Q-IVF
Nationellt kvalitetsregister
för assisterad befruktning

Fertility treatments in Sweden

National report 2021

Refers to treatments started in 2019

RESULTS – TRENDS –COMPARISONS

Table of contents: National report 2021

Notes from the head of the Registry

Christina Bergh, registerhållare

The first child in the world born as a result of in vitro fertilization (IVF) was born in 1978. During the more than forty years since the start of IVF,-techniques has developed immensely, both in terms of birth rates and in terms of maternal and child safety. Furthermore, today IVF can be offered to a wider range of patients, and treatments have been significantly simplified. As a result of IVF, to date over nine million children have been born worldwide.

Since the first child was born in Sweden as a result of IVF in 1982, legislation on assisted reproduction has been changed or amended several times. Applicable regulation on assisted reproduction can today be found in *Lagen om genetisk integritet* (The Genetic Integrity Act, SFS 2006:351).

Some milestones reached in the last twenty years in Sweden are:

- 2003: Oocyte donation becomes allowed
- 2005: IVF-treatment of lesbian couples becomes allowed
- 2016: IVF-treatment of single mothers becomes allowed
- 2019: The legal requirement of maintaining a genetic link between at least one parent and child is removed. Treatments where both the oocyte and the sperm have been donated now becomes allowed, as well as treatments with donated embryos
- 2019: The period during which frozen embryos can be stored is extended to ten years
- 2019: It is decided that commercial or altruistic surrogate motherhood is not allowed in Swedish healthcare

In Sweden, both privately and publicly owned care providers perform IVF. In total, just over 20 000 treatments are performed yearly, including both fresh and frozen embryo treatments. The couple's own gametes are used in a majority of the treatments, with about five percent of the treatments being performed with either donated oocytes or donated sperm (www.qivf.se). Lately, the possibility of freezing unfertilized oocytes with good success rates has also emerged. Among other things, this means that women who suffer from a disease where the cure or treatment may hurt the function of the ovaries can now freeze their oocytes with the possibility of having children at a later date.

The National Quality Registry for Assisted Reproduction (Q-IVF) was introduced in 2007. Consequently, this years' report is the 12th from Q-IVF. It covers all treatments initiated in 2018 at Sweden's - at that time - eighteen IVF clinics. Out of the eighteen clinics, six were public and twelve were private. Public as well as private clinics have linked up with and report to Q-IVF on a broad and reliable scale, meaning that almost 100% of treatments performed in Sweden in 2018 are accounted for in this report.

The aim of Q-IVF is to monitor treatment results and identify potential risks for men and women who have undergone IVF-treatment as well as children born as a result of IVF. The registry likewise is a valuable data source for clinics to benchmark their development and qualitative work, as well as being a base for scientific research.

The Regional Board of Västra Götaland is the authority responsible for the registry and handling of personal data. The head of the Registry is professor Christina Bergh, Gothenburg and the registry coordinator is midwife Kia Borg. The steering group consists of representatives of the various IVF clinics in Sweden, representatives of patient networks, and statistician Karin Källén. Behavioral science competence is provided by Professor Gunilla Sydsjö, Linköping. The steering group meets regularly, with alternating chairpersons. The current chair is Kersti Lundin, Sahlgrenska. The registry is financially supported by Sweden's regional governments, SKR.

From being connected to Uppsala Clinical Research Center (UCR) during the first years, the current IT-platform is now MedSciNet, the same IT-platform used by the Pregnancy Registry. Q-IVF is also affiliated with Registercentrum (QRC) in Stockholm.

Over the last few years, comprehensive development work has been carried out aiming at reporting and presenting data "on-line" with daily updates and continuous presentation of results, a method which is to replace the current system using yearly compilations. The new method is already used by several clinics and is working well. Furthermore, this on-line method allows individual clinics to make use of much more up-to-date data, which is supporting in the clinics' pursuit of qualitative work. New patient groups have been added, for example single mothers, women in need of treatment to preserve their fertility, and patients with gender dysphoria.

Data from Q-IVF is used in several research projects, including projects that involve short and long-term follow-up studies on children born as a result of IVF, and their mothers. Q-IVF reports aggregated data to the Nordic Fertility Society (NFS) and to the European Society of Human Reproduction and Embryology (ESHRE).

Christina Bergh, Head of Q-IVF

Board of directors

Working group

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Kersti Lundin, embryologist, associate professor, Sahlgrenska University Hospital, Gothenburg

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Kia Borg, Registry coordinator

Representative of "The National Association of Involuntary Childlessness"

Terms and definitions

AID	artificial insemination with donor sperm: donor sperm is placed directly into the uterus
Assisted reproduction	use and manipulation of gametes (oocytes and/or sperm) outside of the body
Biochemical pregnancy	a positive pregnancy test (urine or serum) ahead of an ultrasound verification of a gestational sac
Birth	The complete expulsion or extraction from a woman of a fetus after 22 completed weeks of gestational age, irrespective of whether it is a live birth or stillbirth, A single birth refers to an individual newborn; and a delivery of multiple births, such as a twin delivery, would be registered as two births.
Blastocyst	an embryo five to six days after fertilization.
Clinical pregnancy	a pregnancy where a gestational sac is visible on an ultrasound
DET	double embryo transfer: transfer of two embryos
Delivery	The complete expulsion or extraction from a woman of one or more fetuses, after at least 22 completed weeks of gestational age, irrespective of whether they are live births or stillbirths. A delivery of either a single or multiple newborn is considered as one delivery.
Delivery rate	The number of deliveries expressed per 100 initiated cycles, aspiration cycles, or embryo transfer cycles.When delivery rates are recorded, the denominator (initiated, aspirated or embryo transfer cycles) must be specified. It includes deliveries that resulted in the birth of one or more live births and/or stillbirths. The delivery of a singleton, twin or other multiple pregnancy is registered as one delivery.
Double donation	a treatment cycle including both donated oocytes and donated sperm
Embryo	a fertilized egg having reached the cell division stage
Embryo donation	a treatment with donated embryos
ET	embryo transfer: transfer of an embryo or embryos into the uterus
FET	frozen embryo transfer: transfer of a frozen/thawed embryo
Freeze cycle	treatment cycle with frozen/thawed embryos
Fresh IVF-cycle	a treatment cycle with or without hormone stimulation aiming for egg retrieval and embryo transfer
Gamete	an oocyte or a sperm
ICSI	intracytoplasmic sperm injection: fertilization using microinjection, where a sperm is injected directly into the oocyte via a thin needle; a method used when the sperm count is low, where there is low sperm motility, or after a previous cycle with no or very low fertilization
IVF	in vitro fertilization: fertilization occurring outside of the woman's body
Live birth	The complete expulsion or extraction from a woman of a product of fertilization, after 22 completed weeks of gestational age; Live births refer to the individual newborn; for example, a twin delivery represents two live births.

Live birth delivery rate	The number of deliveries that resulted in at least one live birth, expressed per 100 cycle attempts. When delivery rates are given, the denominator (initiated, inseminated, aspirated or embryo transfer cycles) must be specified.
Multiple pregnancies	a pregnancy where the women is pregnant with multiple fetuses
Multiple birth	The complete expulsion or extraction from a woman of more than one fetus, after 22 completed weeks of gestational age, irrespective of whether it is a live birth or stillbirth. Births refer to the individual newborn; for example, a twin delivery represents two births.
OPU	ovum pick up; oocyte retrieval from the ovaries
SET	single embryo transfer
ST. IVF	standard IVF: egg and sperm placed together in a petri dish filled with nutrient solution and the sperm fertilizing the oocyte.
Own gametes	the couple's own oocytes and sperm are used in a treatment
Treatment cycle	a treatment initiated either by hormones or by start of menstruation
Freeze-all	all embryos are frozen for use at a later date, and no transfer of embryos taking place in the fresh cycle

Background (childlessness and its causes)

Infertility, or involuntary childlessness, is defined by the WHO as pregnancy not occurring despite a woman having unprotected sexual intercourse regularly for one year. Primary infertility means that a woman has never been pregnant, or that a man via intercourse has never given rise to a pregnancy. Secondary infertility means that a woman *has* been pregnant, or that a man via intercourse *has* given rise to a pregnancy, but then has difficulty achieving another pregnancy.

Fertility problems affect 10–15% of all heterosexual couples. The cause for these problems differs. About one third of the problems are related to the man (e.g. low sperm count, low sperm motility about one third of the problems are related to the woman, and about one third of the problems are related to both the man *and* the woman. In some cases no explanation is found, then called unexplained infertility.

Fertility treatment

It is estimated that about two thirds of all couples/patients can become pregnant and have children after checkups and treatment. By treatment, we refer to various medical treatments to help a woman get pregnant, including sperm insemination and in vitro fertilization (IVF). Both insemination and IVF can be performed either using own or donated gametes.

During insemination, sperm from the husband or donor is inserted into the woman's uterus at the time of ovulation. This report only presents the results from insemination with donated sperm (AID).

During IVF, oocytes are retrieved from a woman's ovaries and fertilized by sperm in a laboratory. Fertilization is achieved by adding sperm to the oocytes in a special dish (Standard IVF) or by injecting a sperm directly into the oocyte. The latter method is called microinjection or intracytoplasmic sperm injection (ICSI). If the oocyte fertilize and cleave and an embryo is developed, it can be transferred into the uterus. In this report, we use the term IVF to denote both IVF and ICSI, unless otherwise stated. We present data both on IVF using own and donated gametes.

In most cases, the aim of an IVF-treatment is for the woman who undergoes the treatment to get pregnant in the same treatment cycle. However, the treatment can also be used to retrieve oocytes for donation purposes or for oocyte freezing in order to preserve a woman's fertility (see below). For this reason, not all started treatments result in a transfer of an embryo into the uterus.

A treatment cycle

A fertility treatment, such as an IVF-treatment, usually takes a couple of weeks, and is known as a treatment cycle. An IVF treatment can be either in the form of a so-called fresh treatment cycle or by transfer of frozen/thawed embryos. Today, in Sweden, 60% of all started treatments constitutes of fresh treatment cycles, while the remaining 40% are treatments using frozen/thawed embryos. Including only treatments that led to embryo transfer, the proportion of fresh treatments decrease to 55%, while the proportion of treatments using frozen/thawed embryos increase to 45%. In about half of all fresh cycles, the method of fertilization is standard IVF (ST. IVF), and in the other half ICSI.

How we collect data

IVF is an established clinical practice in the field of medicine. The number of treatments in Sweden has increased from around 3 000 in 1992 to just over 22 000 today. Out of all children born in Sweden in the year referenced in this report (2018), 5 043 children have been born as a result of IVF and 343 children through donor insemination. It is important to follow up the results of the treatments for the clinics, to be able to perform these treatments as safely and as effectively as possible.

Q-IVF was launched in 2007, and since then all treatment cycles are reported to Q-IVF. All public as well as privately owned clinics in the country performing IVF-treatments participate. For this reason, Q-IVF is one of the most complete, national IVF registries in the world, with just over 240 000 registered treatments to date. Reporting from the IVF-clinics to Q-IVF was previously done once a year, but since 2020 there is a regular and continuous on-line transfer of data from the clinics to the registry.

How should we interpret data?

A common measure of treatment outcome is the proportion of started treatments that resulted in a live birth. However, an IVF-treatment involves several steps and there are several reasons why a started treatment may not lead to transfer of an embryo. The treatment cycle could be cancelled due to very few or no ovarian follicles being developed, the fertilization process or embryo development might fail, or there may be a risk of other complications, such as ovarian hyperstimulation syndrome (OHSS). When there is a risk of OHSS, one often chooses to freeze all embryos, which will lower the risk. Methods for embryo freezing are very effective today, with a high rate of embryo survival. The woman can then have a thawed embryo transferred at a later date without risk of OHSS and with a remaining high chance of pregnancy and live birth.

In some cases, a treatment cycle is started without the objective of transferring an embryo, for example when women freeze oocytes or embryos ahead of chemotherapy. Only looking at the proportion of started treatments that ended in a live birth can therefore be a misleading way of measuring how effective IVF-treatments are. Comparing the number of live births per embryo transfer is another way to measure effectiveness, and is used in this report. We also observe that the effectiveness of the freeze cycles is increasing, something that is primarily associated with extended culture to the blastocyst stage. Culturing embryos to the blastocyst stage select embryos which are more viable. In addition, the freezing methods have improved, thus a larger share of embryos survive freezing and thawing.

How data can be used

Each of the participating clinics has a secured login and can access their own data via Q-IVF's website, and compare themselves to the results for the country as a whole. A yearly report containing treatment results, birth rates and other relevant statistics and trends is published for public access.

When seeing patients, the clinics can use birth rates for Sweden as a whole to demonstrate how results vary in different age groups. Using Q-IVF's yearly report, patients can also themselves look up the effectiveness of the different methods of assisted reproduction. This information may make it easier to understand what the treatments are about and what the chances of getting pregnant are.

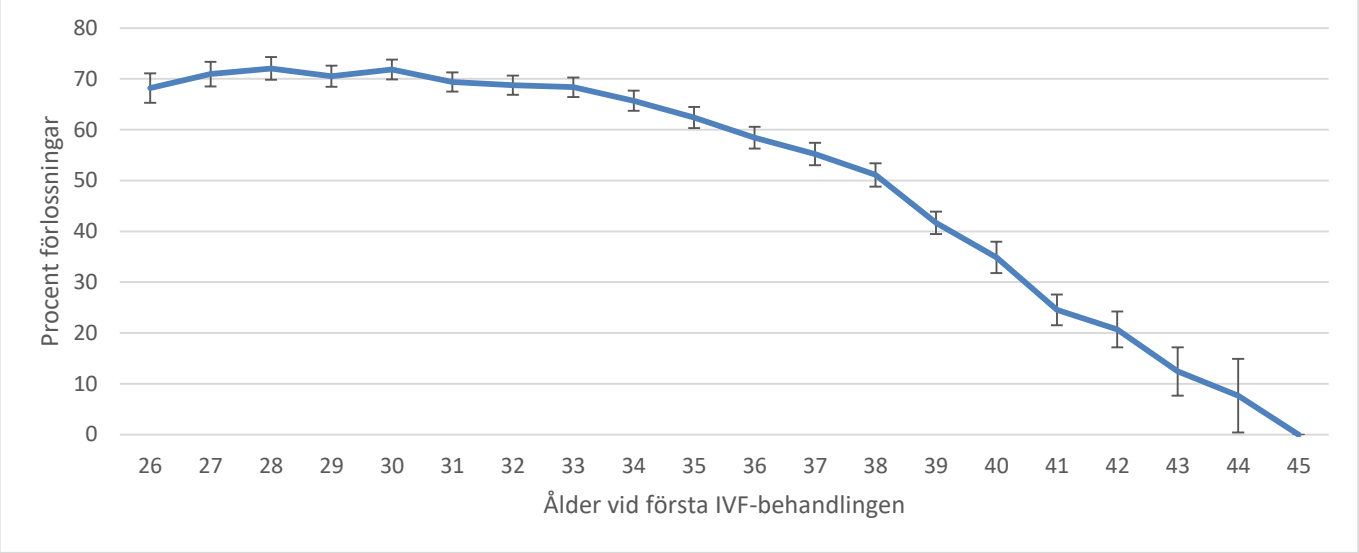
Introduction

Will we/I succeed in having a baby with an IVF treatment?

This question cannot be answered with certainty. You can succeed in having a baby despite poor preconditions and you could be unsuccessful even though your preconditions are good. The different factors affecting chances of having a baby will be discussed at the appointment with the treating doctor at the clinic.

A woman's age is the most important factor in determining chances of success, since the quantity and quality of a woman's oocytes becomes poorer as she ages. A man's age is also of some importance, but much less, since sperm are produced in the testicles continuously. The importance of the age factor is shown in the graph below. The graph shows the chance of delivering a baby after an 18-month-treatment period, a period that may include one or several treatments.

Figure 1. *Proportion of women achieving a delivery after treatment started within 18 months of the first IVF-treatment (own oocytes).*



The graph above includes women who underwent their first oocyte retrieval from January 1, 2012 to June 30, 2018. The numbers 26 to 45 in the graph indicate a woman's age at the start of the first treatment.

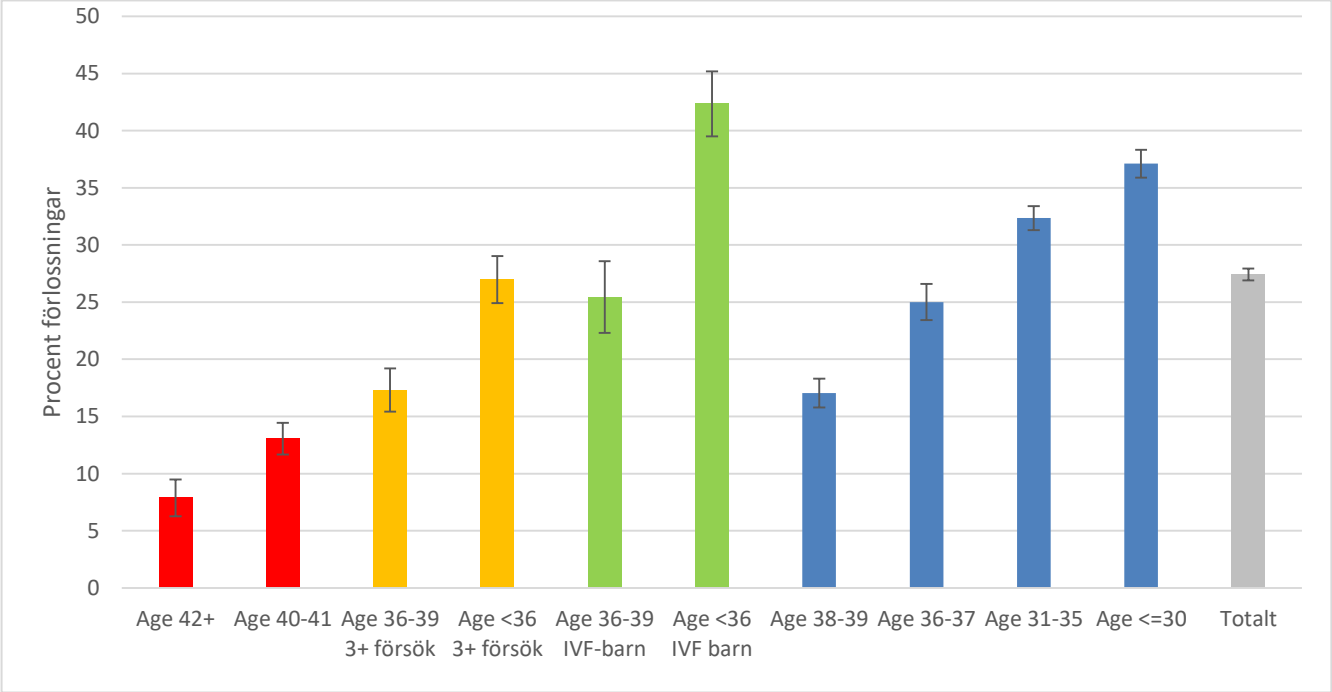
AMH (Anti-Mullerian Hormone) is a substance, which is measured in the blood and shows a woman's ovarian reserve. The level of AMH is used to predict how many oocytes can be retrieved during IVF-stimulation. However, the level of AMH is not associated with the oocyte quality. Another way to evaluate a woman's ability to produce oocytes is to count the number of small (undeveloped) ovarian follicles. The level of AMH can vary greatly between different women of the same age.

The sperm quality (sperm count and motility) also affects one's chance of having a baby with spontaneous conception, but is less important in determining the chance of succeeding with an IVF-treatment.

How long time a couple has tried to become pregnant and have a baby is important for the assessment of when it is reasonable to initiate an IVF-treatment.

Having had an **IVF-baby** in an earlier treatment increases the chance of succeeding again. This increased success rate is shown in Figure 2, where the green bars show the probability of success for women already having IVF children. Figure 2 also shows that unsuccessful IVF-treatments do not affect one's chances very much when it comes to new attempts (yellow bars). The red bars in the chart show the impact of advanced age on success rate.

Figure 2. *Delivery rate per first embryo transfer after a fresh oocyte retrieval (with fresh transfer or, if the first treatment resulted in a so-called "freeze-all", first embryo transfer of a frozen/thawed embryo). Applies for IVF with one's own egg/sperm.*



The graph above shows results from June 1 2017 to June 30 2019. The blue bars indicate the groups who have undergone one, two or three treatments. The yellow bars indicate groups who have undergone more than three treatments. The red bars indicate the groups over 40 years of age. The above-40 group is not divided into sub-categories based on the number of undergone treatments (since this would make the groups small and results statistically more uncertain). The green bars indicate the chance of succeeding again if one already has a baby born as a result of IVF.

Which clinic should we/I choose?

Generally, all IVF-treatments at all clinics in Sweden are of high quality and done in a similar manner. The clinics reporting to Q-IVF are able to compare themselves to other clinics and thereby learn from each other. In the section "Comparison" (Figure 27 and Figure 28) of this yearly report, we have tried to demonstrate the results of the different clinics as fair and accurate as possible.

Other aspects that are important to take into consideration when choosing a clinic is a clinics' location (how long it takes to travel there), and the contact with and perception of the staff. The personal treatment by the staff at the different clinics is evaluated in this yearly report under "Patient satisfaction".

IVF with the patient´s own gametes (autologous)

A summary of the treatments started in 2019

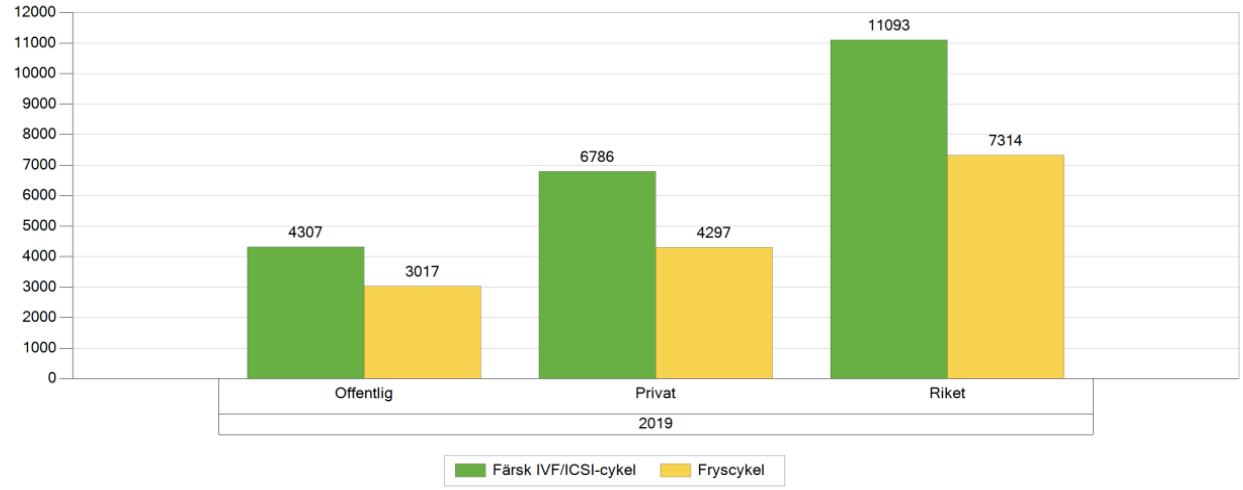
Table 1 *Number of treatments, pregnancies, birth rates per treatment type. Autologous IVF/ICSI (PGD not included).*

	St.IVF	ICSI Ejaculated	ICSI Epididymis/Testicle	Total St.IVF and ICSI	**Total Freeze cycles**	**Total Fresh and Freeze cycles**
Started cycles	**5668**	**5135**	**290**	**11 093**	**7314**	**18 407**
Oocyte aspirations	5349	4784	288	10 421		
Embryo transfer	**4003**	**3583**	**205**	**7791**	**7091**	**14 882**
Positive pregnancy tests	1621	1400	84	3105	3412	6517
Biochemical pregnancies	213	193	7	413	472	885
Clinical pregnancies	**1409**	**1209**	**78**	**2696**	**2940**	**5636**
Spontaneous abortion < gestational week 13	194	160	7	360	370	730
Spontaneous abortion gestational week 13-22	21	17	1	39	50	89
Ectopic pregnancy	11	10	0	21	24	45
Induced fetus reduction	1	1	0	2	0	2
Stillborn, gestational week 22-27	6	1	0	7	7	14
Stillborn, gestational week 28+	8	8	0	14	13	27
Deliveries, singleton	1145	985	68	2198	2434	**4632**
Deliveries, twins	28	28	5	61	47	**108**
Deliveries, triplets	1	0	0	1	1	**2**
Total number of deliveries	**1174**	**1013**	**73**	**2260**	**2482**	**4742**
Total number of live born children	**1205**	**1037**	**78**	**2320**	**2499**	**4819**

Spontaneous abortion < gestational week 13 is including a few legal abortions

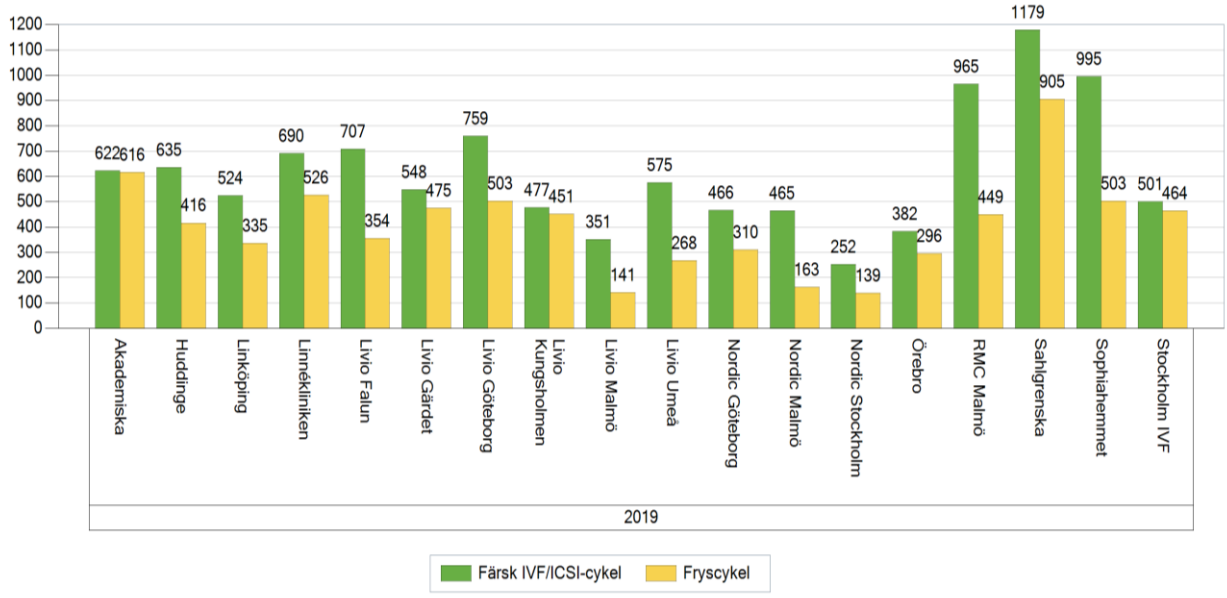
Number of started cycles in Sweden 2019

Figure 3. *Number of started treatments public /private /total. Fresh IVF and freeze cycles. Autologous gametes.*



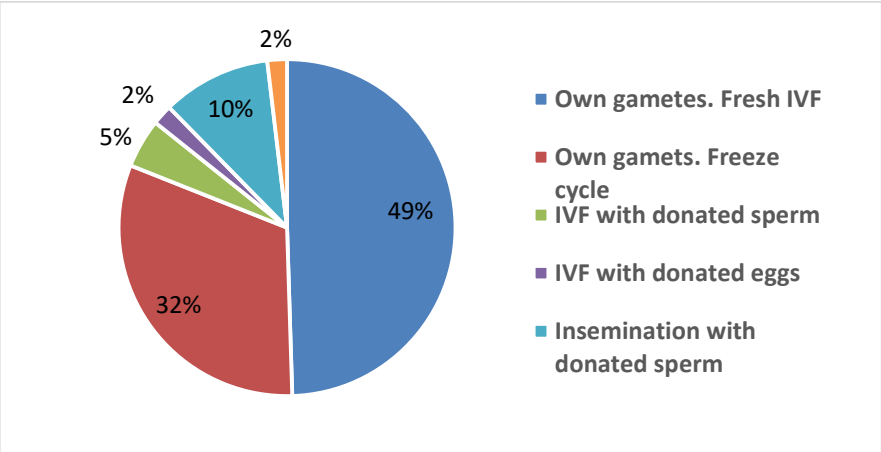
Some of the treatments given at private clinics are paid for by the state since the regional governments sometimes procure treatments from the private clinics. In this yearly report, treatments at private clinics purchased by the state cannot be separated from treatments purchased by individuals.

Figure 4. *Number of started treatments per clinic. Fresh IVF and freeze cycles. Autologous gametes.*



Different treatments started in 2019

Figure 5. *Proportion of initiated treatments.*



In the figure above, the proportions of various treatments started are shown in a pie chart. For details, see tables 1 and 5.
The number of treatments this year is similar to the number of treatments the year before, but there is an increase in the number of donor inseminations (IUI-D), and in oocyte freezing for autologous use.

Figure 6. *Proportion of women who started a fresh IVF-treatment, separated by age.*

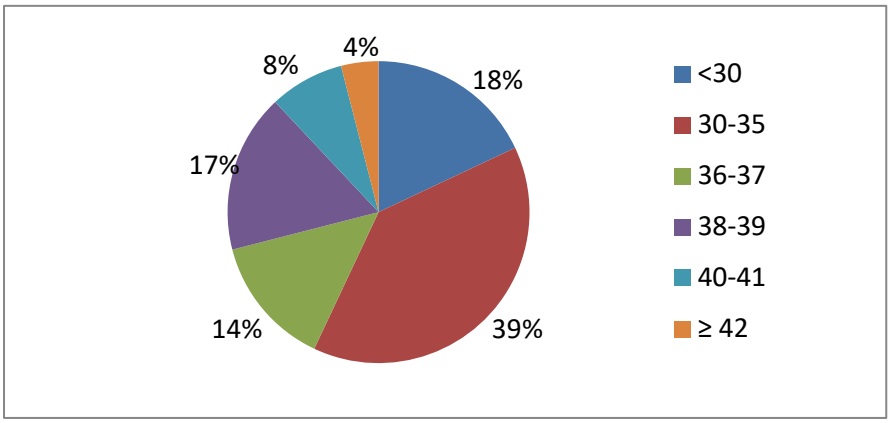
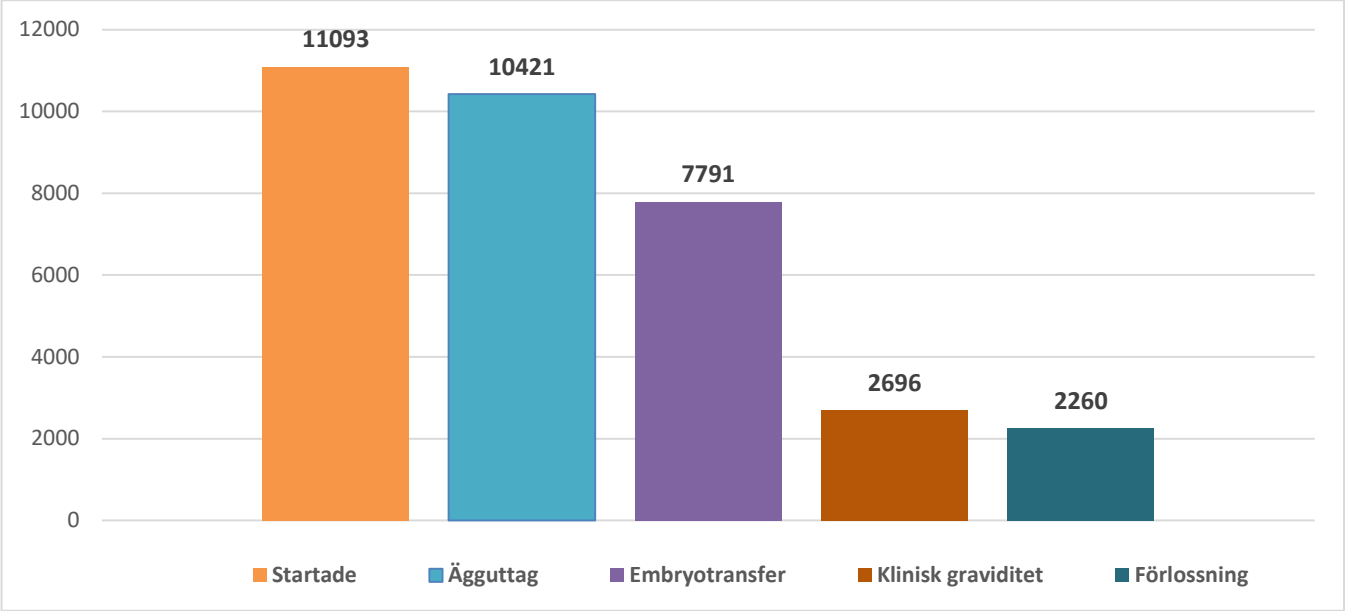


Table 3. *Lost to follow up in 2019, i.e. treatments where we, despite investigations do not have any results. The reason may be because patients come from abroad or patients move abroad.*

	Missing treatment results	Pregnancies with missing outcome	Total
Fresh IVF	8	5	13
Freeze cycles	8	11	19

Figure 7. *Number of treatments reaching different steps in the treatment process. Fresh IVF/ICSI. Autologous gametes.*



Out of the 11 093 started fresh IVF-treatments with autologous gametes, 2 260 resulted in live births, i.e. about 20%. From the treatments reaching the embryo transfer stage, 28 % resulted in a live birth.
Many things can happen during the various treatment stages. Sometimes stimulation is disrupted before the oocyte retrieval. The reasons may be that the number of ovarian follicles is too small, that the prescribed medication is not taken correctly, or for medical or personal reasons.

Out of all treatments that lead to an oocyte retrieval, in around 20% a fresh embryo transfer is not performed. The most common reason for this is that one chooses to freeze all embryos of high quality. Freezing all embryos instead of doing a fresh embryo transfer is a common strategy when there is risk of OHSS. This does not reduce one's chance of becoming pregnant, even though it of course delays the embryo transfer. Other reasons why treatments don't lead to an embryo transfer might be that mature oocytes cannot be retrieved, that oocytes are not fertilized properly, or that no embryo is developed that is suitable for transfer.

Generally, an IVF-treatment is an effective treatment method and most patients/couples manage to get pregnant and have a baby within the first three IVF-treatments.

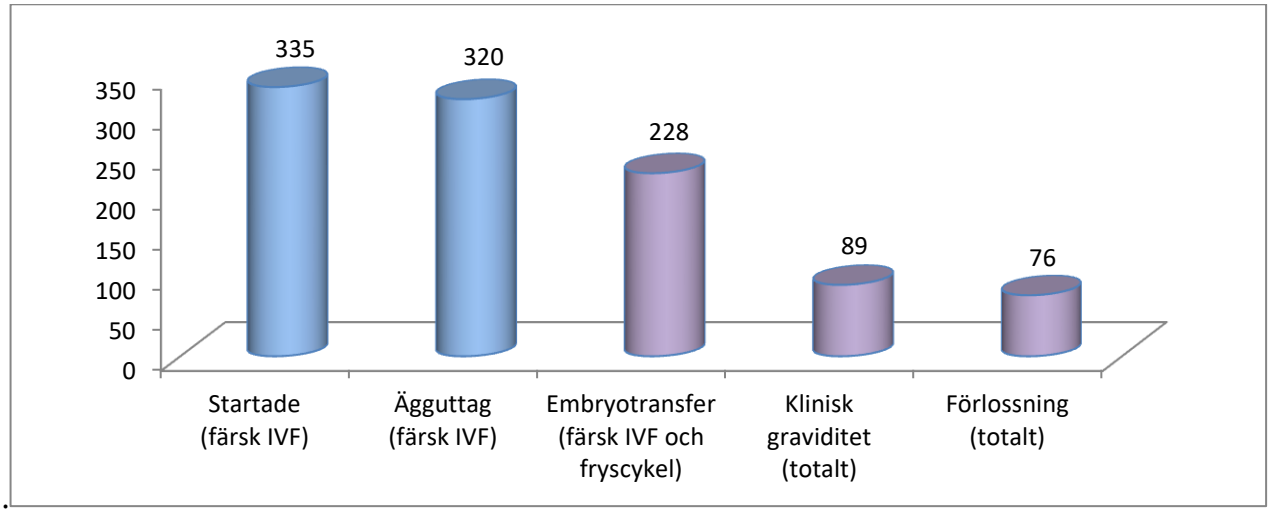
PGT – Preimplantation Genetic Testing

Preimplantation genetic testing was introduced in 1989 as an alternative to prenatal diagnostics for severe genetic diseases, and the first child from a process involving PGT was born in 1992. The technique, earlier named PGD (preimplantation genetic diagnosis) recently changed names to PGT (Preimplantation Genetic Testing), which involves several forms of genetic testing. PGT-A (Preimplantation Genetic testing – Aneuploidy screening) is a variant of the PGT method, the purpose of which is to select an embryo without chromosome abnormalities to increase the birth rate and decrease the time to pregnancy and live birth.

In Sweden, PGT is offered to couples with known monogenic diseases and genetically inherited chromosome abnormalities, while PGT-A is only allowed in clinical trials. During PGT an embryo biopsy is performed, including one to ten cells being sampled from the growing embryo and then analyzed with PCR (Polymerase Chain Reaction), FISH (Fluorescence In Situ Hybridization) technique, array-based technique, or NGS (Next Generation Sequencing).

An embryo, which is considered healthy with regard to the disease in question, can be transferred into the uterus. This reduces the risk of a baby being born with the disease in question from 25%–50% to 0.1%–0.5%. PGT is performed in two clinics in Sweden, in Gothenburg and Stockholm. The first child in Sweden born from a process involving PGT was born in Gothenburg in 1996, and today nearly 500 babies in Sweden have been born from a process involving PGT.

Figure 8. *Number of treatments involving PGT that reached different steps in the treatment process in 2019 and results after fresh and frozen/thawed cycles (combined)..*



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If biopsy is performed at the blastocyst stage, embryos are frozen and transfer are performed in a frozen/thawed cycle.

Complications arising from IVF treatments

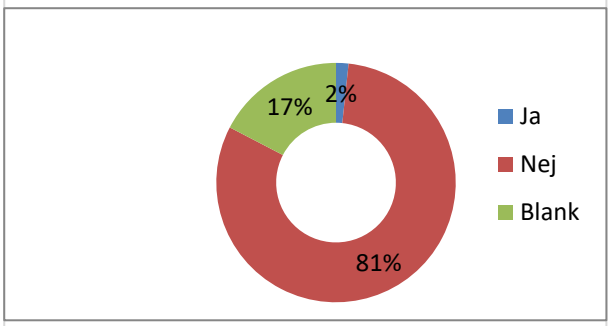
Generally, complications arising from IVF-treatments are few, the most common being OHSS. This syndrome may show up in women with high AMH levels, and in women with many ovarian follicles in their ovaries. During OHSS, blood vessels start leaking fluid into the abdomen. Milder forms of OHSS are quite common and occur in up to 10 % of women. Moderate or severe forms of OHSS are observed in 1%–5% of women. The fluid leaking into the abdomen will eventually be resorbed and returned to the blood stream, but sometimes it is beneficial for the patient if the fluid is drained.

Severe forms of OHSS can today in most cases be prevented through different treatment strategies. The risk of thrombosis increases in case of OHSS and in some cases medical drugs preventing thrombosis needs to be administrated. Severe forms of OHSS resulting in hospitalization or draining of fluid from the abdomen are reported to Q-IVF.

The risk of infection in the ovaries or the abdomen after oocyte retrieval is 0.3%, which is low. Antibiotics are usually not administered, only if the treating doctor considers there being an increased risk of infection.

Minor bleedings after oocyte retrieval is common. These are bleedings from the vagina or from the abdomen that will eventually be absorbed by the body. In 1–2 cases out of 1 000 oocyte retrievals a major bleeding occurs in the abdomen that requires observation at hospital and sometimes surgical/medical intervention.
A few cases of ovarian torsion, when an ovary has twisted over its own stem, occur every year.

Figure 9. *Reported complications at fresh IVF- treatments*



Among the reported complications from fresh IVF-treatments initiated in 2019, there were 60 cases of OHSS where hospitalization was required, 18 cases of bleeding and 10 cases of infection.

Table 4 *Number of reported complications at fresh IVF-treatments*	
Complications - Yes	180
Complications - No	9254
Not reported	2004
Total number of OPU	10421

How many embryos are transferred?

Due to the relatively high incidence of twins as a result of IVF, the Swedish National Board of Health and Welfare decided that, as a rule, only one fertilized oocyte (embryo) can be transferred into the woman. If the risk of a twin pregnancy is estimated to be low, two fertilized embryos can be transferred. As part of this policy, if two embryos are planned to be inserted, the couple or the single woman are to be informed about the risks that twin pregnancies entail. Though most twin deliveries go well, twin pregnancies involve a significantly higher risk of complications than a single-baby delivery.

Before a decision is made on the number of embryos that are to be transferred, there is an individual assessment as to whether there exist any other risk factors, including diseases and previous complications related to pregnancy or delivery, for example caesarean section.

The risk of premature delivery and low birthweight is higher for twin pregnancies than for single-baby pregnancies. Premature births and low birth weight are associated with increased medical risks for the children. Multiple pregnancies also entail an increased risk of hypertensive disorders of pregnancy (HDP) and pre-eclampsia as well as other severe obstetrical complications for the mother. These increased risks are the reasons why in Sweden only one embryo at a time is transferred in the majority of the cycles.

Figure 10a. *Proportion of transfer of one (SET) or two (DET) embryos. Fresh IVF. Autologous gametes.*

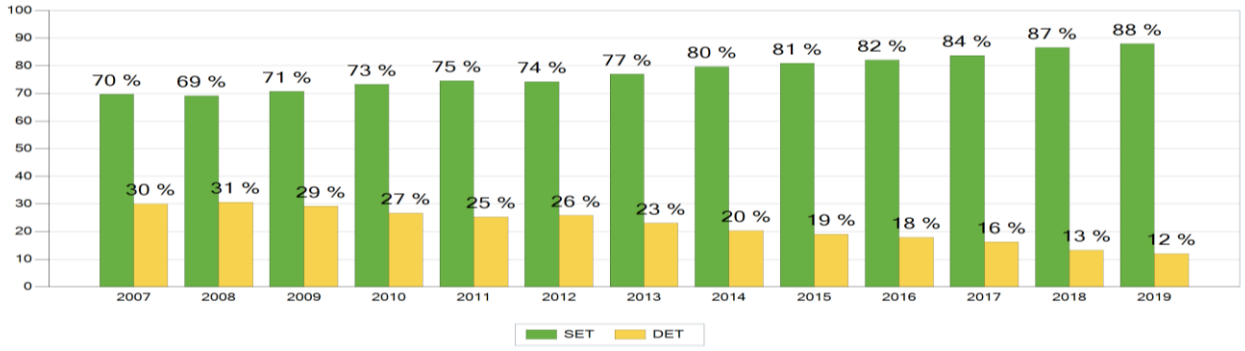


Figure 10b. *Proportion of transfer of one (SET) or two (DET) embryos. Freeze cycles. Autologous gametes.*

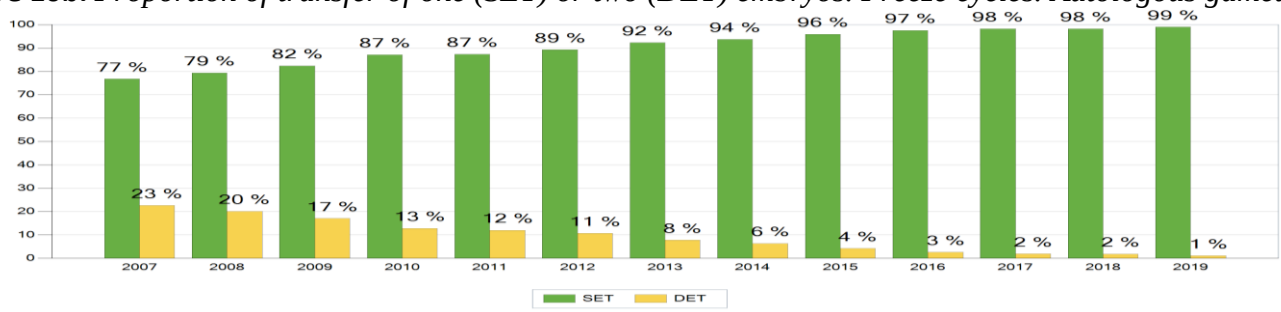
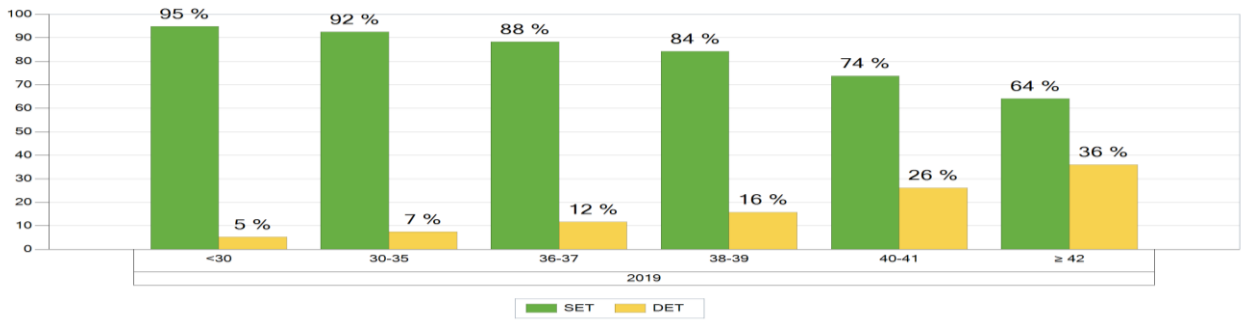


Figure 10c. *Proportion of SET/DET per embryo transfer and age group. Fresh IVF. Autologous gametes.*



Incidence of multiple pregnancies as a result of IVF-treatments in 2018

There has been a dramatic decline in multiple pregnancies in Sweden in the last twenty years due to the one-embryo-transfer policy being introduced and broadly adopted. Despite only one embryo now being transferred at a time, the total delivery rate has remained stable or increased. The increased delivery rate is particularly apparent for IVF with freeze cycles and is associated with modified embryo culture and freezing methods.

The multiple pregnancy rate as a result of IVF in Sweden is among the lowest in the world. Several other countries still have multiple pregnancy rates at 25%–30%. The multiple pregnancy rate for spontaneous conception is about 1%.

Figure 11a. *Multiple birth rate per delivery. Fresh IVF/ICSI and frozen/thawed cycles.*

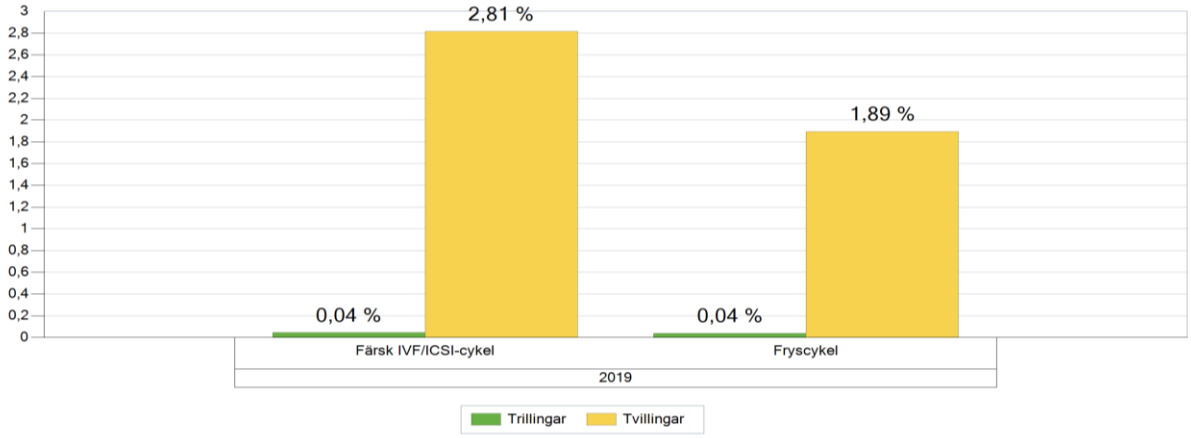


Figure 11b. *Multiple birth rate per delivery at transfer of single embryo (SET). Fresh and frozen/thawed cycle.*

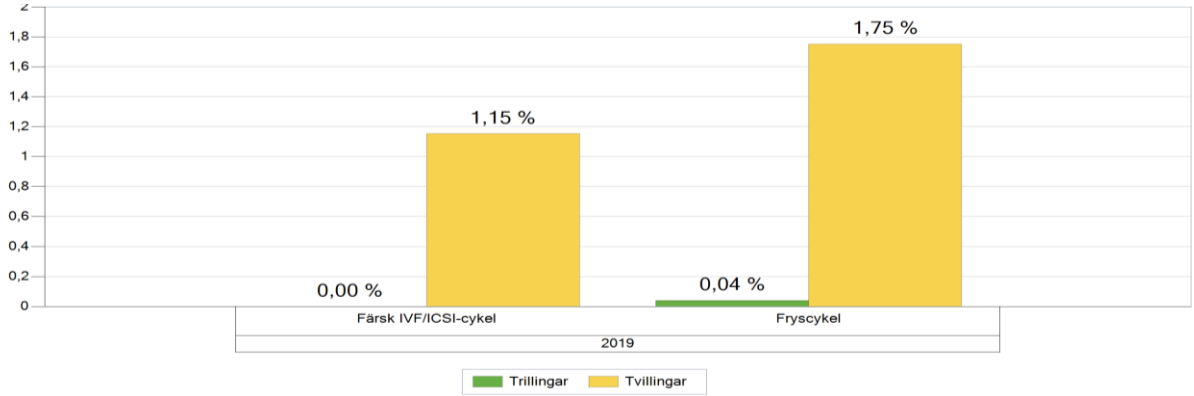


Table 5. Number of multiple births, in total and after transfer of one embryo (SET).

	Deliveries twins	Deliveries triplets		Deliveries twins	Deliveries triplets
Fresh IVF - Total	64	1	*SET*	24	0
Freeze cycles - Total	48	1	*SET*	44	1

For how long was the embryo cultured before transfer?

There are several reasons determining on what day an embryo is transferred. Transferring an embryo that has been cultured for 5–6 days leads to a higher chance of pregnancy per embryo transfer than of an embryo cultured for 2–3 days. This is because embryos that survive in culture until day 5–6 are more viable and therefore have a higher implantation rate. The disadvantage with day 5-6 culture is that it is not known if embryos that do not survive during the prolonged culture period would have been able to generate a child if being transferred on day 2–3. If there is only one or a few embryos by day 2–3, probably nothing is gained from extending the culture until day 5–6. Concerning embryo freezing, embryos that have been cultured for 5–6 days have a higher survival rate (97–98 %) and a better chance of leading to a pregnancy than embryos frozen at day 2 or 3. However, the same potential disadvantages exist here i.e. viable embryos are potentially lost in the culture period from day 2-3 to day 5–6. Today 90% of all freeze cycles take place after culture for 5–6 days since the advantages of day 5–6 are believed to outweigh the disadvantages for the freeze cycles.

Figure 12a. *Proportion of embryo transfers day 2–3 and day 5–6 per age group. Fresh IVF. Autologous gametes.*

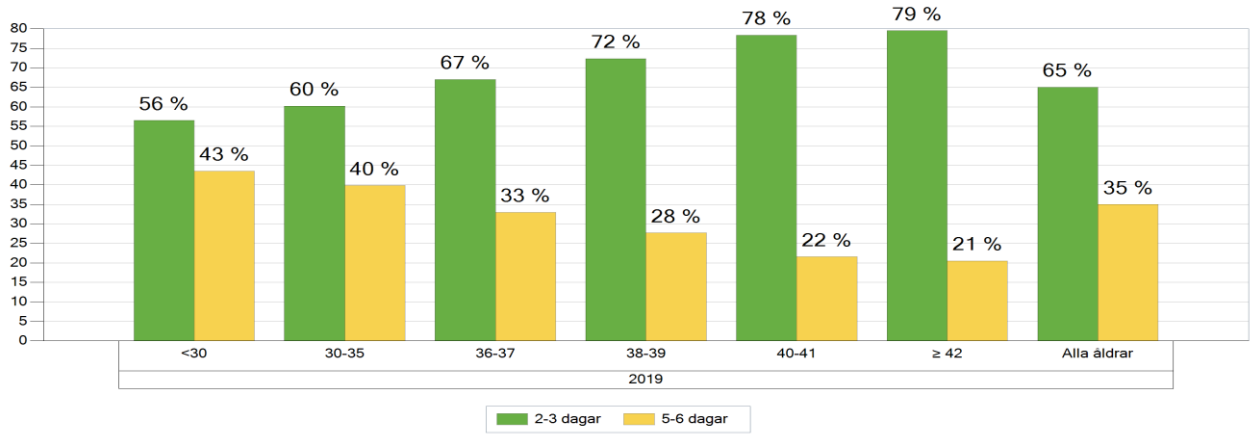
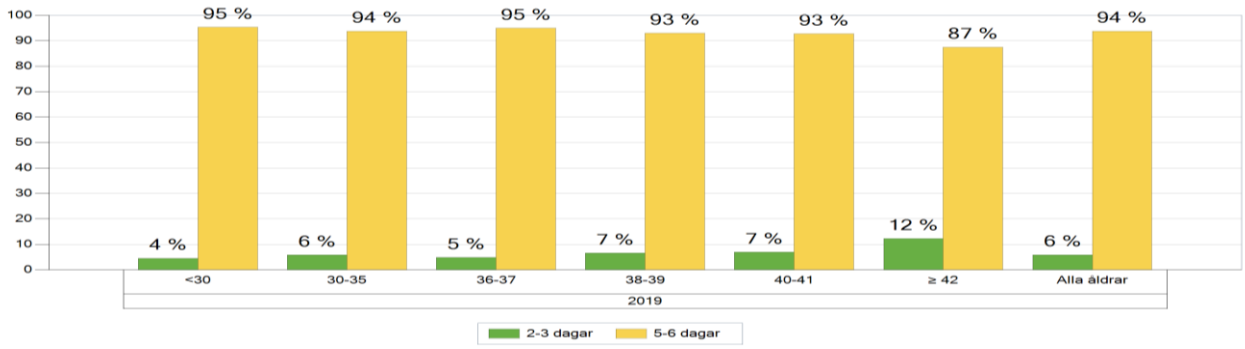


Figure 12b. *Proportion of embryo transfers day 2–3 and day 5–6 per age group. Freeze cycles. Autologous gametes.*



The increased prevalence of blastocyst transfers in freeze cycles compared to fresh cycles are due to the freezing methods for blastocysts (vitrification) having yielded improved treatment results compared to the more traditional "slow freezing" of day 2–3 embryos. The difference for fresh cycles between these culture regimens, however, is not that apparent.

Results

The results from fresh IVF-treatments have been stable over the years, while the results from freeze cycle IVF-treatments have improved in recent years. This is largely associated with extended culture duration aimed for the blastocyst stage and to improved freezing methods. Just over 20%of all women become pregnant and have a child per started IVF-cycle. Younger women have a higher chance, while older women have a lower chance. The woman's age is the most important factor for the chance of becoming pregnant and having a child. At a higher age, both the oocyte numbers and the quality of the oocytes decrease.

Figure 13 *Birth rate per started cycle for different age groups. Fresh IVF/ICSI. Autologous gametes.*

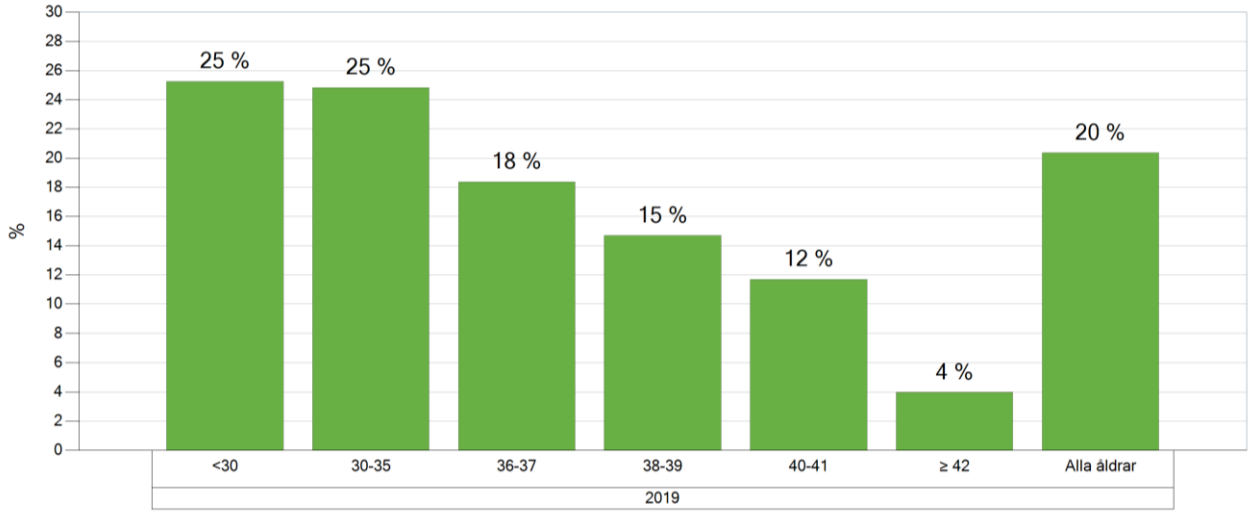
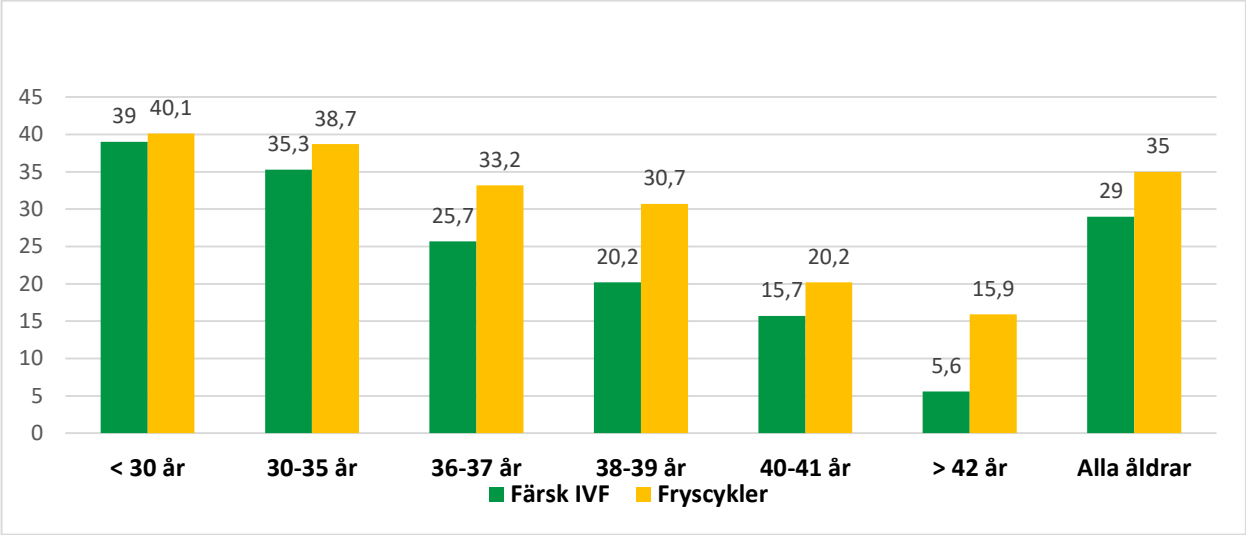
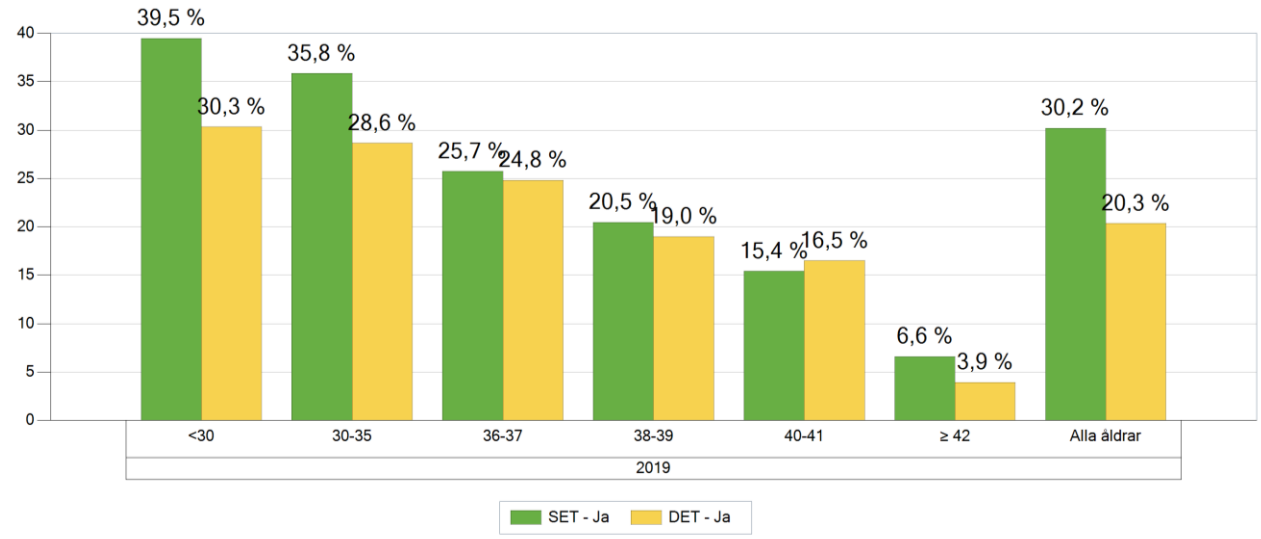


Figure 14 *Birth rate per embryo transfer for different age groups. Fresh IVF/ICSI and freeze cycles. Autologous gametes.*



The reason for a higher birth rate after treatments with frozen embryos compared to fresh treatments for women at a high age is largely because the embryos in the freeze cycles may have been frozen when the women were younger.

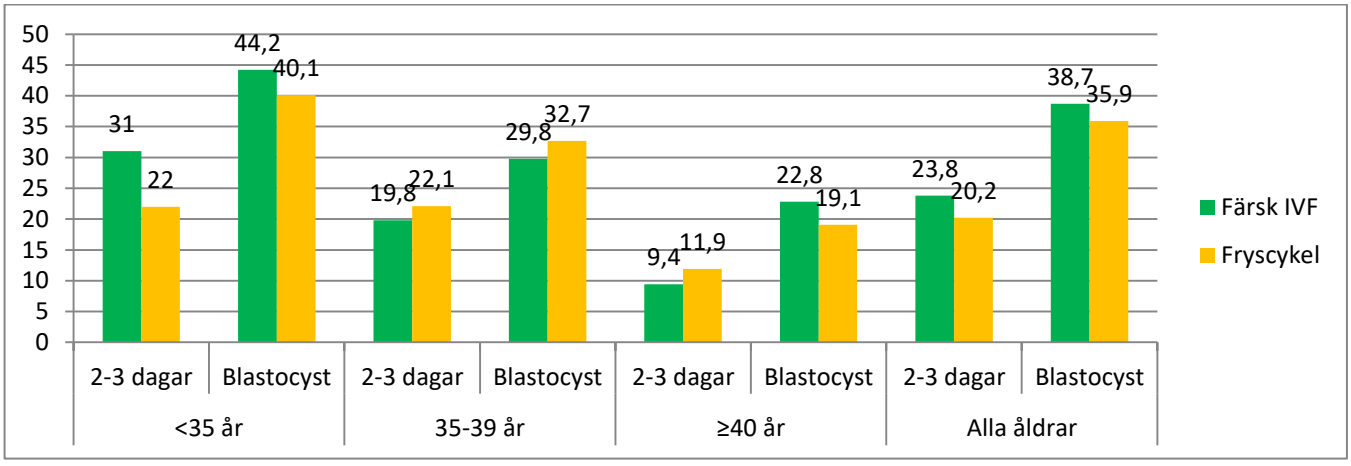
Figure 15. *Proportion of births per embryo transfer and SET/DET for different age groups. Fresh IVF/ICSI. Autologous gametes.*



The birth rate is not directly comparable for SET and DET for the different age groups because the reason why one or two embryos is transferred varies with the prognosis of the patient. Therefore, one cannot draw the conclusion that SET yields a higher birth rate than DET for different age groups nor for all age groups combined. The difference is instead due to that patients with a better prognosis have received SET and patients with somewhat less good prognosis have received DET.

Due to the previously high multiple pregnancy rate for women treated with IVF, the Swedish National Board of Health and Welfare introduced regulations already in 2003 that only one fertilized oocyte could be transferred. If the risk of a twin pregnancy is estimated to be low, however, two embryos are allowed to be transferred.

Figure 16. *Delivery rate per culture time, day 2-3 and blastocysts, and per age group. Fresh IVF/ICSI. Autologous gametes.*



The Figure shows that if one separate treatments in day 2-3 and blastocysts, no apparent differences exist in delivery rates between fresh and frozen/thawed cycles even though a small advantage is observed for fresh cycles (all ages).

Trends (autologous gametes)

Figure 17. *Number of embryo transfers per year for various treatment methods.*

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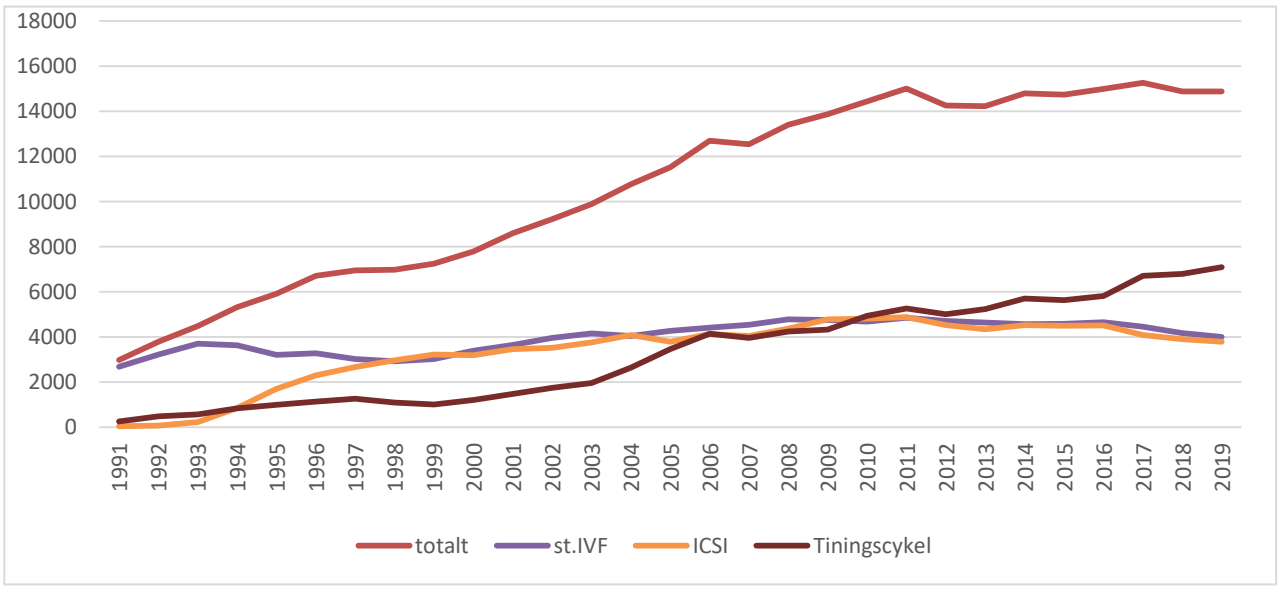


Figure 18. *Proportion of deliveries per embryo transfer and year of treatment for various treatment methods.*

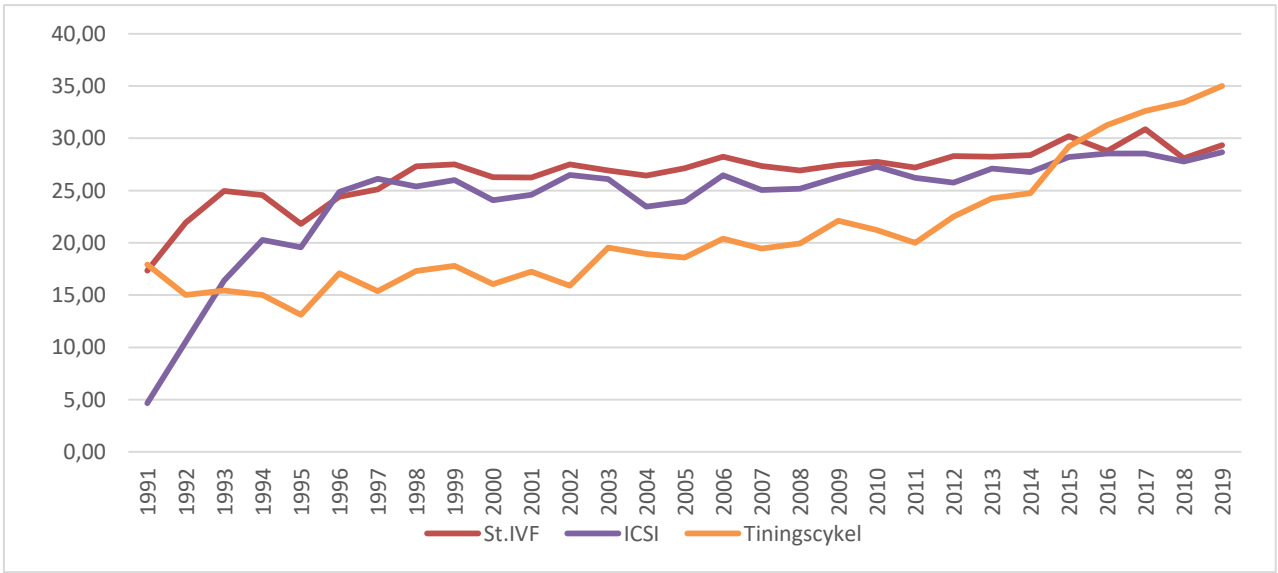
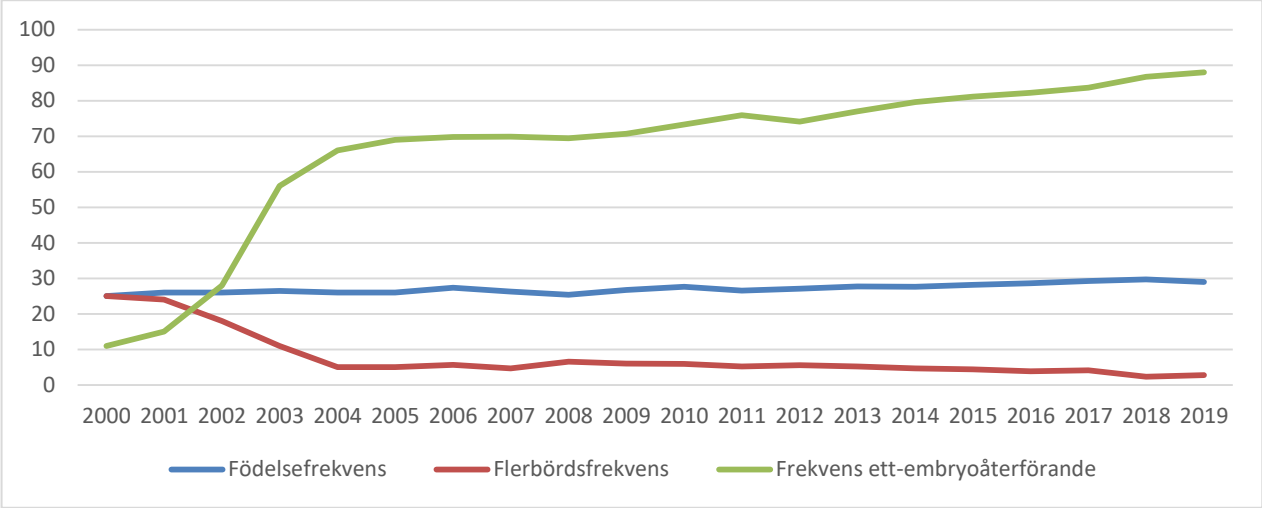
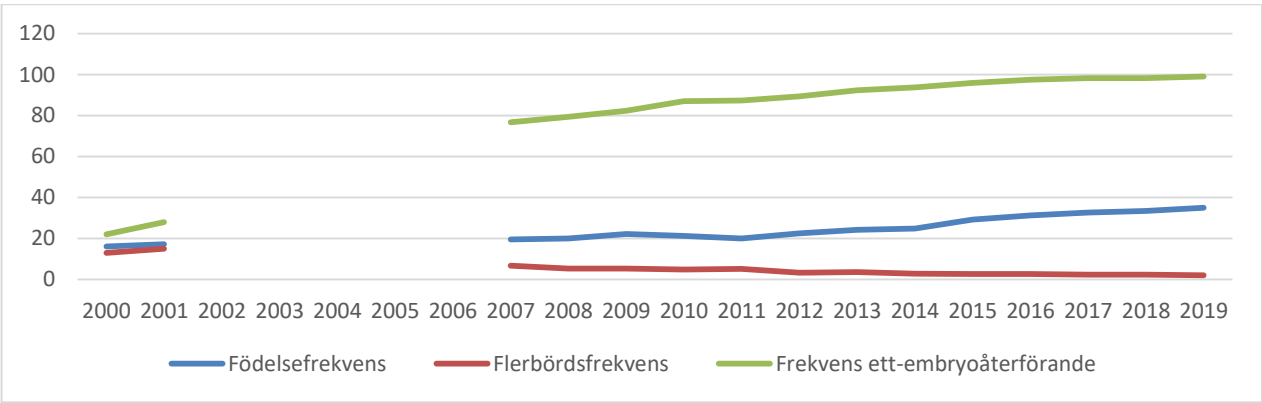


Figure 19a. *Proportion of deliveries per embryo transfer, multiple births and SET per year. Fresh IVF/ICSI.*

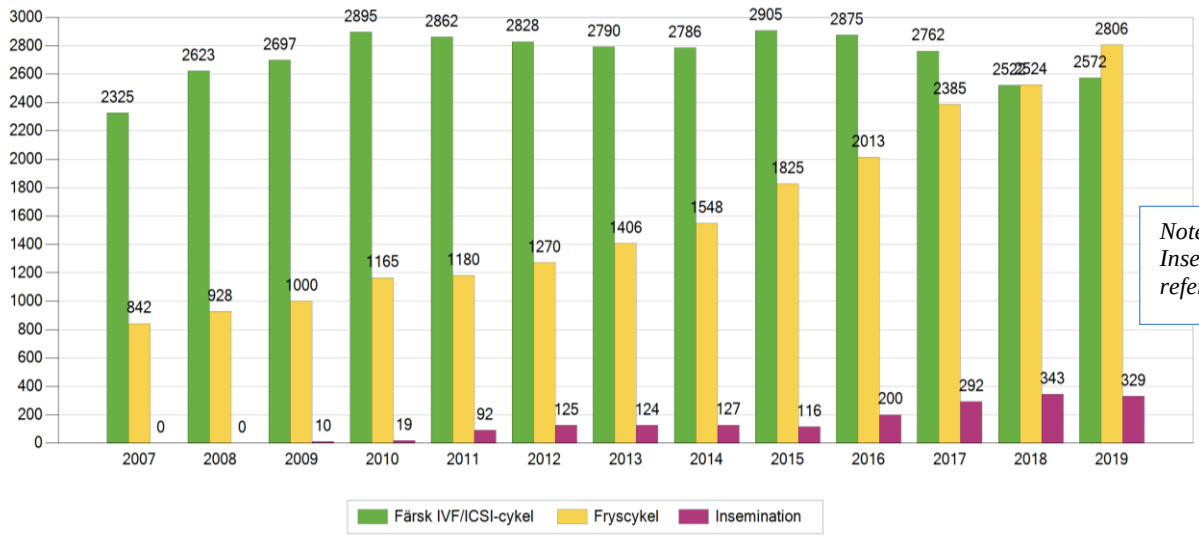


Figur 19b. *Proportion of deliveries per embryo transfer, multiple births and SET per year. Frozen/thawed cycles.*



Data for the years 2002-2006 is missing.

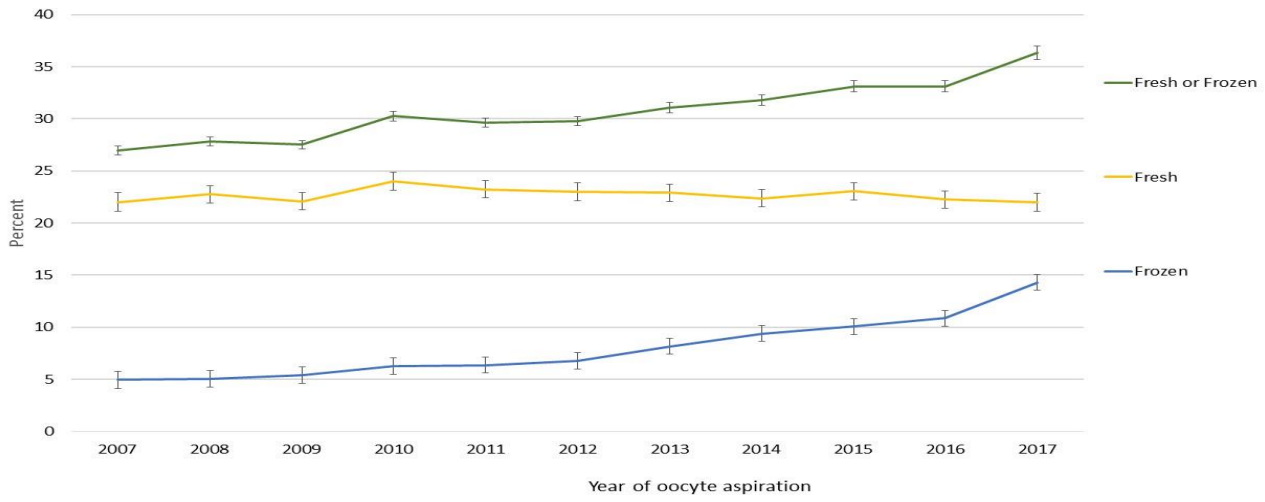
Figure 20. *Number of live born children per year (fresh IVF and freeze cycles include donation and PGT).*



Cumulative result

Cumulative live birth rate is defined as live birth rate per oocyte retrieval, including the fresh cycle and all subsequent frozen/thawed cycles from the same oocyte retrieval. This way to present data may be regarded the most accurate way, since live birth rate is counted per oocyte retrieval. When results are assessed per embryo transfer, the number of transferred embryos may vary as well as culture days, both known to affect the results. Here we present the cumulative live birth rate for all oocyte retrievals performed in Sweden since the start of the registry 2007 and until 2019. We have included live births after transfer of frozen/thawed embryos one year after the oocyte retrieval. The cumulative live birth rate increased from 27.0% to 36.3% within these 11 years, including women not receiving any embryo transfer at all. If, including only women receiving at least one embryo transfer, the live birth rate increased from 30.0% to 43.3% (not shown in figure).

Figure 21. *Cumulative live birth rate per oocyte retrieval and year of treatment, including all embryo transfers within one year after oocyte retrieval.*



Yellow line: Live birth rate after fresh embryo cycle.

Blue line: The additive value of frozen/thawed embryo transfers from the same oocyte retrieval (differ from live birth rate per frozen/thawed embryo transfer) on live birth rate.

Green line: The cumulative live birth rate (fresh and frozen/thawed embryo transfers) per oocyte retrieval.

Reference: Saket Z, Källén K, Lundin K, Magnusson Å, Bergh C. Cumulative live birth rate after IVF: trend over time and the impact of blastocyst culture and vitrification. Hum Reprod Open. 2021 Jun 29;2021(3):hoab021. doi: 10.1093/hropen/hoab021. PMID: 34195386; PMCID: PMC8240131.

IVF with donated gametes (sperm and oocytes)

Sperm and oocyte donation for IVF purposes became legal in Sweden in 2003. However, until 2019 it was only allowed at University hospitals. In 2019, it became allowed for private clinics to offer IVF-treatments with donated oocyte/sperm.

The chance of becoming pregnant and having a child as a result of IVF with one's own oocytes and donated sperm is about 30% for fresh treatments. Still, the chance of success depends on the woman's age, similar to all other IVF-treatments.

The chance of becoming pregnant and having a baby with an embryo that stems from a donated oocyte is not influenced by the age of the woman who receives the embryo is attempting to become pregnant. The donor's age, however, is important. Consequently, the donors are mostly younger women. About 35% of patients become pregnant and have a baby from a fresh oocyte donation treatment.

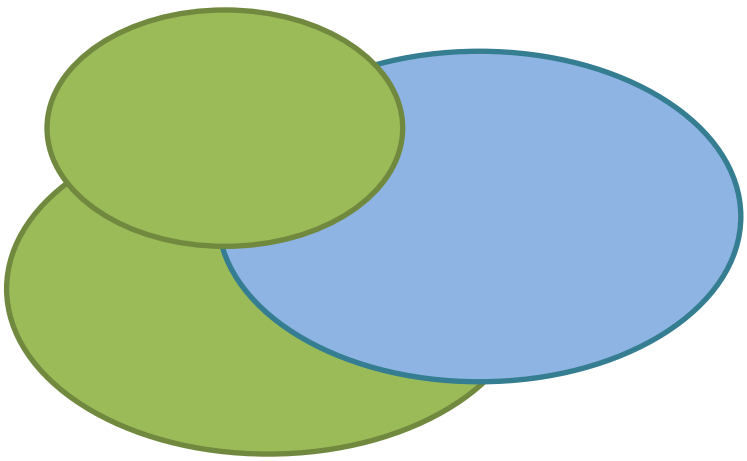


Table 6. *Number of treatments, pregnancies, babies and deliveries. IVF with donated gametes.*

	IVF with donated sperm		IVF with donated oocytes	
	Fresh IVF	**Freeze cycles**	**Fresh IVF**	**Freeze cycles**
Started cycles	1035	541	159	264
Embryo transfers	796	534	76	256
Positive pregnancy tests	308	247	37	97
Biochemical pregnancies	37	29	4	6
Clinical pregnancies	271	218	33	91
Spontaneous abortion < gestational week 13	42	28	5	23
Spontaneous abortion gestational week 13-22	3	3	0	1
Ectopic pregnancy	1	1	0	0
Induced abortion	0	0	0	0
Stillborn gestational week 22-27	0	0	0	0
Stillborn gestational week 28+	1	0	0	0
Deliveries, singleton	220	185	28	66
Deliveries, twins	5	1	0	1
Deliveries, triplets	0	0	0	0
Total number of deliveries	225	186	28	67
Total number of live born children	229	187	28	68

Results

IVF with donated sperm

Figure 22. *Delivery per embryo transfer for different age groups. Fresh IVF and freeze cycles. Donated sperm.*

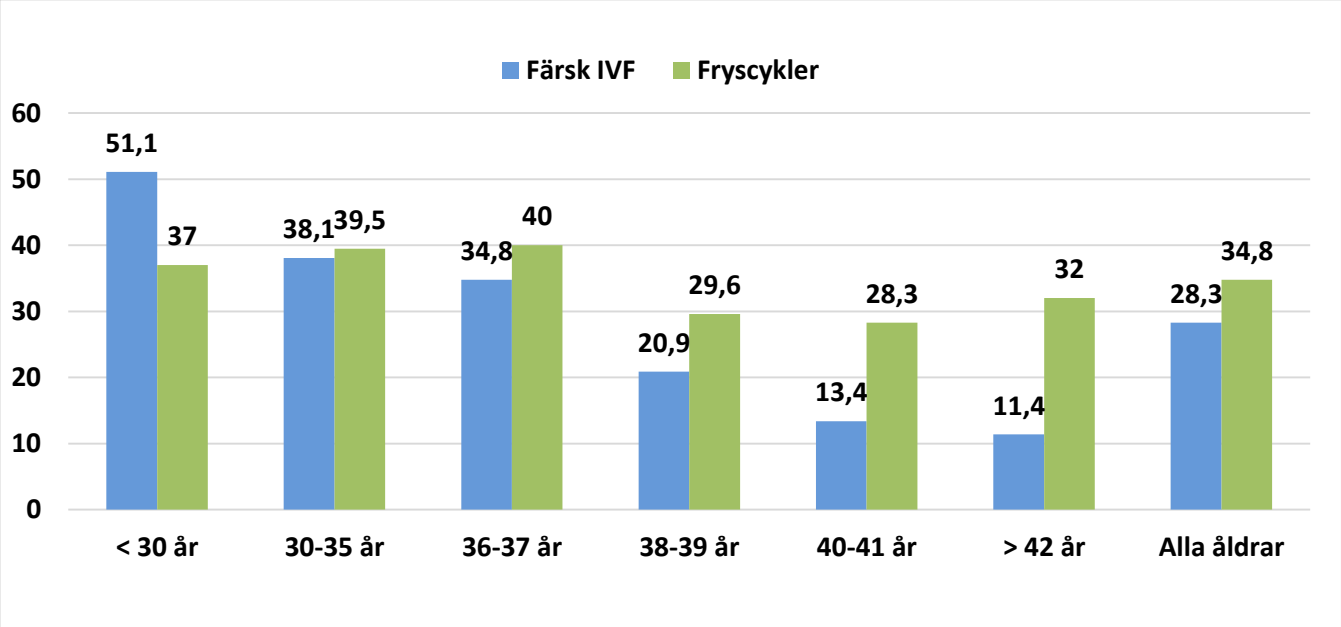


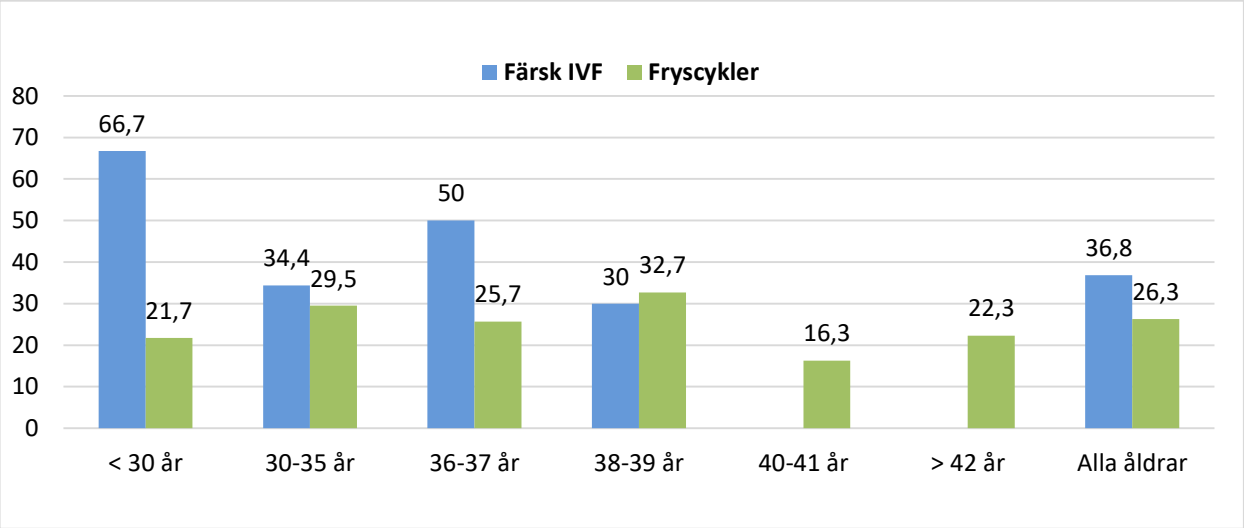
Table 7. *Number of embryo transfers and deliveries for different age groups. Fresh IVF and freeze cycles. Donated sperm.*

Age	Number of ET Fresh IVF	Number of deliveries Fresh IVF	Number of ET Freeze cycles	Number of deliveries Freeze cycles
<30	45	23	54	20
30-35	236	90	185	73
36-37	115	40	65	26
38-39	253	53	115	34
40-41	112	15	92	26
≥ 42	35	4	25	8

Results

IVF with donated oocytes

Figure 23. *Proportion of deliveries per embryo transfer and year. Fresh IVF/ICSI and freeze cycles. Donated oocytes.*



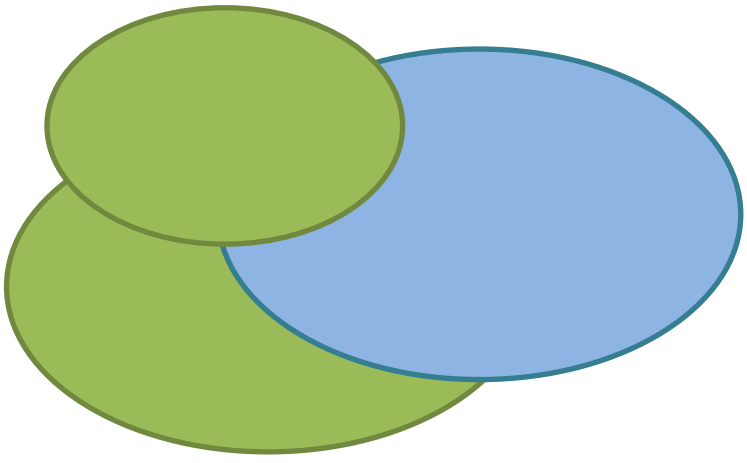
For donated oocytes, the age of the woman who is attempting to become pregnant is not as important for the result of the treatment as when using own gametes. The oocyte donor's age is more important. Please note that the number of oocyte donation treatments is low and that the presented rates therefore may be misleading.

Table 8. *Number of embryo transfers and deliveries for different age groups. Fresh IVF/ICSI and freeze cycles. Donated oocytes.*

Age	Number of ET Fresh IVF	Number of deliveries Fresh IVF	Number of ET Freeze cycles	Number of deliveries Freeze cycles
<30	9	6	23	5
30-35	32	11	96	28
36-37	10	5	35	9
38-39	20	6	49	16
40-41	3	0	43	7
≥ 42	2	0	9	2

Insemination with donated sperm (IUI-D)

In April 2016, a change in the Swedish legislation made it possible for single women to undergo assisted reproduction. At the same time, private clinics could obtain permission from IVO (Inspektionen för Vård och Omsorg, the Health and Social Care Inspectorate), the government body in Sweden overseeing health care providers) to perform insemination with donated sperm (IUI-D). Lesbian couples have had this opportunity since 2005, if performed in public clinics. Among heterosexual couples this treatment is available for couples where the man for some reason lacks sperm or if no fertilization is obtained.



IUI-donor (insemination with donated sperm)

Table 9. *Number of treatments, pregnancies, babies and deliveries, IUI-D*

Insemination with donated sperm	
Started cycles	2492
Insemination	2305
Positive pregnancy tests	430
Biochemical pregnancies	53
Clinical pregnancies	383
Miscarriage < gestational week 13	44
Miscarriage gestational week 13-22	2
Ectopic pregnancy	4
Unknown	4
Stillborn (gestational week 22-27)	0
Stillborn (gestational week 28+)	1
Delivery singletons	317
Delivery twins	6
Delivery triplets	0
Total number of deliveries	**323**
Total number of live births	**328**

Figure 24. *Number of IVF/ICSI and IUI-D treatments started in single women in 2019.*

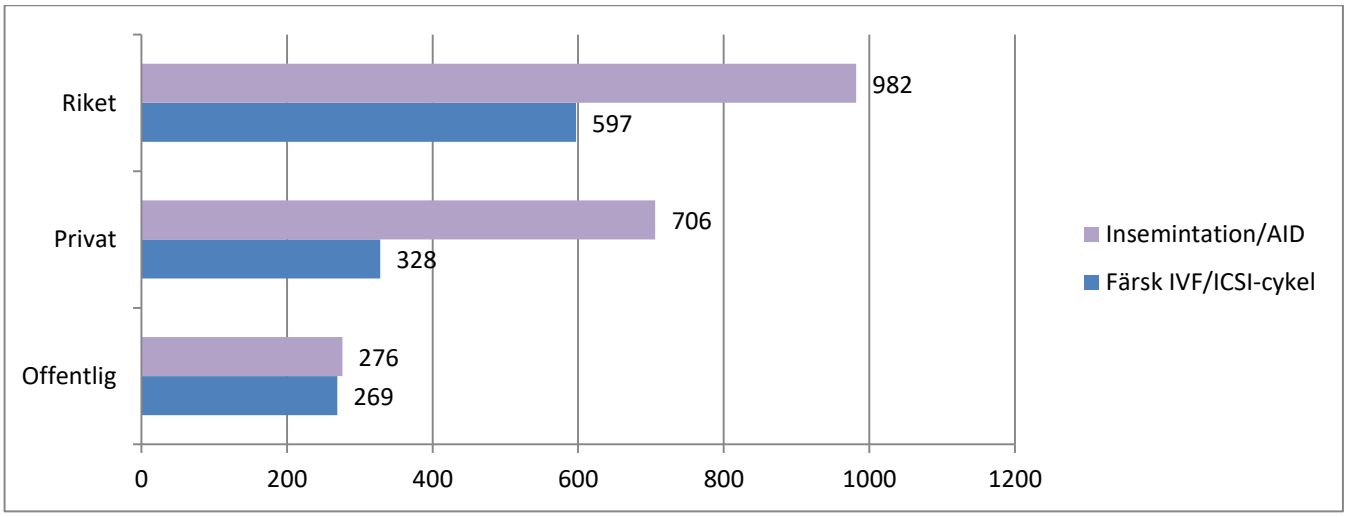


Figure 25. *Number of IUI-D cycles (insemination with donated sperm) per year, public/private/total.*

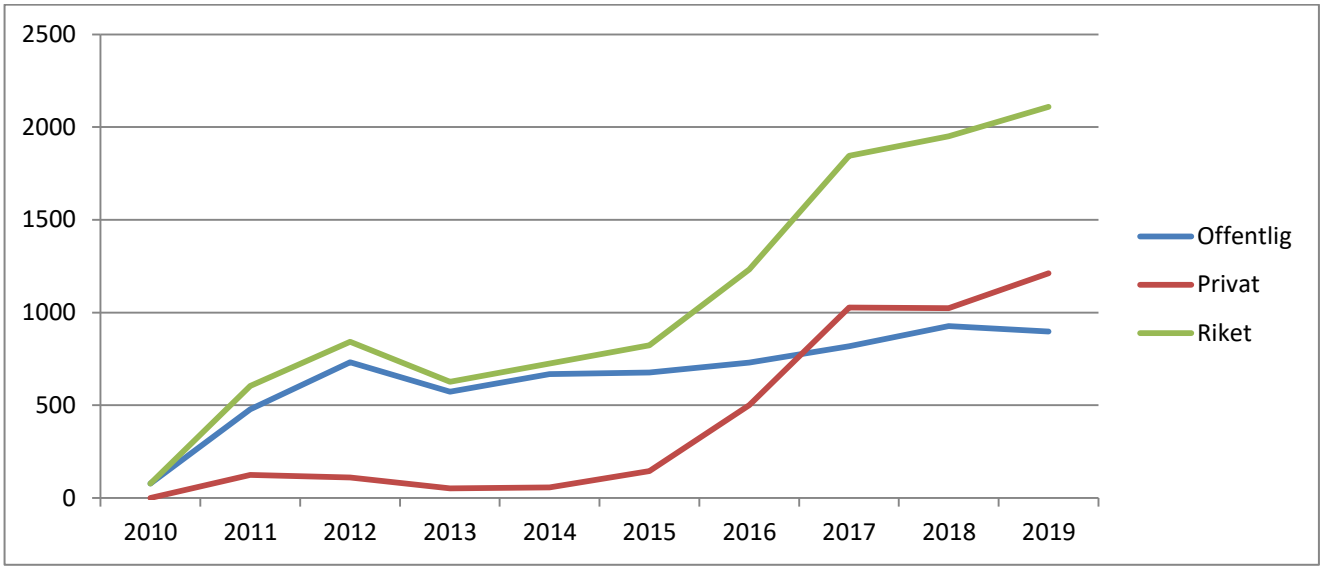


Figure 26. *Delivery per insemination (IUI-D) for different age groups.*

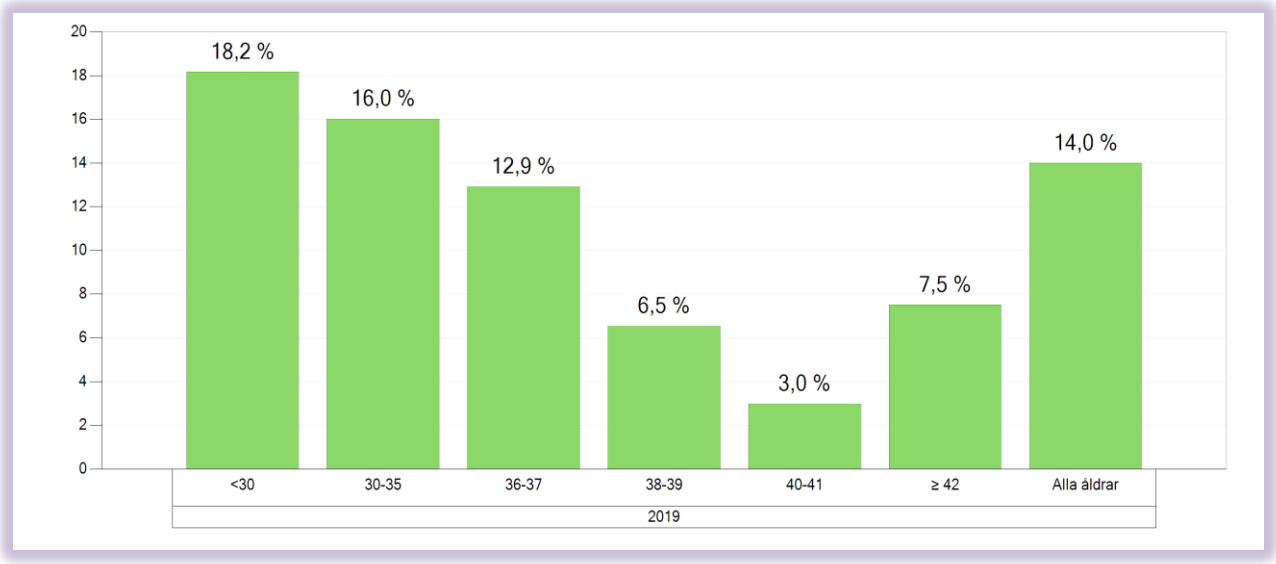


Table 10. *Number of inseminations and deliveries for different age groups. IUI-D.*

Age, years	< 30	30-35	36-37	38-39	40-41	≥ 42
Number of inseminations	391	1112	372	291	101	40
Number of deliveries	71	178	48	19	3	3

Oocyte freezing

The technique of freezing embryos (fertilized oocytes) is reliable and has been used for many years. However, it has been significantly more difficult to freeze unfertilized oocytes. Today the technique of vitrification makes it possible to freeze unfertilized oocytes more effectively than before. Oocyte freezing can be done for medical reasons or non-medical reasons. One medical reason to freeze unfertilized oocytes with the aim to preserve fertility in cases where a woman suffers from cancer and needs to undergo chemotherapy and/or radiation, since the cancer treatment may be harmful to ovaries and oocytes ("oncologic indication"). Other medical reasons to freeze unfertilized oocytes may be sex reassignment surgery/gender confirmation surgery, severe endometriosis or risk of premature menopause. Non-medical reasons for women to freeze unfertilized oocytes could be the desire to delay the starting of a family. It is also possible to freeze donor oocytes in order to more easily coordinate an oocyte donation cycle with a recipient cycle.

In Q-IVF, oocyte freezing for oncologic reasons, for other medical reasons and for non-medical reasons is separated into different categories. In 2018, 139 oocyte freezing treatments were performed on basis of oncologic indication, an increase from the year before. In the same year (2018), 283 oocyte freezing treatments were performed for non-medical reasons. This latter group of treatments has also increased.

Even though the numbers have increased, still rather few of the frozen oocytes have so far been thawed, fertilized and transferred, except for oocyte donation cycles. We can therefore not yet account for the results of those treatments.

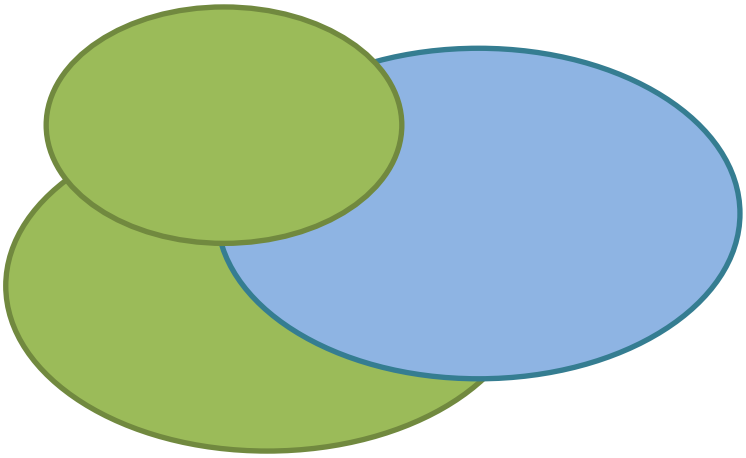


Figure 27. *Number of cycles with freezing of autologous oocytes. Public/private.*

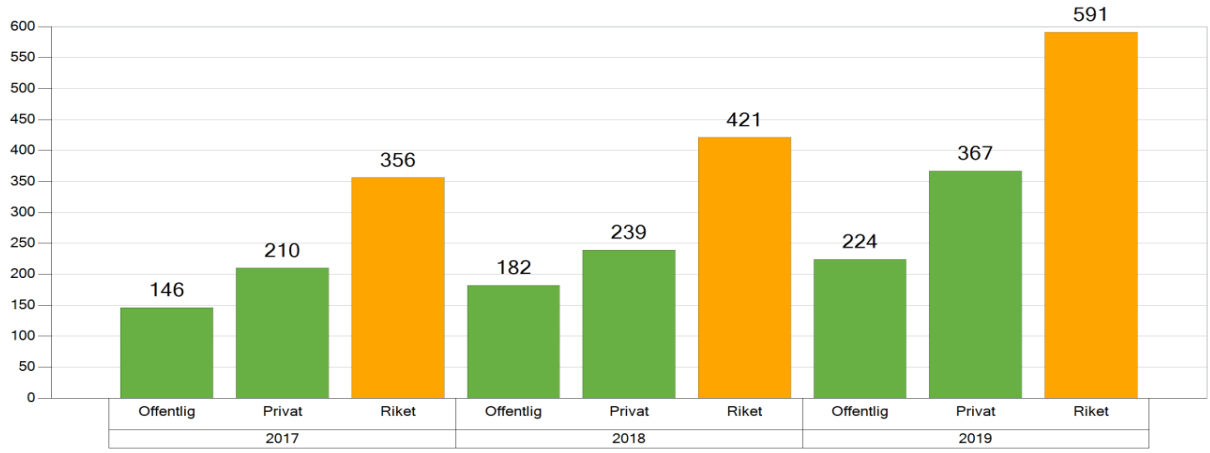


Figure 28. *Reasons for oocyte freezing. Public/private/total.*

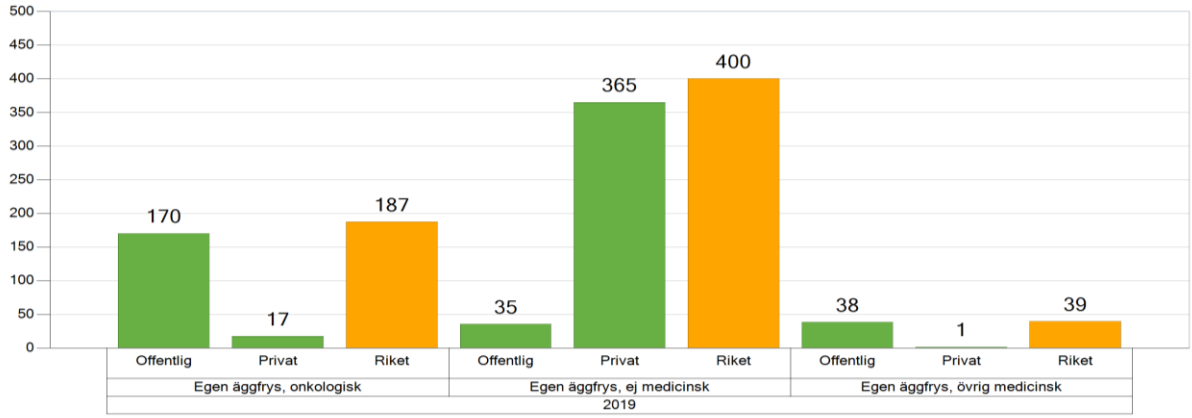
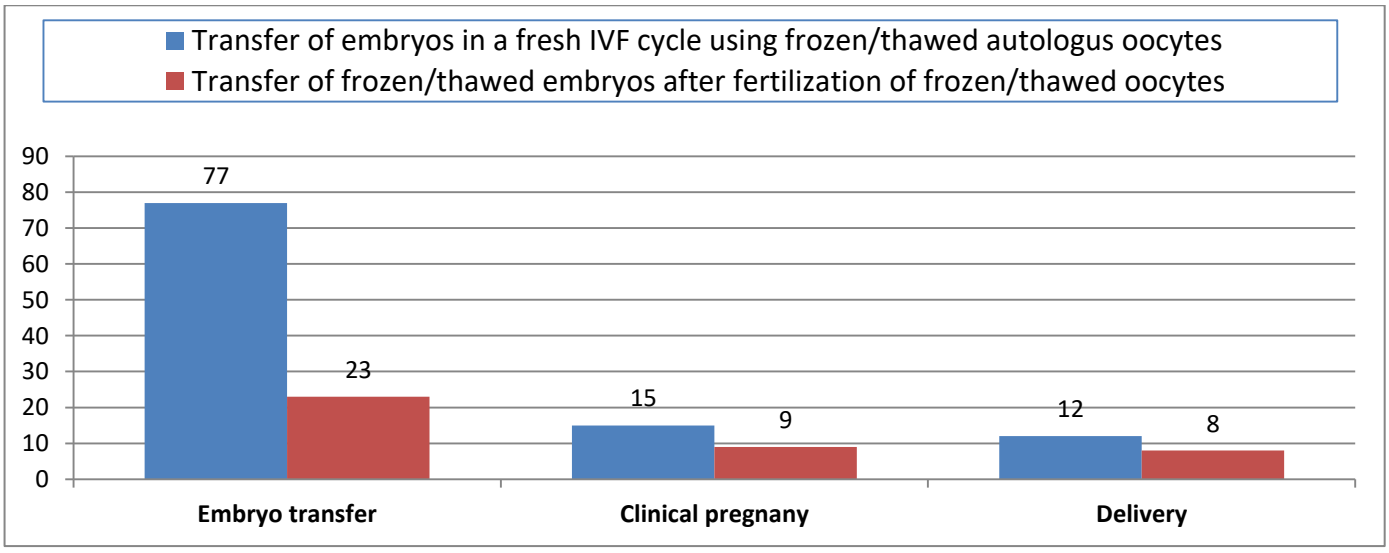


Figure 29. *Number of embryo transfers and deliveries using thawed oocytes after freezing of autologous oocytes.*



Comparisons

In this yearly report, we make comparisons between the clinics. The reader should take into account that the clinics perform treatments on different types of patients and different age groups. A clinic that performs treatments on younger patients will have better results than a clinic that performs treatments on somewhat older women. Furthermore, women who have already had a baby as a result of IVF, and who then undergo another IVF-treatment, have better chances of success than women who have not had an IVF-baby before. In addition, the number of patients treated in each clinic also influences the reliability of the results.

How important are the group sizes for comparisons?

We present many of the results separated into different age groups. In comparisons between groups, one should take into account how large the groups are. The larger the groups are, the more reliable are the results, and the smaller the groups are, the more unreliable the results. In addition, group sizes vary by year and between clinics. If, for example, there are 300 deliveries from 1 000 treatment cycles in the youngest age group one year, the delivery rate is 30%. If, in the same year, only ten treatment cycles are performed in the oldest age group, and they result in three deliveries, the delivery rate for this group is also 30%. Given that the number of treatment cycles for both the youngest and the oldest age group stays exactly the same, one less birth in the youngest age group yields a birth rate of 29,9% (almost no change), while one less birth in the oldest age group would yield a birth rate of only 20% (seemingly a considerable decline).

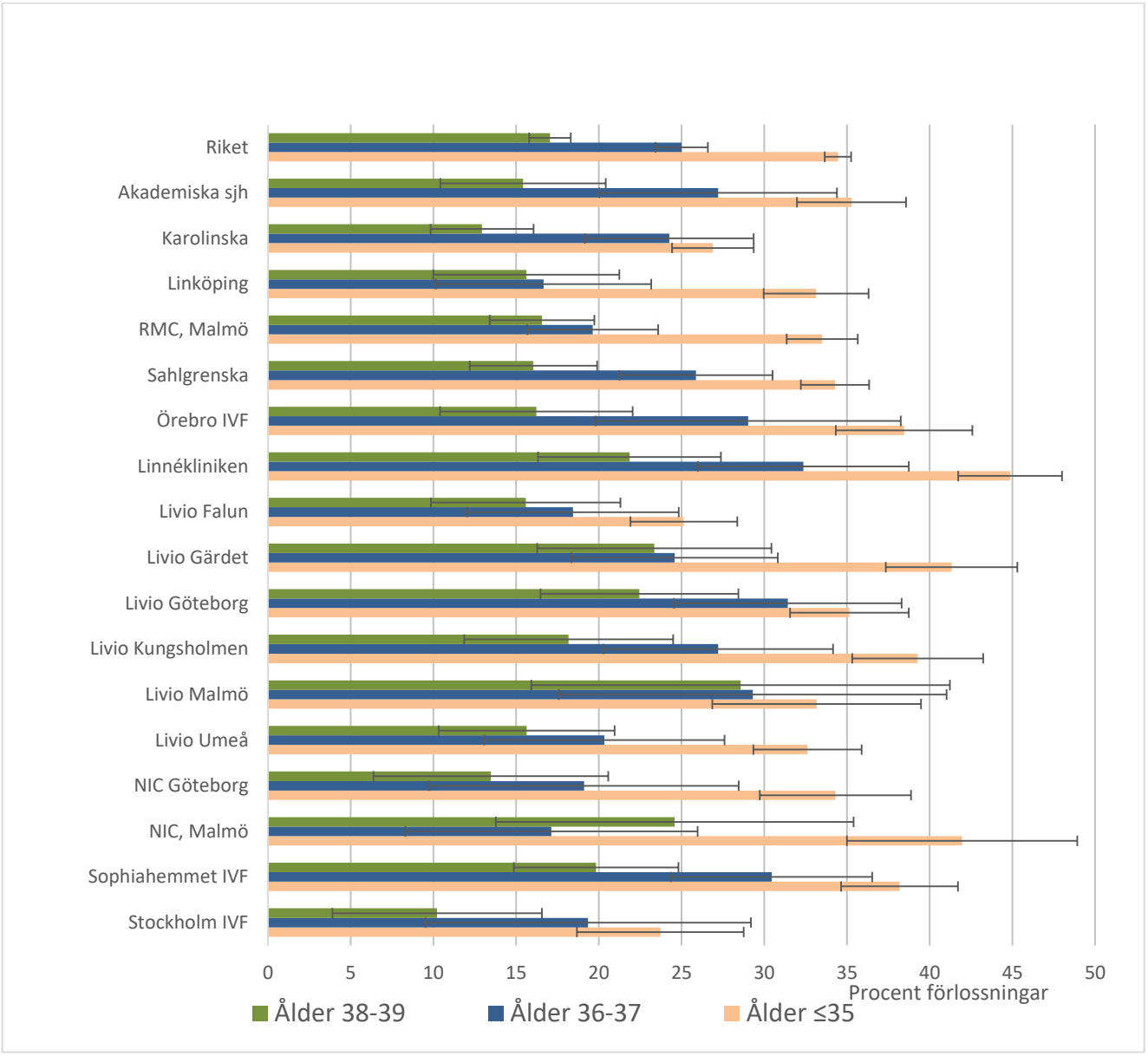
The results are presented in deliveries per embryo transfer. In order to achieve more reliable results, results from multiple years have been combined. Regarding the number of days an embryo has been cultured, graphs we do not discriminate the results between day 2–3 embryos and day 5–6 embryos (blastocysts). Concerning fresh embryo transfers, day 2–3 embryos make up a considerable proportion (67%) of all embryo transfers (Figure 12a), while in freeze cycles day 5–6 embryos are most common (90%, Figure 12b). In Figure 27, results from the first embryo transfer are presented, irrespective of whether it is done in a fresh cycle or in freeze cycle. The reason for this is the growing number of cycles where all embryos have been frozen and where the first transfer logically becomes a freeze transfer. A variation in the number of culture days and other treatment strategies, as well as the spectrum of treated patients, may differ between clinics and could lead to somewhat different results.

As explained above, the reliability of the results vary due to the number of embryo transfers, and a reliability indication, a so-called confidence interval, is shown as a black line at the top of every bar. The longer the black line is, the less embryo transfers are included, and the less reliable are the results. The results for Sweden as a whole are very reliable, since numbers from all clinics are included in these results. New clinics are not always included in the comparisons, since the number of treatments they have performed may be too low.

Comparisons

Figure 30. *Proportion of deliveries per oocyte retrieval and first embryo transfer (fresh transfer, or first embryo transfer with a frozen/thawed embryo if the fresh treatment resulted in "freeze-all"). The compilation only applies for those women doing cycle number 1–3 and who have not had children earlier as a result of IVF.*

Treatments with the patient's own gametes between June 1 2017 and June 30 2019

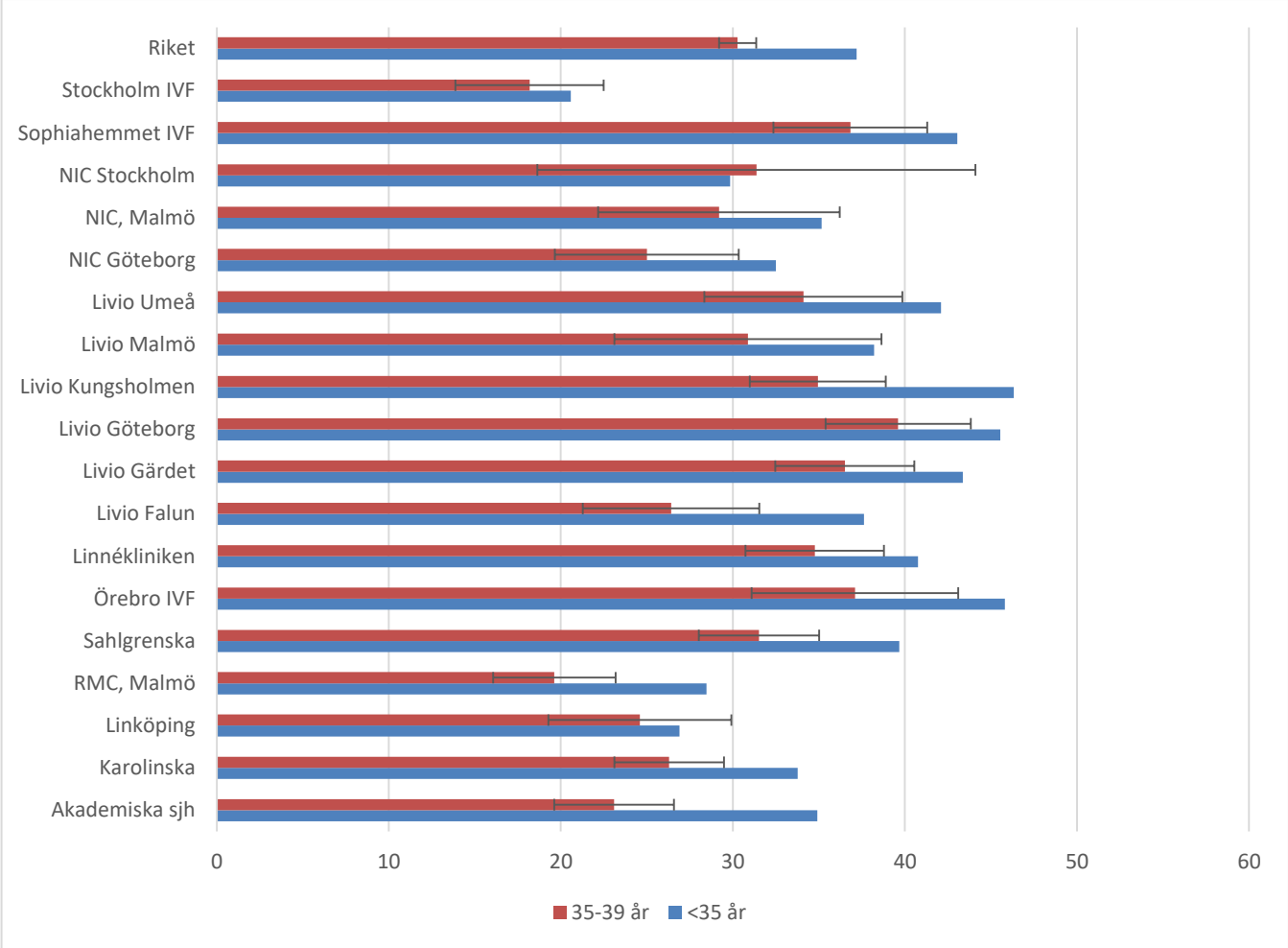


Confidence interval: The lines in the bars denote the so-called confidence interval. The confidence interval is an estimation of a number's reliability. The longer the line is, the more unreliable the birth rate is. The foremost factor affecting reliability is the number of treatments per age group (a low number of treatments equals low reliability).

Comparisons

Figure 31. *Proportion of deliveries per embryo transfer of frozen/thawed embryos. The woman's age at the time of the oocyte retrieval applies.*

Treatments with autologous gametes 2017–2019



Confidence interval: The lines in the bars denote the so-called confidence interval. The confidence interval is an estimation of a number's reliability. The longer the line is, the more unreliable the delivery rate is. The foremost factor affecting reliability is the number of treatments per age group (a low number of treatments equals low reliability).

Figure 32. *Rate of blastocyst transfers among frozen/thawed cycles per year.*

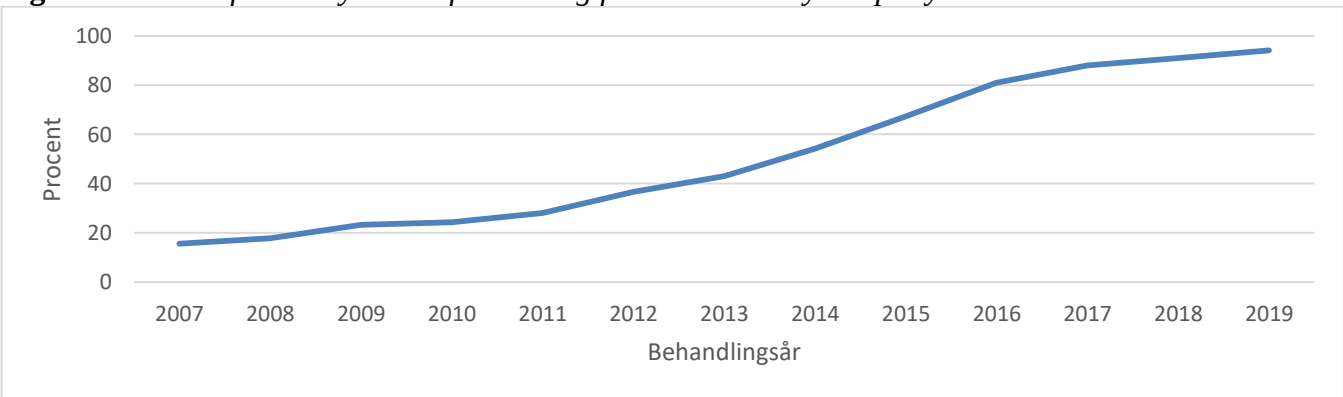


Table 11.

Number of embryo transfers included in the comparisons between IVF clinics (Figure 27). ***Fresh IVF****. The compilation only applies to those women undergoing cycle 1–3 and who has no children earlier as a result of IVF/ICSI. Autologous gametes.*

Public clinics

Age	**Akademiska Uppsala**	**Huddinge Karolinska**	**Sahlgrenska Göteborg**	**RMC Malmö**	**Linköping**	**Örebro**
≤ 35 år	805	1242	2033	1856	845	533
36-37 år	147	272	344	387	126	93
38-39 år	201	448	349	531	160	154

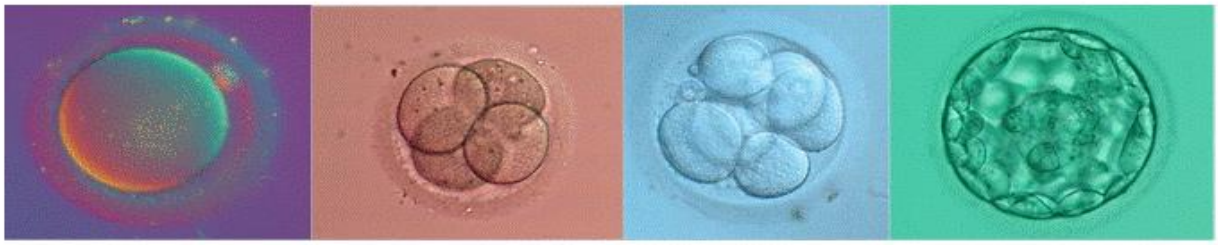
Private clinics

Age	**Linné kliniken**	**Livio Falun**	**Livio Gärdet**	**Livio Göteborg**	**Livio Kungsholmen**	**Livio Malmö**	**Livio Umeå**	**Nordic Göteborg**	**Nordic Malmö**	**Sophia hemmet**	**Stockholm IVF**
≤ 35 år	965	696	588	680	583	214	791	414	193	728	274
36-37	207	141	183	175	158	58	118	68	70	220	62
38-39	215	154	137	187	143	49	179	89	61	247	88

Research

Q-IVFs' data offers great possibilities for researchers. Approval from the ethical committee and a "secrecy assessment" are required. Application forms to access data from Q-IVF can be found on our homepage.

A large number of studies based on Q-IVF data have been performed in Sweden. In many of these studies, the researchers have cross-linked with data from the Medical Birth Registry, the Registry of Birth Defects, the Cancer Registry, the Patient Registry, or other health or national quality registries. In this way, it has been possible to detect what type of risks IVF-children and IVF-mothers may run, compared to children born from spontaneous conception and their mothers. Globally, the largest risk involved in IVF is the large proportion of multiple pregnancies that lead to babies being born prematurely and with low birth weight. In Sweden, we have been able to drastically reduce the number of multiple pregnancies through the one-embryo-transfer policy. This makes Sweden one of the leading countries in the world in this area of IVF. Though some risk remain, these risks are quite limited, and most children born as a result of IVF in Sweden are healthy. Additionally, research into how patients experience the IVF-treatment is performed, especially when the treatment does not succeed. Both childlessness and the IVF-treatment itself are known to be stressful.



Patient satisfaction

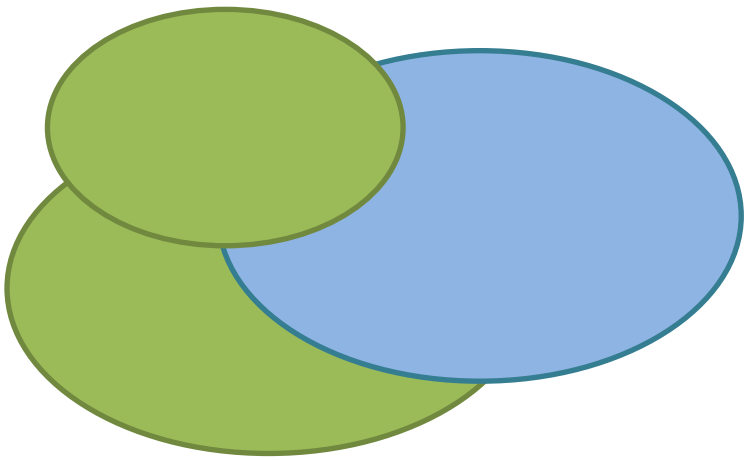
KUPP (Quality from a Patient's Perspective) is a patient survey often used in Swedish health care. All of Sweden's IVF clinics use a variant of this survey named IVF-KUPP, containing specific questions for IVF-patients. The survey is scientifically validated.

The patients answer various types of questions. They are asked to assess how the clinic and the staff handle different parts of the IVF treatment. They are also asked to assess how important the handling and the specific parts of the treatment were to themselves.

The survey is administered by Q-IVF and performed in all of Sweden's IVF-clinics at a one-and-a-half-year interval. The answers in the survey constitute data on which the comparisons between IVF clinics in this report are based. The same comparisons can also be found on Q-IVF's homepage.

In the fall of 2019 (during three months), the survey IVF-KUPP was performed for the fifth time, using questionnaires. Each of the clinics is given the collective results of the questionnaires filled out by their own respective patients, in order to learn and make improvements. In total, 4 855 questionnaires were sent out to women and "partners" who underwent treatment. In 2019, 71% of women and 50% of "partners" answered the questionnaire.

Among responders, 57% underwent IVF-treatment for the first time and the remaining 43% had undergone treatment before. The answers did not differ between these two groups. The group who underwent an IVF-treatment that included donated sperms constituted 13% and increased from 6% in the previous survey.

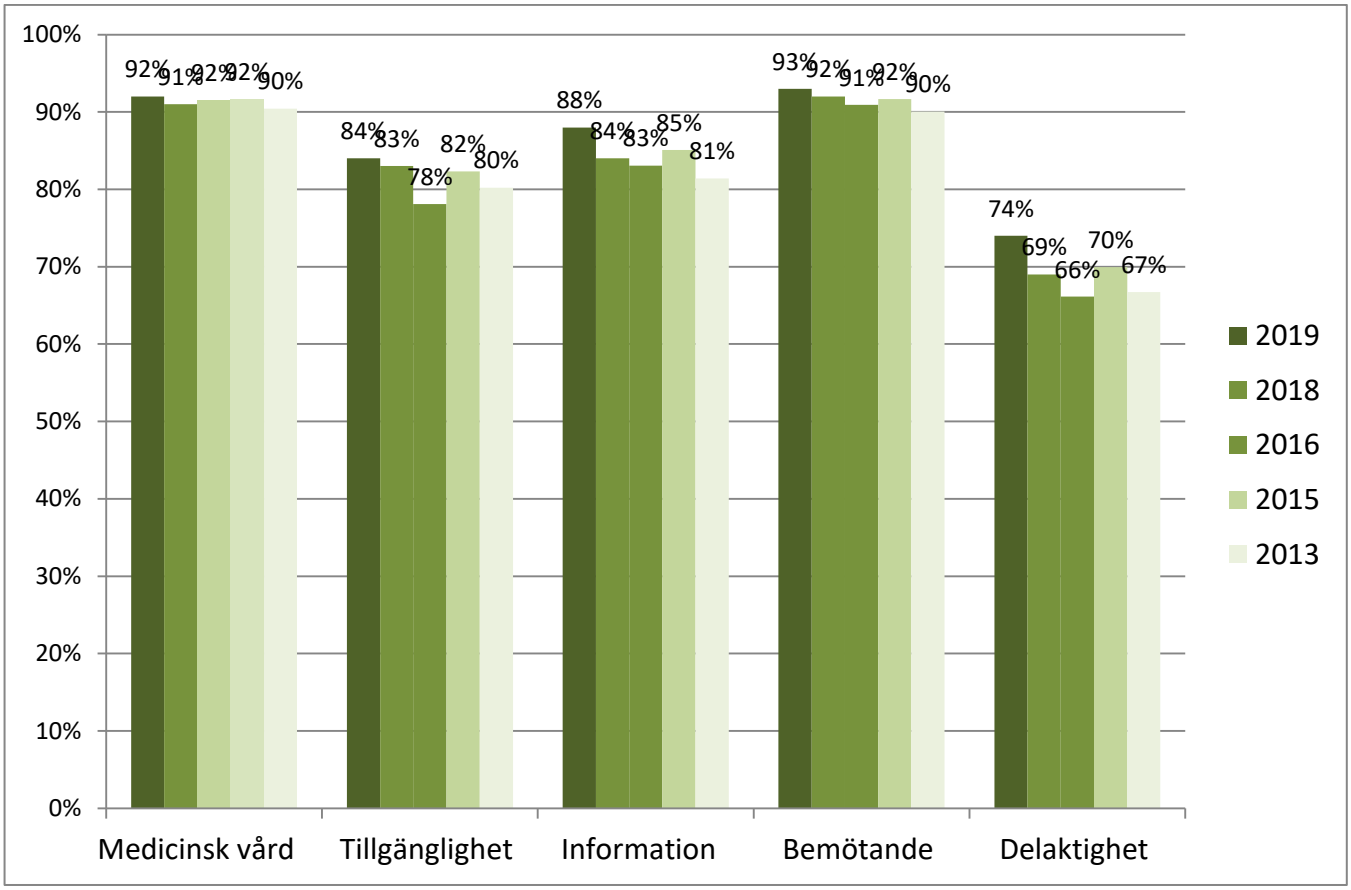


The comparisons have been divided into five main categories;

- Medical care: We received the best possible health care as far as we can tell (1 question)
- Availability: It was easy to come in contact with the clinic, and it was easy to get an appointment (2 questions)
- Information: Treatment, medication, check-up-results, complications (5 questions)
- Approach from staff: Empathy, respect, engagement (6 questions)
- Participation: Participation in decision-making (2 questions)

The answers apply to the proportion of respondents who answered "completely agree" or "mostly agree" to the selected questions from the survey.

Figure 33. *Average for all clinics in Sweden and comparisons to previous years.*



The results have improved for all variables. Satisfaction in general is at a high level, and it has increased. The issue (category) that the clinics have focused on in particular since the latest survey is "Participation", and results have improved (an increase in satisfaction from 69% to 74%). The clinics had also focused on "Information", where an increase in satisfaction from 84% to 88% is observed. The overall improvement is largely due to the clinics commitment to patient wellbeing.

Concluding remarks

Q-IVF is one of the world's most complete quality registries for IVF-treatments, with over 230 000 registered cycles from both public and private healthcare providers. In 2019, more than 23 000 cycles were started, which is a small increase compared to previous year.

The chance of getting pregnant from a fresh IVF-treatment has remained at the same level during the last years (in 2018 the chance of success was 22% per initiated treatment and 29.3% per embryo transfer.) The chance for a woman of achieving a pregnancy is, however strongly related the woman's age. The chance of getting pregnant from a transfer of a frozen embryo has increased, mostly associated with new, effective methods of freezing and extended culture of excess embryos. The proportion of multiple pregnancies in Sweden is very low due to only one embryo being transferred in a majority of the cycles.

In the last years, extended culture of all embryos, if not replaced on day 2/3, has become the norm. Transfer of blastocysts) now constitutes 98% of all transfers with frozen/thawed embryos and 33% of fresh transfers.

Freezing of unfertilized oocytes, a technique very much improved in recent years, is a technique used by both public and private clinics. Since the woman's age is very significant in determining the quality of her oocytes, oocyte freezing is increasing mainly among women younger than 39 years.

Since the change in the Swedish legislation in 2016, which allowed single women to use assisted reproduction, insemination with donated sperm has increased. In upcoming reports, we intend to present the proportion of these treatments performed in single women, and how large part of the treatments performed in either heterosexual or homosexual couples.

Having children is a central part of most people's lives, and those who undergo an IVF-treatment usually have high expectations for the treatment. In the last few years, through the quality survey KUPP, we have been able to measure in a validated manner how well the providers of in vitro fertilization meet the patients' expectations. We are proud to say that the IVF providers meet the patients' expectations well, and strive to become even better. This report is one tool to help the IVF providers make the improvements they aim for.