Assessment of the indications and risks of ICSI (Intracytoplasmic sperm injection) to children born as a result of ICSI

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Aim
To assess the indications and efficacy of ICSI and the risks to children born as a result of ICSI.

Conclusions and results
The literature reports efficacy for each indication mainly in terms of fertilisation rates or pregnancy rates, using a variety of denominators, and rarely in terms of birth rates. The main results have been reported per cycle. The fertilisation rate/cycle ranged from 43% for bilateral absence of the vas deferens to 62.5% for obstructive azoospermia, and the pregnancy rate/cycle from 21.4% for in vitro fertilisation (IVF) failures in cases of non-male infertility to 49.5% for bilateral absence of the vas deferens. Current indications for ICSI are:
- first-line indications, when there is no alternative to ICSI or after failed IVF, i.e. azoospermia and oligoasthenoteratozoospermia, total failure of IVF and reduced (≤ 20%) fertilisation, anti-sperm antibody levels ≥ 80%, and technical indications in cases of viral infection or pre-implantation genetic diagnosis (PGD);
- second-line indications, when poor sperm quality persists despite previous optimal first-line treatment (medical, surgical, sperm collection, etc.) and prevents natural conception, assisted insemination by husband (AIH) or IVF, i.e. acquired azoospermia of the seminal ducts, hypogonadotrophic hypogonadism, spermatic varicocele, and ejaculation disorders. The working group defined poor sperm quality as either fewer than 500 000 motile spermatozoa after preparation or more than 500 000 motile spermatozoa after preparation if their morphology and/or survival was not normal.

The increasing number of ICSI interventions performed in recent years seems to be due to a wider range of indications and earlier use in moderate azoospermia.

No conclusion could be drawn as to whether the risk to the next generation differs between IVF and ICSI pregnancies. The main risk, as for naturally conceived children, is the mortality and morbidity associated with multiple pregnancies. For singleton pregnancies, rates of premature birth (estimated mean 9.3% vs 6.4%; reported odds ratios (OR) 1.24-1.41), low birth weight (estimated mean 9% vs 3.6%; OR 1.23-2.01), and major congenital malformations (estimated mean 5.9% vs 3.6%; OR 1.23-1.41) were significantly higher in children resulting from ICSI than in naturally conceived children. The frequency of chromosomal anomalies passed on to children born as a result of ICSI was significantly higher than that observed for naturally conceived children (mean 1.4% vs 0.3%). Five-year follow-up studies revealed no significant difference in physical, cognitive or psychological development between children conceived through ICSI and those conceived naturally. No conclusions may be drawn from currently available data regarding the occurrence of epigenetic anomalies, oncological events or the existence of specific risks in ICSI connected with either the technique itself or the use of surgically collected spermatozoa.
Methods
The assessment was based on an analysis of the literature published between 1995 and 2006 (388 publications examined, including 120 on efficacy (of which 9 were health economics studies) and 71 on risks) and on expert opinion (18-member multidisciplinary working group) and 16 peer reviewers.

Further studies
Further studies are needed on long-term follow-up to evaluate:
- the efficacy of ICSI according to relevant criteria (i.e. birth rates)
- the risks to children conceived by means of assisted reproduction technology and to their descendents.