



# Prevention of in-vitro fertilization twins should focus on maximizing single embryo transfer

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Twin pregnancy is an iatrogenic complication of in vitro fertilization (IVF) associated with severe as well as subtle adverse outcomes (1). With higher implantation rates (IRs) and refined cryopreservation protocols for extra embryos (2), many centers like ours worldwide have made single embryo transfer (SET) the default choice for most IVF couples. When accompanied by preimplantation genetic screening, elective SET (eSET) pregnancy rates at all ages have reached 50% or higher (3), whereas double embryo transfer (DET) would carry an unacceptable risk of twins. Equivalent or superior results can be achieved with sequential transfer of the two embryos (4-6). We provide detailed counselling at the initial visit so that a couple has the opportunity to seek another provider if they disagree with our center's policy. Once a comprehensive presentation of the risks and alternatives has been made, it is our experience that most couples prefer single embryo transfer.

In addition to more serious risks outlined below, it is now known, compared to births at 39 weeks, early-term births (37-38 weeks) are associated with an increase in adverse neonatal outcomes by a magnitude of up to 4-fold at 37 weeks and 2-fold at 38 weeks (7, 8). These are primarily respiratory and with Caesarian delivery (9), which is the mode of delivery for most IVF twins, but also include other neonatal complications. Because the modal week (highest frequency) for assisted reproductive technology (ART) twin births is 37 weeks, 39.2% of twins are born earlyterm (1). If we add the risk of preterm birth (53.8% in this study) plus early-term, twins have over a 90% risk of being born before 39 weeks and at risk of an adverse outcome.

The brain grows rapidly during the final four weeks of pregnancy, with a nearly 50% increase in cortical gray matter

(10), a nearly threefold increase in myelinated white matter (10), and increasing neuronal and gyral differentiation (11). In a large study of third grade children, math and reading scores progressively increased from 37 to 40 weeks (12). In children born at 34 to 36 weeks there is an increased incidence of a variety of abnormalities of intellectual and neurologic function (12), and with greater degrees of prematurity, such deficits are increasingly common.

A further risk of twin pregnancies is the impact of complications on families. Birth of a severely handicapped child can be devastating, and siblings of a disabled child can be psychologically affected (13). Mothers of twins have a higher risk of depression, and divorce is more common (14, 15).

It has been suggested eSET is not appropriate in older women or younger women facing a progressive decrease in ovarian function, and that twins are a desirable outcome to help them complete their family. However, twins will significantly increase the risk of maternal complications in older women (16). An alternative is to undergo two or more banking cycles to store multiple euploid embryos while fertility is higher, which will also reduce miscarriage and its associated delays and psychological trauma. DET may decrease the chance of later pregnancies if only one of the embryos implants, because a further cycle will be delayed until after delivery.

Insurance companies in the U.S. are increasingly encouraging eSET by choosing referral centers based on the number of embryos transferred, due to high costs of providing medical care to preterm babies (14), further magnified now that more extremely premature babies are surviving (14). Lifetime expenses of medical care for resulting disabilities further increase costs.

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