

**Assisted Reproductive Technology
National Summary Report
Belgium 2017**



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Collège de Médecins Médecine de la Reproduction
College of Physicians Reproductive Medicine**

15 October 2019

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Data provided to the Belgian registration system of Assisted Reproductive Technology (ART) give an overall national picture of factors that contribute to the quality and success of ART treatment performed in Belgium with the aim to obtain one healthy live-born infant. Some of these factors are patient-related and therefore outside a center's control (e.g. woman's age, cause of infertility, ...).

Information about the factors that contribute to a successful ART treatment give potential ART users an idea of the average chances of success. Average chances do, however, not always apply to a particular individual or couple pointing consequently to the need to take complementary medical advice.

This report summarizes data of all individual A (16) and B (18) ART centers.

The 37125 cycles performed in 2017 at these reporting centers led to 5692 live births. The 2017 National summary table is presented on page 6.

The report also includes a number of charts and graphs to answer specific questions on ART treatments or trends. The figures are organized according to the type of ART procedure used. Some ART procedures use a woman's own eggs (nondonor), and others use donated eggs or embryos, although sperm used to create an embryo may also be either from a woman's partner or from a donor. Data are presented according to the source of the egg.

Embryos that develop may be transferred back to the woman during the days following the retrieval of eggs (named here fresh embryo transfer) or after cryopreservation for transfer at a later date (named here frozen embryos). Data on frozen embryos include therefore data on embryos that may have been frozen many years before the cycle started in 2016.

The National report has 5 sections:

Section 1 (Figures 1 through 3) presents general information on the number and location of ART centers, number and types of ART cycles performed; age of women having undergone these treatments and number of infants born from ART cycles.

Section 2 (Figures 4 through 16) presents information on the ART cycles that used only fresh nondonor eggs or fresh embryos from nondonor eggs.

Section 3 (Figures 17 through 21) presents information on ART cycles that used only frozen embryos from nondonor eggs.

Section 4 (Figures 22 and 23) presents information on ART cycles that used only donated eggs.

Section 5 (Figures 24 through 28) presents trends in the number of ART procedures performed over the last 10 years and their success rates.

Percentages in figures do not always add up to 100 due to rounding.

National Summary Table

2017 ART CYCLE PROFILE

Type of ART^a

IVF	17%	With social security	85%
ICSI	75%	Used PGD	6%
Mixed (IVF + ICSI)	8%		

2017 ART SUCCESS RATES

Type of Cycle^b

Age of Woman

<36 36-39 40-42 ≥43 Total

Fresh Embryos from Nondonor Eggs

Number of cycles	10345	4829	4116	424	19714
Percentage of cancellations	6.7	12.0	14.3	15.6	9.7
Percentage of cycles with freeze-all	14.2	7.3	3.5	3.5	10.0
Average number of embryos transferred	1.2	1.4	1.7	1.9	1.4
Percentage of embryos transferred resulting in clinical implantation ^c	27.2	15.9	8.5	3.6	19.3
Percentage of single embryo transfer	79.8	60.2	48.0	42.1	68.2

Outcomes per Cycle

Percentage of cycles resulting in clinical pregnancy	23.8	16.6	10.1	6.5	18.8
Percentage of cycles resulting in live birth	18.6	11.2	5.7	1.9	13.7

Outcomes per Cycle excluding freeze-all cycles

Percentage of cycles resulting in clinical pregnancy	27.9	17.9	10.4	6.7	20.9
Percentage of cycles resulting in live birth	21.8	12.1	6.0	2.0	15.3

Outcomes per Transfer

Number of transfers	6857	2989	2436	235	12517
Percentage of transfers resulting in clinical pregnancy	36.5	27.3	17.2	11.8	30.0
Percentage of transfers resulting in live birth	28.6	18.4	9.8	3.5	22.0

Outcomes per Pregnancy

Number of pregnancies	2394	781	407	27	3609
Percentage of pregnancies resulting in live birth	80.9	69.4	58.6	33.3	75.5

Outcomes per Live Birth Delivery

Number of live births	1866	526	232	8	2632
Percentage of live births resulting in singleton live births	93.0	90.9	93.1	87.5	92.6
Percentage of live births resulting in twin live births	7.0	9.1	6.5	12.5	7.4

Frozen Embryos from Nondonor Eggs

Number of cycles	9441	2970	1476	336	14223
Number of transfers	8264	2507	1230	257	12258
Average number of embryos transferred	1.2	1.2	1.3	1.4	1.2
Percentage of embryos transferred resulting in clinical implantation ^c	22.8	18.0	11.6	9.2	20.3
Percentage of transfers resulting in clinical pregnancy	32.2	27.6	19.1	16.5	29.6
Percentage of transfers resulting in live birth	23.5	18.2	10.4	9.2	20.8

All Ages Combined

Donor Eggs (Fresh and Vitrified Oocytes)

Number of cycles	846
Number of transfers	574
Percentage of embryos transferred resulting in clinical implantation ^c	14.4
Percentage of transfers resulting in clinical pregnancy	33.6
Percentage of transfers resulting in live birth	20.7

^a Reflects features of fresh non-donor cycles (N=19714)

^b Includes all initiated cycles with own or donor sperm.

^c Clinical implantation, including fetal heart beat.

Section I: Overview

Where are Belgian ART clinics located, how many ART cycles did they perform in 2017, and how many infants were born from these ART cycles?

ART clinics are located throughout Belgium; the largest number of ART centers is concentrated in the Brussels Region. Figure 1 shows the locations of A (16) and B (18) centers. While B centers may, following legislation, perform the entirety of the ART procedure i.e. egg retrievals, fertilization of eggs and embryo transfers, A centers transport their retrieved eggs and sperm specimen to the B center to complete the procedure. All of them report their data which are gathered in this report.

In Belgium, the number of centers is defined by the Royal Decree of the 15th February 1999. This law limits the number of centers to 1 A center per 700,000 inhabitants, 1 B center per university hospital and 1 non-university center per province with at-least 1 center in a public hospital.

The 37125 cycles performed in 2017 at these reporting centers led to 5402 live births.

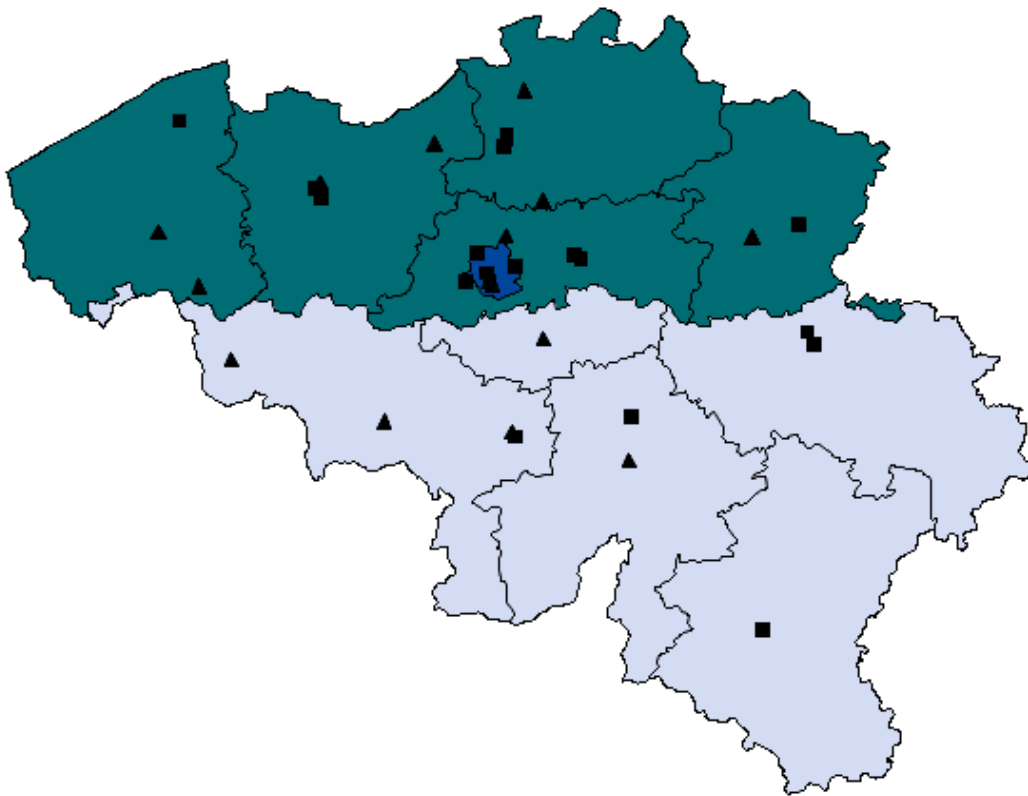


Figure 1. Location of the 18 ART B-centers (■) and 16 ART A-centers (▲) in Belgium.

What types of ART cycles were performed in Belgium in 2017?

Figure 2 shows the types of ART cycles performed in Belgium in 2017. For approximately 53% of ART cycles performed, fresh nondonor eggs were used. ART cycles using frozen nondonor embryos were the next most common type, accounting for approximately 38% of the total. In about 2% of cycles, fresh donor eggs were extracted. Recipients of such fresh eggs represented 2% of all ART procedures and recipients of thawed eggs less than 1%. A very small number of cycles (1%) involved different treatment procedures (embryo donation, surrogate carrier, eggs sharing or, mixed cycle).

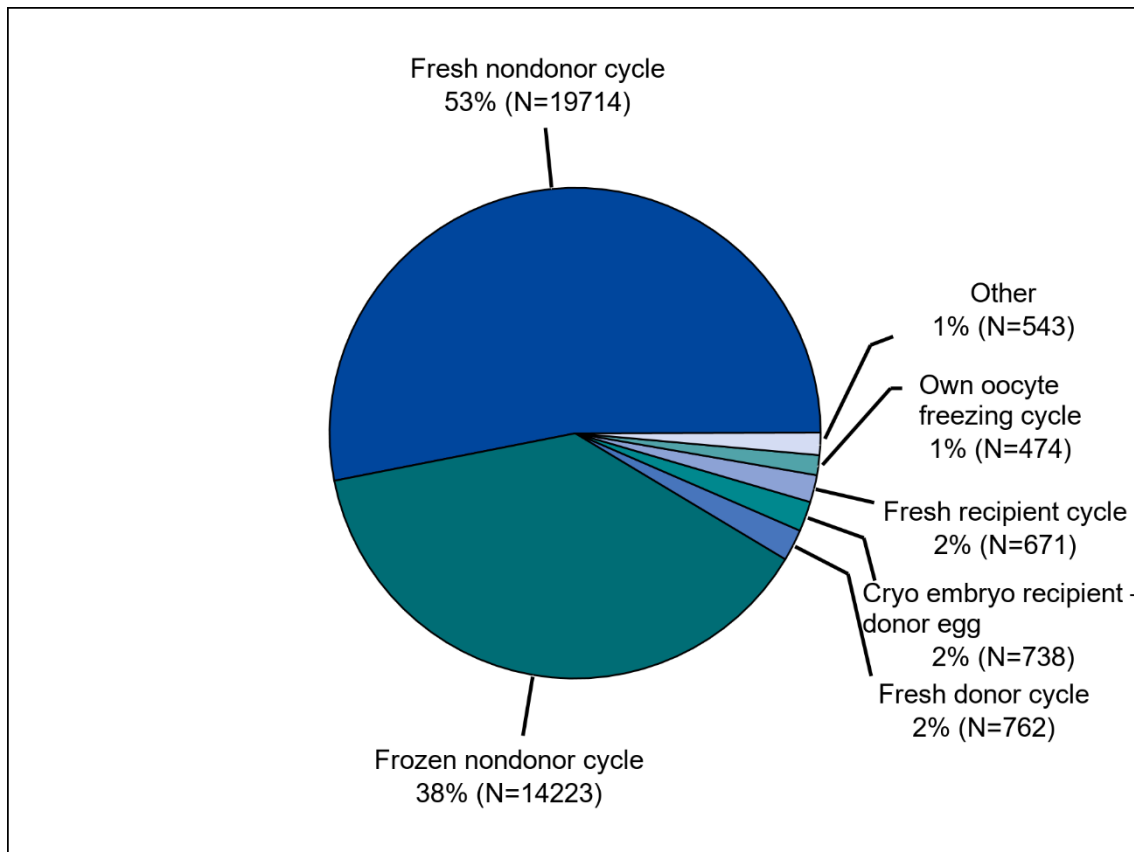


Figure 2. Type of ART cycles.

How old were women who used ART in Belgium in 2017?

Figure 3 presents ART cycles performed in Belgium according to the age of all the women treated (own and donor eggs, fresh and thawed cycles). The largest proportion of women using IVF was younger than age 36, representing 57.6% of all IVF cycles performed in 2017, 22.8% of ART cycles were performed among women aged 36–39, 16.2% for women aged 40–42 and, 3.4% for women aged ≥ 43 .

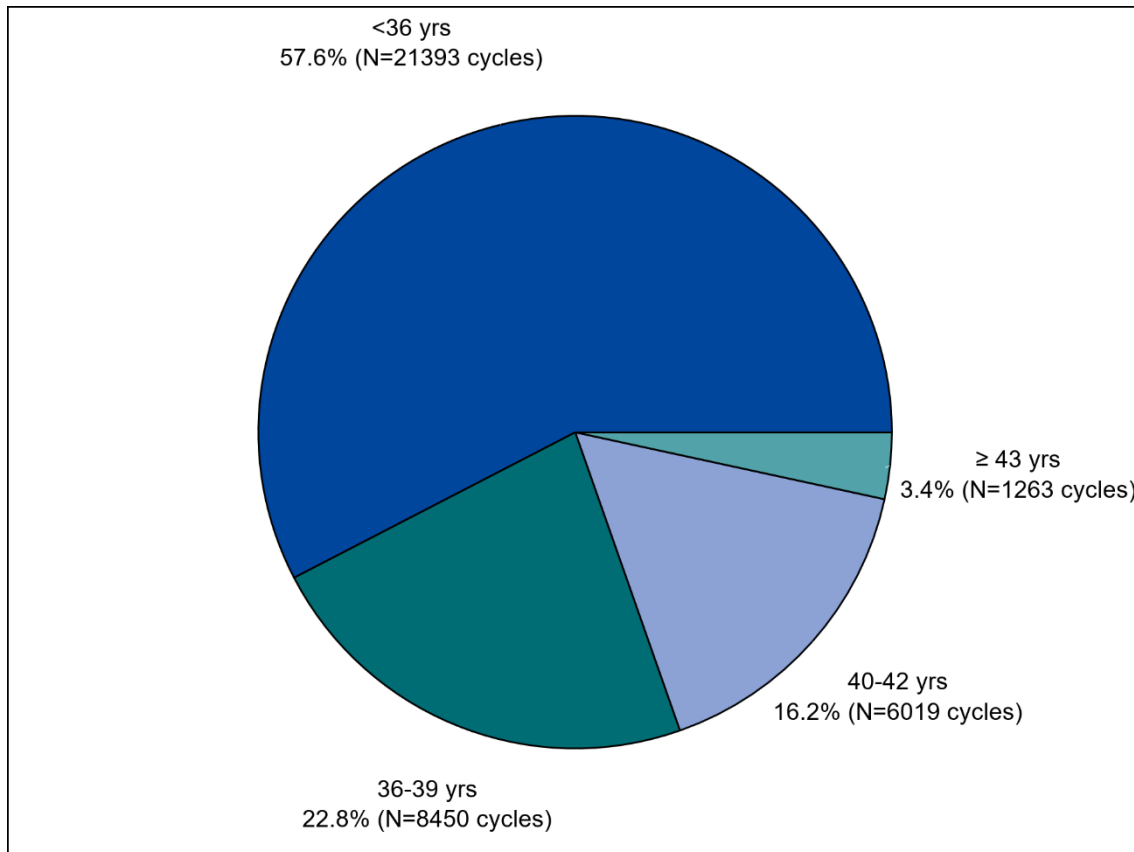


Figure 3. ART use by age group.

Section 2: ART cycles using fresh nondonor eggs or embryos

What are the steps for an ART cycle using fresh nondonor eggs or embryos?

Figure 4 presents the steps for an ART cycle using fresh nondonor eggs or embryos and shows how ART users in 2017 progressed through these stages towards embryo transfer and cryopreservation.

An ART cycle is initiated when women begin taking medication to stimulate the ovaries to develop eggs or when women begin ovulation monitoring by ultrasound or blood tests in case of natural cycles. If the ovarian follicles grow, mature eggs are developing and the cycle then progresses to egg retrieval (aspiration), a surgical procedure to collect the eggs from a woman's ovaries.

Once retrieved, eggs are inseminated with sperm in the laboratory leading to 80.3% of cycles where at least one egg was fertilized.

Among fertilized eggs, one or more of the resulting embryos are selected to be transferred into a woman's uterus through the cervix.

Supernumerary embryos of sufficient quality will ultimately be frozen in 43.0% of initiated cycles to be transferred in a subsequent cycle.

A cycle may be canceled at any step for specific medical reasons (e.g., no eggs are produced or retrieved, fertilization failed, or no embryo developed) or rarely for a non-medical reason because of a patient's choice.

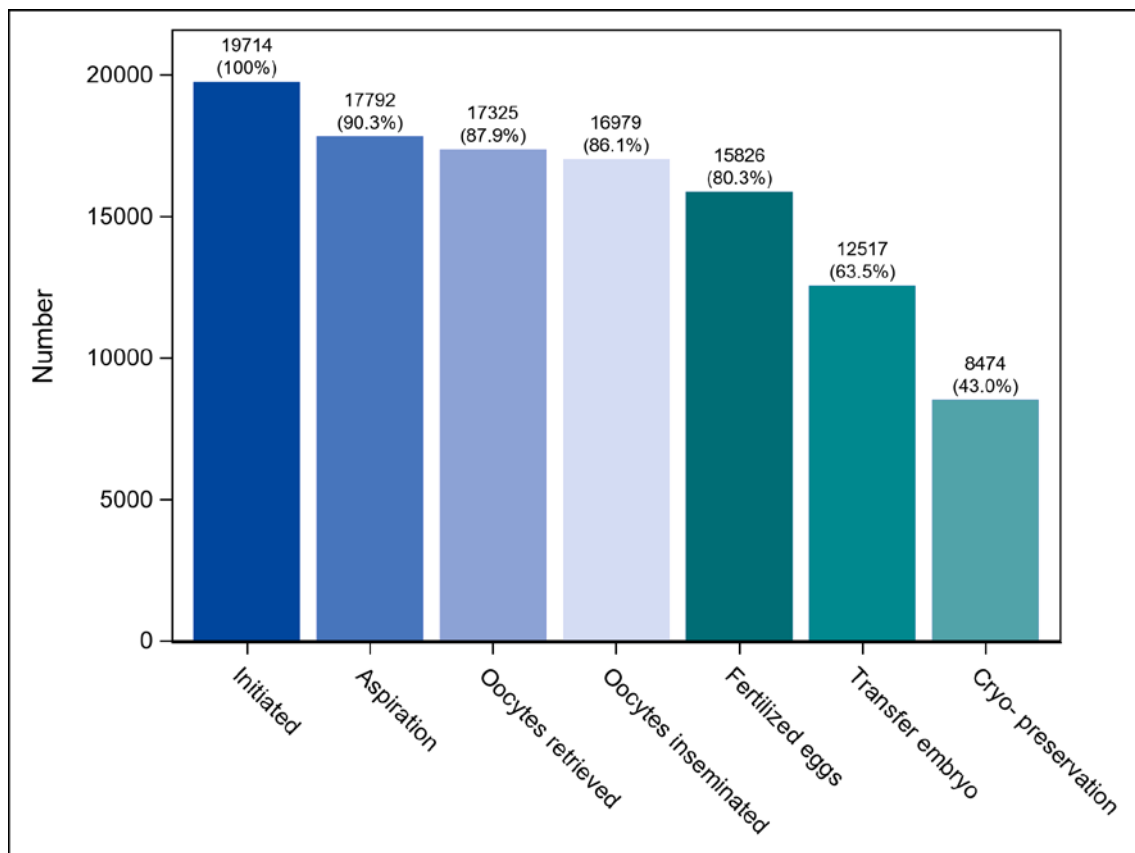


Figure 4. Outcomes of ART cycles using fresh nondonor eggs or embryos by stage.

Why are some ART cycles canceled?

In 2017, a total of 1922 IVF cycles were canceled before egg retrieval (Figure 5). The main reason for cancelling cycles (43%) was an insufficient ovarian response. On the contrary, a too-high ovarian response with a risk of major complications (ovarian hyperstimulation syndrome (OHSS)) was responsible for 1% of the cancelled cycles. Premature LH and/or progesterone rise was observed in 15% of cases and patient withdrawal for other non-medical reasons in 11% of cases. Finally, in 26% of cases, cancellation was due to other medical reasons and in 4% the cause was unknown.

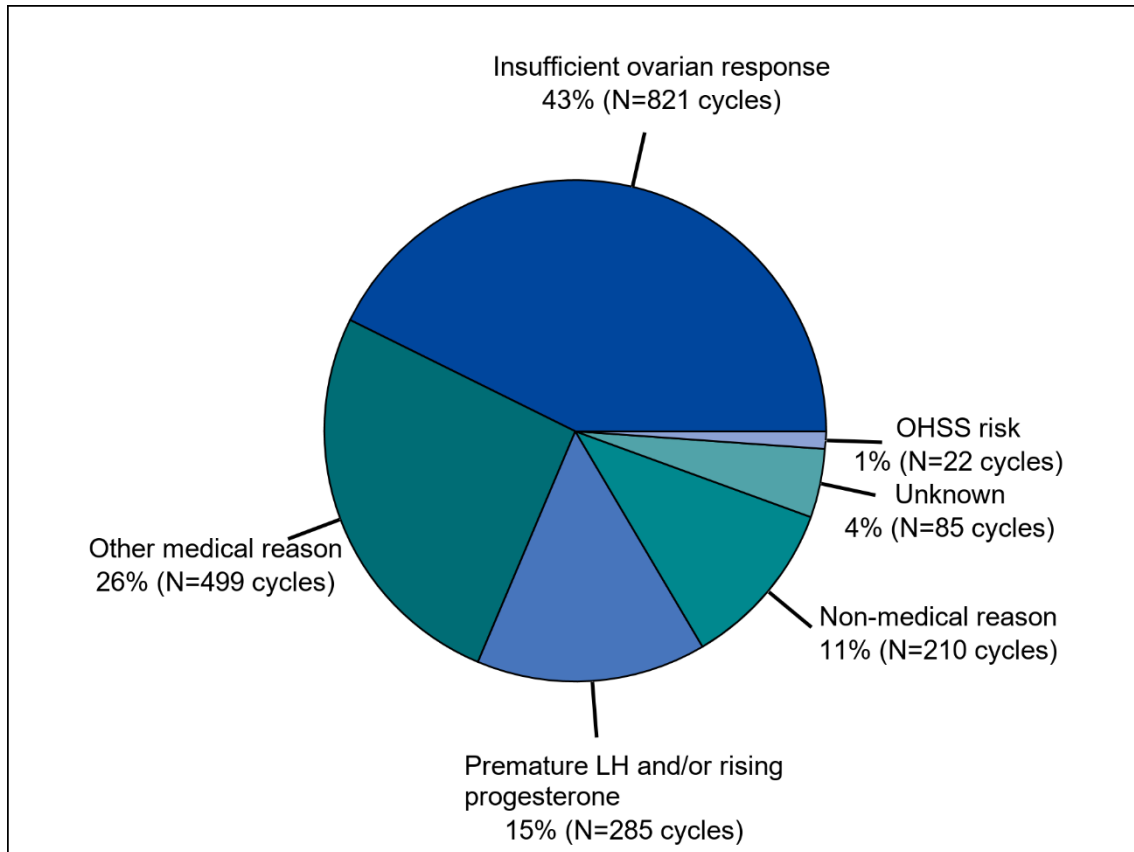


Figure 5. Reasons ART cycles using fresh nondonor eggs or embryos were canceled.

How are success rates of ART measured?

Figure 6 shows success rates based on three different measures for ART cycles using fresh nondonor eggs or embryos in 2017, each providing slightly different information.

We can consider the success rate per cycle (dark blue), per cycle excluding freeze all cycles (green) or per embryo transfer (light blue).

The success rate per cycle includes *de facto* couples who have cancelled their treatment (Figure 5), and cycles stopped before reaching embryo transfer (Figure 4: retrieval and/or fertilization failure, absence of embryo development). Such calculation is more realistic for couples who will start treatment. However, in an increasing number of cycles, it is decided to freeze all available embryos and not to proceed to fresh embryo transfer. This usually occurs for reasons such as avoiding of ovarian hyperstimulation syndrome, endometrial pathology, progesterone rise, ... These are the cycles excluding freeze all cycles (green).

The success can be appreciated in terms of pregnancy (clinical) or live birth (which excludes miscarriages, induced abortion, ectopic pregnancy or stillbirth).

Considering the occurrence of multiple pregnancies being a side effect of ART, according to the risk of adverse infant health outcomes, including prematurity, low birth weight, disability, and death, evaluation of percentages of transfers or cycles that resulted in a singleton live birth is the best way to appreciate the quality of the work performed in ART.

The most appropriate indicator to inform couples facing an ART treatment is therefore the "singleton live birth rate per cycle", i.e. 12.7% per fresh nondonor egg cycle.

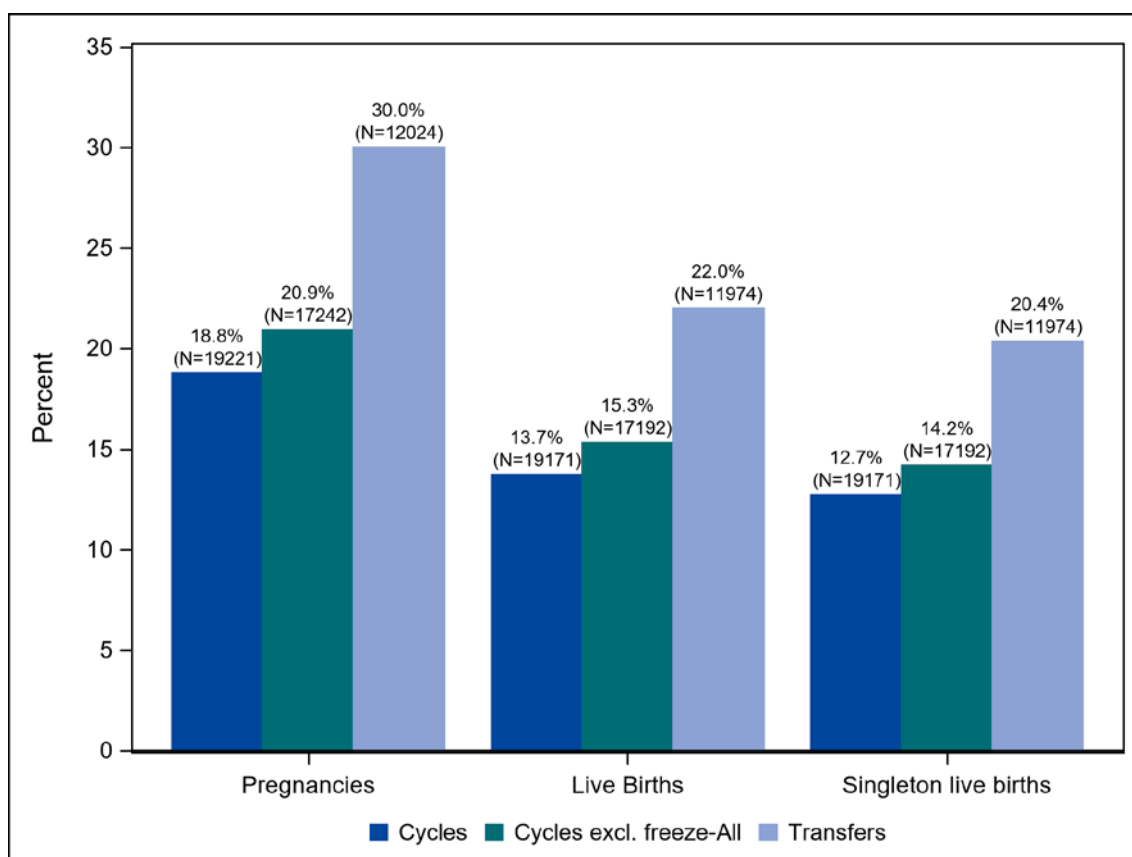


Figure 6. Measures of success for ART cycles using fresh nondonor eggs or embryos.

Using ART, what is the risk of having multiple infant live birth?

Multiple-infant births are associated with greater health problems for both mothers and infants, including higher rates of caesarean section, prematurity, low birth weight, and infant disability or death.

In Belgium since July 2003, the number of embryos to transfer is regulated by a Royal Decree. It is a condition to obtain reimbursement of IVF laboratory costs.

For fresh embryos: at the first IVF trial, for patients under 36 years, only one embryo may be transferred. For these patients, at the second IVF trial, two embryos may be transferred only if their quality is not optimal. From the third trial, two embryos can be transferred, regardless of their quality.

For patient aged 36 to 39 years, two embryos can be transferred for the two first trials and three from the third one.

Beyond 40 years, no regulation on the maximum number of embryos to be transferred exists.

For frozen embryos, regardless of age, no more than 2 embryos may be replaced. Since the application of such regulations, the rate of twins decreased by more than 50% to reach in 2017 a figure of 7.4%. The triplets' rate was less than 1% (Figure 7).

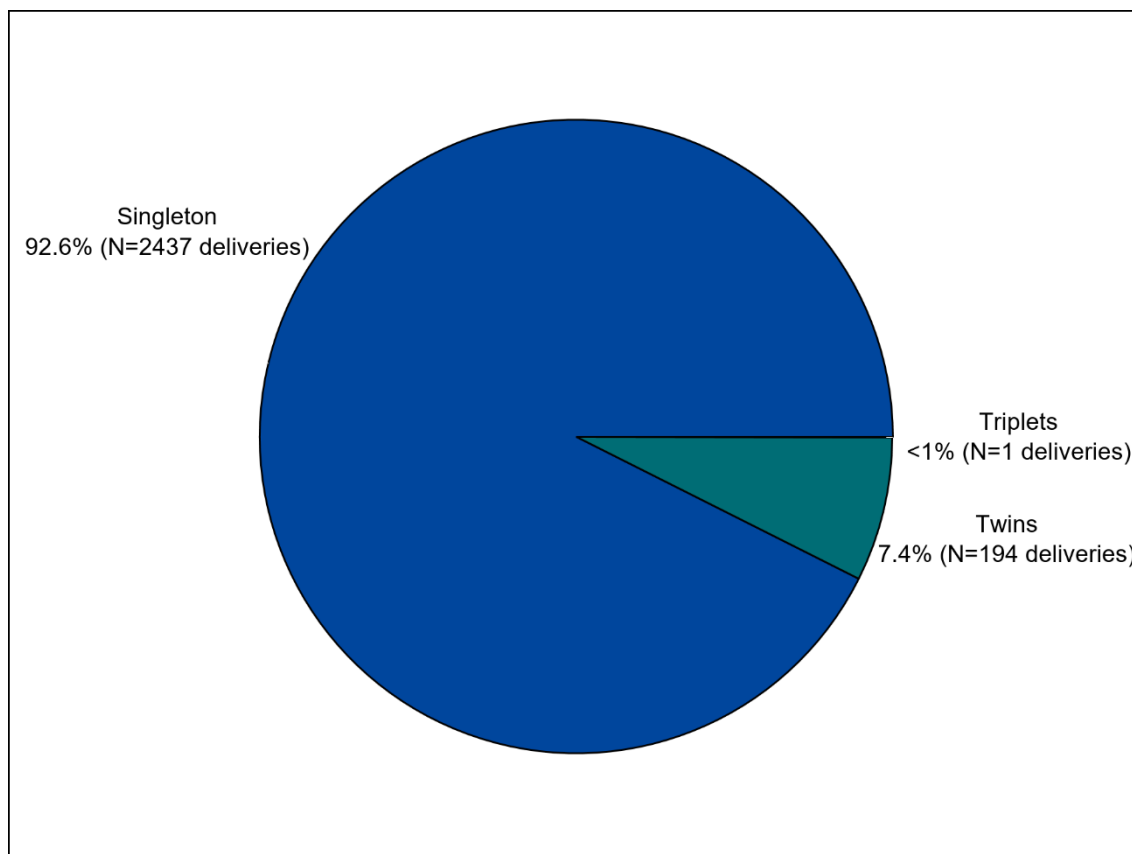


Figure 7. Distribution of multiple infant live births from ART cycles using fresh nondonor eggs or embryos.

Using ART, what are the risks of having a preterm birth infant?

Preterm birth occurs when a woman gives birth before 37 full weeks of pregnancy. In case of preterm delivery, infants are at greater risk of death in the first few days of life, as well as other adverse health outcomes, intellectual and learning disabilities, and behavioral and emotional problems throughout life. Preterm births also cause substantial emotional and economic burdens for families.

Figure 8 shows percentages of preterm births resulting from IVF cycles that used fresh nondonor eggs or embryos in 2017, by number of infants born.

Prematurity is defined as very preterm births with births before 32 weeks of pregnancy and preterm births with births before 37 weeks of pregnancy.

The percentage of very preterm live birth was 1.6% for singletons and 9.8% for twins. The percentage of preterm live birth was 7.7% for singletons and 45.4% for twins. In Belgium, in 2011, the rate of preterm births between 32-37 weeks for singletons in the general population was 5.5% and 1.05% for very preterm birth (Roelens et al, 2014).

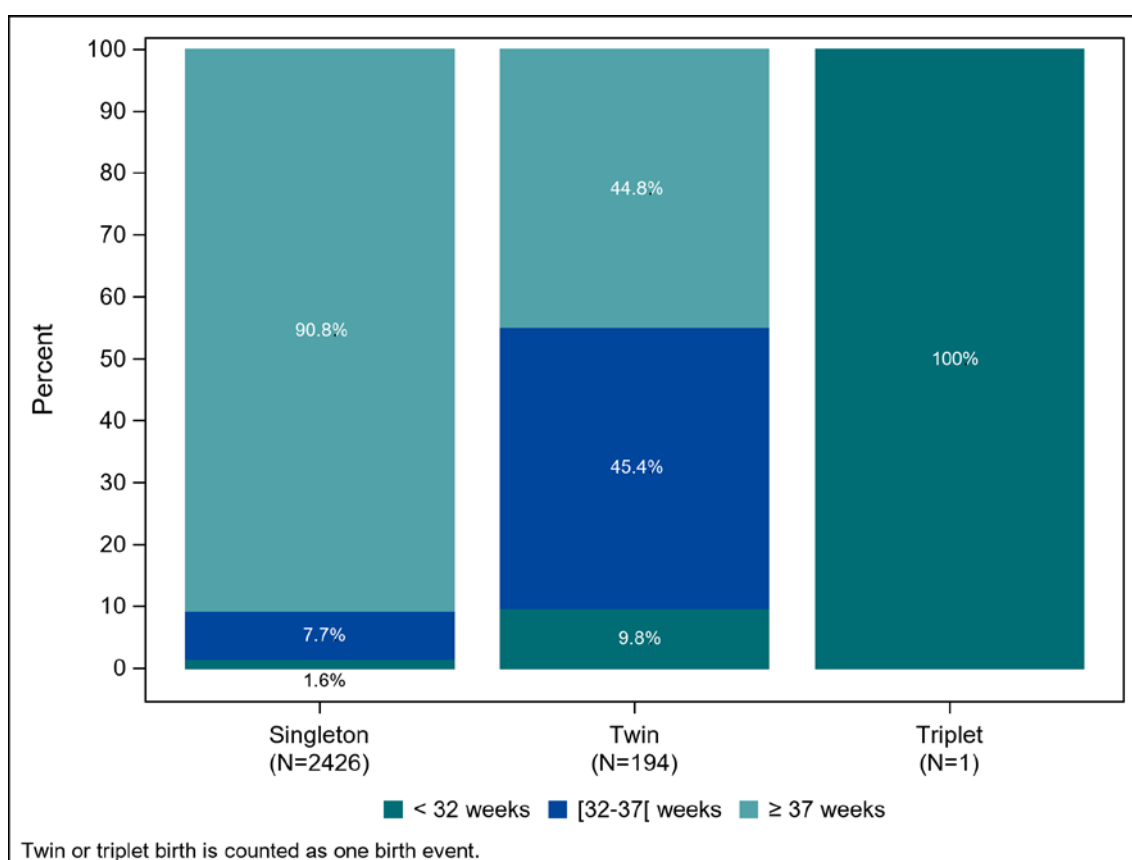


Figure 8. Percentages of live births that were preterm from ART cycles using fresh nondonor eggs or embryos, by number of infants born.

Using ART, what are the risks of having a low-birth-weight infant?

Low birth weight means birth weight less than 2500 grams, very low birth weight means birth weight less than 1500 grams.

Low birth weight has comparable consequences to prematurity for health and development of the children. In Figure 9, the results are presented for singletons, twins and triplets according to the weight (less than 1500 g, between 1500 and 2500 g and over 2500 g).

In 2017, children born alive weighing less than 1500 g represented 1.3% of the singletons and 8.0% of the twins. Birth weight between 1500 and 2500 g represented 7.8% of the singletons and 42.9% of the twins.

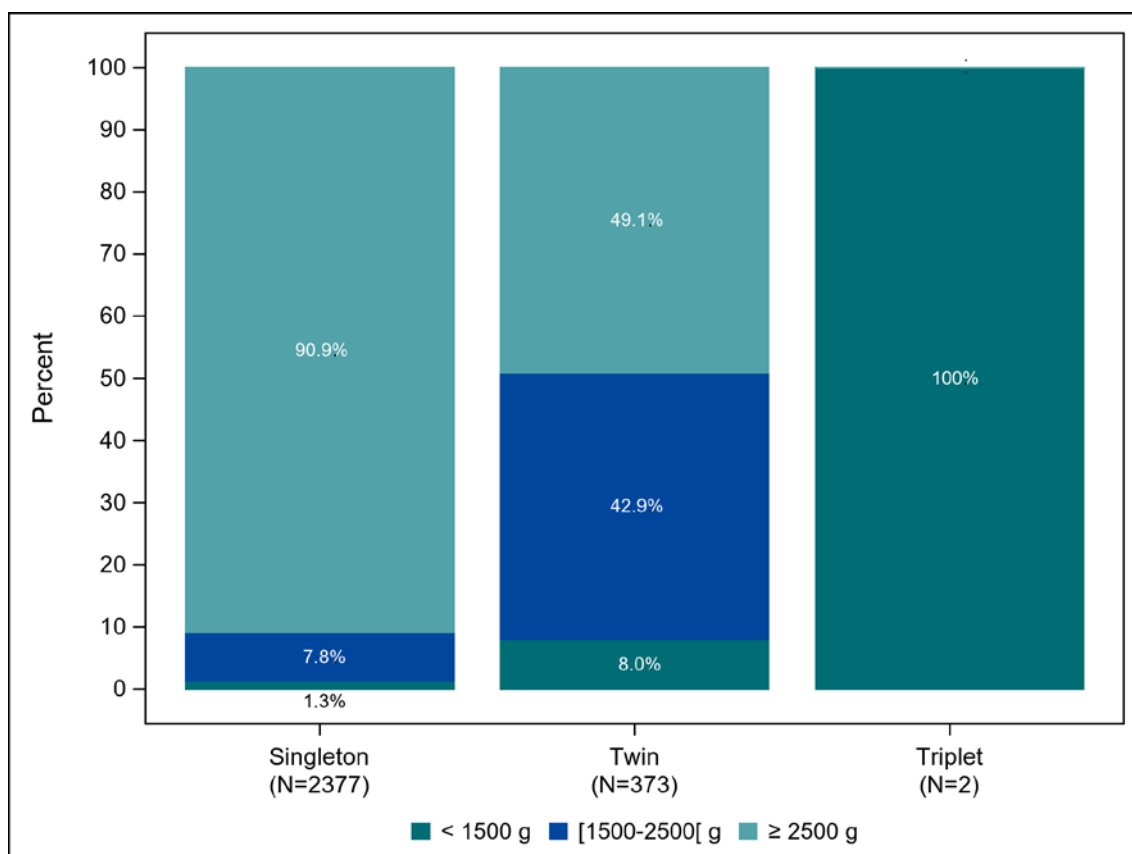


Figure 9. Percentages of live births that were low birth weight from ART cycles using fresh nondonor eggs or embryos, by number of infants born.

Do percentages of ART cycles that result in pregnancies and live births differ among women of different ages?

A woman's age is the most important factor affecting the chance of a live birth when her own eggs are used. In general, there is a decline in the percentage of ART cycles resulting in pregnancies and live births as a woman's age increases, but only after a woman entered her 30s. Figure 10 shows percentages of pregnancies and live births among women of different ages who had ART procedures using fresh nondonor eggs or embryos in 2017. Among women in their 20s, percentages of ART cycles resulting in pregnancies and live births were relatively stable. However, percentages declined steadily among women in their mid-30s onward leading to very low success in the group >40 years of age.

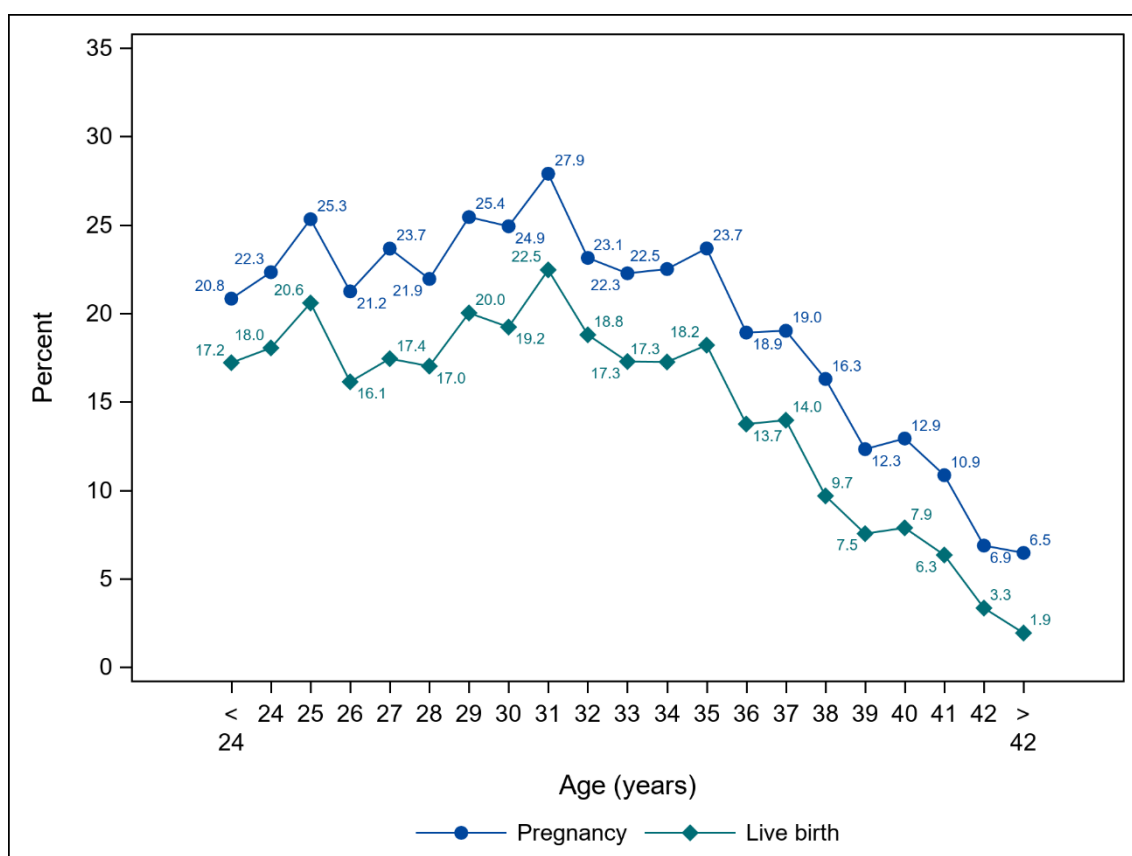


Figure 10. Percentages of ART Cycles using fresh nondonor eggs or embryos that resulted in pregnancies and live births, by age of woman.

How does a woman's age affect her chances of progressing through the various stages of ART?

As women get older, the likelihood of a successful response to ovarian stimulation and egg aspiration decreases (these are the cancelled cycles increasing from 7% in women <36 years to 16% in women ≥ 43). Using 2017 data, Figure 11 shows that cycles that have progressed to egg aspiration are less likely to reach embryo transfer with increasing age and cycles that progress to embryo transfer are less likely to progress to pregnancy and live birth.

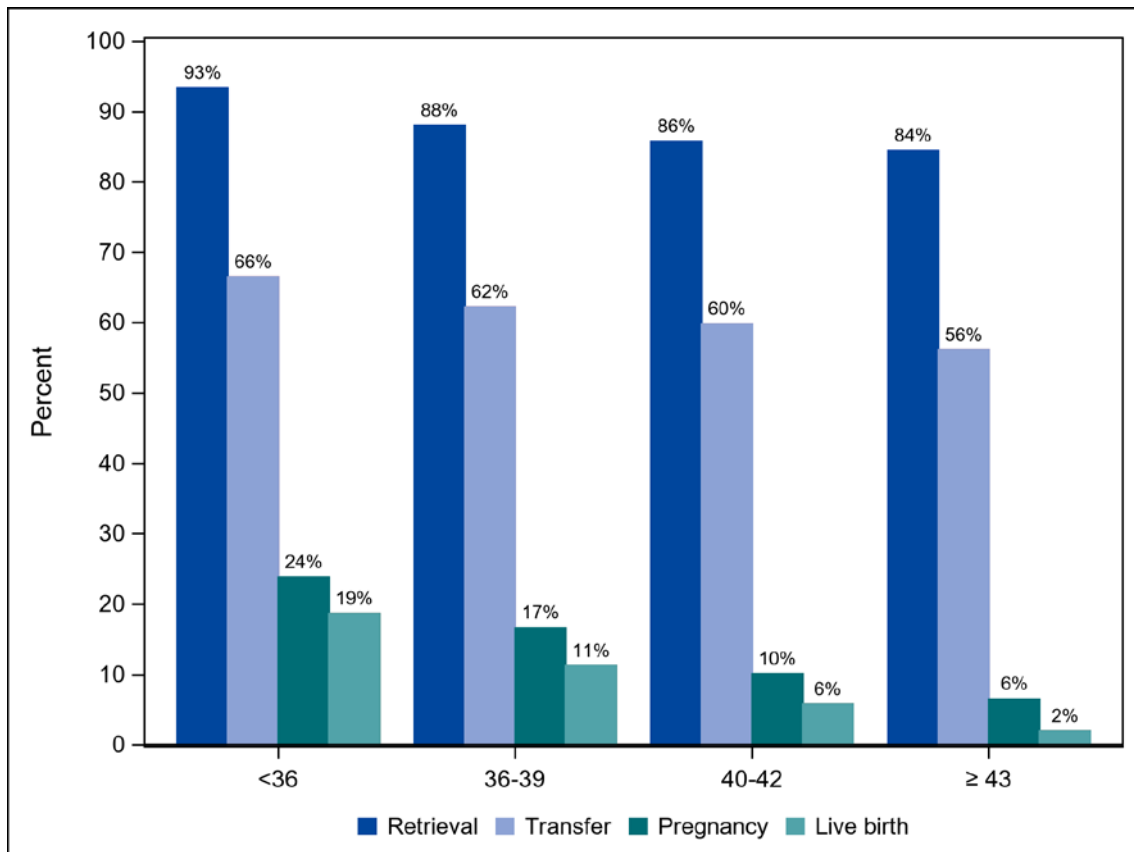


Figure 11. Outcomes of ART cycles using fresh nondonor eggs or embryos, by stage and age group.

What are the causes of infertility among users of ART?

The causes of infertility among ART patients include female factor, male factor, combined female and male pathology or remains unexplained which means that no clear cause of infertility is found in either partner.

Pathology in the female can be caused by:

- **Tubal factor.** Fallopian tubes are blocked or damaged, making it difficult for the egg to be fertilized or for an embryo to travel to the uterus.
- **Ovulatory dysfunction.** Ovaries are not producing eggs normally. A frequent cause is polycystic ovary syndrome.
- **Endometriosis.** The presence of tissue similar to the uterine lining in abnormal locations. This condition can affect both fertilization of the eggs and embryo implantation.
- **Uterine factor.** A structural or functional disorder of the uterus that results in reduced fertility.
- **Genetic factor.** The woman carries a genetic problem.
- **Premature ovarian insufficiency.** The ovary does not have the ability to produce eggs. This diagnosis often leads to use of donor eggs.

Male factor means that a low sperm count or problems with sperm function make it difficult for a sperm to fertilize an egg under normal conditions or that a genetic factor is present.

Figure 12 shows infertility diagnoses reported for each ART cycle using fresh nondonor eggs or embryos performed in 2017. Female infertility was diagnosed in 24% of the cycles, male factor infertility in 28%, mixed male and female pathology was present in 18% of the cycles and unexplained infertility was present in 24% of the ART cycles.

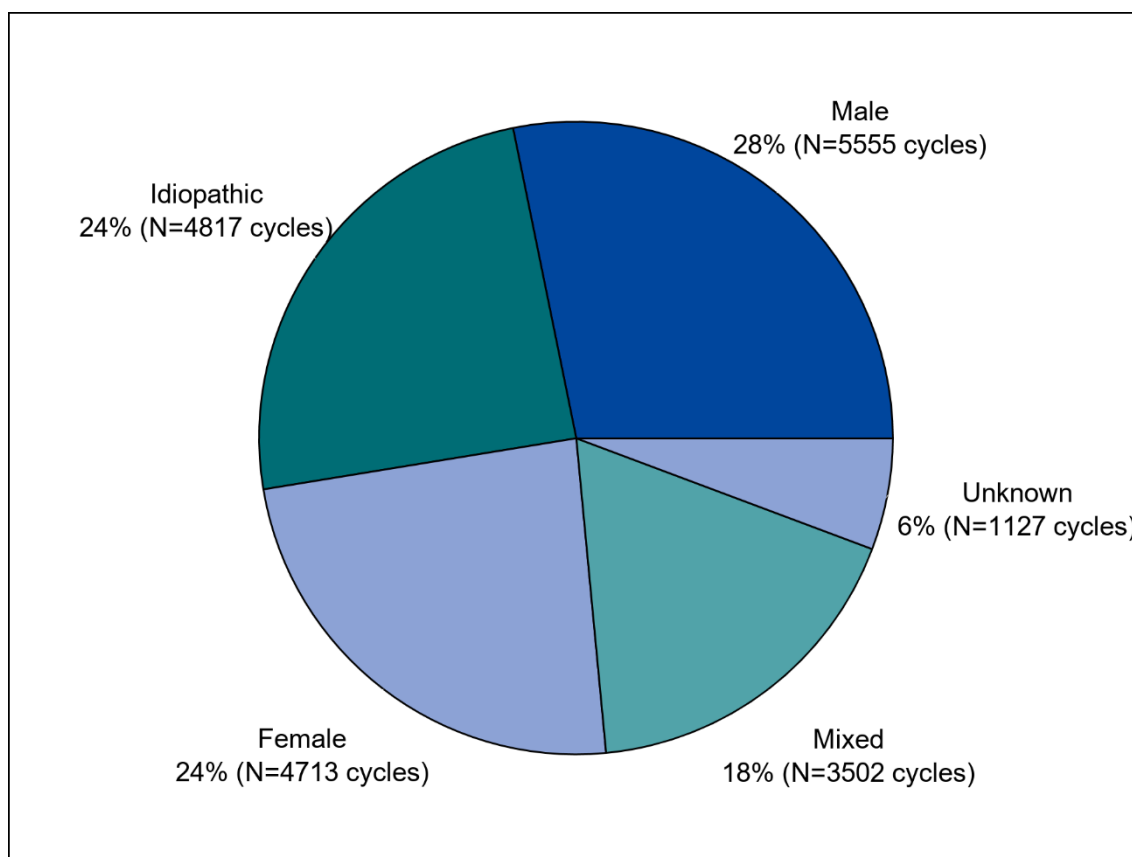


Figure 12. Infertility diagnoses among patients who had ART cycles using fresh nondonor eggs or embryos.

Do percentages of ART cycles that result in live births differ for women who use ART for the first time compared with women who previously used ART?

The percentages of ART cycles that resulted in live births among women who previously had one or more unsuccessful ART cycles were similar or lower to those among women who had no previous ART cycles and no previous births in all age groups. Figure 13 shows the relationship between the success of ART cycles performed in 2017 using fresh nondonor eggs or embryos and a history of previous ART cycles among women with no previous births. The first three bars show the chances of live birth during the 6 reimbursed cycles where live birth rates vary per age category but are maintained over 6 fresh ART cycles. Note that the percentages for women ≥ 43 y and for 6 or more previous cycles are estimated with high uncertainty due to a low number of cycles and should therefore be interpreted with caution.

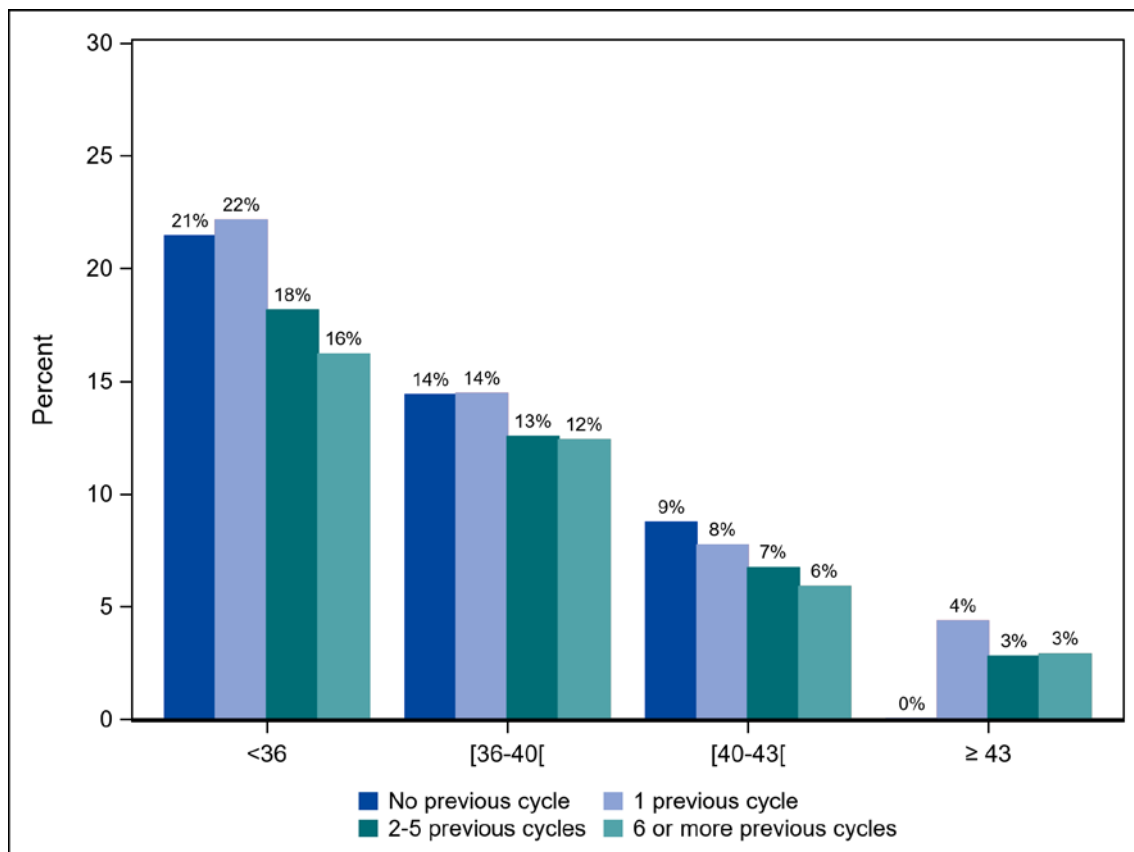


Figure 13. Percentages of ART cycles using fresh nondonor eggs or embryos that resulted in live births, by age group and number of previous ART Cycles, among women with no previous live births.

How many embryos are transferred in an ART procedure?

Figure 14 shows that in 2017, in 68.2% of ART cycles that used fresh nondonor eggs or embryos one embryo was transferred, in 27.9% two embryos were transferred, in 3.4% three embryos and in 0.5% four or more embryos were transferred.

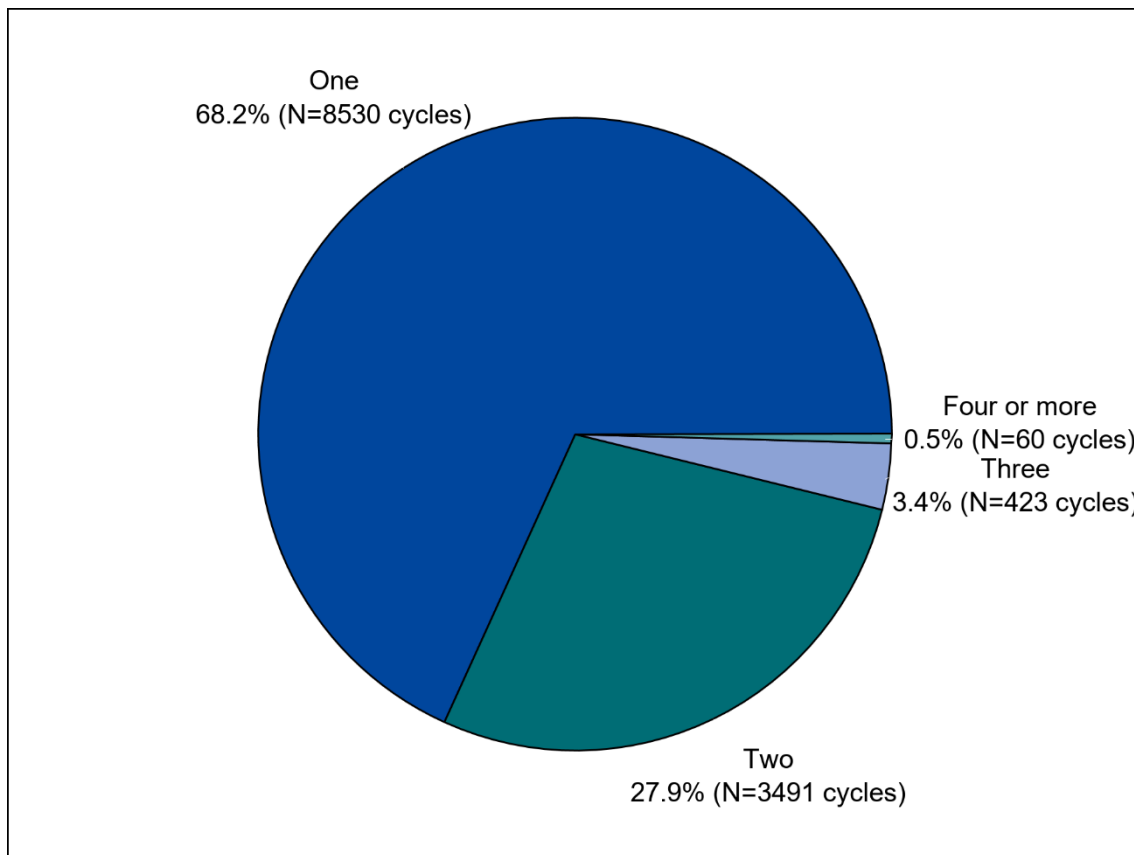


Figure 14. Numbers of embryos transferred during ART cycles using fresh nondonor eggs or embryos.

How do percentages of embryos transferred that result in implantation differ among women of different ages?

The implantation rate decreases steadily as the age of the woman increases. Figure 15 presents the relationship between the implantation percentage for fresh nondonor embryos transferred and a woman's age. In 2017, the percentage of embryos transferred that resulted in implantation was 27.2% among women younger than age 36. There was a decline with age from 15.9% between 36 and 39 years to 8.5% between 40-42 years. The implantation rate for women 43 and older was only 3.6%.

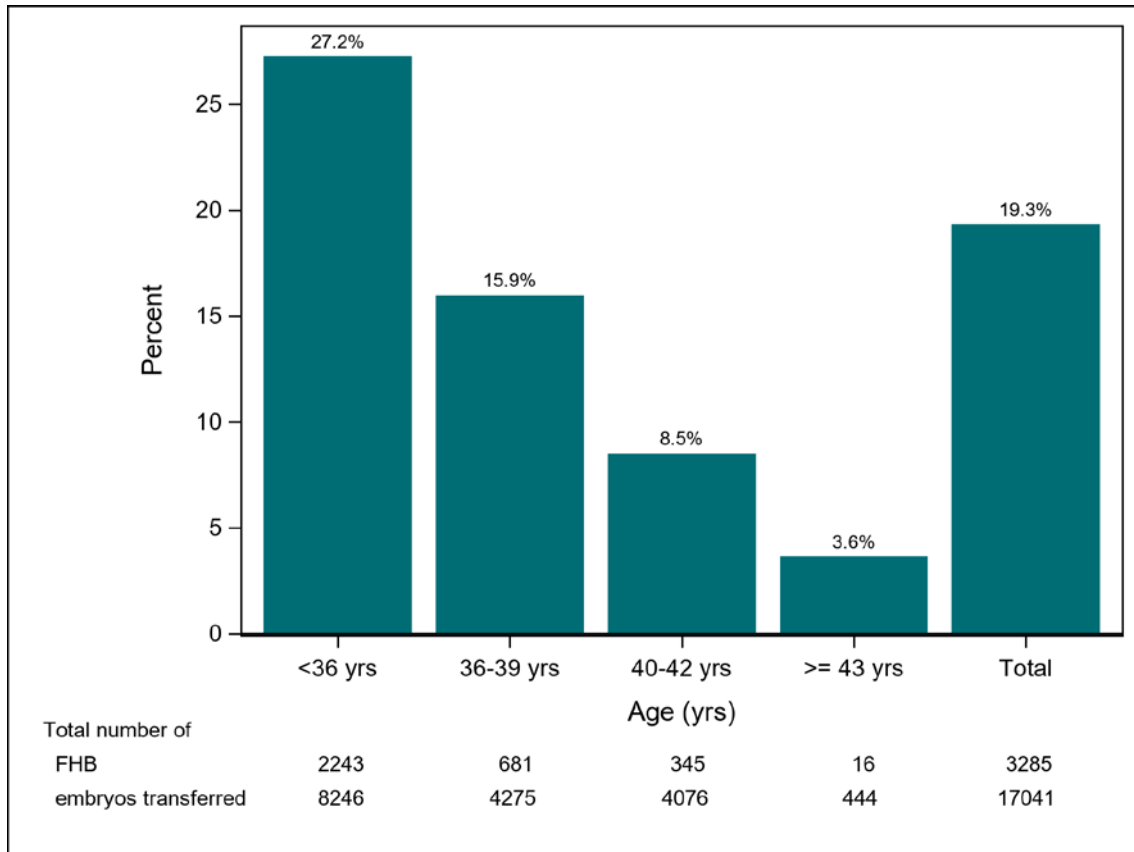


Figure 15. Percentages of embryos transferred that resulted in implantation among women using fresh nondonor eggs or embryos, by age group.

How long after egg retrieval does embryo transfer occur?

After fertilization, the embryo(s) can be transferred into the woman's uterus 1 up to 6 days after fertilization. Figure 16 shows that 58.8% of the fresh nondonor ART cycles were day 3 transfers (3 days after eggs aspiration) and 34.0% were day 4-5-6 transfers.

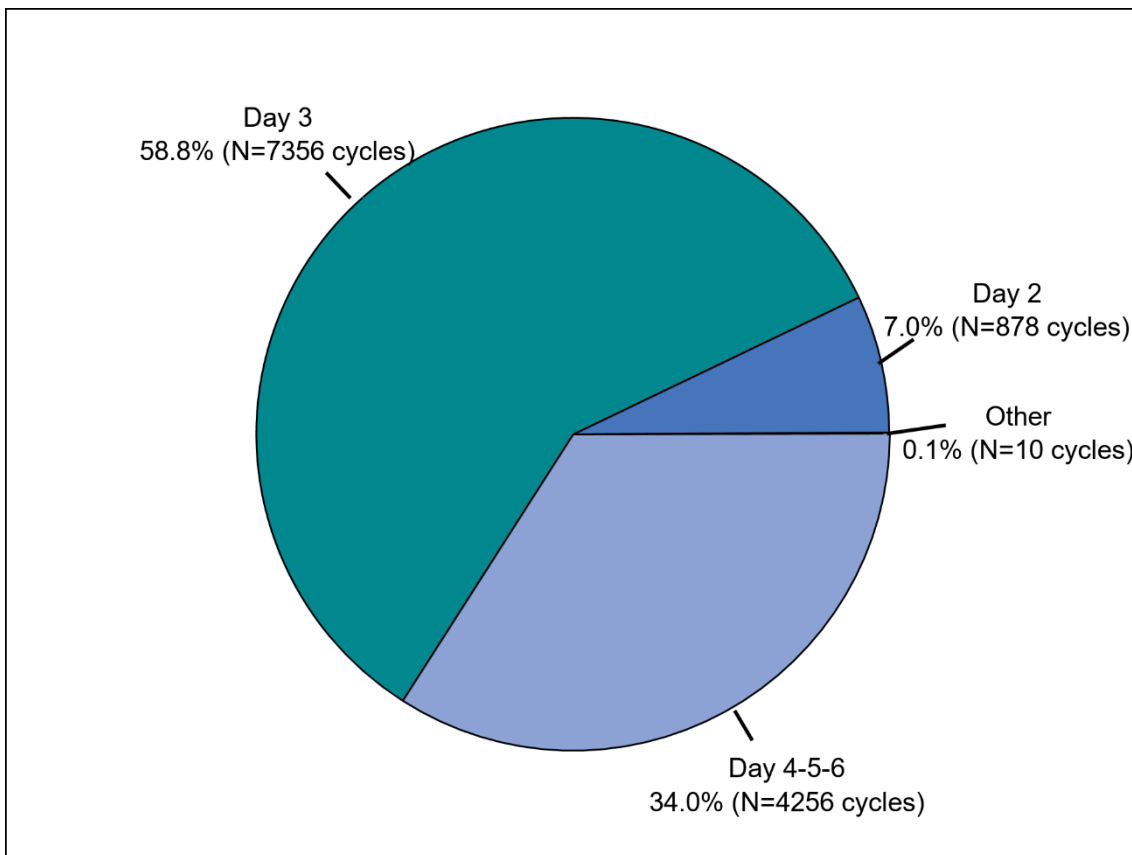


Figure 16. Day of embryo transfer among ART cycles using fresh nondonor eggs or embryos.

Section 3: ART cycles using frozen nondonor embryos

How do percentages of embryos transferred that result in implantation for frozen nondonor embryos differ among women of different ages?

The implantation rate decreases steadily as the age of the woman increases. Figure 17 presents the relationship between the implantation percentage for frozen nondonor embryos transferred and a woman's age. In 2017, the percentage of embryos transferred that resulted in implantation was 22.8% among women younger than age 36. There was a decline with age from 18.0% between 36 and 39 years to 11.6% between 40 and 42 years. The implantation rate for women 43 and older was 9.2%.

A comparison can be made with implantation rates in fresh nondonor ART cycles in Figure 15. Note that for frozen cycles, the age of the woman at the time of retrieval has a larger effect on implantation rates than the age of the woman at the time of transfer.

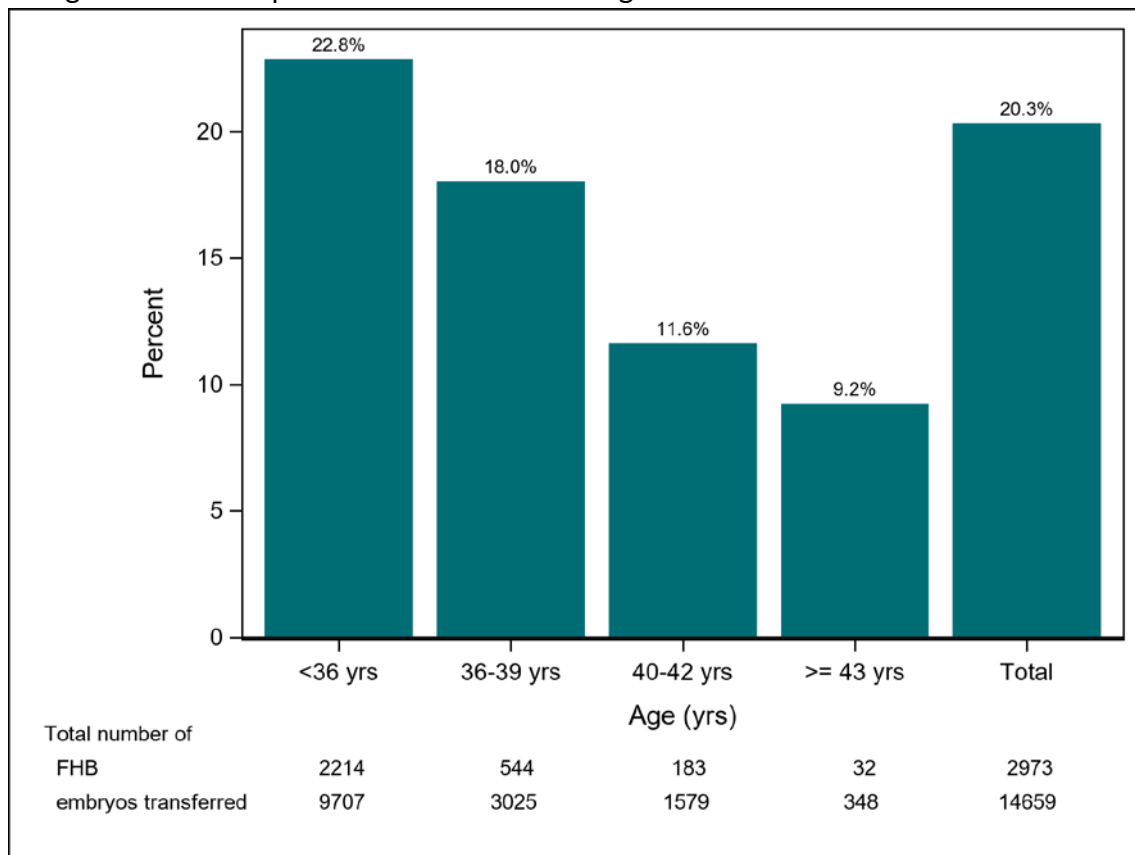


Figure 17. Percentages of embryos transferred that resulted in implantation among women using frozen nondonor embryos, by age group.

What is the percentage of transfers that results in pregnancies and live births for ART cycles?

In general, there is a decline in the percentage of ART cycles using frozen nondonor embryos resulting in pregnancies and live births as a woman's age increases. Figure 18 shows percentages of pregnancies and live births among women of different ages who had ART procedures using frozen nondonor eggs or embryos in 2017. Among women in their 20s, percentages of ART cycles resulting in pregnancies and live births were relatively stable. However, percentages declined steadily among women in their mid-30s onwards leading to very low success in the group >40 years of age.

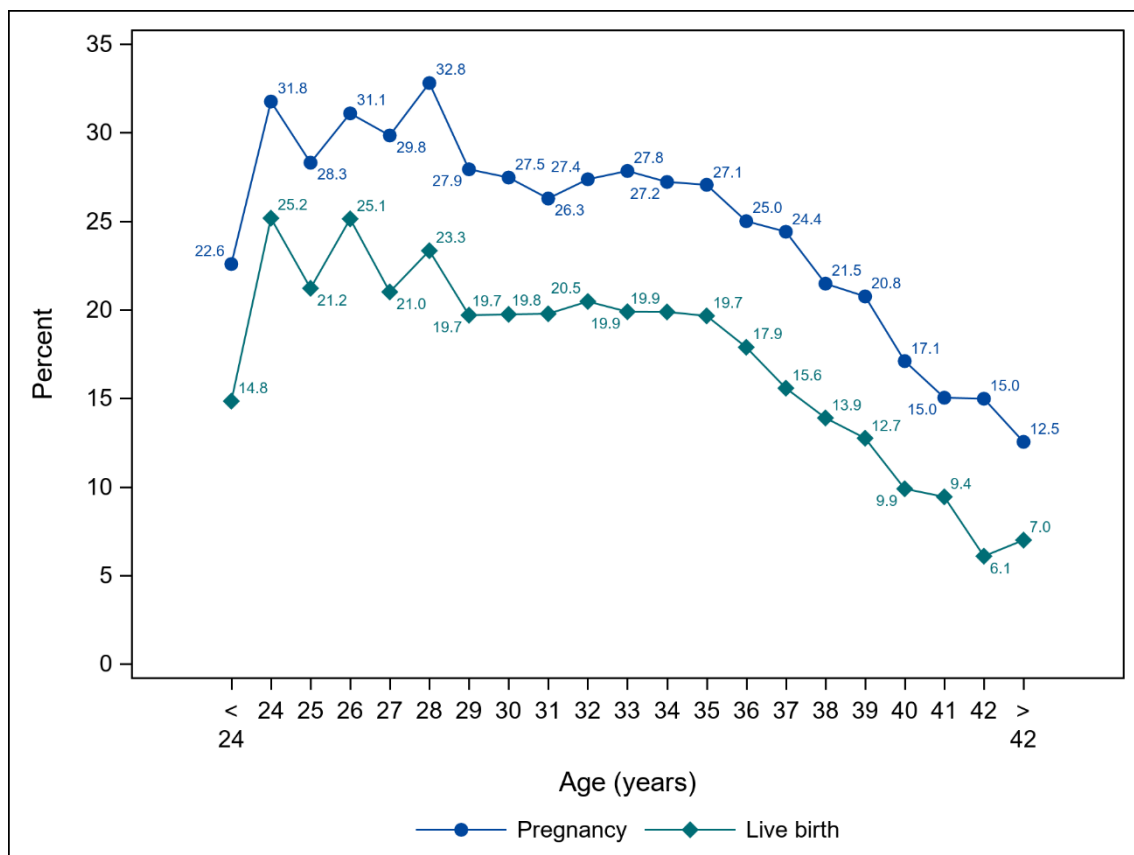


Figure 18. Percentages of ART Cycles using frozen nondonor embryos that resulted in pregnancies and live births, by age of woman.

Using frozen nondonor ART cycles what is the risk of having multiple infant live births?

As shown in Figure 19, among 2430 deliveries that resulted from ART cycles using frozen nondonor embryos in 2017, 94% were singleton pregnancies, 6% twins and less than 1% triplets. No higher order pregnancies were recorded. In comparison, there is a 7.4% multiple infant birth rate using fresh nondonor eggs or embryos (Figure 7) and a multiple live birth rate of about 3.7% in the general Belgian population (data from FPS Economy, report 2010).

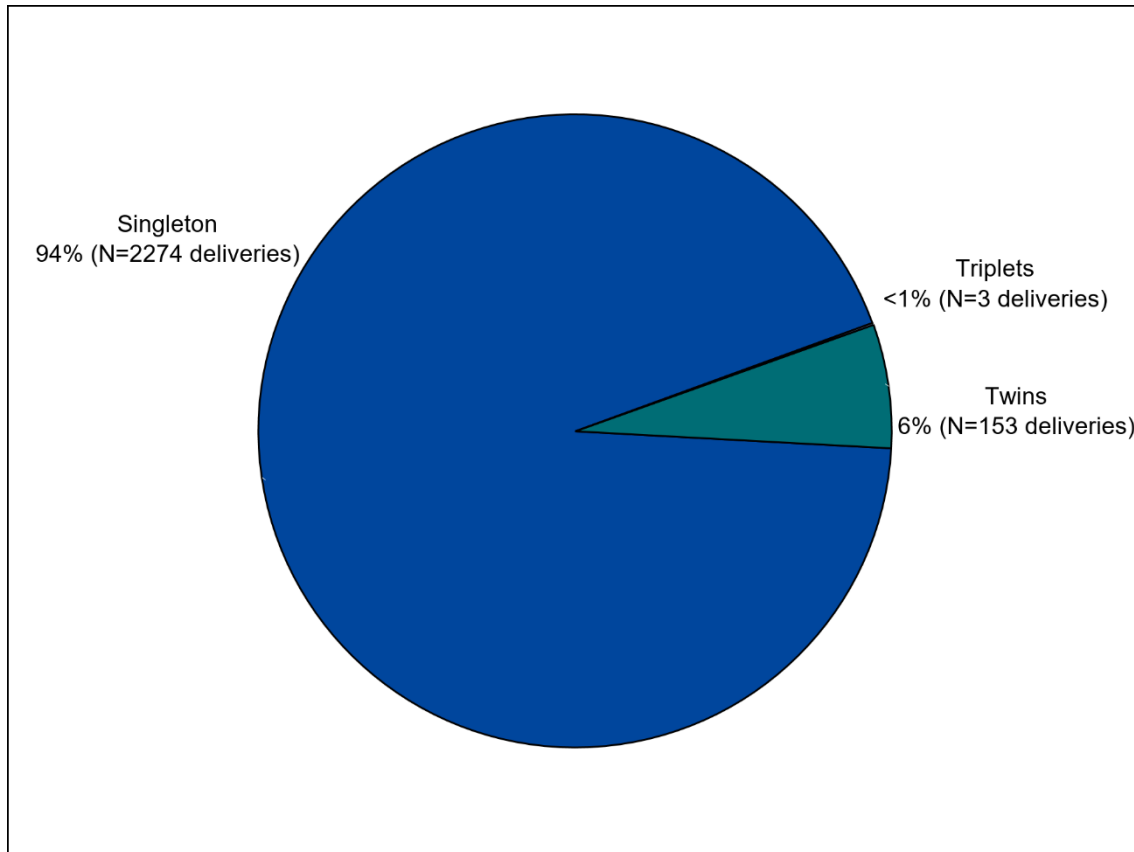


Figure 19. Distribution of multiple infant live births from ART cycles using frozen nondonor embryos.

Using frozen nondonor ART cycles, what are the risks of having a preterm birth infant?

Preterm birth occurs when a woman gives birth before 37 full weeks of theoretical amenorrhea (calculated from 2 weeks before ovulation in a natural cycle or from the induction of a luteal phase in artificial cycles).

Figure 20 shows preterm live births categorized as very preterm births (<32 weeks) or preterm births (>32<37 weeks) resulting from ART cycles using frozen nondonor embryos in 2017 by number of infants born. Preterm live birth occurs in approximately 9.2% of singleton pregnancies and 63.8% of twin pregnancies. In comparison there are 55.2% from ART cycles using fresh nondonor eggs or embryos for singletons or twins, respectively. In the general Belgian population there are approximately 8.0% preterm births (data from FPS Economy, report 2010).

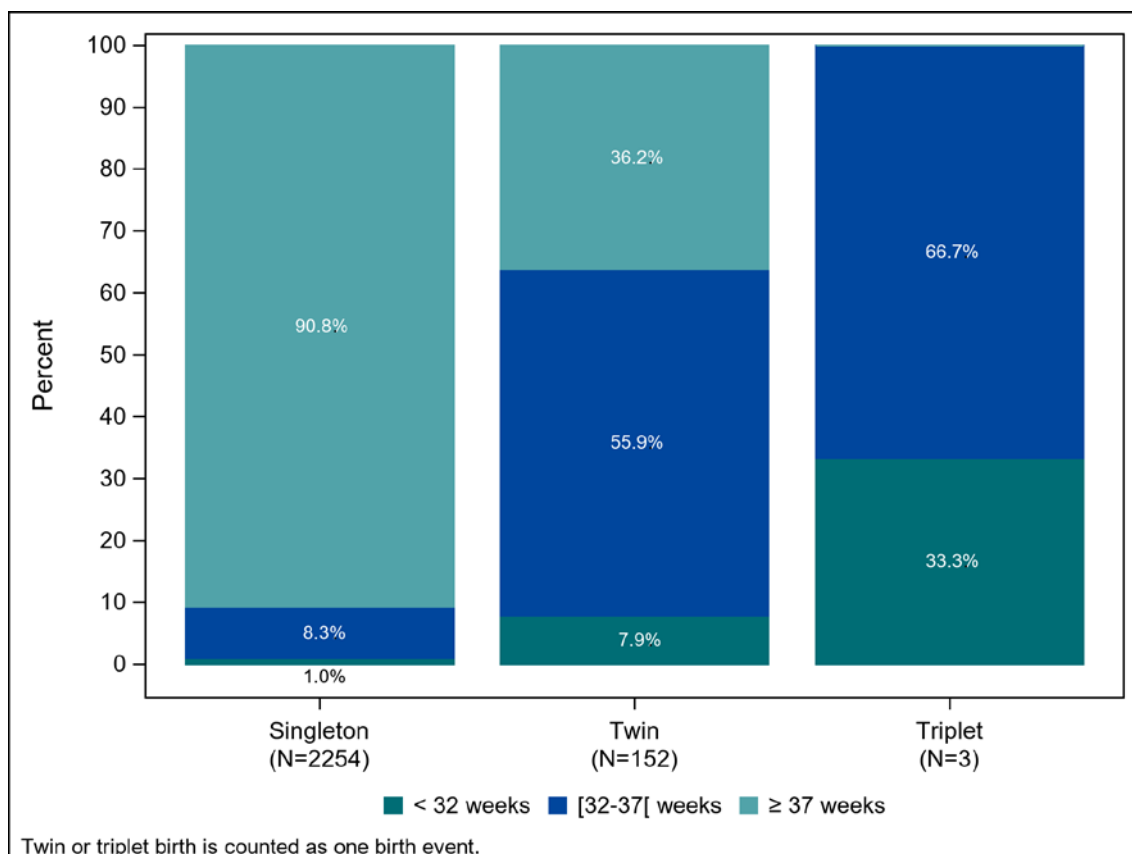


Figure 20. Percentages of live births that were preterm from ART cycles using frozen nondonor embryos, by number of infants born.

Using frozen nondonor ART cycles, what are the risks of having a low-birth-weight infant?

Figure 21 shows low-birth-weight infants (<2500 g) or very low birth weight (<1500 g) resulting from ART cycles using frozen nondonor embryos in 2017 by number of infants born. Low-birth-weight occurs in 5.4% of singleton live births and 53.1% of twin live births. In comparison, there was 9.1% and 50.9% of low-birth-weight infants from ART cycles using fresh nondonor eggs or embryos for singleton or twin live births, respectively. There is 5.9% of low-birth-weight infants in the general Belgian population (data from FPS Economy, report 2010).

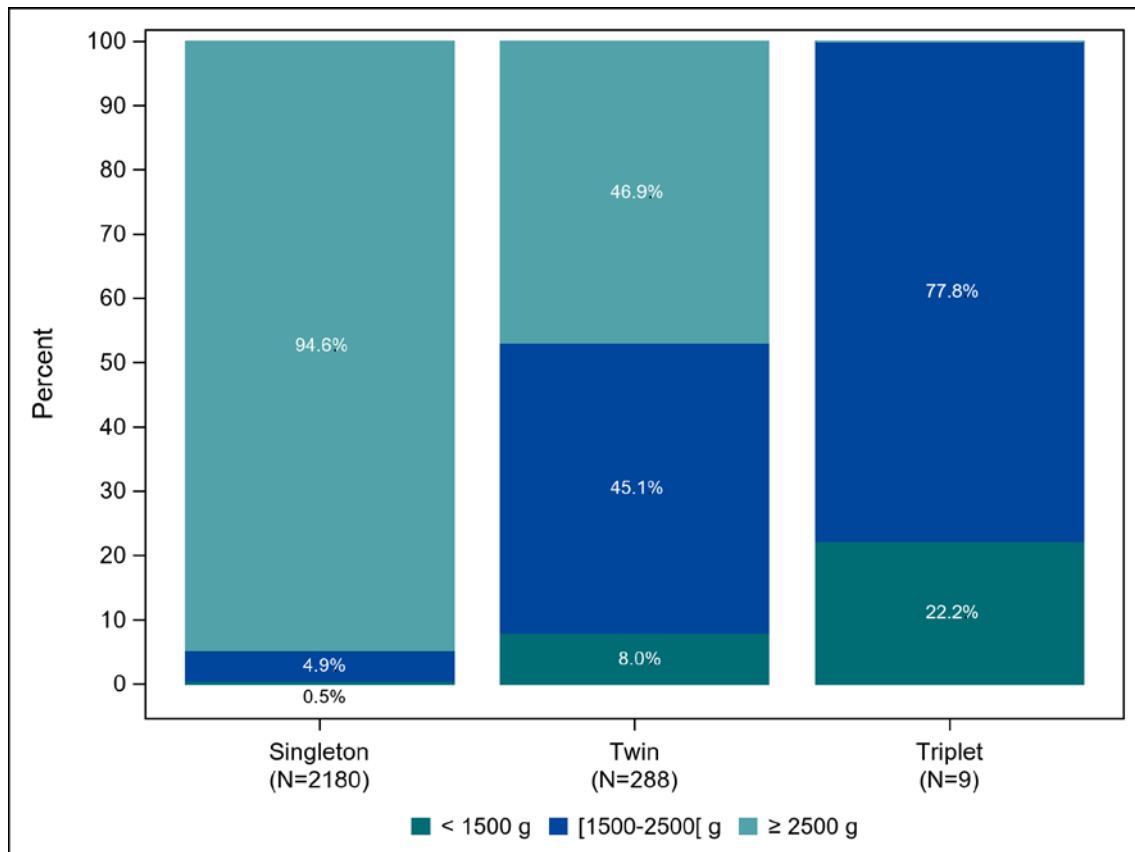


Figure 21. Percentages of live births that were low birth weight from ART cycles using frozen nondonor embryos, by number of infants born.

Section IV : ART cycles using donor eggs

Do percentages of transfers that result in live births differ by recipient age between women using ART with fresh donor eggs and those using ART with their own eggs?

Figure 22 compares percentages of transfers that resulted in live births for ART cycles performed in 2017 using fresh embryos from fresh donor eggs with those of ART cycles using a woman's own fresh eggs, related to the woman's age. The likelihood of a fertilized egg to implant is linked to the age of the women who produced the egg. Therefore, and as expected, the percentages of transfers resulting in live births for cycles using own eggs declines when the woman gets older (see Figure 10). For donor eggs, the age of the donor determines the outcome and the percentage of live births remains quite stable considering common age limitations for egg donors (usually less than 36 year-old). For recipients older than 40 years, percentages of transfers using donor eggs leading to a live birth are several times higher than when own eggs are used.

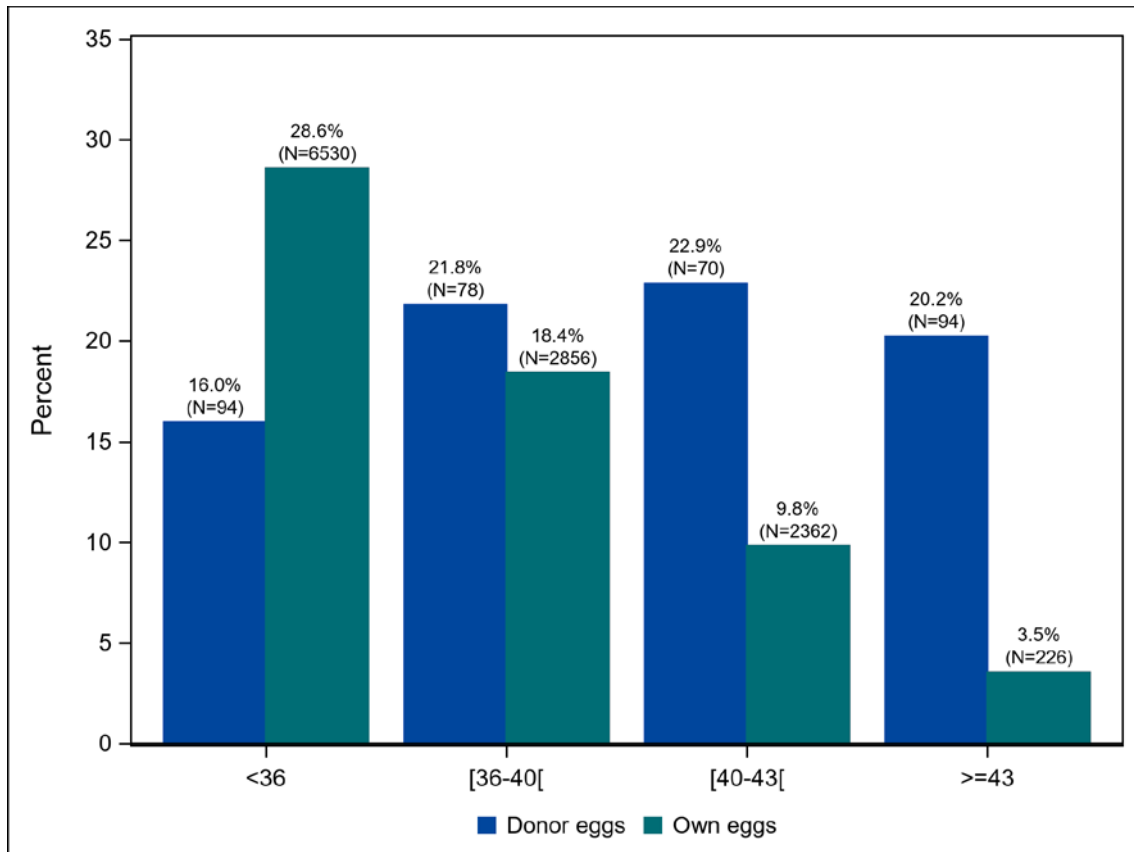


Figure 22. Percentages of transfers that resulted in live births for ART cycles using fresh embryos from own eggs and ART cycles using fresh embryos from donor eggs, by age of recipient.

What is the risk of having a multiple infant live birth from an ART cycle using fresh donor eggs?

Figure 23 shows 67 live births in 2017 resulting from ART cycles using fresh embryos from donor eggs. 18% of these live births produced were twins or triplets. When using nondonor eggs this was only 9.2%. Such outcome could be explained by the fact that the restriction on the number of embryos to be transferred depends on the age of the recipient and thus not on the age of the donor which determines the implantation rate (see Figure 15).

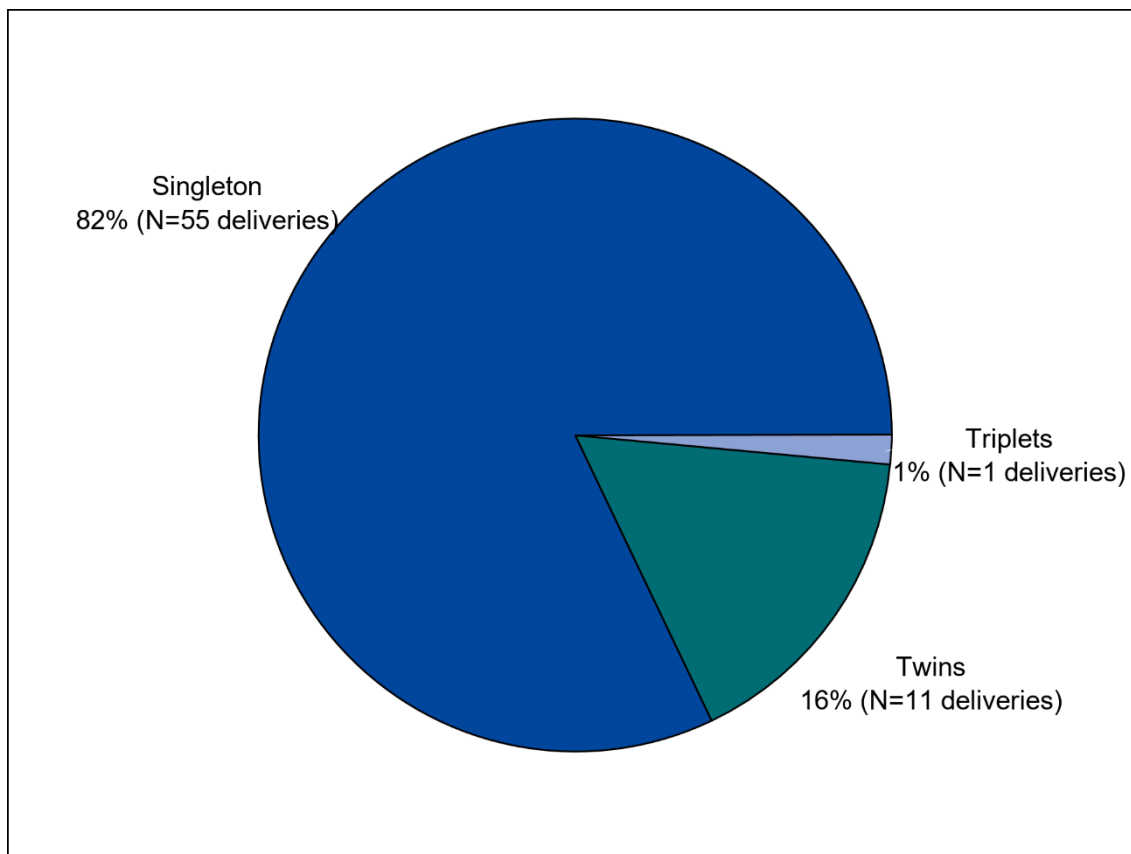


Figure 23. Distribution of multiple-fetus pregnancies and multiple-infant live births among ART cycles using fresh embryos from donor eggs.

Section 5 : ART Trends

Since 1999 when the College of Physicians in Reproductive Medicine became responsible for quality control including compulsory registration of ART activities in Belgium under the national public health authority, many years of data collection provide us with the opportunity to examine trends in ART use and success rates over time. This report features analysis of trends for the most recent 5 to 10 year periods. Figures for the earlier years are available in previous annual reports (see www.belrap.be).

Is the use of ART increasing?

Figure 24 shows the number of ART cycles performed from 2008 to 2017. Since the reimbursement of the majority of ART related costs in 2003, an increase in the number of cycles was observed until 2011 but stabilized thereafter.

Over the whole period, the proportion of cycles performed in patients with social security and complying with reimbursement criteria varied from 71% to 78%.

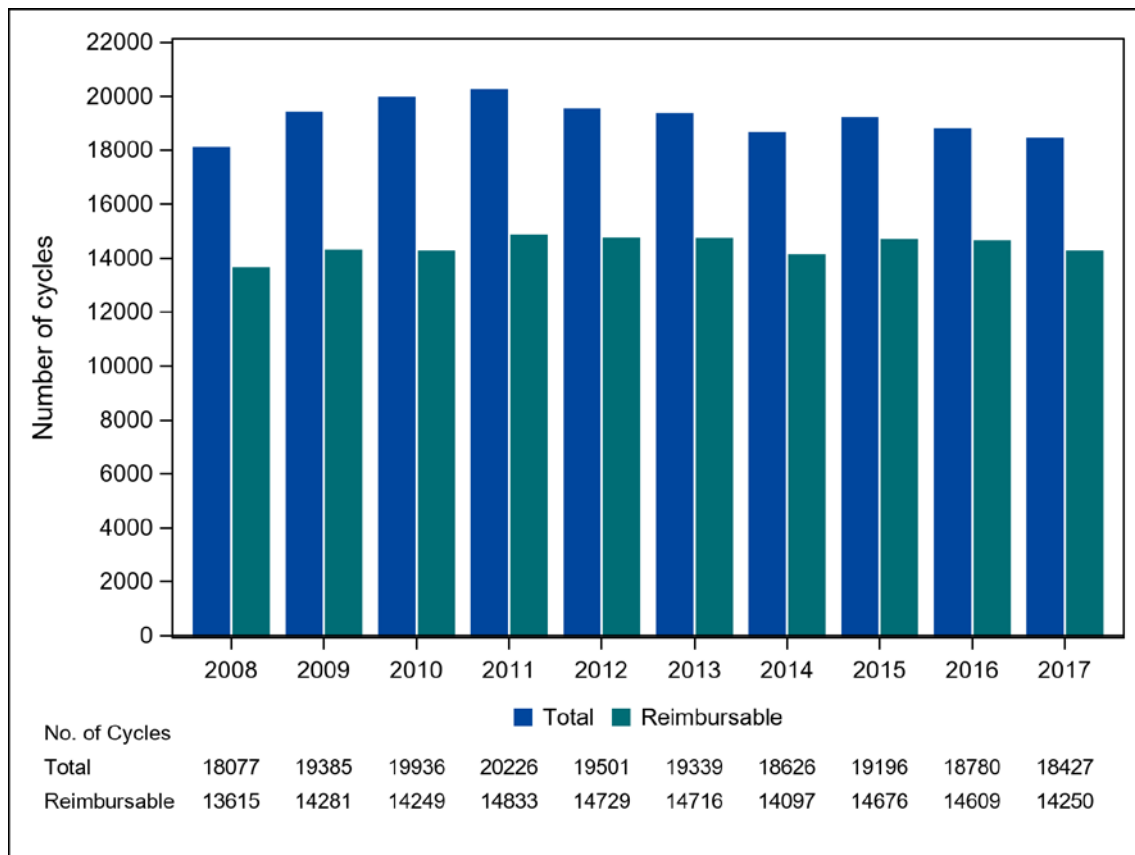


Figure 24. Number of non-cancelled ART cycles using fresh nondonor eggs or embryos, over time.

Is the use of ICSI increasing?

Intracytoplasmic sperm injection (ICSI) was originally developed and used for severe male infertility. The procedure became further more widely applied when fertilization rates were abnormal in previous ART cycles, when sperm parameters after preparation did not reach thresholds expected to be sufficient for optimal outcomes or for ART cycles with PGD.

Figure 25 shows the number of ART cycles using fresh nondonor eggs or embryos performed with ICSI from 2007 to 2017. During the past 10 years, the number of cycles using ICSI increased from 75.5% to 83.4%.

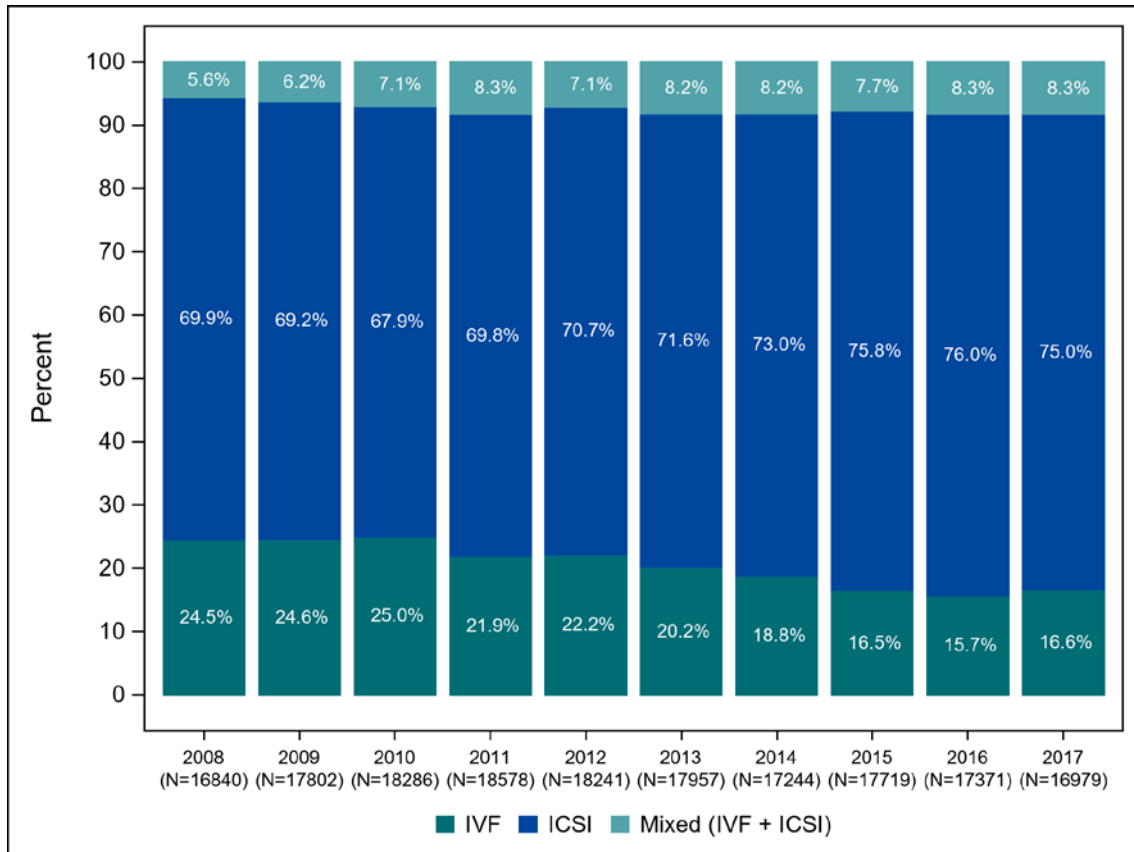


Figure 25. Percentage of ICSI cycles for ART cycles using fresh nondonor eggs or embryos, over time.

Has the percentage of transfers that resulted in live births for all ART patients changed?

Figure 26 shows the evolution of the percentages of transfers that resulted in live births for ART cycles using fresh nondonor eggs or embryos for a **reference group** including first cycles and excluding PGD cycles per age category over a five year period from 2013 to 2017.

A trend to a subtle increase in live birth rates is observed for all age categories except for the women ≥ 43 y. Interpretation of the data should consider implementation of the European directive in the Belgian legislation in December 2009 with adapted quality control in ART including authority auditing.

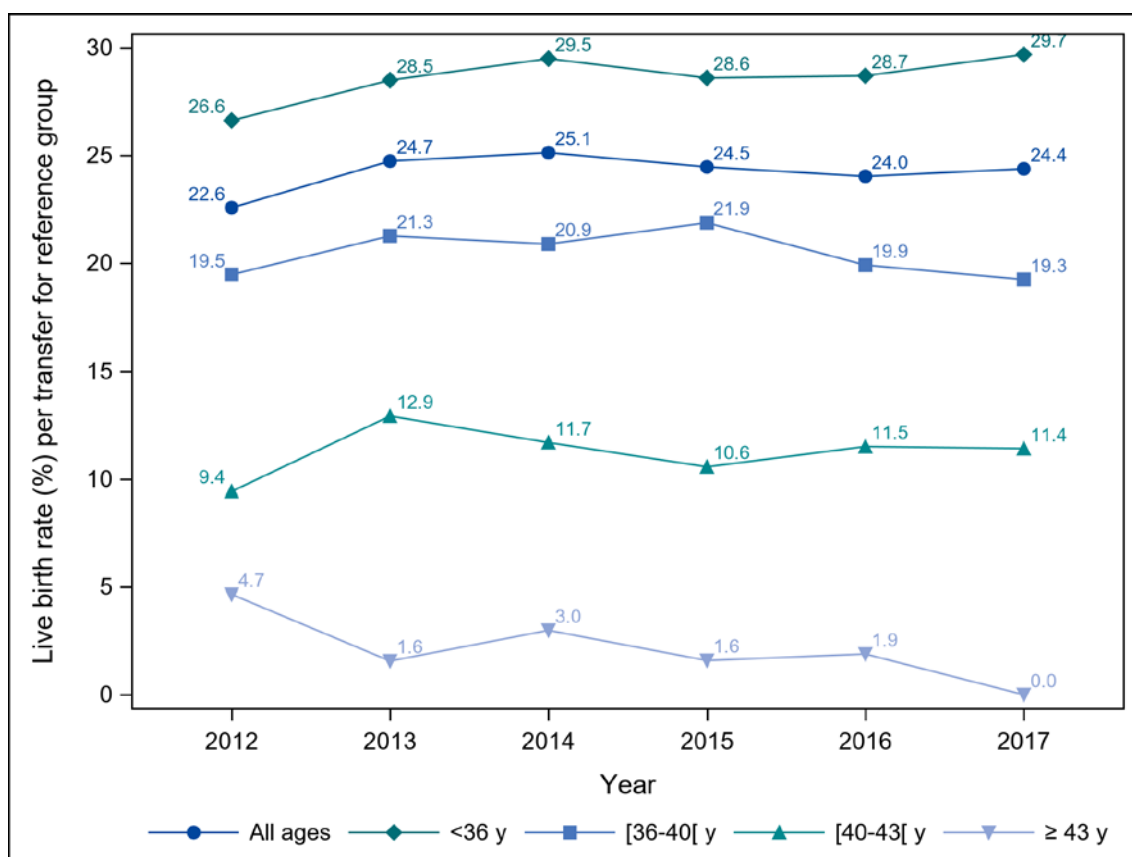


Figure 26. Percentage of transfers that resulted in live births for ART cycles using fresh nondonor eggs or embryos, over time for a reference group of rank 1 cycles excluding PGD cycles per age category and age categories combined (all cycles).

Has the number of embryos transferred changed in fresh nondonor cycles?

Figure 27 presents trends in percentages for the number of embryos transferred in fresh nondonor cycles over a 10 year period from 2008 to 2017.

Cycles that involved the transfer of one embryo increased from 50.4% to 68.2% and cycles involving the transfer of 3 or more embryos decreased from 9.8% to 3.9%.

Interpretation of the data should consider that the reimbursement policy of ART has been linked to the number of embryos transferred according to age and cycle rank since July 2003.

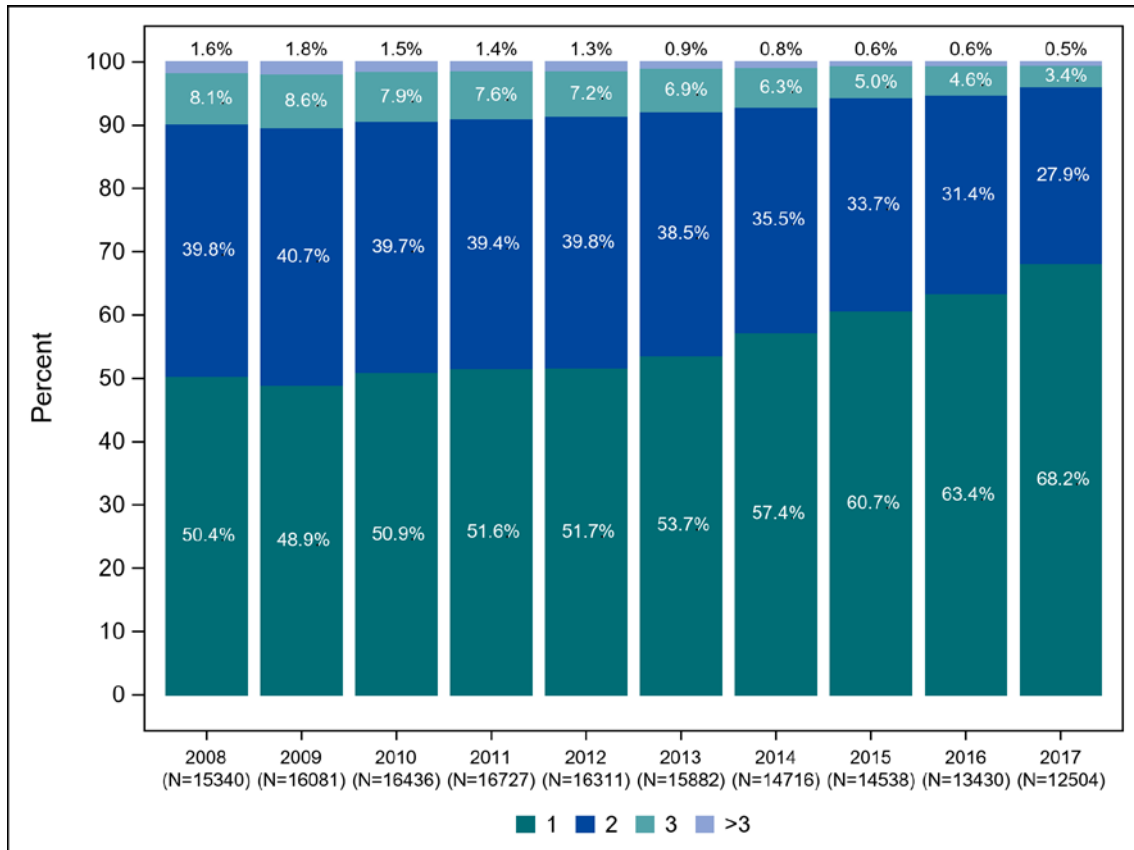


Figure 27. Percentages of fresh nondonor cycles that involved the transfer of one, two, three, or four or more embryos over time.

Have percentages of singletons and twins changed for ART cycles using fresh nondonor eggs?

Figure 28 shows the evolution of the percentages of singleton and multiple infants for ART cycles using fresh nondonor eggs from 2007 to 2017. Percentages of twins decreased from 11.5% to 7.4% and triplets remains on average at 0.2% over this period of time.

Interpretation of the data should consider reimbursement policy of ART cycles that has been linked to the number of embryos transferred according to age and cycle rank since July 2003. Since 1998, the percentage of singleton pregnancies increased to 92.6% with a decrease of multiples to 9.1%.

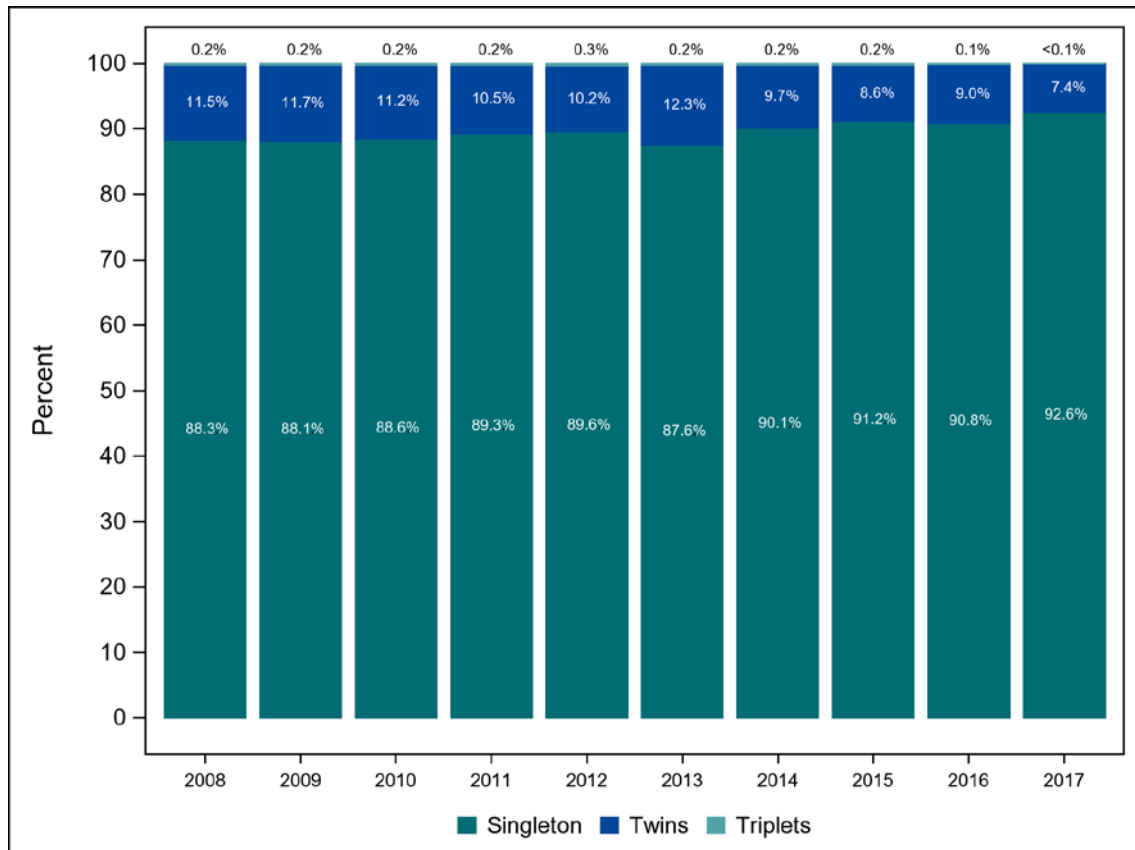


Figure 28. Percentage singletons and twins for ART cycles using fresh nondonor eggs or embryos over time.

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Appendix

Appendix A: Glossary of Terms

ART (assisted reproductive technology). All treatments or procedures that include the in vitro handling of both human eggs and sperm or of embryos for the purpose of establishing a pregnancy. This includes, but is not limited to, in vitro fertilization and embryo transfer, gamete intrafallopian transfer, zygote intrafallopian transfer, tubal embryo transfer, gamete and embryo cryopreservation, oocyte and embryo donation, and gestational surrogacy. ART does not include assisted insemination (artificial insemination) using sperm from either a woman's partner or a sperm donor.

ART cycle. An ART cycle starts when a woman begins taking fertility drugs or having her ovaries monitored for follicle production. If eggs are produced, the cycle progresses to egg retrieval. Retrieved eggs are combined with sperm to create embryos. If fertilization is successful, at least one embryo is selected for transfer. If implantation occurs, the cycle may progress to clinical pregnancy.

Artificial cycle. An artificial cycle starts when a woman begins taking hormonal drugs to prepare the endometrium for implantation.

Belrap: Belgian Register for Assisted Procreation. www.Belrap.be

Canceled cycle. An ART cycle in which ovarian stimulation or monitoring has been carried out with the intention to treat, but which did not proceed to follicular aspiration, or in the case of a thawed embryo, to embryo transfer.

Cryopreservation. The freezing or vitrification and storage of gametes, zygotes, embryos, or gonadal tissue.

Donor egg cycle. A cycle in which oocytes are collected from a donor for clinical application or research. An embryo is formed from the egg of one woman (the donor) and then transferred to another woman (the recipient).

Embryo donation. The transfer of an embryo resulting from gametes (spermatozoa and oocytes) that did not originate from the recipient and her partner.

Ectopic pregnancy A pregnancy in which implantation takes place outside the uterine cavity.

Egg. A female reproductive cell, also called an oocyte or ovum.

Egg retrieval (also called oocyte retrieval or oocyte aspiration). A procedure to collect the eggs contained in the ovarian follicles.

Embryo. The product of the division of the zygote to the end of the embryonic stage, 8 weeks after fertilization. (This definition does not include either parthenotes – generated through parthenogenesis – or products of somatic cell nuclear transfer.)

Embryo transfer. The procedure in which one or more embryos are placed in the uterus or fallopian tube.

Endometriosis. A medical condition that involves the presence of tissue similar to the uterine lining in abnormal locations.

eSET (elective single embryo transfer). The transfer of one or more embryos, selected from a larger cohort of available embryos.

Female factor infertility. Infertility due to ovulatory disturbances, pelvic abnormalities affecting the reproductive tract, or other abnormalities of the reproductive system.

Fertilization. The penetration of the egg by the sperm and combination of their genetic material resulting in the formation of a zygote.

Follicle. A structure in the ovaries that contains a developing egg.

Freeze-all cycle. An ART cycle in which, after oocyte aspiration, all oocytes and/or embryos are cryopreserved and no oocytes and/or embryos are transferred to a woman in that cycle.

Fresh eggs, sperm, or embryos. Eggs, sperm, or embryos that have not been frozen. Fresh embryos, however, may have been conceived using either fresh or frozen sperm and/or eggs.

Frozen embryo transfer cycle. An ART procedure in which cycle monitoring is carried out with the intention of transferring frozen/thawed embryo(s).

Gamete. A reproductive cell, either a sperm or an egg.

Gestational age. Age of an embryo or fetus calculated by adding 2 weeks (14 days) to the number of completed weeks since fertilization. Note: for frozen/thawed embryo transfers, an estimated date of fertilization is computed by subtracting the embryo age at freezing from the transfer date of the cycle.

Gestational carrier (also called a gestational surrogate). A woman who carries a pregnancy with an agreement that she will give the offspring to its intended parents. Gametes can originate from the intended parent(s) and/or a third party (or parties).

Gestational sac. A fluid-filled structure associated with early pregnancy, which may be located inside or outside the uterus (in case of an ectopic pregnancy).

ICSI (intracytoplasmic sperm injection). A procedure in which a single sperm is injected directly into the cytoplasm of an egg.

Implantation rate. A measurement of ART success. The number of gestational sacs divided by the number of embryos transferred.

Induced or therapeutic abortion. The termination of a clinical pregnancy by deliberate interference that takes place before 20 completed weeks of gestational age (18 weeks after fertilization) or, if gestational age is unknown, of an embryo/fetus of less than 400 g.

Infertility. A disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.

IVF (in vitro fertilization). An ART procedure that involves removing eggs from a woman's ovaries and fertilizing them outside her body. The resulting embryos are then transferred into a woman's uterus through the cervix.

Live birth. The delivery of one or more infants with any signs of life.

Low birth weight: Birth weight less than 2,500 grams.

Male factor infertility. Any cause of infertility due to low sperm count or problems with sperm function that makes it difficult for a sperm to fertilize an egg under normal conditions.

Miscarriage (also called spontaneous abortion). The spontaneous loss of a clinical pregnancy before 20 completed weeks of gestational age (18 weeks after fertilization) or, if gestational age is unknown, the loss of an embryo/fetus of less than 400 g.

Multiple pregnancy. A pregnancy with two or more fetuses.

Multiple birth. A pregnancy that results in the birth of more than one infant.

Oocyte. The female reproductive cell, also called an egg.

Ovarian hyperstimulation syndrome. An exaggerated systemic response to ovarian stimulation characterized by a wide spectrum of clinical and laboratory manifestations. It is classified as mild, moderate, or severe according to the degree of abdominal distention, ovarian enlargement, and respiratory, hemodynamic, and metabolic complications.

Ovarian monitoring. The use of ultrasound and/or blood or urine tests to monitor follicle development and hormone production.

Ovarian stimulation. The use of drugs (oral or injected) to stimulate the ovaries to develop follicles and eggs.

Ovulatory dysfunction. A diagnostic category used when a woman's ovaries are not producing eggs normally. It is usually characterized by irregular menstrual cycles reflective of ovaries that are not producing one mature egg each month. It includes polycystic ovary syndrome and multiple ovarian cysts.

PGD (preimplantation genetic diagnosis). Analysis of polar bodies, blastomeres, or trophoctoderm from oocytes, zygotes, or embryos for the detection of specific genetic, structural, and/or chromosomal alterations prior to implantation, that is, before the pregnancy is established.

Pregnancy (clinical). A pregnancy diagnosed by ultrasonographic visualization of one or more gestational sacs or definitive clinical signs of pregnancy.

Premature ovarian insufficiency. The ovary does not have the ability to produce eggs. This diagnosis often leads to use of donor eggs.

Preterm birth. A live birth or stillbirth that takes place after at least 20 but less than 37 completed weeks of gestational age.

Singleton. A single infant.

Sperm. The male reproductive cell.

Spontaneous abortion. See Miscarriage.

Stillbirth. The birth of an infant that shows no sign of life after 20 or more weeks of gestation.

Stimulated cycle. An ART cycle in which a woman receives oral or injected fertility drugs to stimulate her ovaries to develop follicles that contain mature eggs.

Tubal factor infertility. A diagnostic category used when the woman's fallopian tubes are blocked or damaged, making it difficult for the egg to be fertilized or for an embryo to travel to the uterus.

Ultrasound. A technique used in ART for visualizing the follicles in the ovaries, the gestational sac, or the fetus.

Unknown cause of infertility. A diagnostic category used when no cause of infertility is found in either the woman or the man.

Uterine factor infertility. A structural or functional disorder of the uterus that results in reduced fertility.

Very low birth weight. Birth weight less than 1,500 grams.

Very preterm birth. Alive birth or stillbirth that takes place after at least 20 but less than 32 completed weeks of gestational age.

Zygote. A diploid cell resulting from the fertilization of an oocyte by a spermatozoon, which subsequently divides to form an embryo.

References : When available ICMART definitions were used.

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