



<b>Title</b>	<b>Assessment of the Indications and Risks of ICSI (Intracytoplasmic Sperm Injection) to Children Born as a Result of ICSI</b>
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<b>Reference</b>	HAS report, December 2006. <a href="http://www.has-sante.fr/portail/display.jsp?id=c_500307">www.has-sante.fr/portail/display.jsp?id=c_500307</a>

## Aim

To assess the indications and efficacy of intracytoplasmic sperm injection (ICSI) and the risks to children born as a result of ICSI.

## Conclusions and results

The literature reports efficacy for each indication, mainly in fertilization or pregnancy rates, using several denominators, and rarely in terms of birth rates. The main results have been reported per cycle. The fertilization 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 fertilization (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, ie, azoospermia and oligoastheno-teratozoospermia, total failure of IVF and reduced ( $\leq 20\%$ ) fertilization, antisperm antibody levels  $\geq 80\%$ , and technical indications in cases of viral infection or preimplantation 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, or IVF, ie, 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 morphology and/or survival were 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 mortality and morbidity associated with multiple pregnancies. For singleton pregnancies, rates of premature birth, low birth weight, and major congenital malformations were significantly higher in ICSI children 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. Five-year followup 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 available data regarding the occurrence of epigenetic anomalies, oncological events, or existence of specific risks in ICSI connected with either the technique itself or the use of surgically collected spermatozoa.

## Methods

Assessment was based on an analysis of literature published between 1995 and 2006 (388 publications examined, including 120 on efficacy, whereof 9 were economic studies, and 71 on risks) and on expert opinion of an 18-member multidisciplinary working group and 16 peer reviewers.

## Further research/reviews required

Long-term followup studies are needed to evaluate:

- efficacy of ICSI according to relevant criteria (ie, birth rates)
- risks to children conceived via assisted reproduction technology and to their descendents.