

Possible health effects of IVF



In the hands of experts, IVF procedures are safe and medical complications are rare. However, as with all medical procedures, there are some possible health effects to consider for women and men undergoing treatment and for children born as a result of treatment.

Possible health effects of IVF

The purpose of this document

VARTA provides independent information and support for individuals, couples, and health professionals on fertility, infertility, assisted reproductive treatment (ART) and the best interests of children born from ART.

This brochure provides an overview of the known possible physical and emotional health effects of IVF for women and men and of outcomes for children born as a result of treatment. Information in this brochure refers to IVF and intracytoplasmic sperm injection (ICSI) but does not include ovulation induction alone.

The information represents the state of knowledge about health effects of IVF at the time of publication and is drawn from studies published in scientific literature. It was compiled with the assistance of experts in the field. It does not take into consideration your personal circumstances and medical history and should not be seen as a substitute for advice from doctors and other health professionals.

If you have other questions that are not addressed here, please raise them with your health care provider.

The first Australian baby conceived through in-vitro fertilisation (IVF) was born in 1980. Since then, more than five million babies, conceived using IVF and other assisted reproductive technologies have been born worldwide. In 2013, four per cent of all babies born in Australia were conceived with the help of assisted reproductive treatment (ART), including IVF.

Why it is difficult to determine if there are IVF-related health effects

The results of studies examining the health effects of IVF can be difficult to interpret. For example, some health effects of IVF may not be related to the procedure itself but to an underlying cause of infertility or the fact that, on average, those who use IVF are older than those who conceive spontaneously.

Another potential problem with studies of IVF-related health effects is the unintentional bias in the way people are selected and assessed. For example, if babies born through IVF are examined more thoroughly and reporting to health registers about them is more complete, then it might seem that health problems are more common than in spontaneously-conceived children.

Possible emotional effects of IVF

IVF treatment is psychologically demanding. For some couples, the strain of IVF causes relationship problems while others describe feeling closer and able to support each other through the demands of treatment.

Women often experience symptoms of depression and anxiety during IVF treatment, particularly when waiting for results after embryo transfer and when treatment fails. When IVF fails, people often feel very disappointed and sad. However, follow-up studies show that within a few years of ending treatment, there are very few differences in terms of emotional wellbeing and life satisfaction between those who had a baby as a result of IVF and those who did not.

Deciding whether to continue or stop treatment can be difficult for people. Couples who have frozen embryos they are not intending to use often find it hard to decide what to do with these embryos.

In the first few months after giving birth, women who conceive with IVF have a higher rate of parenting difficulties than women who conceive spontaneously, including anxiety about caring for the baby. However, these difficulties lessen with time. The rate of exclusive breastfeeding three months after the birth is lower after IVF than spontaneous conception and this may be related to worry about the ability to nourish the baby.

In Australia, counselling services are available in all IVF clinics. Women who have IVF treatment and their partners are encouraged to use these if they experience emotional difficulties.

Possible health effects of IVF



Possible physical effects of IVF for women

During treatment

Physical complications requiring hospital admission occur in about one per cent of all stimulated treatment cycles. The most common complication is ovarian hyperstimulation syndrome (OHSS). This condition can develop as a result of the fertility drugs which are used in IVF to stimulate the ovaries to produce multiple eggs. OHSS is a potentially serious condition which, in very rare cases, can lead to blood clots, kidney failure and death. In 2013, 294 women (0.7 per cent of all stimulated cycles) were hospitalised as a result of OHSS. All IVF programs monitor patients carefully to minimise the risk of OHSS. If a patient develops an excessive number of follicles in response to the fertility drugs, the patient's doctor may recommend that the cycle be cancelled or a shorter-acting ovulation drug be used before an egg collection in order to avoid OHSS. As OHSS is worsened by pregnancy, if the doctor has reason to believe that the woman is at risk of OHSS after the egg collection procedure, the advice may be to freeze all the embryos and then transfer them, one at a time, when the ovaries return to normal.

Surgical complications which require hospital admission, such as bleeding and infection from egg collection, occur in less than 0.5 per cent of IVF cycles.

The risk of serious complications from general anaesthesia and sedation is approximately one in 50,000 treatment cycles.

Long-term

There have been very few studies examining long-term health effects of IVF for women, other than some studies relating to cancer. Those undergoing treatment are often concerned that the use of fertility drugs may increase a woman's risk of cancer.

A number of large studies have investigated the relationship between the use of fertility drugs and breast cancer. Combining these studies, the risk of using fertility drugs has been investigated in over 45,000 women and no overall increase in the rate of breast cancer has been found.

Ovarian and uterine cancers are less common and therefore more difficult to study. Although some reports have implied that they may increase the risk of ovarian and uterine cancer, there does not appear to be conclusive evidence that fertility drugs increase the risk of these cancers.

Some studies have raised questions about whether there is an increase in cancer risk associated with the duration of fertility drug use, or use of specific types of fertility drugs among certain groups of infertile women. To date, there is no conclusive evidence that these factors increase the risk of any type of cancer, however new studies are emerging all the time.

Although the findings of existing studies are reassuring, it is important to remember that IVF has only been available for about 35 years and that it is only in the past two decades that IVF has been used by large numbers of women. Therefore, questions remain about the long-term risks of using fertility drugs, particularly for rare forms of cancer. Also, little is known about the effect of fertility drugs in women with a strong family history of breast or ovarian cancer, or in women with a personal history of cancer prior to fertility treatment.



Possible physical effects of intracytoplasmic sperm injection (ICSI) for men

In some infertile men, sperm for intracytoplasmic sperm injection (ICSI) cannot be obtained from the ejaculate. In such cases, sperm may be retrieved surgically either by needle biopsy of the testicles under local anaesthesia, or open biopsy under general anaesthesia. These procedures are associated with minor risks related to the operation itself and use of anaesthetics. Local bleeding or infection occurs in less than one per cent of open biopsies; needle biopsies carry an even lower risk of complications. However, in rare cases, severe bleeding may occur with the risk of losing the testis.

Some men with severely reduced sperm production have low testosterone levels, or risk developing testosterone deficiency later in life. Biopsies of the testes can, on occasion, further reduce testosterone production, resulting in the need for lifelong testosterone replacement therapy.

Possible health effects of IVF

Outcomes of IVF pregnancies

The risks of pregnancy loss and adverse birth outcomes after IVF must be viewed in the context of how often problems occur in spontaneously-conceived pregnancies in Australia.

As discussed below, some of these are more common after IVF. For both IVF and spontaneously-conceived pregnancies, older maternal age, obesity, and smoking increase the risk of pregnancy complications and adverse birth outcomes. If you are proceeding with treatment, you should discuss potential pregnancy-related risks with your fertility specialist, who can provide advice relevant to your particular circumstances.

Current Australian data for **all pregnancies** shows that approximately:

- one pregnancy in six will miscarry
- one baby in 14 will be premature
- one baby in 25 will have a birth defect
- one baby in 100 will die around the time of birth
- one baby in 400 will have cerebral palsy and be disabled.

Although most pregnancies after IVF proceed without complications, studies show that women who conceive with IVF are more likely to:

- experience bleeding during the pregnancy
- develop blood clots in early pregnancy
- develop high blood pressure and diabetes in later pregnancy
- deliver prematurely.

Birth outcomes for babies born as a result of IVF

The vast majority of babies born as a result of IVF are healthy and have no short or long-term problems. It is important to know that birth outcomes are more favourable for single babies than for twins and triplets.

Single babies

Australian data show that compared with spontaneously-conceived babies, IVF-conceived babies have a higher risk of certain outcomes. In 2013, 10.5 per cent of single babies born after IVF were pre-term (born before 37 weeks gestation) compared with 6.9 per cent of spontaneously conceived babies. Also, seven per cent of IVF-conceived single babies were low birth weight (weighed less than 2.5kg) compared with 4.7 per cent of spontaneously-conceived single babies. The risk of a baby dying around the time of birth is marginally higher after IVF than spontaneous conception.

Recent studies have found that the risk of bleeding during pregnancy, premature birth, and low birth weight is lower among babies born as a result of transfer of a frozen/thawed embryo in an unstimulated cycle than among babies born as a result of a fresh embryo transferred in a stimulated cycle.

A single IVF baby is more likely to be born by caesarean section than a single baby conceived spontaneously. There are a number of possible reasons for this but the important implication is that a mother's physical and emotional recovery following caesarean birth may be slower than after a vaginal birth.

Twins and more

Multiple births are about three times more common after IVF than they are after spontaneous conception. A multiple pregnancy creates a greater risk for the mother and her babies than a pregnancy with one baby. A major risk is pre-term delivery. Other risks include bleeding during pregnancy and high blood pressure, or pre-eclampsia¹.

Babies born from a multiple pregnancy are more likely than those from single pregnancies to have cerebral palsy or to die close to the time of birth, mainly due to a higher risk of pre-term birth. Risks for the baby are substantially greater in a triplet or quadruplet pregnancy than in twin or single pregnancies.

There are higher rates of psychological distress in mothers of multiples because caring for more than one baby is more difficult than caring for a single baby.

Single embryo transfer (SET) is the only way to reduce the rate of multiple births associated with IVF and to give all babies born after IVF the best possible start in life. When several embryos are available after a stimulated cycle, one can be transferred and the remainder frozen. If the first embryo does not result in a pregnancy, frozen embryos can be thawed and then transferred, one at a time, in subsequent cycles. This way, the cumulative chance of having a baby is the same as if two or more embryos are transferred together but the risk of a multiple birth is substantially eliminated. With improved pregnancy rates associated with IVF, single embryo transfer has become more common. The proportion of SET in Australia and New Zealand increased from 40 per cent in 2004 to 79 per cent in 2013. As a result, the multiple birth rate for IVF-conceived babies in Australia fell to 5.6 per cent in 2013, one of the lowest in the world.

¹Pre-eclampsia is a serious disorder of pregnancy characterised by high maternal blood pressure, protein in the urine and severe fluid retention. It is the most common serious medical complication of pregnancy, affecting around 5 to 10 per cent of all pregnancies in Australia. One to two per cent of cases are severe enough to threaten the lives of both the mother and her unborn child.

Possible health effects of IVF

The risk of birth defects after IVF

Studies investigating the risk of birth defects in babies born following IVF suggest there is a small increased risk of birth defects compared with spontaneously-conceived babies. Between five and six per cent of IVF-conceived babies have a birth defect compared with approximately four per cent of spontaneously-conceived babies.

Whether children born after ICSI have an added risk of birth defects compared with those born as a result of IVF is still not clear.

Many of the defects are minor. The severe birth defects that appear to be more common occur in the early stages of fetal development and can often be detected by ultrasound monitoring of pregnancy. One extremely rare condition that appears to be more common in children born after IVF is a growth disorder called Beckwith-Wiedemann Syndrome (BWS). In several studies, BWS has been shown to occur in about one in 4,000 IVF babies compared with one in 14,000 to 35,000 spontaneously-conceived babies.

The increased risk of birth defects after IVF may relate to parental characteristics such as age or cause of infertility rather than the laboratory handling of sperm, eggs, and embryos. If difficulty conceiving is caused by a genetic or chromosomal disorder, the baby may be affected by the same disorder.

For example, about three per cent of men with severe defects of sperm production and low or zero sperm counts are missing parts of the Y chromosome, where genes responsible for sperm production are located. Men with so called 'Y chromosome microdeletion' may become fathers with the aid of ICSI but their sons will have the same genetic problem and therefore in all likelihood will be infertile.

Also, in men with unexplained severe male infertility, chromosomal imbalances are much more common than in men with a normal sperm count. In these cases, a chromosomal test (karyotype) is performed. If a problem is found, genetic counselling is offered to inform the couple about the chance of success with ART, potential risks to the offspring, and the possibility of using embryo screening to only transfer unaffected embryos.

It is also possible that the process itself or the fertility drugs affect the uterine environment at the time of implantation and impair fetal development.

Health and development in children and adults born after IVF

Studies of the growth, health and development of young children born after IVF have found few differences between them and other children. However, as multiple births have historically been more common after IVF and children from multiple pregnancies are more likely to be born pre-term and to have a low birth weight than single children, there is an overall increased risk of developmental problems and cerebral palsy. Children who are born very prematurely have more learning difficulties and attention and behavioural problems than those born at term. In adulthood some health problems such as high blood pressure and reduced lung function are more common among extreme pre-term survivors.

Childhood cancer is a rare condition. Most major studies of the frequency of cancer in children born after IVF have shown that the incidence is similar to that in the general population. Further studies are needed to investigate the effects of particular forms of fertility treatments on specific types of cancer.

The few studies that have followed IVF-conceived children beyond puberty have not detected major differences between them and other young people. An Australian study of more than 700 IVF-conceived young adults aged between 18 and 28 years found that they were more likely to have a respiratory problem and to have experienced a hospital admission than a comparison group of young adults who were spontaneously-conceived. However, the two groups showed no differences in terms of other aspects of physical health and development, emotional well-being, and quality of relationship with the parents. Research is continuing in this area as an increasing number of IVF-conceived people reach adulthood.

If you have further questions

It is important that you collect information from independent sources and then discuss any questions regarding treatment with your healthcare provider.

For more information about IVF and other assisted reproductive treatments, visit our website at www.varta.org.au or call 03 8601 5250

Useful sources of information

Access Australia

Australia's national infertility network

www.access.org.au

Your Fertility

for information on how to improve your chance of conceiving and having a healthy baby

www.yourfertility.org.au

Andrology Australia

for information on male infertility

www.andrologyaustralia.org

Better Health Channel

for health and medical information

www.betterhealth.vic.gov.au



The **Victorian Assisted Reproductive Treatment Authority** is an independent statutory authority funded by the Victorian Department of Health and Human Services.

Phone: +61 3 8601 5250

Email: varta@varta.org.au