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SYMPOSIUM: FUTURES IN REPRODUCTION REVIEW

Selecting the 'best' embryos: prospects for improvement




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Abstract This review considers why and how embryos are selected for transfer and with what consequences. It concludes that: (i) current selection methods are inadequate or at least inadequately subjected to evidential scrutiny; (ii) decisions about number of embryos should be based not solely on input (numbers transferred) but on the likelihood of the transfer resulting in multiple pregnancies – out turn; and (iii) what is needed are better methods not just for selecting better embryos, but also for selecting responsible clinicians who collude less with their patients' demands but advise them more responsibly. 

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KEYWORDS: embryo quality, evidence base, IVF, morphokinetics, multiple pregnancy, PGS, responsibility

VIDEO LINK: <http://sms.cam.ac.uk/media/1400963>

Introduction

In the attempt to select the 'best' embryo for transfer, clinicians need to address three factors: (i) Why are embryos selected? (ii) What outcome is hoped to achieve by this selection? and (iii) Are patients being served well by embryo selection?

In the days when IVF started, especially when either mild stimulation with clomiphene was used or natural cycles advocated, and when in-vitro development of embryos

was suboptimal, there were few embryos available for transfer (Edwards and Steptoe, 1980; Trounson et al., 1981). In the USA, and later in other countries, where ovarian superovulation was the norm, many more oocytes were collected and embryos derived, prompting decisions as to which embryos to select for transfer and how many (Cohen et al., 2005). The 'surplus' also led to the first steps in embryo cryopreservation (Trounson and Mohr, 1983).

It had been clear for some time, and was demonstrated recently in a statistical analysis of over 400,000 cycles in

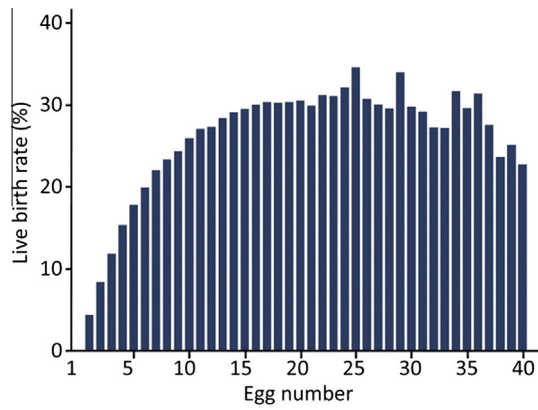


Figure 1 Association between live birth rate and number of eggs retrieved per cycle. Graph compiled from 400,135 cycles from the HFEA database for IVF cycles performed in the UK from 1991 to 2008. Reproduced from [Sunkara et al. \(2011\)](#).

the Human Fertilisation and Embryology Authority database ([Sunkara et al., 2011](#)) that, since the quality of eggs is variable and the development of embryos similarly so, the chances of pregnancy increase significantly with increasing numbers of eggs retrieved ([Figure 1](#)). However, the returns from ovarian stimulation are limited; success begins to plateau around 15 eggs ([Figure 1](#)), and obtaining numbers beyond that may be detrimental ([Figure 2](#)). Furthermore, successful outcome is age related – as the woman becomes older, so the likelihood of a successful outcome will reduce ([Figure 2](#); [Sunkara et al., 2011](#)), either because increasing the dose of gonadotrophins has no further effect or because the additional eggs that are obtained are less likely to be viable. Indeed, one problem today is that women are delaying attempts at childbearing ([Bewley et al., 2005](#)). Thus, the median age of women undergoing IVF in UK is around 36 and by that time more than 90% of the ovarian pool has been lost, and the chances of a live birth following IVF are severely compromised ([Figure 3](#)). Not surprisingly, these women are vulnerable to the marketing ploys of those who offer any alternative that might improve their already slender chances to avoid involuntary childlessness. These

desperate women fall victim to a myriad of treatment variations despite the facts that there are no data as to their proven clinical efficacy such as to justify their ubiquitous use and, even worse, available evidence has failed to demonstrate benefit in their use. Examples of such alternatives are acupuncture, aspirin, sildenafil (Viagra), steroids, heparin, growth hormone, immune therapies including intravenous immunoglobulin and endometrial biopsy ([Segev et al., 2010](#)).

One anecdote illustrating this type of problem appeared in *Hello* magazine in December 2010 in which the treatment of a famous singer was recounted – then supported in various internet blogs:

At 42 years old and on her sixth attempt at IVF with her 68 year old husband and assisted by acupuncture, the treatment finally worked. She was originally expecting triplets, which spontaneously reduced to twins, and were delivered prematurely by Caesarean section at just over 5lbs.

This example says everything about the modern practice of assisted reproduction: the expectations of the technology, especially by older woman, how clinicians collude with alternative treatments despite absent or negative data and how they transfer multiple embryos knowing full well that multiple birth is the single biggest risk to the health and welfare of children born after IVF due to the increased hazard of significant prematurity with twin and triplet pregnancy ([Braude, 2006](#); [Grady et al., 2012](#)).

The fact that all clinicians, all nurses, all obstetrician gynaecologists are aware of the statistics, and most will have some first hand experience of their consequences, why is it still the case, as documented by the Practice Committee of the ASRM ([Figure 4](#)) that 50% of all children conceived by assisted reproduction in the USA are born in a multiple pregnancy? ([ASRM, 2012](#)). Clinicians recognize the problem but for various reasons fail to act responsibly. It is our duty to try to improve IVF outcome by improving efficacy and safety: efficacy for those women not yet pregnant and desperate to be so – through better embryo selection; and safety by avoiding complications in those who do

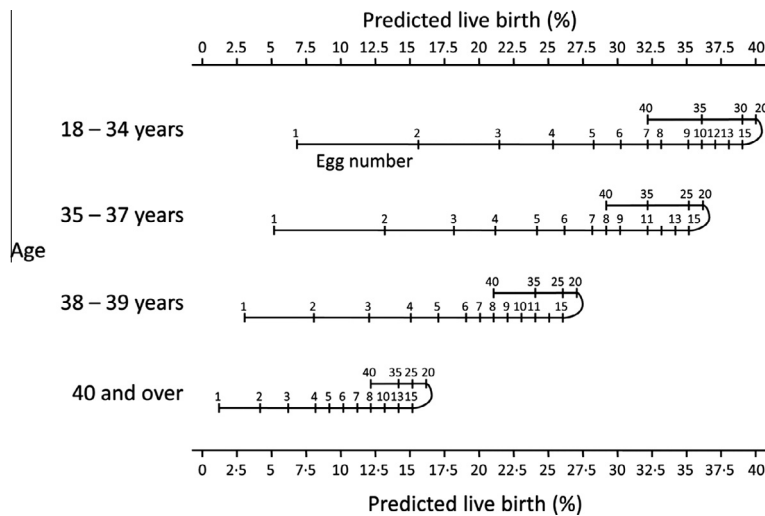


Figure 2 Nomogram to calculate predicted live birth probability given egg number and age. Reproduced from [Sunkara et al. \(2011\)](#).

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