



# **EXECUTIVE SUMMARY for 2021**

## **IARTR THE ITALIAN ASSISTED REPRODUCTIVE TECHNOLOGY REGISTER**

**MONITORING THE ACTIVITY AND  
OUTCOMES OF ITALIAN ASSISTED  
REPRODUCTIVE TECHNOLOGY CENTRES  
2021**



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# MONITORING THE ACTIVITY AND OUTCOMES OF ITALIAN ART CENTRES IN 2021

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## SUMMARY OF OUTPUTS GENERATED FROM IARTR, 2021

	Patient gametes			Donor gametes		
	Fresh cycles (IVF and ICSI)	FET	FO	oocyte donation	double donation	sperm donation
N° of patients	41,172	21,846	1,254	9,071	802	1,711
N° of initiated cycles/thawings	50,297	27,204	1,445	10,584	910	1,967
N° of aspirations	45,817	-	-	-	-	-
N° of transfers	24,665	26,360	1,056	9,733	849	1,416
<i>with 1 embryo (%)</i>	50.7	81.6	48.0	81.9	81.9	67.2
<i>with 2 embryos (%)</i>	44.1	17.7	49.1	17.9	17.9	32.1
<i>with 3+ embryos (%)</i>	5.2	0.8	2.8	0.3	0.2	0.7
N° of clinical pregnancies*	7,258	9,268	278	4,000	355	536
Pregnancies per initiated cycles/thawings (%)	14.4	34.1	19.2	37.8	39.0	27.2
Pregnancies per initiated cycles without freeze-all cycles (%)	17.3					
Pregnancies per aspirations (%)	15.8					
Pregnancies per aspirations without freeze-all cycles (%)	19.4					
Pregnancies per transfers (%)	29.4	35.2	26.3	41.1	41.8	37.9
Cumulative pregnancies per initiated cycles (%)		33.4				
Pregnancies lost to follow-up (%)	15.1	11.8	13.3	9.8	17.5	14.9
Pregnancies loss per monitored pregnancy (%)	24.5	24.7	28.2	21.2	14.7	20.8
N° of deliveries	4,652	6,158	173	2,844	250	361
<i>single (%)</i>	88.9	96.2	87.3	95.7	95.6	92.2
<i>twin (%)</i>	11.0	5.0	12.1	4.3	4.2	7.8
<i>triplets or more (%)</i>	0.2	0.0	0.6	0.0	0.4	0.0
Deliveries per aspirations/thawings (%)	10.2	22.6	12.0	26.9	27.5	18.4
Estimated deliveries per aspirations/thawings (%)	12.0	25.7	13.8	29.8	33.3	21.6
Estimated deliveries per aspiration without freeze-all cycles (%)	14.6					
N° of live born babies	5,156	6,370	196	2,959	262	387
Live born babies per initiated cycles/thawings (%)	10.3	23.4	13.6	28.0	28.8	19.7

\*Clinical pregnancy: A pregnancy diagnosed by ultra-sonographic visualization of one or more gestational sacs or definitive clinical signs of pregnancy. In addition to intra-uterine pregnancy, it includes a clinically documented ectopic pregnancy<sup>1</sup>.

## SUMMARY OF OUTPUTS GENERATED FROM IARTR, 2021

	Intrauterine Insemination		
	patient semen	donor semen	IUI total
N° of patients	9,765	469	<b>10,234</b>
N° of initiated cycles	14,999	661	<b>15,660</b>
N° of inseminations	13,672	652	<b>14,324</b>
N° of clinical pregnancies*	1,579	130	<b>1,709</b>
Pregnancies per initiated cycles (%)	10.5	19.7	<b>10.9</b>
Pregnancies per inseminations (%)	11.5	19.9	<b>11.9</b>
Pregnancies lost to follow-up (%)	12.6	13.1	<b>12.6</b>
Pregnancies loss per monitored pregnancy (%)	20.1	10.6	<b>19.4</b>
N° of deliveries	1,102	101	<b>1,203</b>
<i>single (%)</i>	92.5	89.1	<b>92.2</b>
<i>twin (%)</i>	7.3	10.9	<b>7.6</b>
<i>triplets or more (%)</i>	0.3	0.0	<b>0.2</b>
Deliveries per initiated cycles (%)	7.3	15.3	<b>7.7</b>
Estimated deliveries per initiated cycles (%)	8.4	17.5	<b>8.8</b>
N° of live born babies	1,184	111	<b>1,295</b>
Live born babies per initiated cycles (%)	7.9	16.8	<b>8.3</b>

## **ITALIAN ASSISTED REPRODUCTION TECHNOLOGY REGISTER (IARTR)**

IARTR has been established at the *Istituto Superiore di Sanità* (Italian National Institute of Health) by a Decree of the Ministry of Health issued on the 7<sup>th</sup> of October 2005 (G.U. n. 282, 3<sup>rd</sup> December 2005) in implementation of article n° 11 paragraph 1 of Law 40/2004 (G.U. n. 45, 24<sup>th</sup> February 2004).

The Register collects descriptive, technical, structural and organizational information of Assisted Reproductive Techniques (ART) centres authorized by their regional health authority, to conduct assisted reproductive technology, and anonymous, aggregate data sets on all the ART treatments, plus information on the infertile couples, on embryos created and on children born after ART.

The main objectives of the Register are:

- ASSESS and REGISTER all the centres performing ART treatments and Intrauterine Insemination (IUI) procedures in the country and the number of embryos created and cryopreserved;
- COLLECT and EVALUATE data regarding centres characteristics, type of service offered (public, private or private covered by the National Health Service), different techniques performed, activity, availability, efficacy and safety of performed techniques;
- PROMOTE research and study on couple infertility causes, long-term evaluation of the children born after ART procedures; research on gametes characteristics and new cryopreservation procedures;
- MONITORE time trends in ART applications to compare different attitudes with other countries.

The Register prepares an annual epidemiological report on the ART centres' activity for the Minister of Health to illustrate to the Italian Parliament the situation of ART application.

The IARTR is linked to the European IVF Monitoring (EIM – European *In-vitro* fertilization Monitoring) Consortium, which collects data on ART from 39 European countries. In turn, the EIM sends data to the World Register ICMART (International Committee Monitoring Assisted Reproductive Technologies). Professor Jacques de Mouzon, Secretary of the ART World Register (ICMART), audited the activity of IARTR till 2018.

## **HOW DOES IARTR WORK?**

Dr Giulia Scaravelli, MD-Gynaecologist and PhD-Obstetrics and Gynaecology, is the managing director of the IARTR. Within the staff, there are many researchers with different skills: statistics, epidemiology, gynaecology, biology, psychology and informatics.

Data on efficacy, safety and outcomes of reproductive techniques, including IUI, are collected on a website in a reserved area with username and password. Data collection is based on summary data sent from each centre according to a national law on privacy protection (Dlgs. 196/2003).

The data collection is organized in two different time frames:

- The first phase of the collection is related to the activity conducted till pregnancies obtained in 2021 and it was carried out from May to June 2022;
- The second phase of the collection is related to the outcomes of pregnancies obtained from ART treatments started in 2021 and it was carried out from October to December 2022.

Data collection is made on number of cycles performed for each technique, number of patients treated, kind of infertility diagnosed, embryos created and eventually transferred, pregnancies outcomes, babies born and complications eventually occurred during treatments.

## IARTR WEBSITE

[www.iss.it/rpma](http://www.iss.it/rpma)

The Register website has the goal to collect and disseminate data and information related to IUI and ART procedures.

The website represents:

- A service to the citizens: they can consult the list of all the authorized ART centres by different regions and can have information about the techniques they perform, and the availability of service. They can find on the home page all the information regarding ART and IUI techniques and their application in Italy. They can find also the links to patient associations, scientific reproductive societies, government institutions, National Health Service, European and international registries on ART. Moreover, there are a lot of information to better understand problems related to infertility reasons, news on reproductive and infertility issues, and a steady overview on Italian and European legislation on the reproductive field.
- A service for all centres: they can fill the forms on their activity each year and they have access to their local authority and to the national Register staff. They can also see on their reserved area some KPIs (Key Performance Indicators) on clinical and laboratory activity to check how they perform in respect with the national values and with the other centres of their region.
- A service for all 20 Italian Regional Authorities: they can see all the data relating to the centres operating on their territory and all the KPIs related to each centre to monitor and elaborate data on their specific activity.

## **The recovery of ART activity in Italy in 2021 after the SARS-CoV-2 pandemic breakdown**

Italy was the first European country to have to deal with the spread of the SARS-CoV-2 infection in the first months of 2020. Since February 2020 the contagion has spread dramatically and many cases have been discovered especially in the northern regions of Italy. A system for the surveillance of cases of infection was promptly set up at the Istituto Superiore di Sanità. This Surveillance System managed by the Regions in collaboration with the ISS has made it possible to outline in detail the impact of the Covid-19 infection in the various regions and provinces. In order not to burden the National Health System (NHS), which had to adapt to the hospitalization of an exponential number of patients in a very short period of time, all medical procedures not deemed urgent were suspended or postponed with a Government Decree issued on March 9<sup>th</sup>, 2020. Among non-urgent procedures included ART treatments. Only the preservation of fertility in cancer patients with cryopreservation techniques of gametes and gonadal tissue continued because they could not have been deferred. Although after the first "lockdown" period in June 2020 the activity of the ART centres gradually resumed, throughout the year in some regions the activity was frequently suspended especially in public structures always in relation to the number of cases of infection with hospitalization for that particular region. ART cycles treatment in 2021 recorded a decrease of 17.6% compared to those carried out in 2020 (see Executive Summary in 2020).

In 2021, 92,407 ART total cycles (II-III level techniques) were recorded. Treatments increased overall by 36% from 2020 to 2021 and by 12% from 2019 to 2021 confirming the trend started before the stop in 2020 due to the pandemic of Covid-19 and the resulting health restrictions.

The greatest decrease of 53.2% of cycles was found in donor cycles with fresh embryo transfer, following by the ART cycles that utilized thawed embryos with 40.9%. The fresh cycles with an increase of 29.7% reached the level of activity of the pre Covid-19 period (-0.1% respect to 2019). The increase of the Intrauterine Insemination (IUI) treatment (+28.7%) did not allow it to reach the same level as 2019 (-5.6% respect to 2019) (**Table I**).

**Table I. Number of initiated cycles according to the type of technique used, 2019-2021**

	2019	2020	2021	Difference 21 vs 20 (%)	Difference 21 vs 19 (%)
<b>ART technique</b>					
Fresh cycle (IVF-ICSI)	50,324	38,728	50,297	+29.7	-0.1
Frozen/thawed Embryo Transfer (FET)	21,796	19,314	27,204	+40.9	+24.8
Frozen/thawed Oocyte (FO)	1,361	1,099	1,445	+31.5	+6.2
Donor gametes	8,995	8,787	13,461	+53.2	+49.6
<i>oocytes</i>	6,867	6,738	10,584	+57.1	+54.1
<i>semen</i>	1,596	1,536	1,967	+28.1	+23.2
<i>oocytes and semen</i>	532	513	910	+77.4	+71.1
<b>ART Total</b>	<b>82,476</b>	<b>67,928</b>	<b>92,407</b>	<b>+36.0</b>	<b>+12.0</b>
<b>Cryopreserved</b>					
Cryopreserved embryos cycles	17,713	15,434	2,031	+40.6	-2.7
Cryopreserved oocytes cycles	2,088	1,445	21,629	+40.1	+22.1
<b>Cryopreserved cycles total</b>	<b>19,801</b>	<b>16,879</b>	<b>23,660</b>	<b>+40.2</b>	<b>+19.5</b>
<b>IUI</b>					
IUI-H (husband semen)	15,895	11,679	14,999	+28.4	-5.6
IUI-D (donor semen)	691	492	661	+34.3	-4.3
<b>IUI Total</b>	<b>16,586</b>	<b>12,171</b>	<b>15,660</b>	<b>+28.7</b>	<b>-5.6</b>

In different healthcare contexts both the decrease of activity in 2020 and the increase in 2021 occurred differently. In 2020, private centres were able to decrease the number of cycles offered up to a mere 4.1% reduction in cycles applied compared to 2019, while the public ones suffered a decrease of 29.2%. In 2021, private centres recorded an increase of 35.6% of activity compared to the previous and public centres of 36.3% (Table II). However, if we take into consideration the percentage changes between 2019 and 2021, it can be deduced that the NHS have recovered the amount of activity compared to the period before the pandemic (+1.4% respect to 2019), while private centres have increased by 30.1% in respect to 2019, reducing the gap between cycles paid for by the NHS and the private ones, mainly thanks to the increase in cycles with gamete donation (Figure A).

**Table II. Number of cycles initiated with ART techniques according to centres setting, 2019-2021**

centres setting	2019	2020	2021	Difference 21 vs 20 (%)	Difference 21 vs 19 (%)
public and private accreditate by the NHS	51,974	38,669	52,719	+36.3	+1.4
private	30,502	29,259	39,688	+35.6	+30.1
<b>ART total</b>	<b>82,476</b>	<b>67,928</b>	<b>92,407</b>	<b>+36.0</b>	<b>+12.0</b>

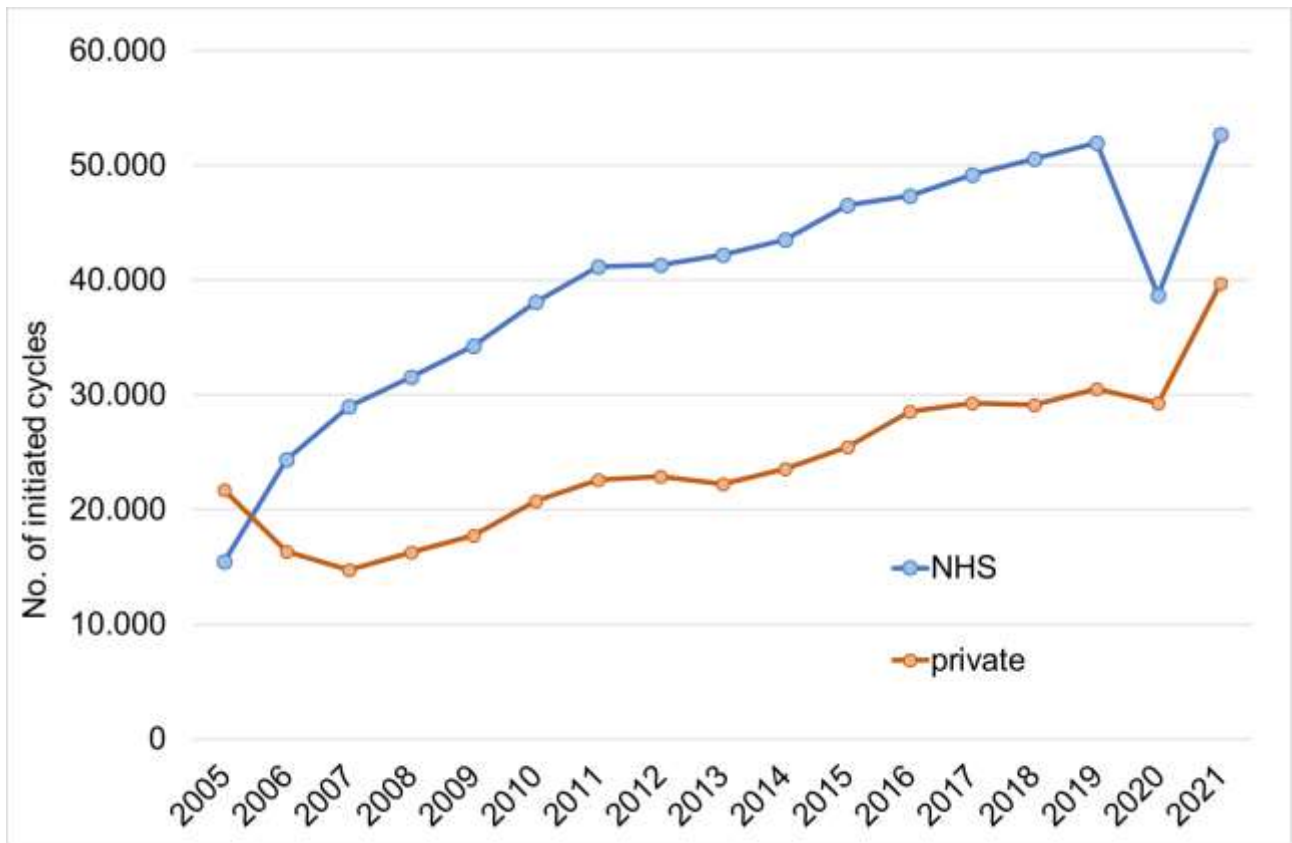


Figure A. Number of ART initiated cycles according to the centres setting, 2005-2021

# 1. ACCESS AND UTILIZATION OF ART SERVICES IN ITALY, 2021

## 1.1. Access to ART service

**Figure 1** shows the regional distribution of the 202 ART authorized centres in 2021, but only 185 performed at least one ART cycle.

The largest number of ART centres is concentrated in northern Italy (82 centres, 40.6% of the total) and in southern Italy (72 centres the 35.5% of the total), irrespectively of the amount of their activities.



**Figure 1. Regional distribution of the ART authorized centres and in brackets the number of centres per 100,000 women of reproductive age (15-45 years)\*, 2021**

\*Average resident population in Italy in 2021: source ISTAT.

**Table 1** shows the geographical distribution of ART centres according to the type of services offered. Overall, the number of active centres was 202 in 2021: 89 (44.1%) operating within the National Health Service (public and private) and 113 (55.9%) which provided only private service. The higher percentage of ART centres providing public service was concentrated in the North of Italy, i.e. in the North West 78.9%, while in the central and in the south of Italy, there were mainly private facilities (60.4% and 72.2%, respectively).

**Table 1. ART authorized centres distribution by region and type of service, 2021**

Region and geographical area	ART centres	Art centres by type of service					
		public		private covered by NHS		private	
		N	%	N	%	N	%
Piemonte	12	5	41.7	1	8.3	6	50.0
Valle d'Aosta	1	1	100	0	0	0	0
Lombardia	23	12	52.2	9	39.1	2	8.7
Liguria	2	2	100	0	0	0	0.0
<b>North-West</b>	<b>38</b>	<b>20</b>	<b>52.6</b>	<b>10</b>	<b>26.3</b>	<b>8</b>	<b>21.1</b>
A.P. Bolzano	3	1	33.3	0	0	2	66.7
A.P. Trento	1	1	100	0	0	0	0
Veneto	19	8	42.1	0	0.0	11	57.9
Friuli Venezia Giulia	3	2	66.7	1	33.3	0	0
Emilia Romagna	18	7	38.9	0	0	11	61.1
<b>North-East</b>	<b>44</b>	<b>19</b>	<b>43.2</b>	<b>1</b>	<b>2.3</b>	<b>24</b>	<b>54.5</b>
Toscana	15	5	33.3	5	33.3	5	33.3
Umbria	2	1	50.0	0	0	1	50.0
Marche	4	2	50.0	0	0	2	50.0
Lazio	27	5	18.5	1	3.7	21	77.8
<b>Central</b>	<b>48</b>	<b>13</b>	<b>27.1</b>	<b>6</b>	<b>12.5</b>	<b>29</b>	<b>60.4</b>
Abruzzo	4	2	50.0	0	0	2	50.0
Molise	1	0	0	0	0	1	100
Campania	28	7	25.0	0	0	21	75.0
Puglia	11	2	18.2	0	0	9	81.8
Basilicata	1	1	100	0	0	0	0
Calabria	5	1	20.0	0	0	4	80
Sicilia	19	4	21.1	0	0	15	78.9
Sardegna	3	3	100	0	0	0	0
<b>South and islands</b>	<b>72</b>	<b>20</b>	<b>27.8</b>	<b>0</b>	<b>0.0</b>	<b>52</b>	<b>72.2</b>
<b>Italy</b>	<b>202</b>	<b>72</b>	<b>35.6</b>	<b>17</b>	<b>8.4</b>	<b>113</b>	<b>55.9</b>

## 1.2. Utilization of ART services

**Table 2** shows the time-trends of ART initiated cycles per million inhabitants and per million women of reproductive age (between 15 and 45 years), in comparison with the same indicators for Europe. Since 2005 in Italy, both the indicators were constantly growing, with an increase of 893 cycles (+140.3%) and of 6,394 cycles (+238.3%), respectively. The latest European data available refers to the activity of year 2018<sup>1</sup>.

The number of started cycles per million inhabitants (calculated only for the 21 countries that have reported data of 100% of the centres) was 1,402 cycles in Europe versus 1,297 in Italy, both under the proposed optimal level of demand calculated as 1,500 of ART services per million inhabitants per year<sup>2</sup>.

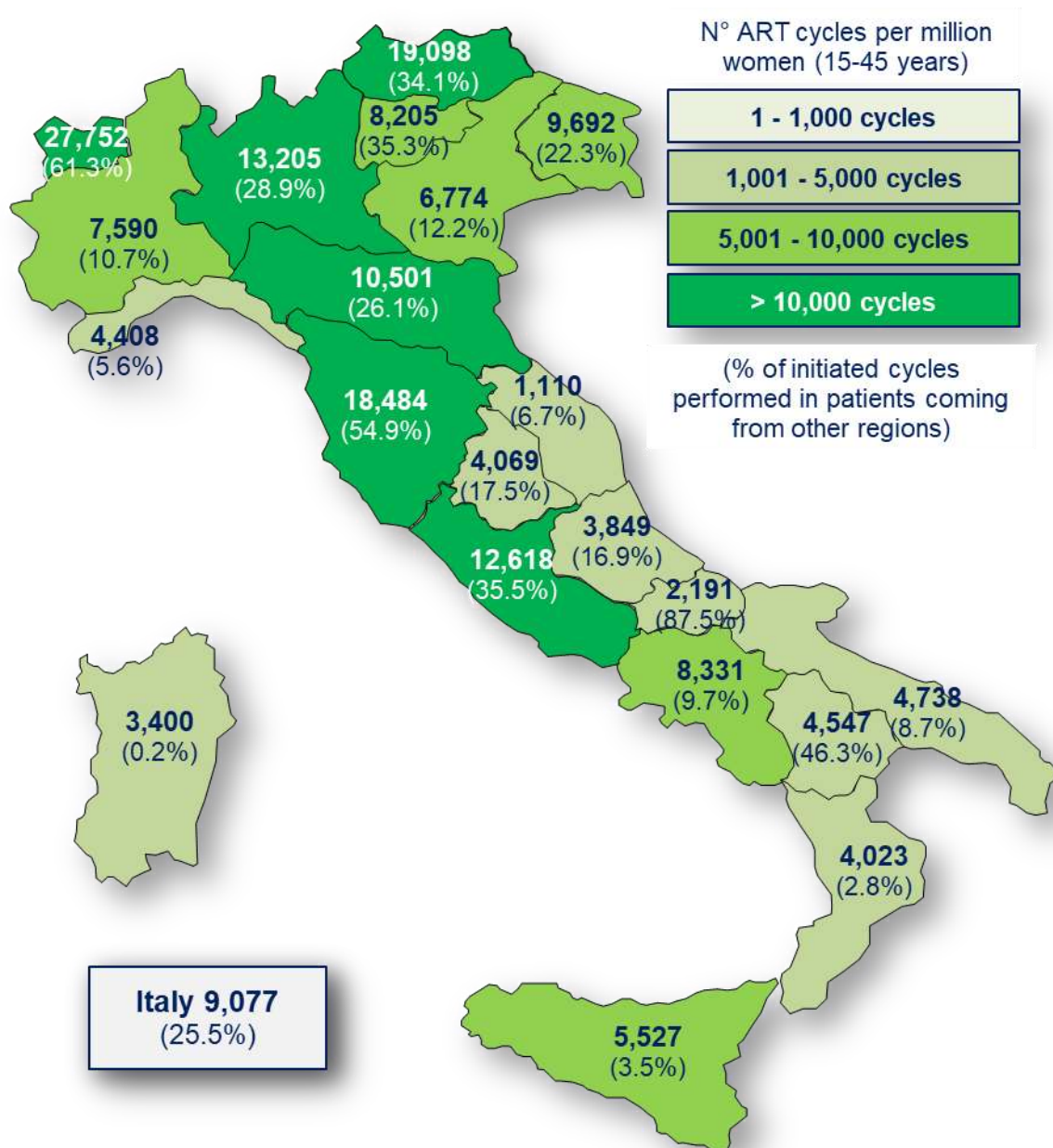
**Table 2. Number of initiated ART cycle per million inhabitants and per million women of reproductive age (15-45 years) annually in Italy (2005-2021) and in Europe (2005-2018)**

Years	ART cycles/ million population		ART cycles/ million women (15 - 45 years)	
	Italy	Europe <sup>a</sup>	Italy	Europe <sup>a</sup>
2005	636	1,115	2,683 <sup>b</sup>	4,008 <sup>b</sup>
2006	692	850	3,328	3,503
2007	736	886	3,569	4,320
2008	800	947	3,905	4,661
2009	865	1,067	4,265	5,455
2010	973	1,221	4,863	6,258
2011	1,063	1,269	5,392	6,556
2012	1,078	1,252	5,562	6,519
2013	1,070	1,175	5,601	6,210
2014	1,102	1,399	5,855	7,608
2015	1,175	1,432	6,341	7,795
2016	1,237	1,410	6,781	7,794
2017	1,275	1,435	7,106	7,662
2018	1,297	1,402	7,341	7,581
2019	1,341	-	7,697	-
2020	1,117	-	6,525	-
2021	1,529	-	9,077	-

a: data for Europe refers only to those countries where data coverage was 100% in every year.

b: in 2005, ART cycles are related to the number of women aged between 15 and 49 years.

**Figure 2** shows the distribution of initiated cycles per million women of childbearing age per geographical region. There is a great difference in the number of cycles performed among regions. If we select regions with more than five hundred thousand women in reproductive age, the distribution of cycles ranges from 4,738 cycles offered in Puglia region to 18,484 cycles provided in Toscana region. More in general, only seven regions in Northern and central area have numbers above the national average (9,077 cycles), while all the Southern regions have numbers below the average.



**Figure 2. Regional distribution of the number of initiated ART cycles per million women of reproductive age (15-45 years)\* and in brackets the percentage of initiated cycles performed in patients coming from other regions, 2021.**

\*Average resident population in Italy in 2021: source ISTAT.

Since its establishment, IARTR collected data on 200,557 infants, of which 169,346 born from ART and 31,211 born from IUI cycles. These data have to be considered with caution due to the proportion of pregnancies lost to follow-up that however changed to the better: from a maximum of 21.5% in 2006 to a minimum of 9.7% in 2018. In 2021, 15,330 babies are born alive from ART procedures in Italy that represent the 3.8% of the national babies born in the country in the same year. These values are an expression of the application of the ART in the different regions, but they do not faithfully reflect the number of births because the cycles carried out also include the treatments performed on patients coming from outside the region (for example in Toscana region, 54,9% of cycles are performed on patients coming from other regions).



**Figure 3. Regional distribution of the babies born in 2021 from ART cycles, also with donation, and the percentages in relation to the annual number of children born\*.**

\*Number of live babies born in Italy in 2021: source ISTAT.

**Figure 4** shows the percentages of live-born babies conceived by ART compared with the national total number of children born in Italy. The percentage of infants born with ART procedures increased more than 5.0 times from 2005 to 2021, with a slight decline in 2020 due to the impact of the Covid-19 pandemic on ART activity

The value of 3.8% for ART treatments in 2021 is higher to that of the European average in 2018 (3.0%) and in other similar country such as the United Kingdom (2.9%). However, it should be considered that a part of this increase is due to a strong contraction in births in Italy.



**Figure 4.** Time-trends of the percentage of live babies born after ART also with donation cycles and after ART & IUI with donation cycles in relation to the annual national number of children born in Italy, 2005-2021.

## 2. EFFICACY OF ART IN 2021 AND TIME TRENDS FROM 2005 TO 2021

## 2.1. Overview of ART

### 2.1.1. What types of ART cycles were performed?

When an ART treatment is applied without using cryopreserved oocytes or embryos, is defined as a “**fresh cycle**”, and it includes:

- **In Vitro Fertilization with embryo transfer (IVF)**: an ART procedure that involves extracorporeal fertilization of gametes<sup>3</sup>;
- **Intra Cytoplasmic Sperm Injection (ICSI)**: a procedure in which a single spermatozoon is injected into the oocyte cytoplasm<sup>3</sup>.

An ART treatment in which cryopreserved oocytes or embryos are utilized is defined as a “**frozen/thawing cycle**”, and it includes:

- **Frozen/thawed Embryo Transfer (FET) cycle**: ART procedure in which cycle monitoring is carried out with the intention of transferring to a woman a frozen/thawed or vitrified/warmed embryo(s)/blastocyst(s)<sup>3</sup>;
- **Frozen/thawed Oocyte (FO) cycle**: ART procedure in which cycle monitoring is carried out with the intention of fertilizing thawed/warmed oocytes and performing embryo transfer<sup>3</sup>.

An ART treatment in which are used gametes that did not originate from the female recipient and/or her male partner is defined as a “**donation cycle**”, and it includes:

- **Oocyte Donation (OD) cycle**: an ART cycle in which a woman receives oocytes from a donor to be used for reproductive purpose<sup>3</sup>;
- **sperm donation**: a cycle in which a woman receives spermatozoa from a person who is not her sexually intimate partner<sup>3</sup>;
- **double donation**: an ART cycle in which oocytes and spermatozoa both originating from donors are used.

The major part of the 92,407 ART cycle performed in Italy in 2021 was made with a fresh procedure with partner gametes (54.4%). Then 29.4% of the cycles were performed with a FET, 1.6% with a FO and the remaining 14.6% (13,461 cycles) with a gamete donation (see **Figure 5**).

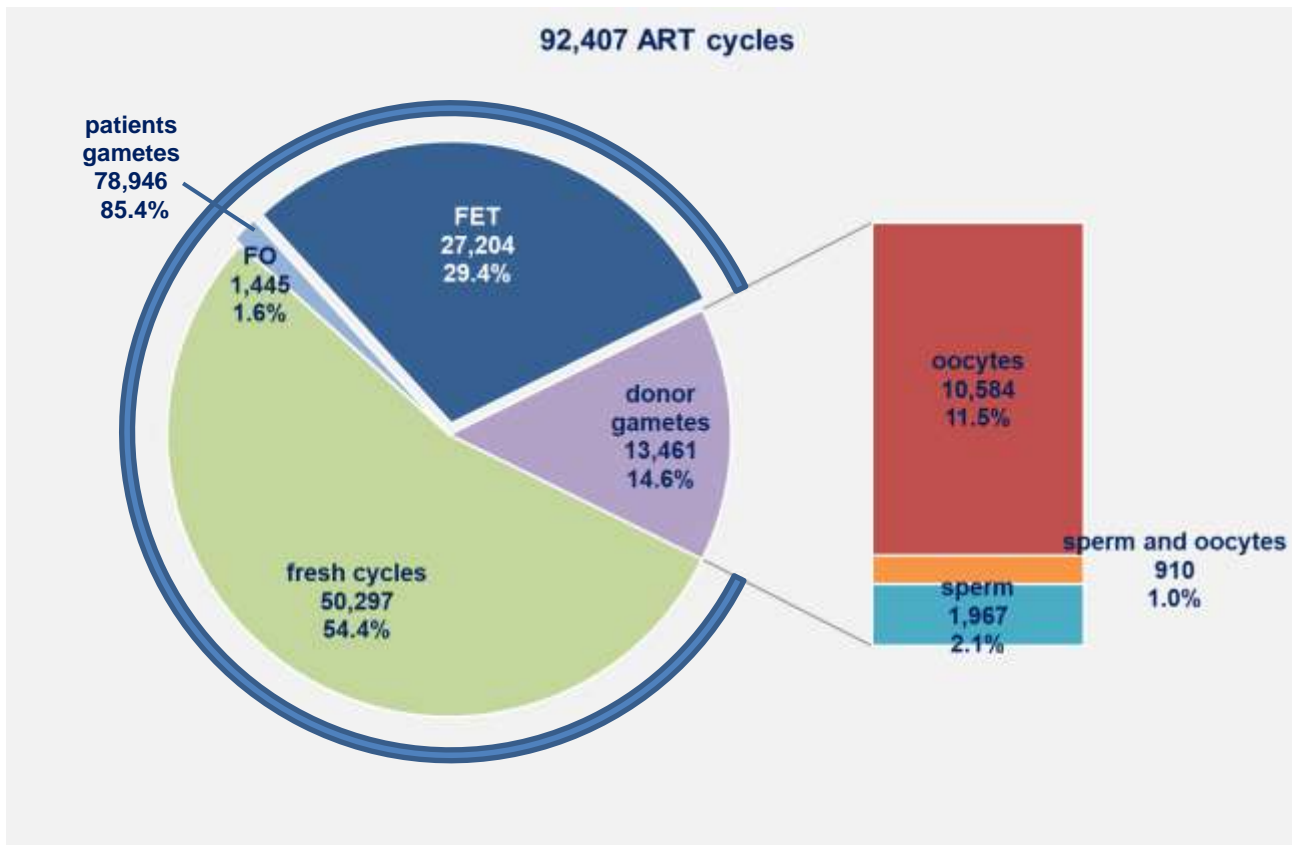


Figure 5. ART cycles performed in 2021.

### 2.1.2. How did the types of ART treatments change according to transfers among women of different ages?

The patient's age is the variable that influences at the most the success of assisted reproduction technologies, and therefore the probability of obtaining a pregnancy. **Figure 6** shows the percentage of ART transfers performed in 2021 according to women's age. As expected, ART treatment with their own oocytes is the most applied treatment in women from  $\leq 34$  years till 42 years of age, while after 42 years of age the cycles performed with donor gametes reach 56.7% of application. FET was the most commonly used ART procedure in patients younger than 40 years.

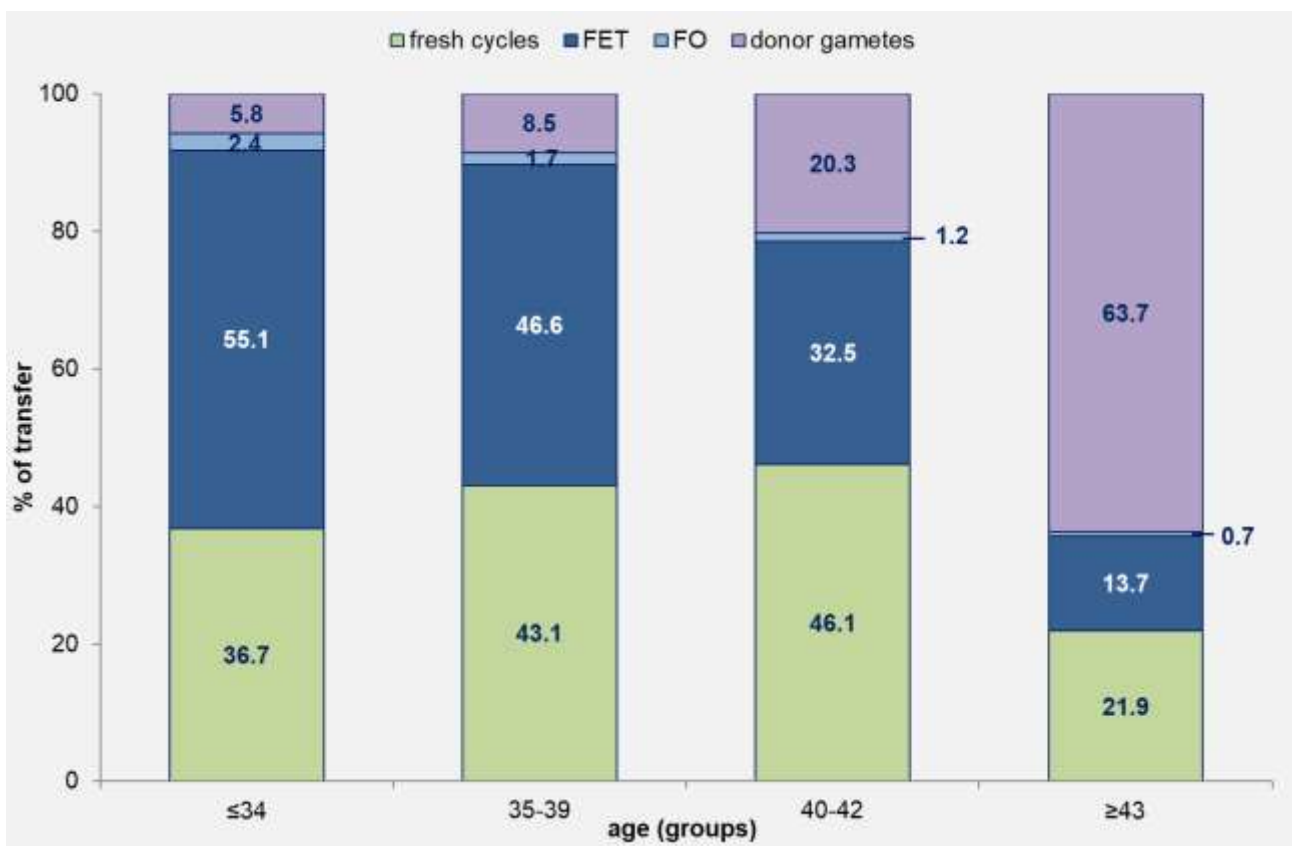


Figure 6. Types of ART procedure performed by female patients' age groups, 2021.

## 2.2. ART non-donor cycles

### 2.2.1. What are the reasons of infertility of couples in ART treatment using fresh cycles in 2021?

#### - *Female factor:*

- **tubal factor** - fallopian tubes are blocked or damaged, could prevent sperm from getting to the egg and eggs from getting to the uterus<sup>3</sup>;
- **ovulatory dysfunction** - ovaries are not producing eggs normally. The ovaries develop many small cysts instead of ripening and maturing one egg in each cycle.
- **endometriosis** – a disease characterized by the presence of endometrium-like epithelium and stroma outside the endometrium and myometrium. This condition can affect both fertilization of the egg and embryo implantation<sup>3</sup>.
- **diminished ovarian reserve** – indicate a reduced number and/or reduced quality of oocytes, such that the ability to reproduce is decreased<sup>3</sup>;
- **multiple abortions**-when there were two or more miscarriages without any full-term pregnancy.
- **multiple factor, female** - more than one female's cause of infertility.

- *Male factor* – abnormal semen parameters or function; anatomical, endocrine, genetic, functional or immunological abnormalities of the reproductive system; chronic illness; and sexual conditions incompatible with the ability to deposit semen in the vagina<sup>3</sup>.

- *Male and female factors* - one or more female and male causes of infertility.

- **Genetic factor** - Due to chromosomal abnormalities (numerical and/or structural) or to genetic alterations. They can be both male and female factors

- *Unexplained infertility* - no cause of infertility was found in either woman or man<sup>3</sup>.

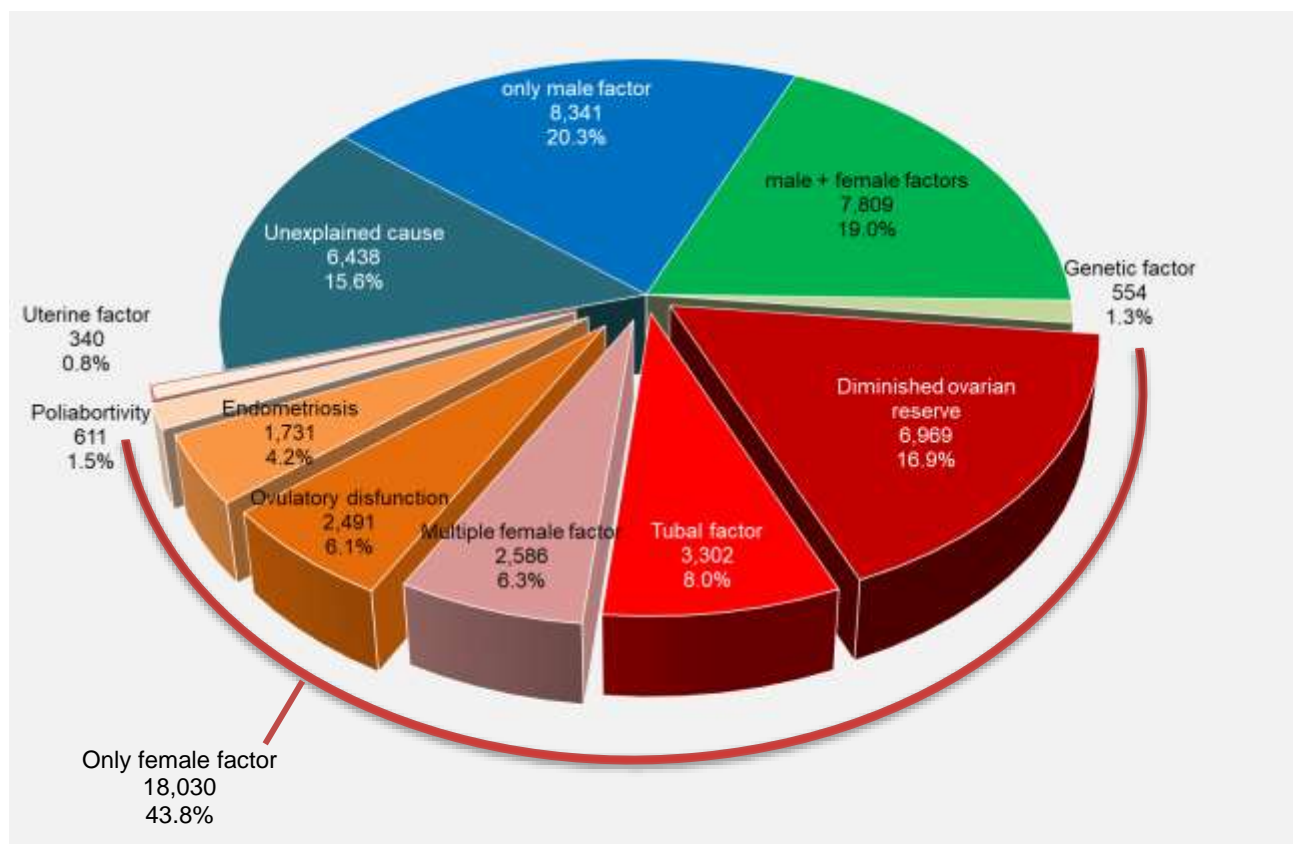


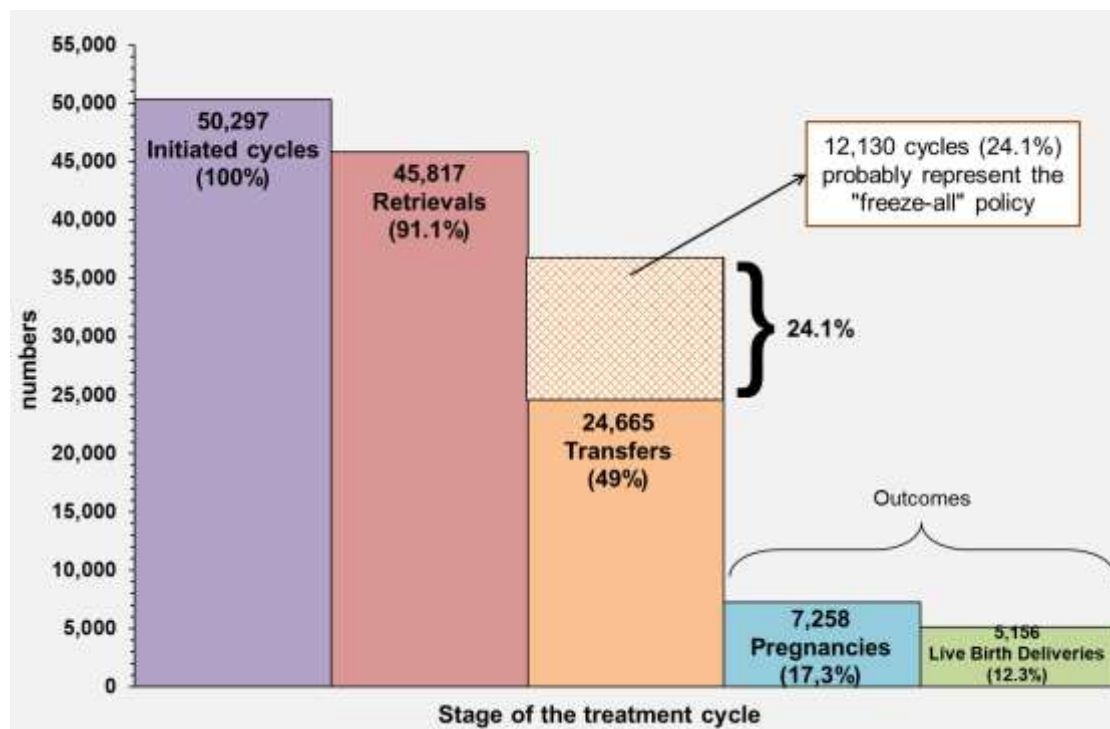
Figure 7. Causes of infertility of couples in ART treatment using fresh cycle, 2021

## 2.2.2. What are the steps for an ART treatment using fresh cycles?

An ART cycle using fresh gametes includes the following steps:

- starts when a woman begins taking fertility drugs to stimulate the ovaries to produce eggs or having her ovaries monitored for follicle production, if no drugs are given (**initiated cycle**);
- continues, if the egg follicles are produced, by an ovarian follicular aspiration performed with the aim of retrieving oocytes (**retrieval**);
- after eggs collection, a process initiated by entry of a spermatozoa into a mature oocyte followed by formation of the pronuclei (**fertilization**);
- if fertilization occurs, the embryo(s) are cultured from day 1 to day 7, and then embryo(s) (generally 1 or 2) is(are) transferred to the woman's womb either at day 2 to 3 (cleavage stage) or at day 5 to 7 (blastocyst stage) (**transfer**);
- the attachment and subsequent penetration by a zona-free blastocyst into the endometrium (**implantation**);
- if implantation is successful, a pregnancy diagnosed by ultra-sonographic visualization of one or more gestational sacs or definitive clinical sign of pregnancy occurs (**clinical pregnancy**);
- generally, in 75-80% of cases a **live birth delivery** occurs. A birth of twins, triplets or more are counted as one live birth.

**Figure 8** shows outcomes resulting from various steps of fresh cycles performed with partner gametes in 2021. Of the 50,297 cycles, 91.1% resulted in an egg retrieval, 49% in an embryo transfer, and 24.1% were estimated in “freeze-all” cycles. We can choose to use the “freeze-all” strategy for different reasons: either to avoid the risk of OHSS (*Ovarian Hyper Stimulation Syndrome*) or to perform PGT (*Pre-implantation Genetic Testing*). Because of the “freeze-all cycles”, we decided to compute the pregnancy rate per cycle removing them from the results of the fresh cycles. They will be included only when we are going to compute the cumulative pregnancy rate (see **Figure 11** and **19**). Among the outcomes, we must also consider the 15.1% of pregnancies lost to follow-up and the 24.5% of monitored pregnancies that do not reach the delivery due to miscarriages or ectopic pregnancies (see **Figure 12**).



**Figure 8.** Outcomes of ART using fresh cycles by stage of the treatment cycle, 2021.

### 2.2.3. Did the number of embryos transferred differ among women of different age groups?

Figure 9 shows the distribution of the ART transfers performed with partner gametes, divided by the number of embryo(s) transferred according to women's age (due to the aggregate data collection we cannot have this information for each ART treatments). The number of transfers with two or more embryos increased with women's age when they use their own oocytes. The single embryo transfers (SET) are increasing both generally and in every age classes. In particular, SET have increased from 67.5% in 2020 to 72.1% in 2021 in younger patients and from 53.7% to 55.1% in older ones.

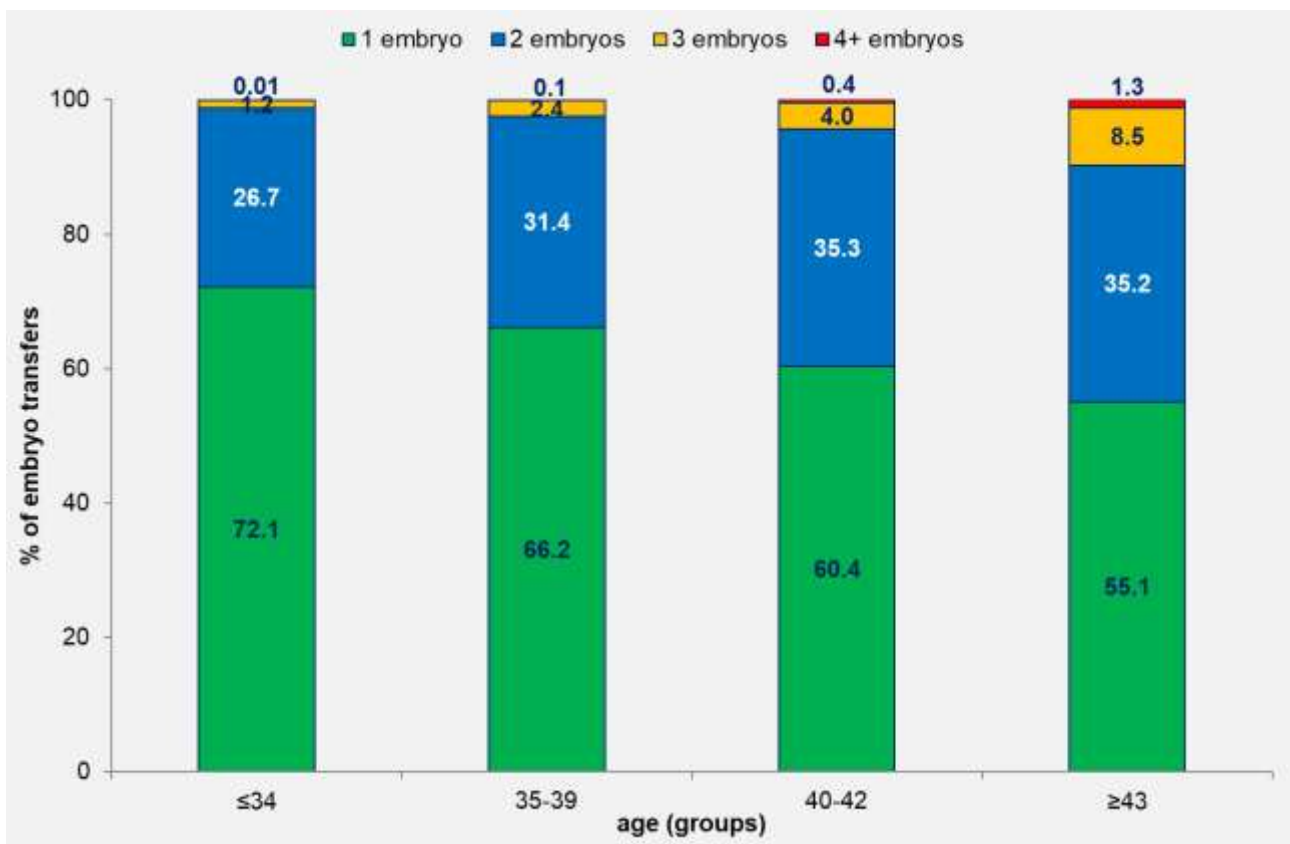
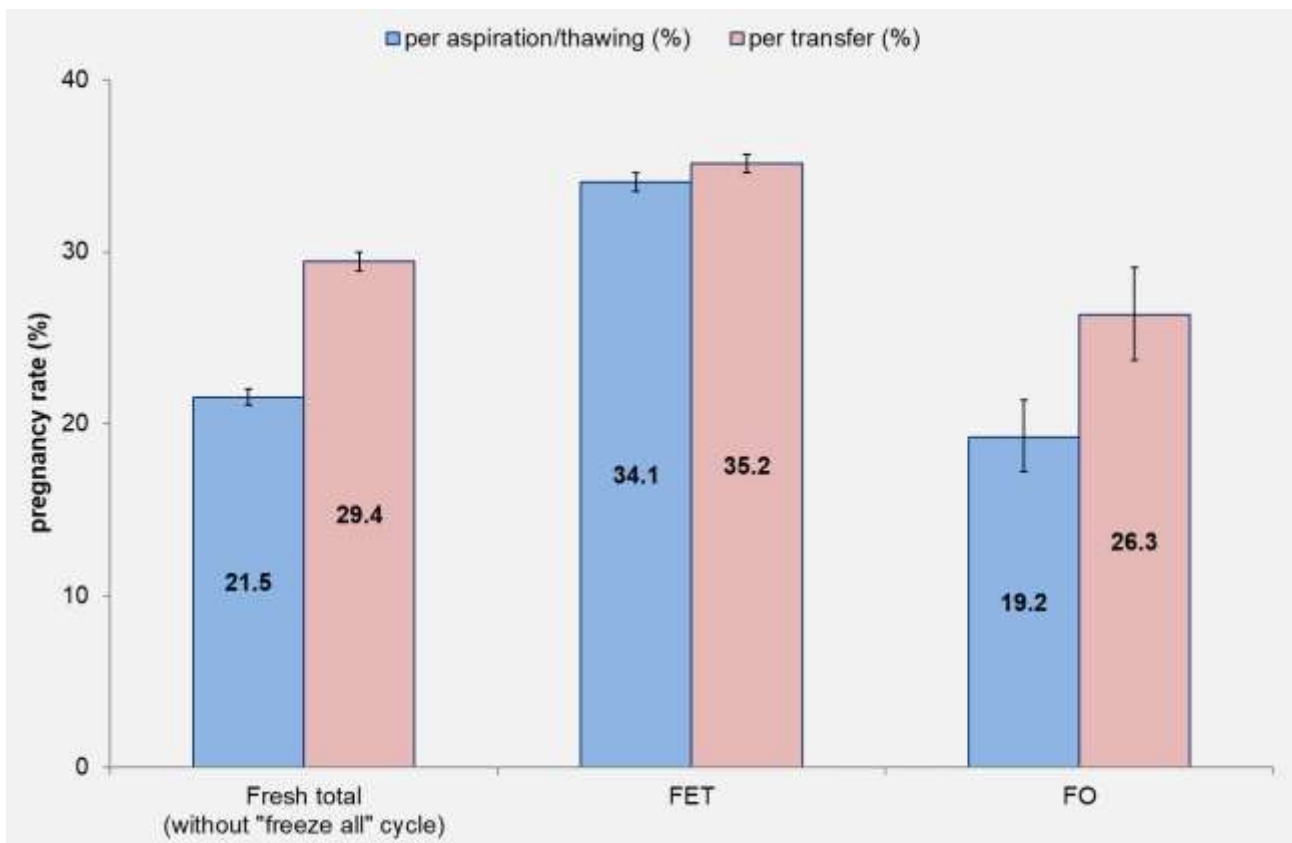


Figure 9. Distribution of embryo transfers according to the number of embryos transferred (ART total) by female patients' age groups, 2021.

## 2.2.4. What are the percentages of initiated cycles or thawings, and transfers that result in pregnancies for ART cycles?

**Figure 10** shows the pregnancy rates per aspiration/thawing and per transfer for the ART treatments. Overall, the rates after FET (Frozen Embryo Transfer) were higher than others treatments, while the FO (Frozen Oocytes) ones were the lowest. The better results obtained with frozen embryos could be partially due to the selection of “good prognosis” patients (freeze-all strategy and/or more efficient single embryo transfer) in cryopreservation techniques. These results are observed also at the European level<sup>1</sup>.

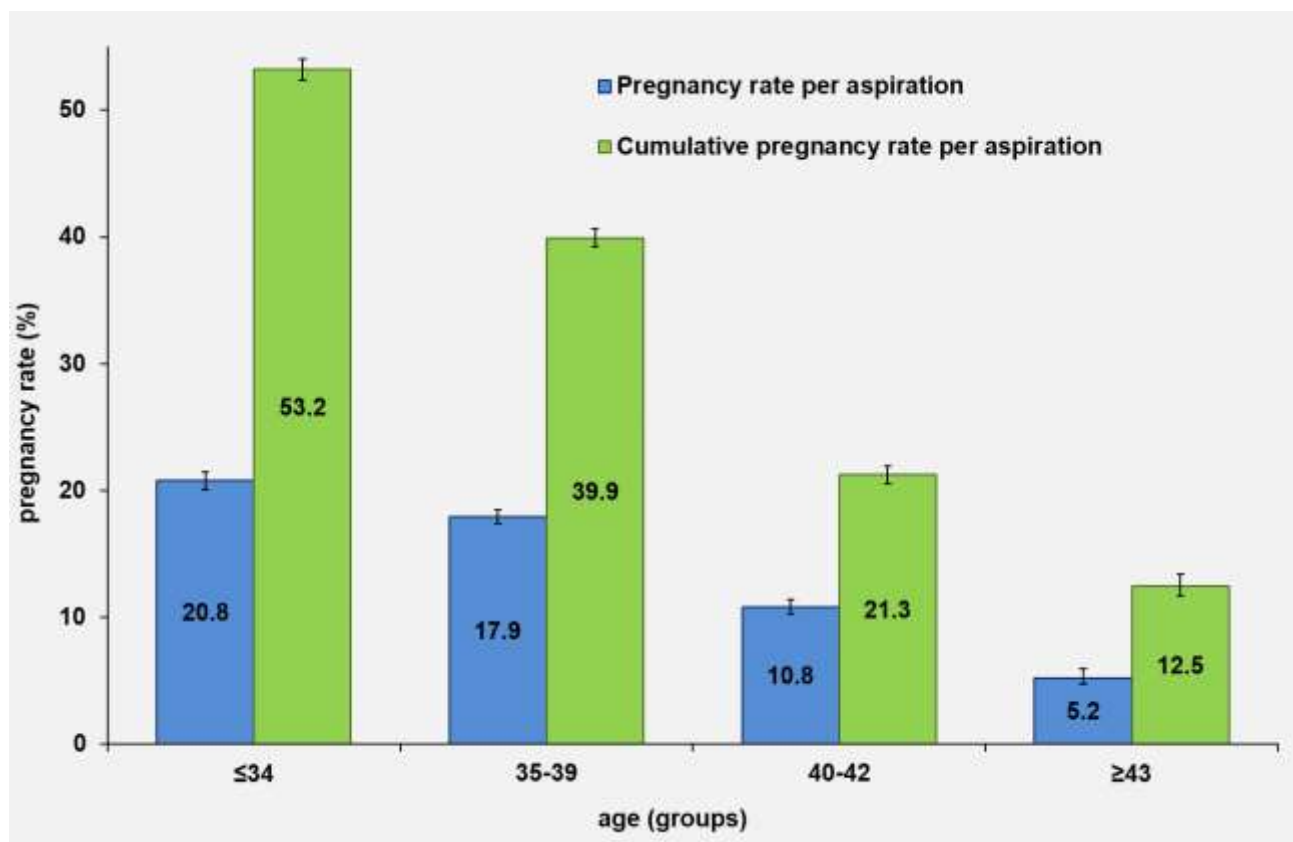


**Figure 10. Pregnancy rates per aspiration/thawing and per transfer according to different ART procedures, 2021.**

### 2.2.5. What is the “Cumulative Pregnancy Rate”?

The cumulative pregnancy rate (CPR) is the overall chance of obtain a pregnancy from all fresh and frozen embryo transfers coming from one egg retrieval. Individual data instead of summary data collection would be needed to precisely calculate the CPR. Unfortunately, IARTR as well as other Registries around the world collects information only in aggregated form. To overcome these limitations and calculate CPR using aggregated data like EIM and ICMART, we add up the number of pregnancies obtained from fresh and frozen cycles divided by the number of aspirations per year. CPR may provide a broader view of pregnancies that are achieved in Italy in a year of activity. Moreover, the comparison of pregnancy rates from fresh cycles vs. cumulative pregnancy rates may show the estimated added value of embryo and oocyte cryopreservation.

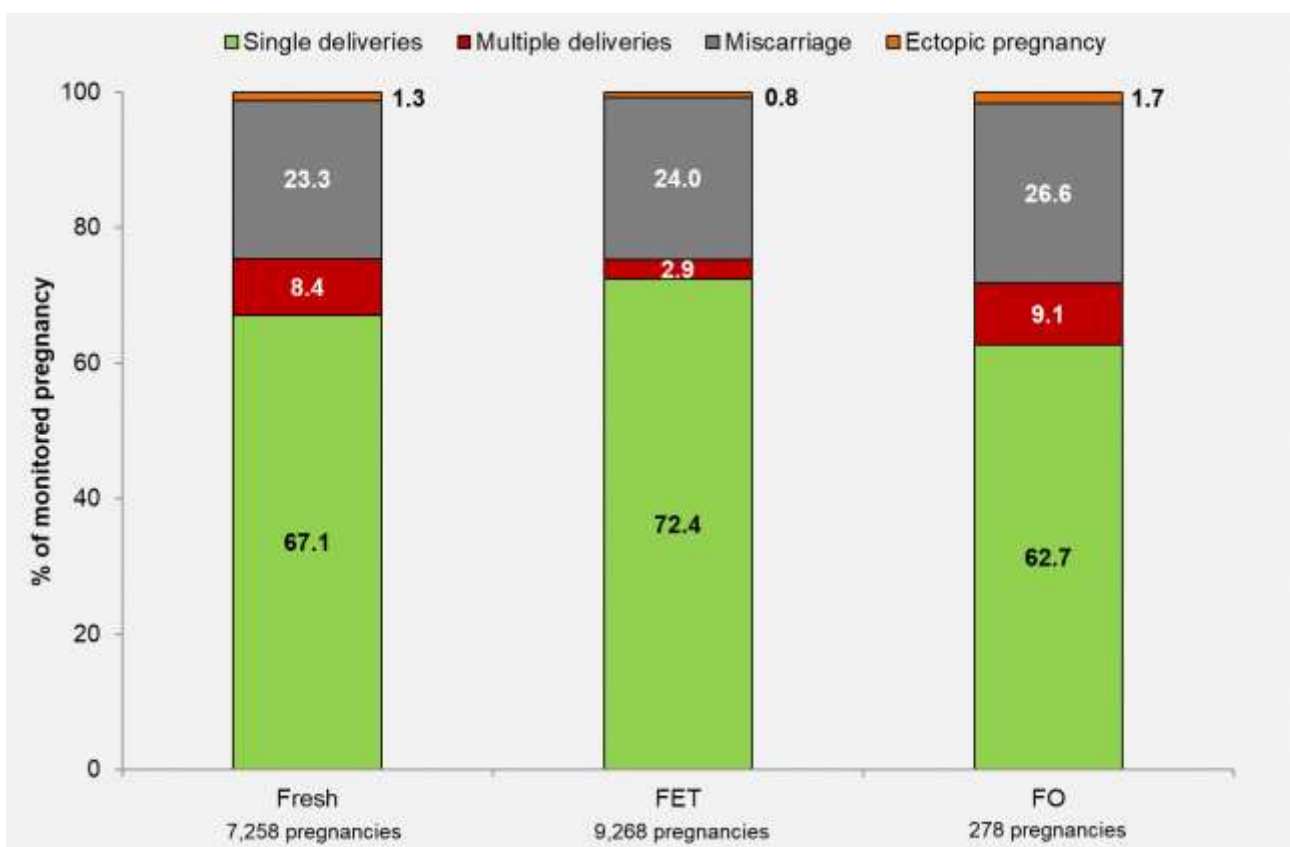
**Figure 11** shows pregnancy rate per aspiration in fresh cycles and cumulative pregnancy rate per aspiration by women age groups. Overall, embryo and oocyte cryopreservation double the chances of achieving a pregnancy per aspiration. It should be emphasized that as we cannot consider the weight of the "freeze-all" policy in every age group of female patients (data not collected by the Registry), hence the pregnancy rates per aspiration could be underestimated in each age group.



**Figure 11.** Pregnancy rates per aspiration and cumulative pregnancy rates per aspiration, by female patients' age groups, 2021.

## 2.2.6. What percentage of ART pregnancies resulted in a delivery?

**Figure 12** shows the outcomes of the monitored clinical pregnancies obtained from the application of ART performed with partner gametes in Italy in 2021. Of the 7,258 monitored pregnancies issued from fresh cycles 75.5% resulted in a delivery, of which 8.4% were multiple, and the 23.3% in a miscarriage. In FET and FO procedures the 75.3 % and 71.8%, respectively, resulted in a delivery. The percentages of multiple deliveries in FET (2.9%) are significantly lower than in fresh cycles, while the percentage of miscarriages shows no significant difference both in FET (24%) and FOR (26.6%) when compared with fresh one.



**Figure 12. Comparison of the outcomes of monitored clinical pregnancies that resulted from ART non-donor procedures, 2021.**

### 2.2.7. What is the gender distribution of infertility factors among ART users?

Figure 13 shows the trend of major reasons of infertility among patients who had ART using fresh cycles from 2005 to 2021. Diagnoses range from one infertility factor within the patient or partner to multiple infertility factors in either one or both members of the couple. The male factors have been decreasing since 2009, while the female ones have been increasing since 2015. Overall, considering also the reasons of infertility present in both members of the couples, female factors were diagnosed in more than 50% of couples in each year of data collection, reaching the maximum values of 64.1% in 2021.

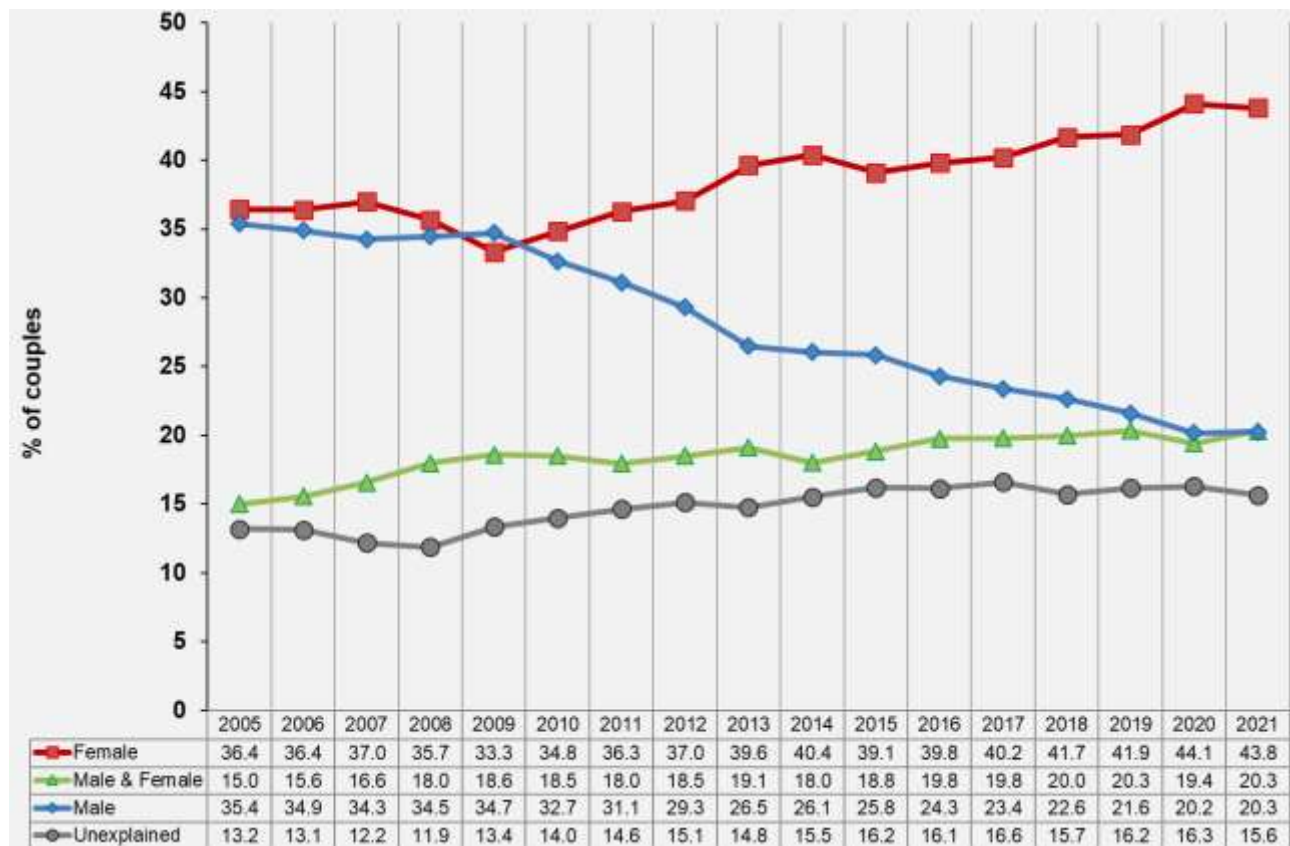


Figure 13. Time-trends of gender distributions of infertility causes among patients who had ART using fresh cycle, 2005-2021.

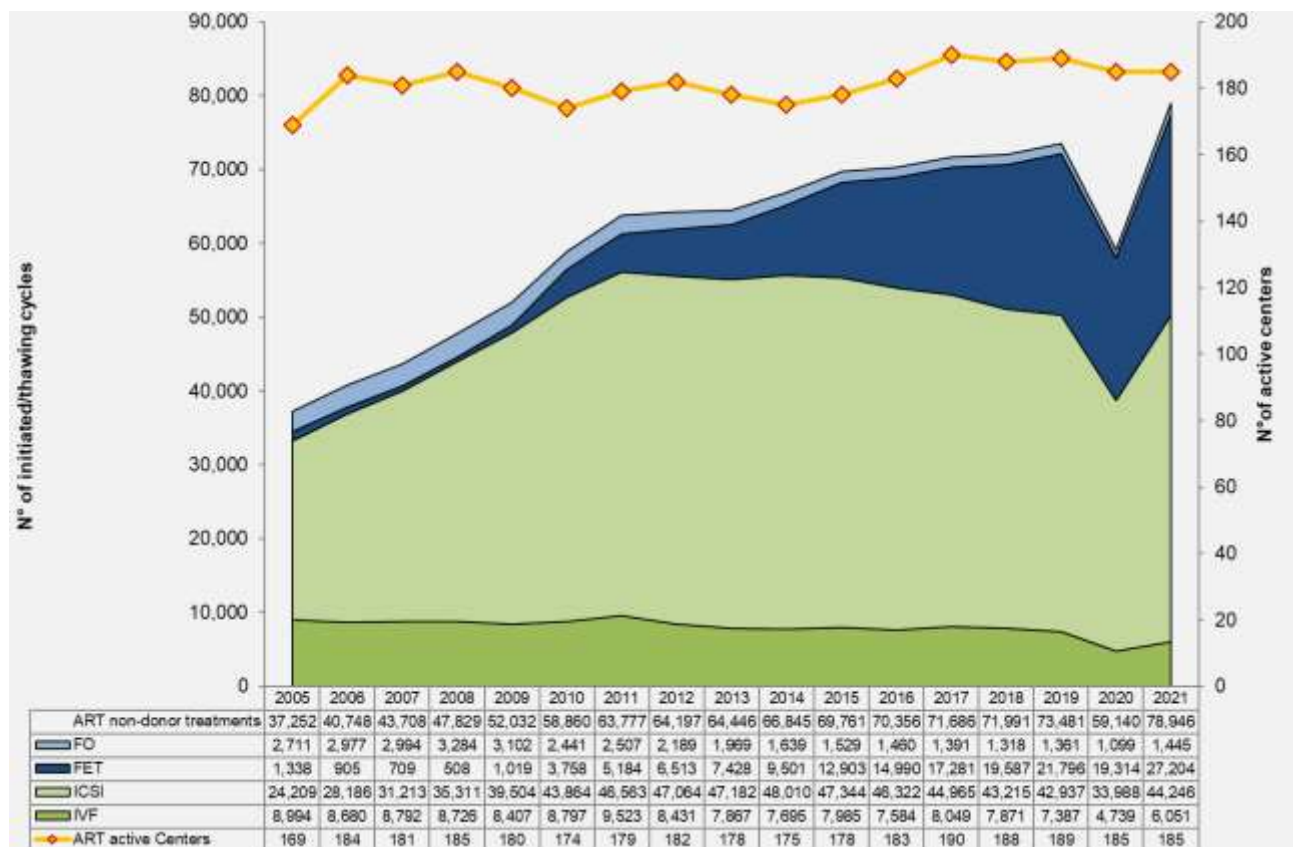
## 2.2.8. Is the use of ART non-donor procedures change over time?

**Figure 14** shows the number of ART non-donor initiated/thawing cycle and the number of ART active centres (with at least 1 cycle performed in the year) from 2005 to 2021.

After the decrease in activity due to “lockdown” caused by the Covid-19 pandemic, the numbers of initiated cycles increased again in 2021, resuming the growth trend observed until 2019.

Intra-Cytoplasmic Sperm Injection (ICSI) was originally developed to improve fertilization rates in couples with severe male factor infertility indication. Today, this procedure is widely used even without a reported diagnosis of male factor infertility.

The number of ICSI cycles increased from 24,209 in 2005 to 44,246 in 2021, while IVF cycles decreased from 8,994 to 6,051. In addition, FET thawing increased from 1,338 to 27,204, while FO procedures decreased from 2,711 to 1,445.



**Figure 14. Time-trends of ART non-donor initiated cycles/thawings and number of active ART centres, 2005–2021.**

### 2.2.9. Did the use of FET (Frozen Embryo Transfer) procedures differ in Italy compared to the other European countries over time?

In 2004, the Italian Parliament approved a Law (40/2004) regulating ART in which embryo cryopreservation was banned. In 2009 Italian Constitutional Court removed some limitations set out in the Law, including the practice of embryo freezing, now permitted under specific conditions. For this reason, the use of FET has declined consistently after 2004 and resumed steadily after 2009 (Figure 14). As shown in Figure 15, percentage of FET transfer performed highly increased from 2.5% in 2009 reaching in 2021, for the first time, more than a half of the ART transfer performed in Italy. In comparison with some European countries<sup>1</sup>, such as France, Spain and Sweden, for 2018 last European data available, Italy still shows the lowest number of FET cycles performed, but they are steadily increasing.

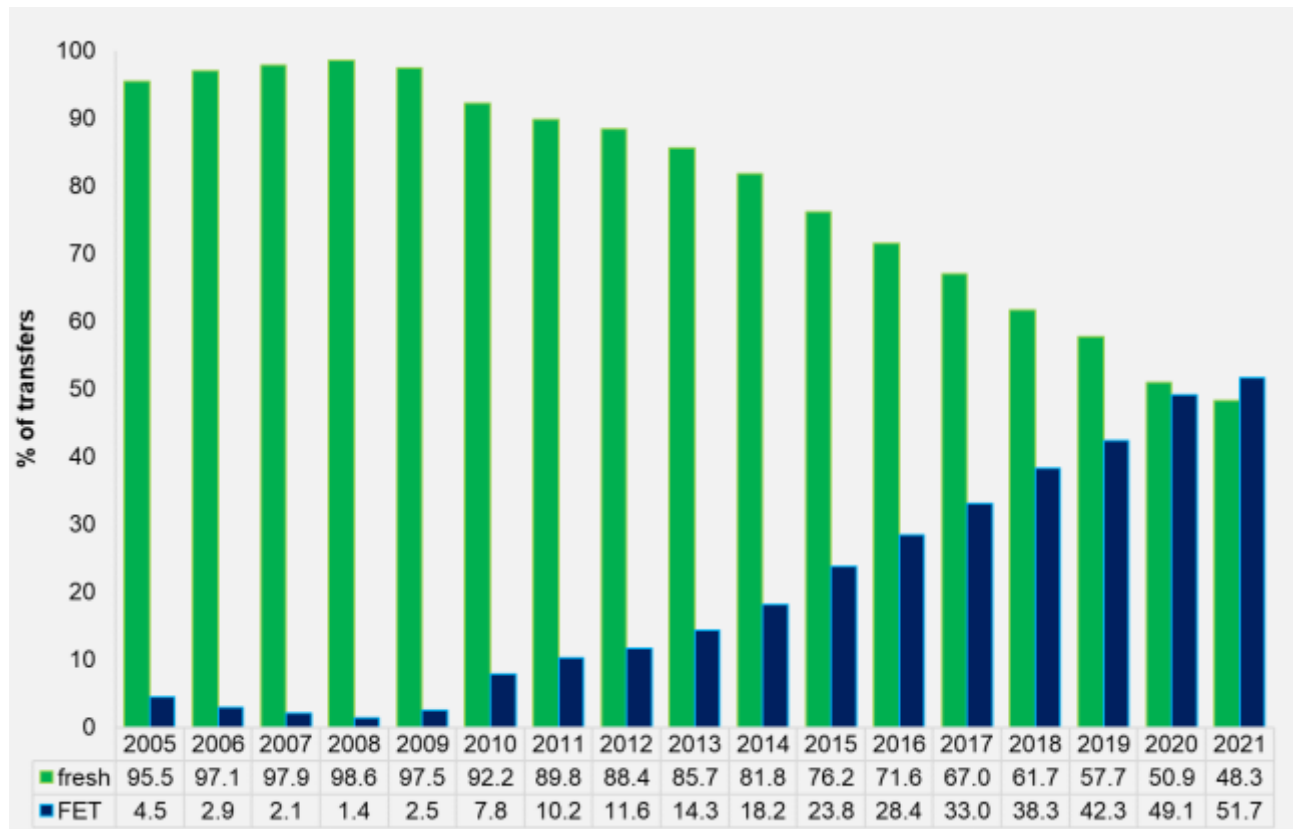


Figure 15. Time-trends of proportion of fresh versus frozen transfer (2005-2021).

### 2.2.10. Has the age of ART female patients changed over time?

Figure 16 shows the distribution of fresh cycles by age groups of women, from 2005 to 2021.

For women older than 40 the percentage of fresh cycles performed increased from 20.7% in 2005 to 34.5% in 2021, while the percentage of fresh cycles performed in women  $\leq 34$  years old decreased from 39.3% in 2005 to 27.1% in 2021. Overall, the mean age of women who had fresh cycles increase over time from 35 to 37 years.

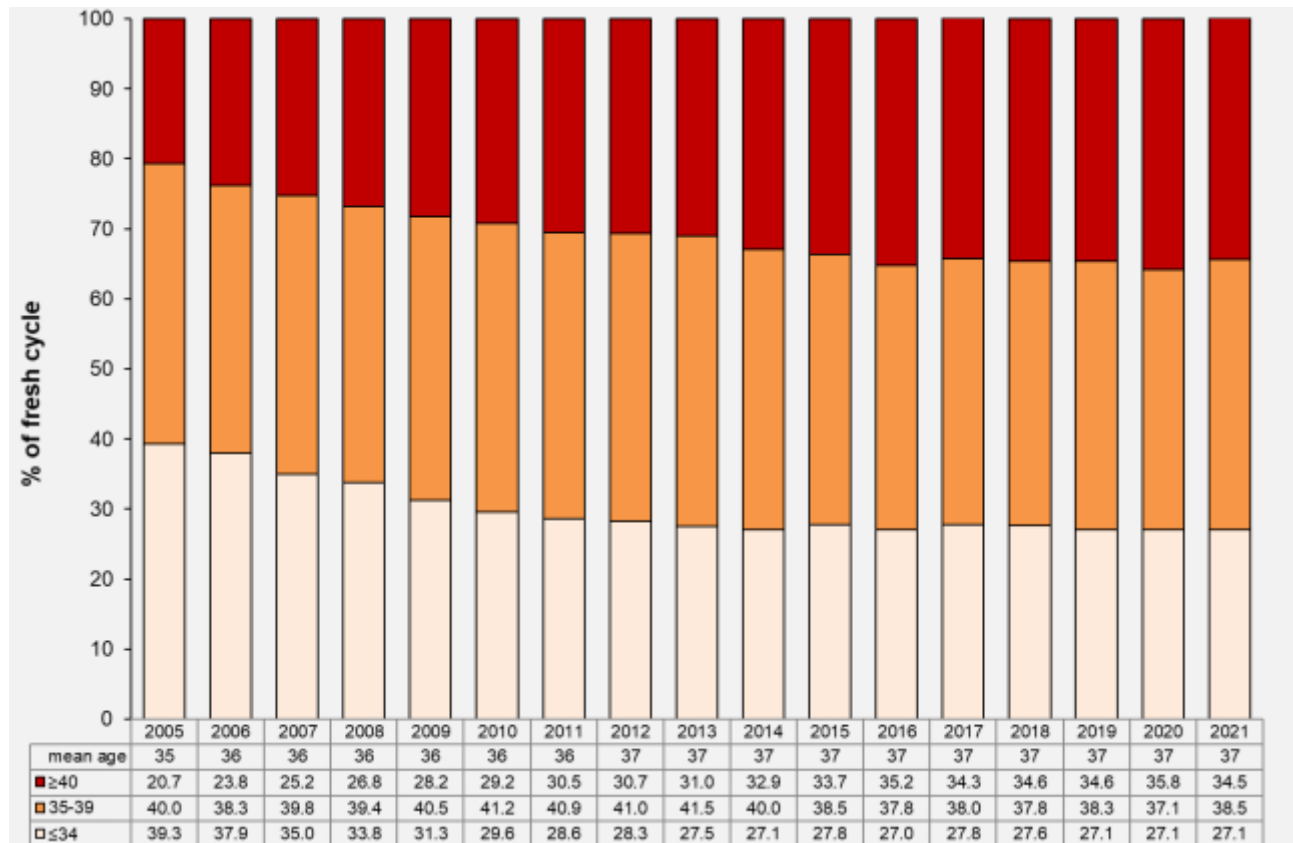
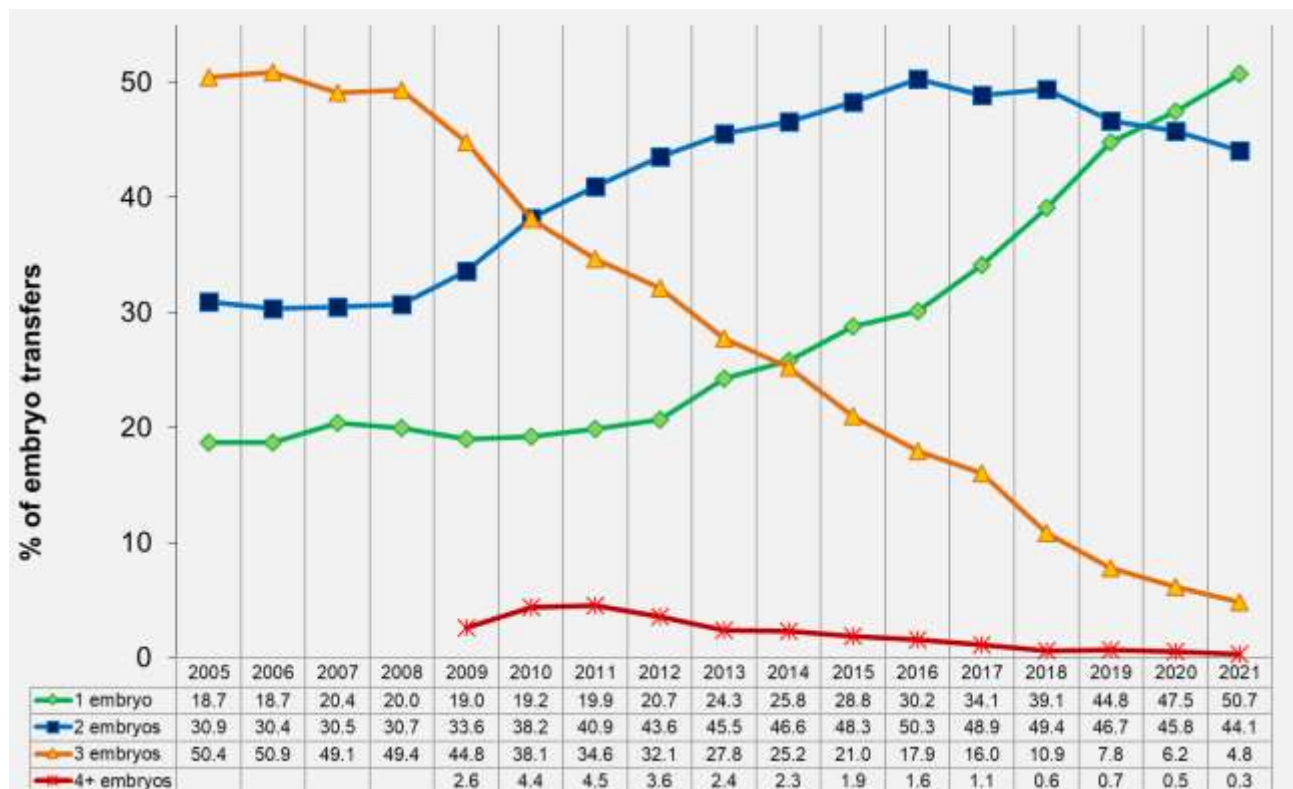


Figure 16. Time-trends of fresh initiated cycle's distributions by age classes of female patients, 2005-2021.

## 2.2.11. Has the number of embryos transferred changed in fresh cycles?

**Figure 17** shows trends with the percentage of the number of embryos transferred in fresh cycles. From 2005 to 2021, the single embryo transfers increased from 18.7% to 50.7% exceeding the proportion of the double embryo transfers. On the other hand, transfers with three embryos dramatically decreased from 50.4%, first to 38.1% in 2010 to reach 4.8% in 2021. As shown in the figure, this trend began from the end of 2009 when Law 40/2004 was changed, by the Parliament, and the limit to transfer all the embryos created for a maximum of three removed. Values of transfers with four or more embryos decreased to 0.3% in 2021, after having been quite stable during time. The average number of embryos transferred decreased from 2.3 embryos per transfer in 2005 to 1.5 in 2021. This trend is similar in most European countries<sup>1</sup>.



**Figure 17. Time-trends of transfer by number of embryos transferred, 2005-2021.**

## 2.2.12. Did pregnancy rates per transfer changed over time among different ART procedures?

Figure 18 shows pregnancy rates per transfer in order to compare cycles with fresh oocytes and embryos vs. those using frozen embryos (FET) or frozen oocytes (FO).

Overall, FET cycles showed the best pregnancy rates increasing highly from 16.3% in 2005 to 35.2% in 2021, those with fresh oocytes increased from 24.5% to 29.4%, and those with frozen oocytes doubled from 11.4% to 26.3%. Since 2014, FET pregnancy rates have been higher than the fresh ones. The consolidation of the probability of obtaining a pregnancy for the fresh techniques and the increase for those of thawing takes place despite the fact that the number of embryos transferred has decreased over the years.

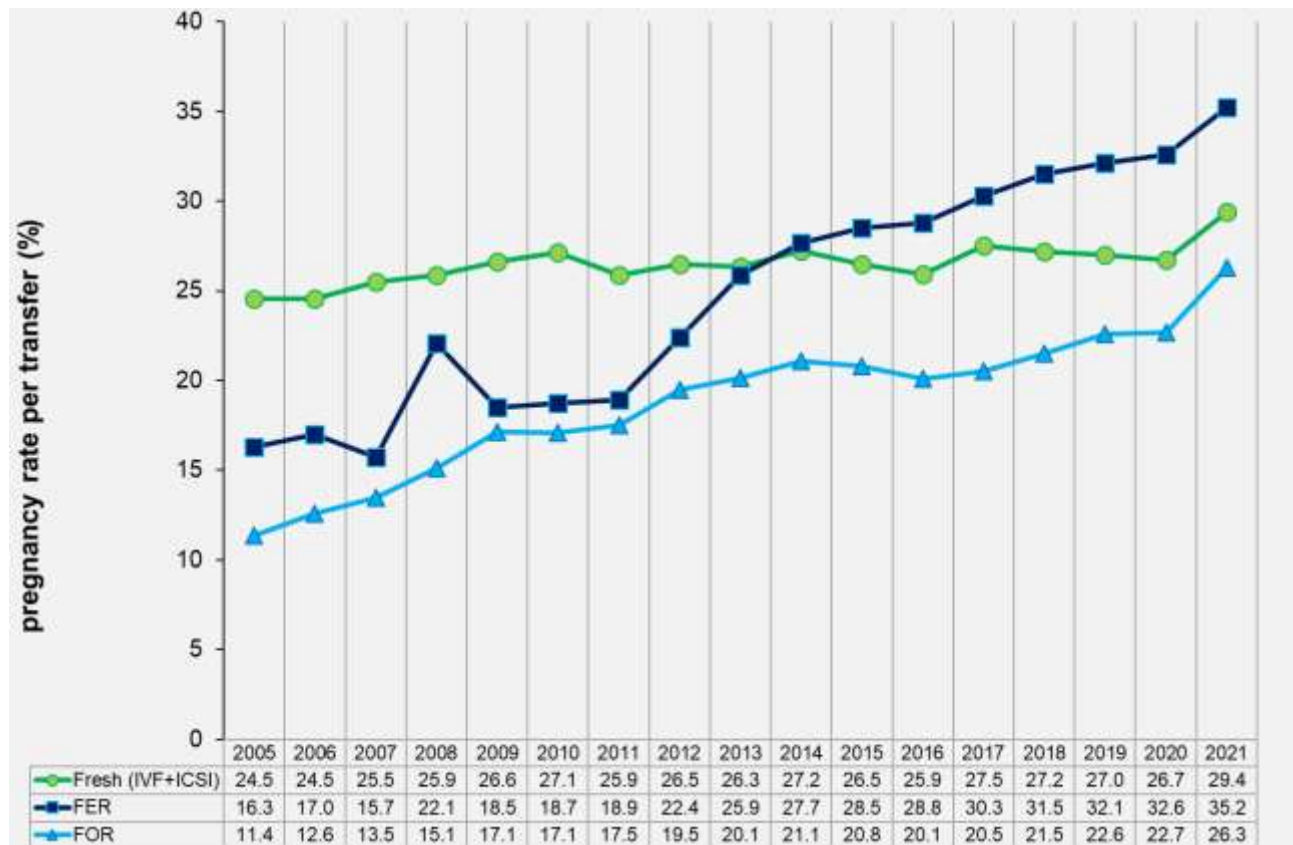
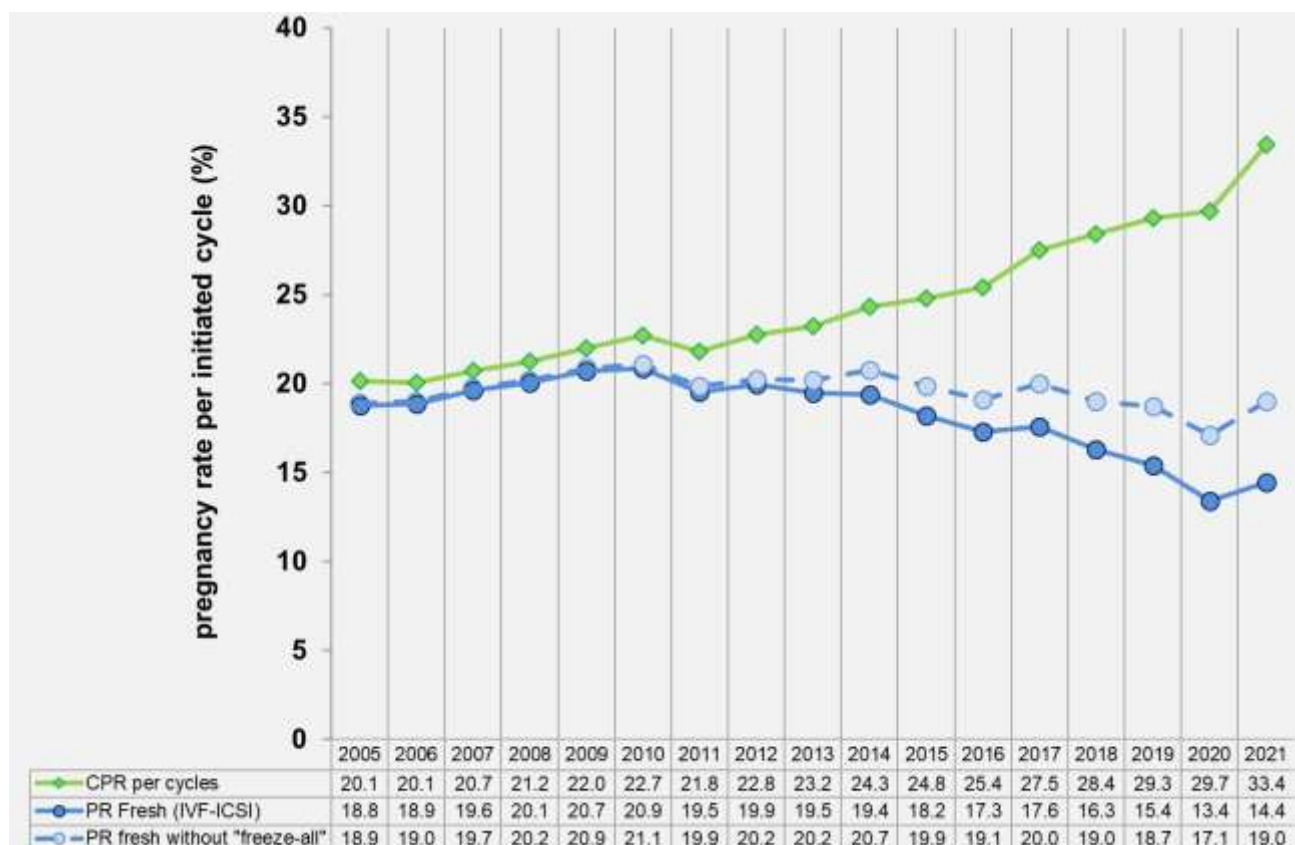


Figure 18. Time-trends of pregnancy rate per transfer for fresh, thawed embryos (FET) and thawed/warmed oocytes cycles (FO), 2005-2021.

### 2.2.13. Did cumulative pregnancy rates per initiated cycle changed over time?

**Figure 19** compares the percentage of pregnancies obtained on fresh initiated cycles with the Cumulative Pregnancy Rate (CPR) over time. As described in **Chapter 2.2.5**, CPR is presented as the sum of pregnancies obtained from fresh cycles and frozen/thawing cycles (FET and FO) as nominator and the number of initiated cycles with fresh techniques of the same year as denominator. CPR gives an estimate of the likelihood of obtaining a pregnancy for a woman undergoing an ART cycle, also having the opportunity to perform oocyte and/or embryo thawing cycles. Moreover, the comparison of pregnancy rate from fresh cycles vs. CPR may show the estimated benefit of embryo and oocyte cryopreservation. As the figure shows, this value is constantly growing from +6.6% in 2005 to a +75.7% in 2021. The trend of the pregnancy rate, calculated by excluding the “freeze-all cycles” from the count of the fresh ones, shows the impact on the outcomes of the fresh techniques of this new and increasingly widespread procedure. The declining trend of the pregnancy rate in fresh cycle is similar to that shown by the European data<sup>1</sup>.



**Figure 19. Time-trends of pregnancy rate per initiated cycle for fresh and cumulative pregnancy rate per initiated cycle, 2005-2021.**

### 2.2.14. Does the risk of pregnancy loss differ among women of different age groups?

Increasing female age also increases the risk of negative pregnancy outcomes (spontaneous or therapeutic abortions and ectopic pregnancies). As shown in **Figure 20** pregnancy loss rates were much higher in older age groups. Rates of missed pregnancies have an unstable trend for patients over 42 years due to small numbers, while they are quite stable in the remaining age groups.

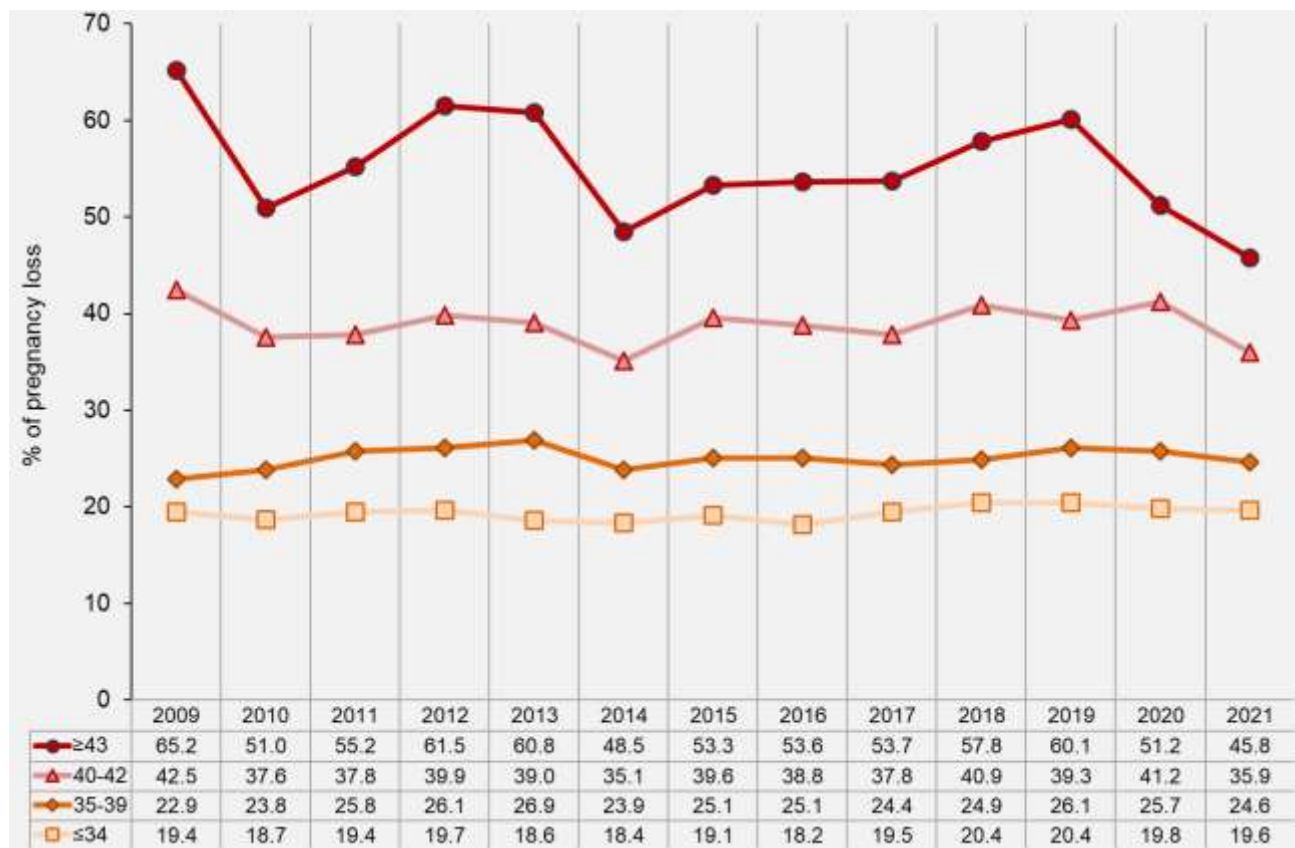


Figure 20. Time-trends of percentages of total pregnancy loss using ART non-donor cycles by female age groups, 2009-2021.

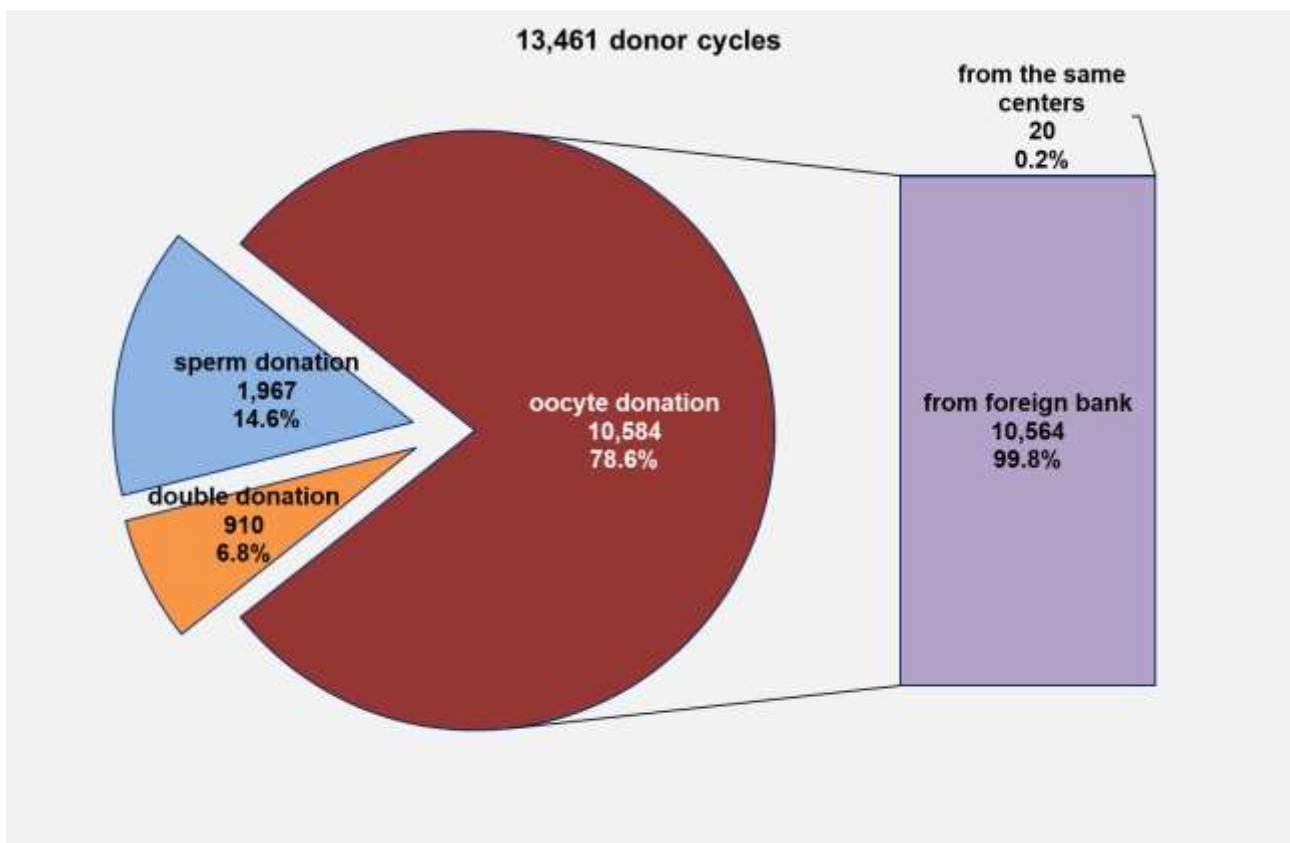
## 2.3. ART donor cycles

In April 2014 Italian Constitutional Court removed the prohibition (set out in the Law 40/2004), regarding the practice of ART techniques using donor gametes. Currently oocyte donation, semen donation and double donation are allowed.

See the Summary table ([see page 59](#)) for more detailed data on activity and outcomes regarding ART donor cycles in 2021.

### 2.3.1. Which gametes were used in ART donor cycles in 2021?

**Figure 21** shows the distribution of the types of the 13,461 ART cycles using donor gametes applied in Italy in 2021 and the origin of the donated frozen oocytes. In about 85.4% of ART donor cycles, fresh or frozen donated eggs were used, in 14.6% of cycles there is a donation of male gametes only. In the oocyte donation cycles, almost all cycles (99.8%) were performed with oocytes obtained from a foreign bank.



**Figure 21.** Distribution of all ART cycles using donor gametes and origin of the oocytes for the donor oocyte cycles, 2021. Total cycles = 13,461.

### 2.3.2. How did the types of donated gametes change among the recipient women of different age classes?

Figure 22 shows the distribution of performed transfers according to the recipient female age group at the start of a donation cycle. The different types of gametes utilised in the different age distribution reflects the treatment indication. Meanwhile, within the group of the youngest women is more frequent a sperm donation (58.3%), the using of donated oocyte growing considerably with the age of the recipient women.

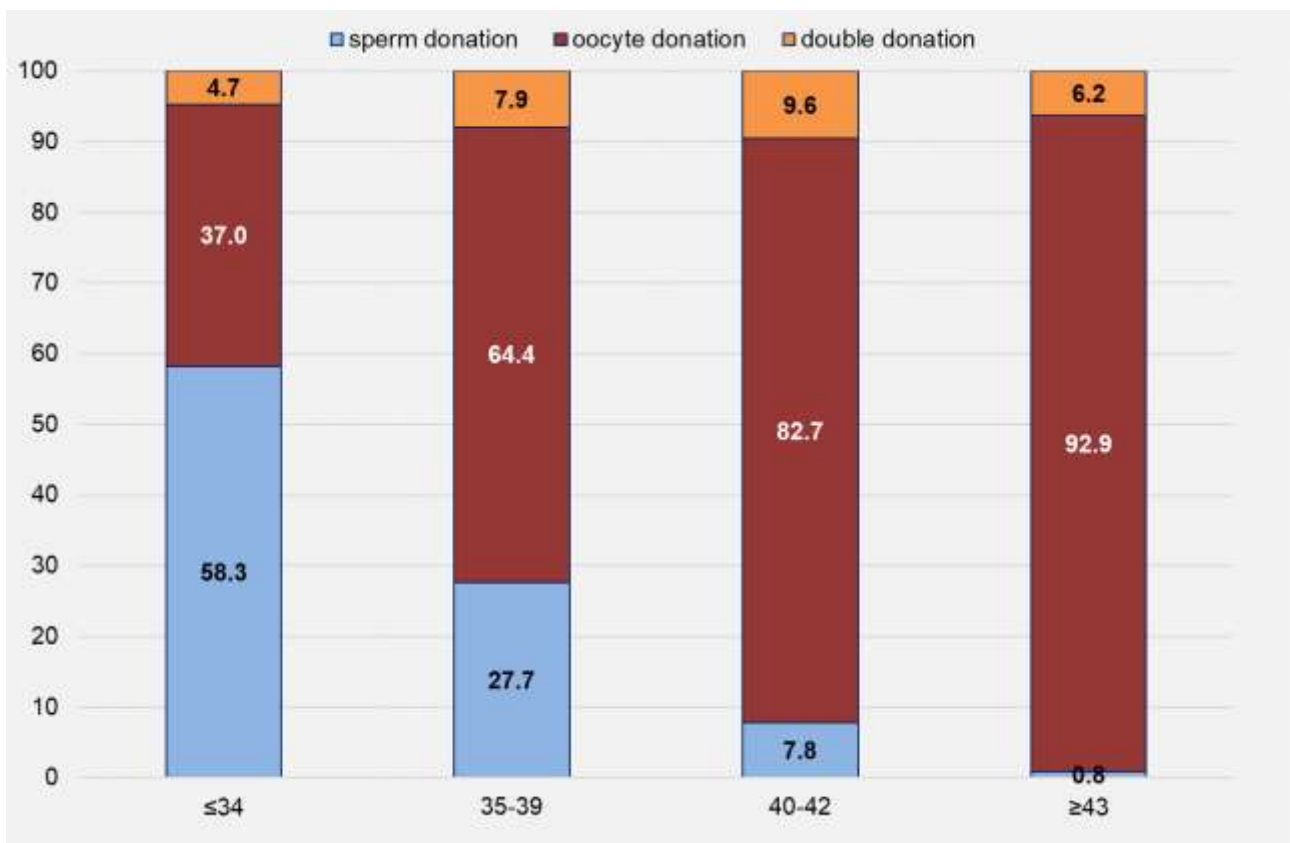


Figure 22. Distribution of donated gametes by recipient female age groups, 2021.

### 2.3.3. What was the percentage of transfers that result in pregnancies in ART donor cycles in 2021?

Figure 23 shows the pregnancy rate per transfer in ART donor techniques. In 2021, 4,891 pregnancies were achieved using ART techniques with donated gametes. Of these pregnancies, 536 were obtained after sperm donation, 987 after fresh oocyte donation, 3,013 after cryopreserved oocyte donation and 355 after double donation. In the case of sperm donation the pregnancy rate per transfer is 37.9%, for fresh egg donation 42.7%, for cryopreserved egg donation 40.6%, and for double donation 41.8%.

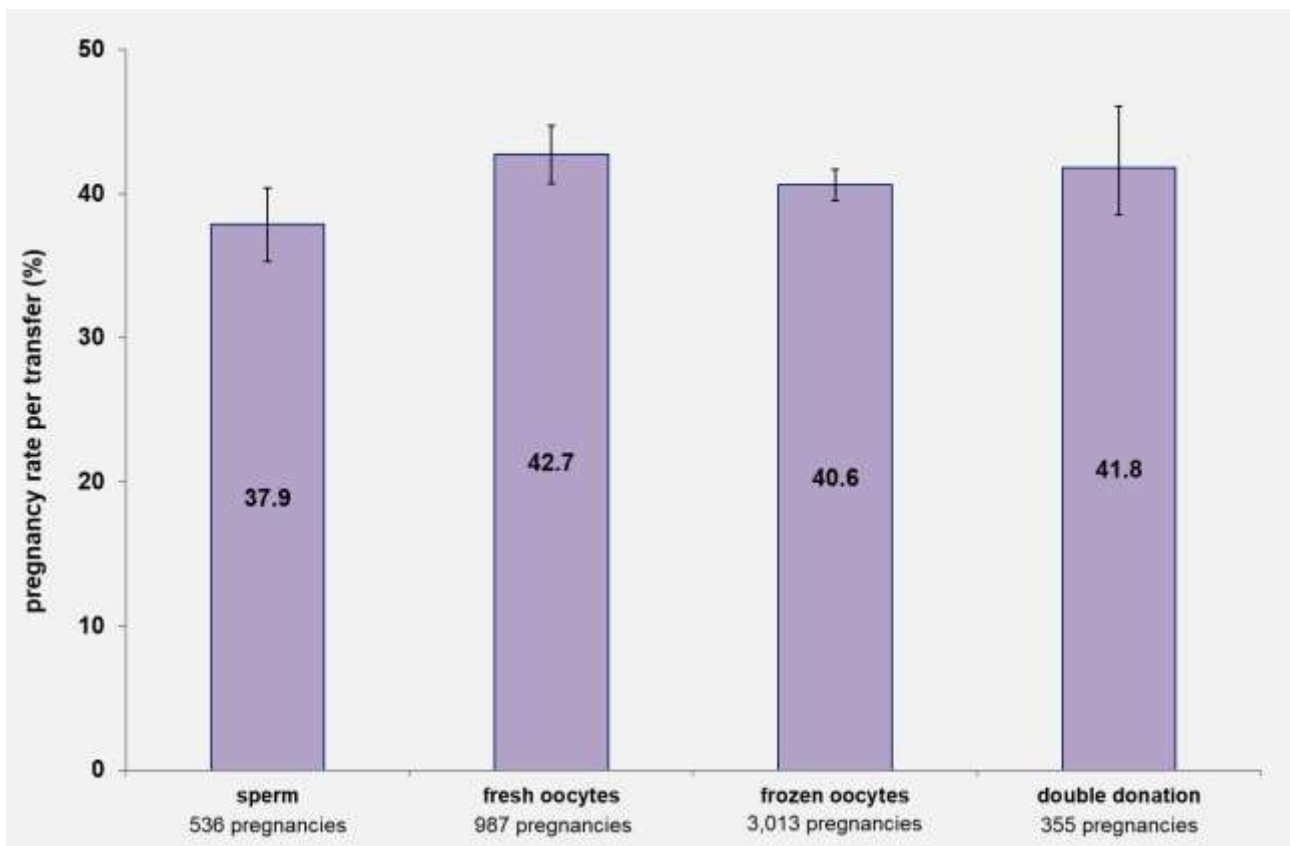


Figure 23. Distribution of pregnancy rate per transfer using donor gametes, 2021.

### 2.3.3. What were the outcomes of the monitored pregnancies in ART donor cycles in 2021?

Figure 24 shows the outcomes of the 4,357 monitored clinical pregnancies obtained from the application of ART donor procedures in Italy in 2021. Of the 456 monitored pregnancies obtained from sperm donation 6.1% resulted in multiple deliveries and 20.4% in an abortion. In frozen donor oocyte cycles the multiple deliveries rate (3.9%) were significantly higher than in fresh donor oocyte ones (1.8%), meanwhile the percentage of abortion were similar (19.1% and 21.1% respectively). The percentage of abortions seems to be lower when both donated gametes are used rather than just one, but the low number of pregnancies obtained with a double donation does not allow speculation.

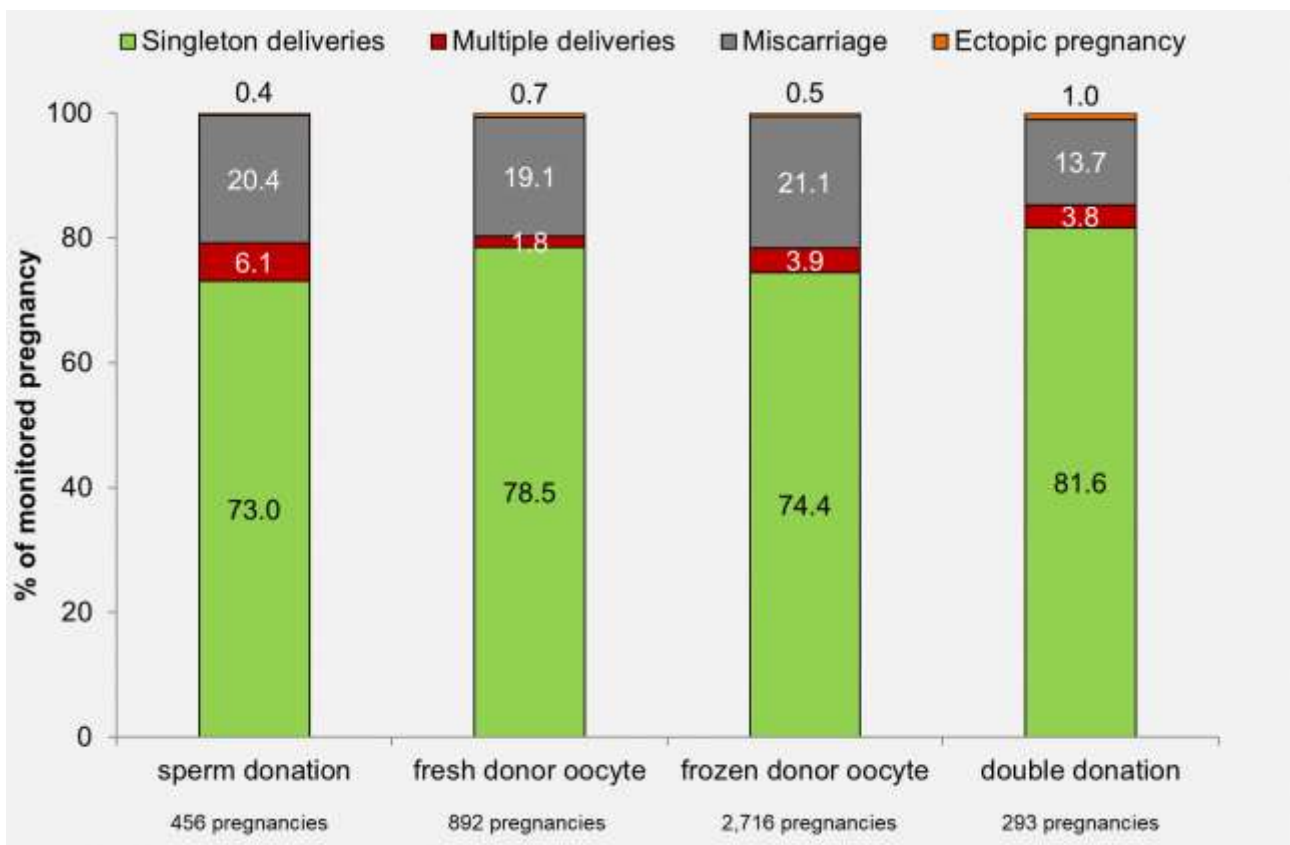


Figure 24. Comparison of the outcomes of monitored clinical pregnancies that resulted from ART donor cycles, 2021.

## 2.4. PGT (Pre-implantation Genetic Testing) activity

During an ART treatment, some investigation could be performed to analyse the DNA from embryos (at cleavage stage or blastocyst) for HLA-typing or for determining genetic abnormalities. These investigations include:

- **PGT-A** - test for the detection of aneuploidies;
- **PGT-M** – test for monogenic/single defects;
- **PGT-SR** – tests for chromosomal structural rearrangements.

### 2.4.1. Which types of genetic tests were performed in ART cycles in 2021?

PGT activity, recorded from 62 centres, involved 5,195 tests performed. **Figure 25** shows the distribution of the application of PGT cycles in Italy with a majority of PGT-A test performed (94.9% if considering also in combination with another test). The application of PGT resulted in a total of 1,587 pregnancies (48.4% per transfer) and 1,291 deliveries (39.4% per transfer). Please check on summary table ([see page 58](#)) for more detailed data on activity and outcomes regarding trend on PGT cycles.

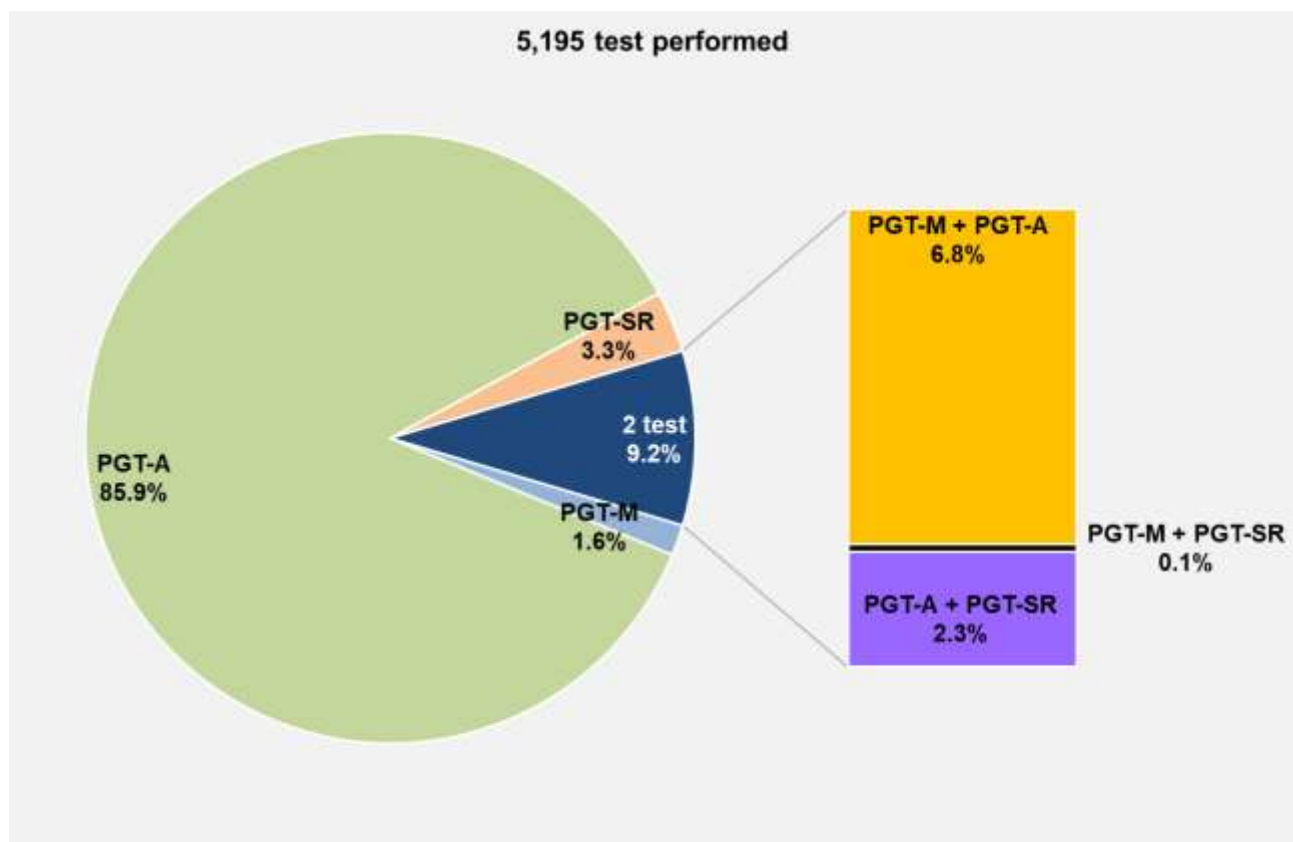


Figure 25. Distribution of PGD/PGS tests, 2021.

## 2.4.2. Did the use of different genetic analysis in ART change over time?

Figure 22 shows the progress of the application of the preimplantation genetic tests in the different phases that occur in a complete cycle of ART. Since the first data collection on PGT cycles performed on 2014 activity, the number of centres performing at least one cycle increased from 22 in 2014 to 62 in 2021. At the same time, the number of analysis performed increased from 1,695 cycles in 2014 to 5,195 cycles in 2021. Since 2014, the Registry has been collected information on a total of 22,868 cycles in which genetic tests were performed, 7,136 pregnancies obtained and 5,739 children born alive. The children born alive with the application of techniques that involved carrying out PGT have increased, from 398 children in 2014 to 1,293 in 2021.

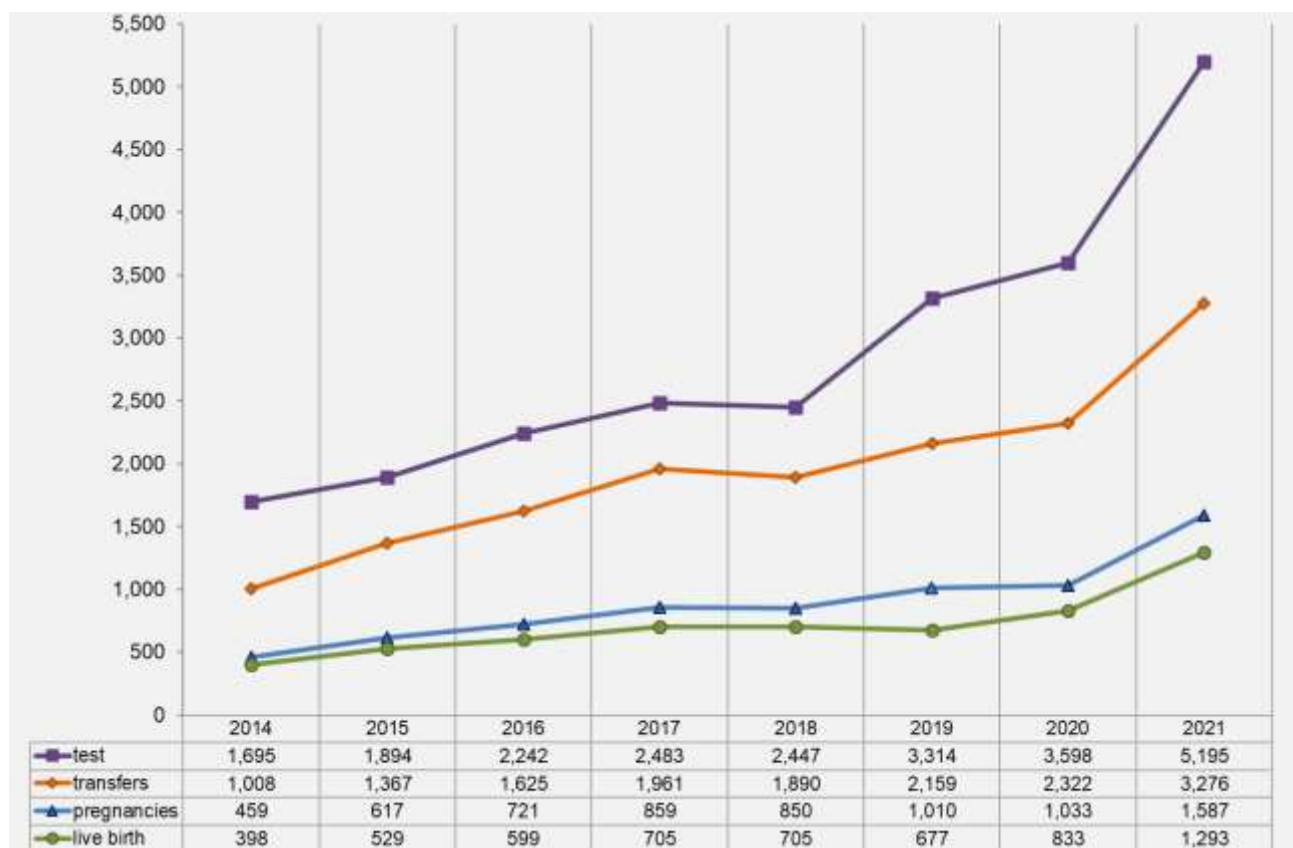


Figure 26. Time-trend of number of tests, transfer pregnancies and live birth after a PGT test, 2014-2021.

### 3. ART SAFETY INDICATORS

### 3.1. Safety in ART procedures

Although ART treatments are considered a safe medical procedure, in few cases some complications could arise during the treatment. These complications could arise at the moment of the ovarian stimulation or during pick-up procedure. Both could affect women’s health. Another type of complication for mother and child it is strictly related to embryo transfer policies. The transfer of more than one embryo could result in multiple pregnancies, therefore multiple deliveries and multiple births that could lead to prematurity, morbidity and perinatal mortality of the babies.

#### 3.1.1. Did the numbers of complications for ART cycles change over time?

In an ART treatment complications are considered:

- **Ovarian Hyper Stimulation Syndrome (OHSS):** An exaggerated systemic response to ovarian stimulation characterized by a wide spectrum of clinical and laboratory manifestations. It may be classified as mild, moderate or severe according to the degree of complications<sup>3</sup>. It is registered as a complication in the ART Register when it is diagnosed as “severe” (at least grade 3).
- **Bleeding:** Significant bleeding, internal or external, after oocyte aspiration retrieval requiring hospitalization for blood transfusion, surgical intervention, clinical observation or other medical procedure<sup>3</sup>.
- **Infection:** The presence of a bacterial or viral infection that can occur during any surgical procedure.

Cases of bleedings and infections are decreasing during time, while the number of OHSS is quite stable.

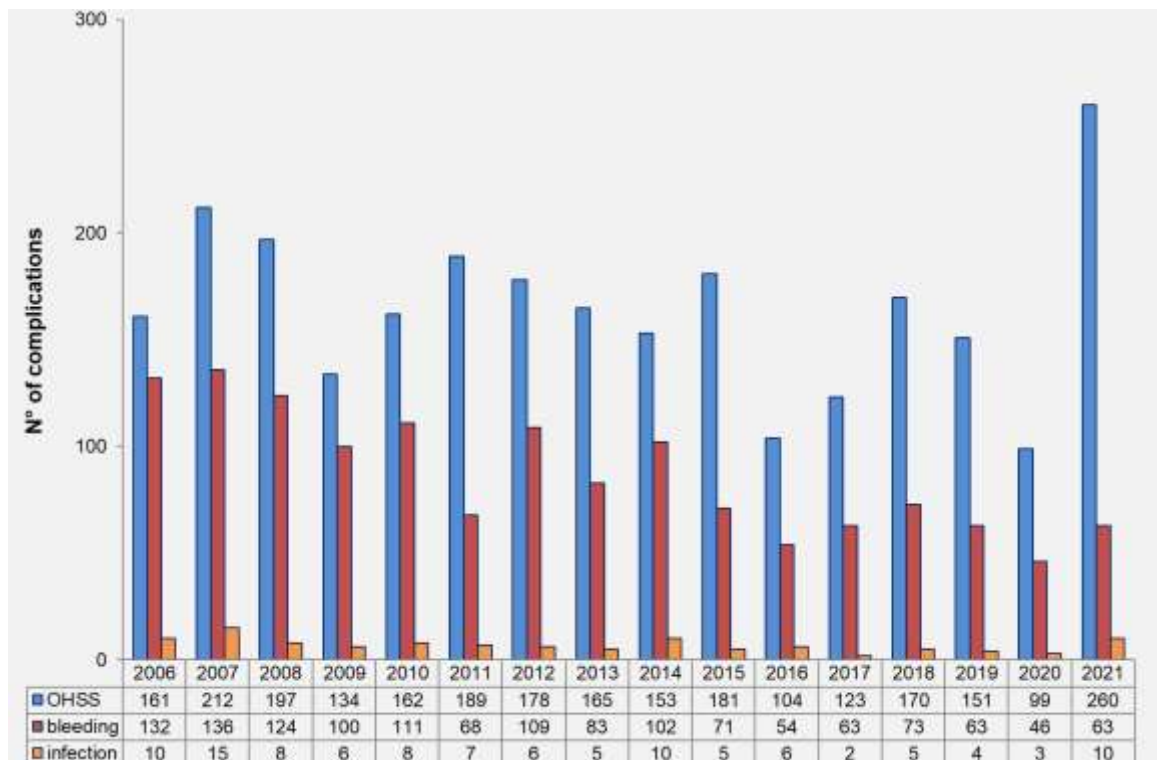
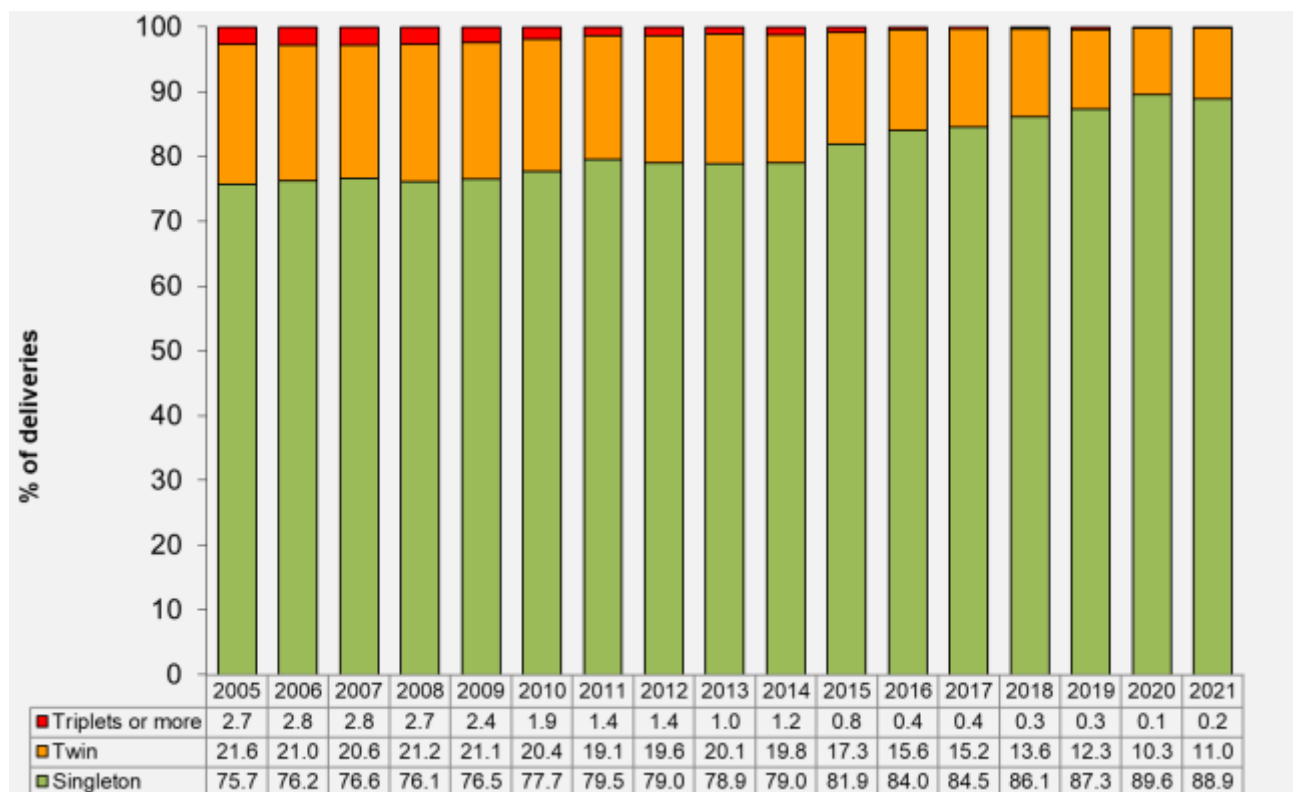


Figure 27. Time-trends of complications in fresh non-donor ART treatments, 2006-2021.

### 3.1.2. Did the percentages of multiple deliveries for ART non-donor cycles change over time?

**Figure 28** shows trends for multiple deliveries in fresh cycles. From 2005 to 2021, twin delivery percentage decreased from 21.6% to 11% while percentages of triplets and more deliveries decreased from 2.7% to 0.2%. These values are similar to the average European values of respectively 12.5% and 0.2% reported in 2018 EIM data<sup>1</sup>. We should remember that from 2004 till 2009 the Law obliged to transfer at once, all the embryos created for a maximum of three.



**Figure 28. Time-trends of deliveries from fresh cycles according to gestational order, 2005-2021.**

The same trends in percentage of the multiple deliveries are found in FER (**Figure 29**). On the other hand, the FO technique shows an unstable trend in twin deliveries (**Figure 30**).

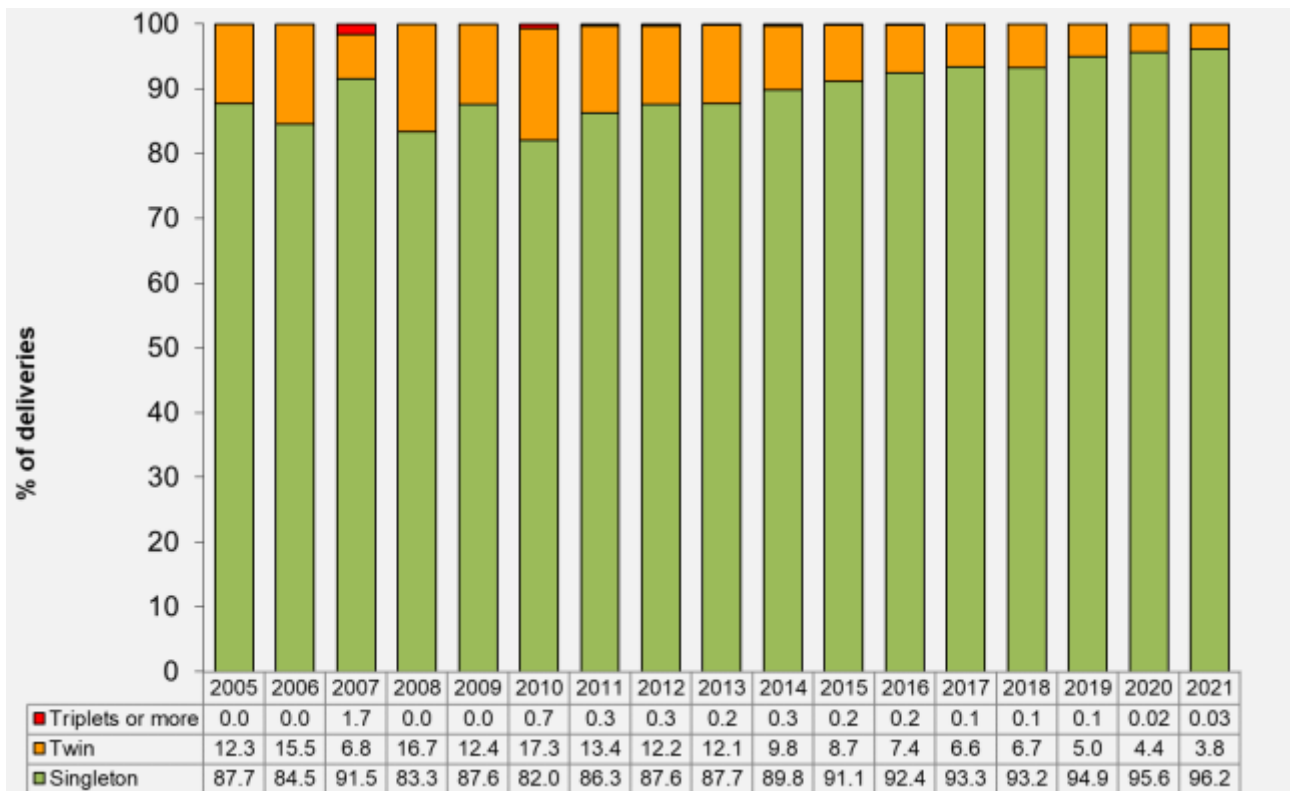


Figure 29. Time-trends of deliveries from FER thawing according to gestational order, 2005-2021

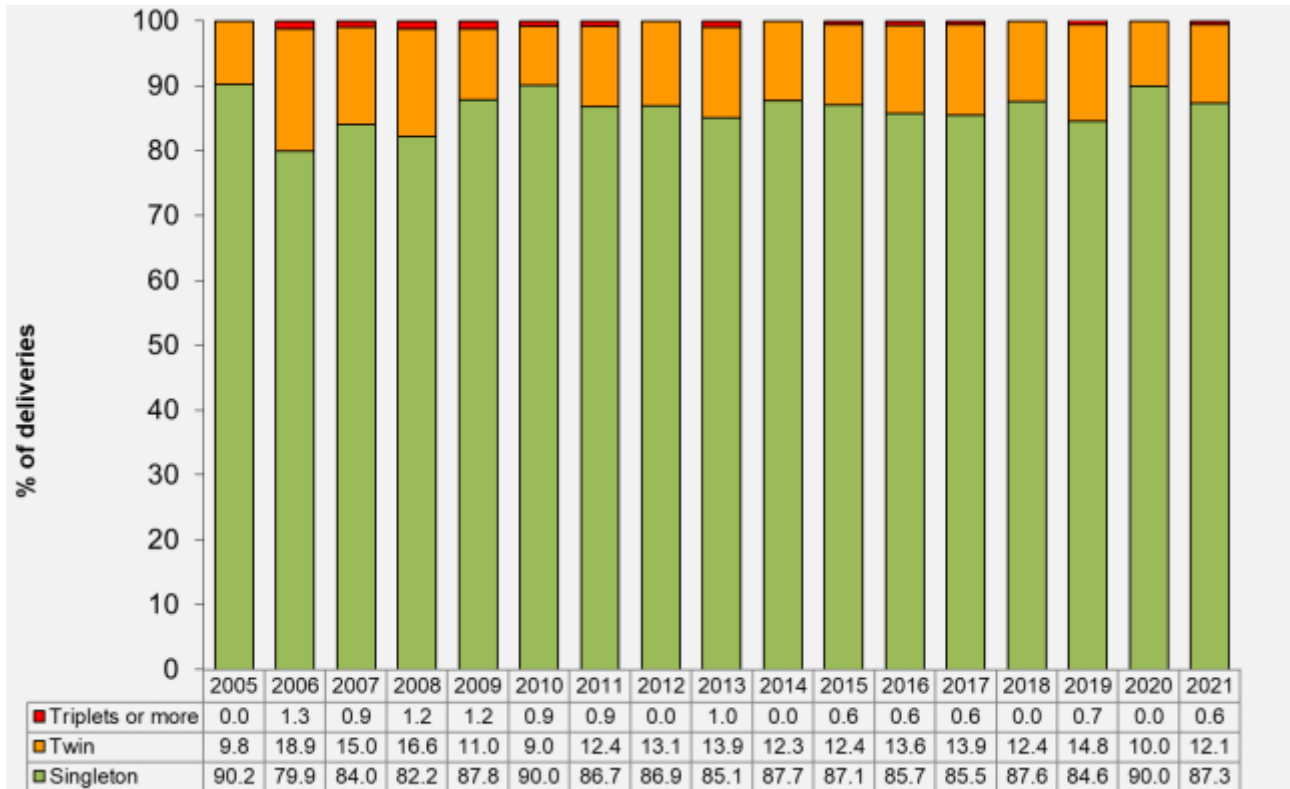


Figure 30. Time-trends of deliveries from FO thawing according to gestational order, 2005-2021

### 3.1.3. Did the percentages of preterm live babies change over time?

Figure 31 shows trends of ART preterm live born babies that are highly correlated with the multiplicity of deliveries.

Overall, the percentage of children born preterm has halved over time, decreasing from 25.8% in 2005 to 12.1% in 2021. Specifically, observing trends related to birth multiplicity, the rate of preterm singleton births decreased from 8.6% to 6.6%, while in multiple births, it decreased from 53.7% to 47.7%.

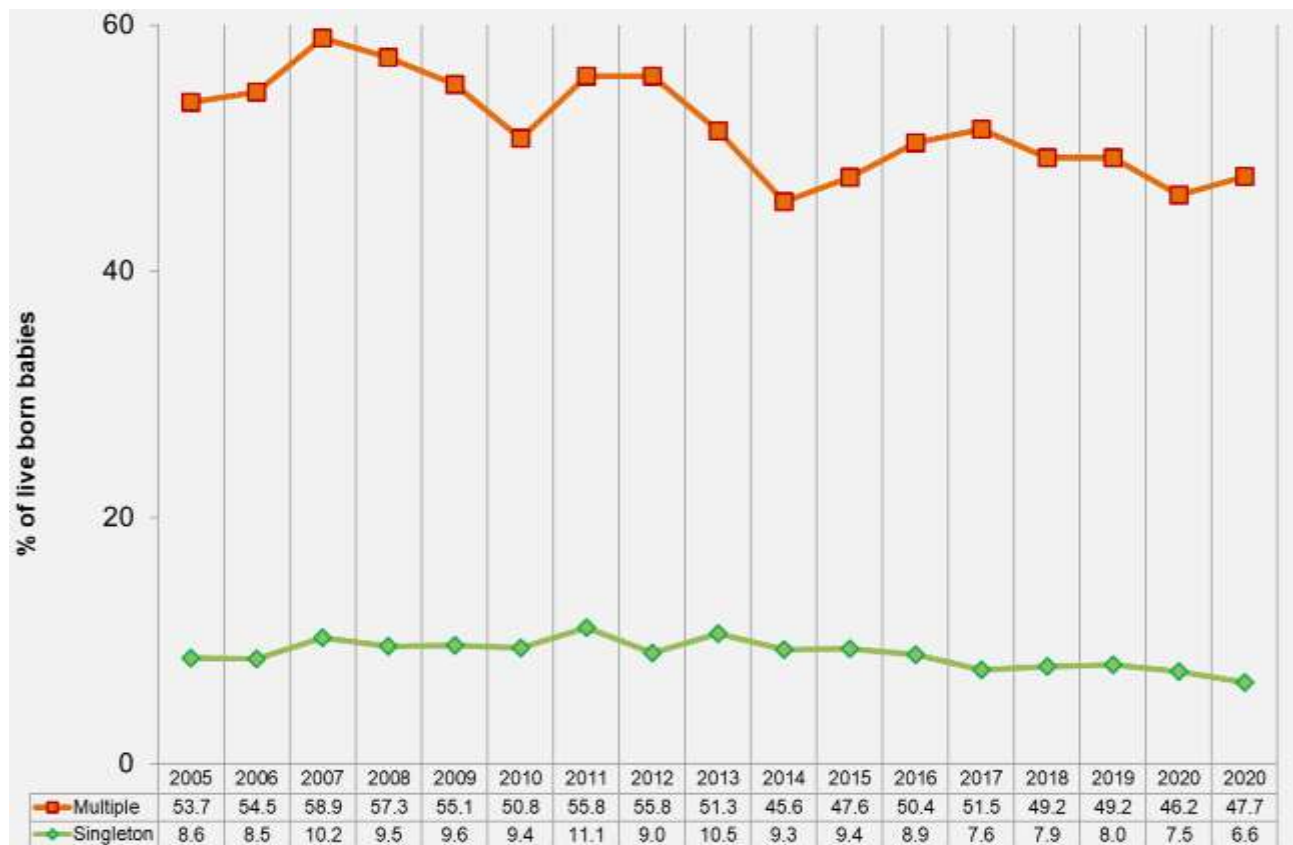


Figure 31. Time-trends of percentage of preterm ART live born babies (<37 week of gestation) by gestational order, 2005-2021.

### 3.1.4. Did the percentage of underweight live babies change over time?

Figure 32 shows the trends of ART live born babies underweight that are highly correlated with the multiplicity of deliveries as already described in respect to prematurity.

Overall, the percentage of children born underweight has also halved over time, decreasing from 26.7% in 2005 to 12.6% in 2021. Specifically observing trends based on birth multiplicity, the rate of underweight births decreased among singleton from 7.5% to 6.2% and among multiple births from 57.7% to 54%.

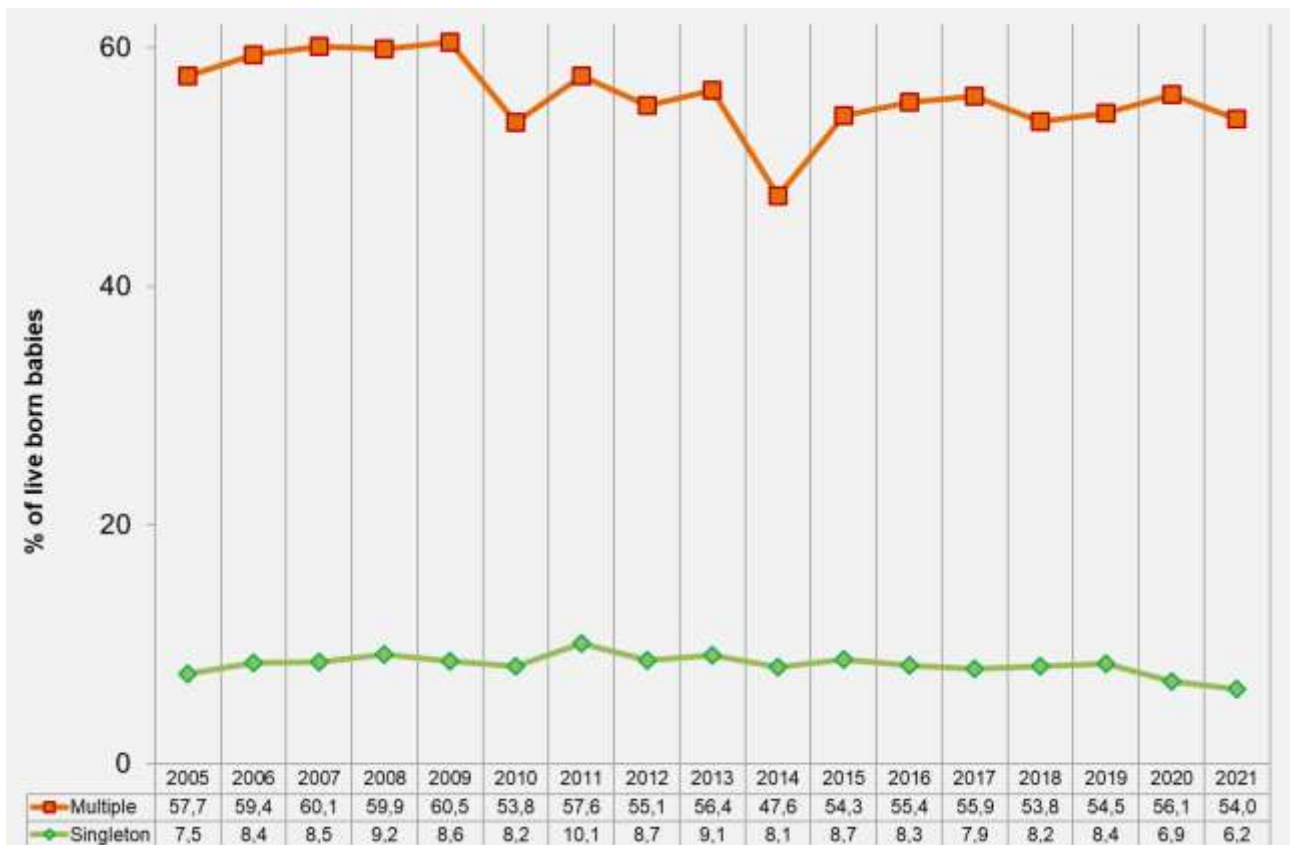


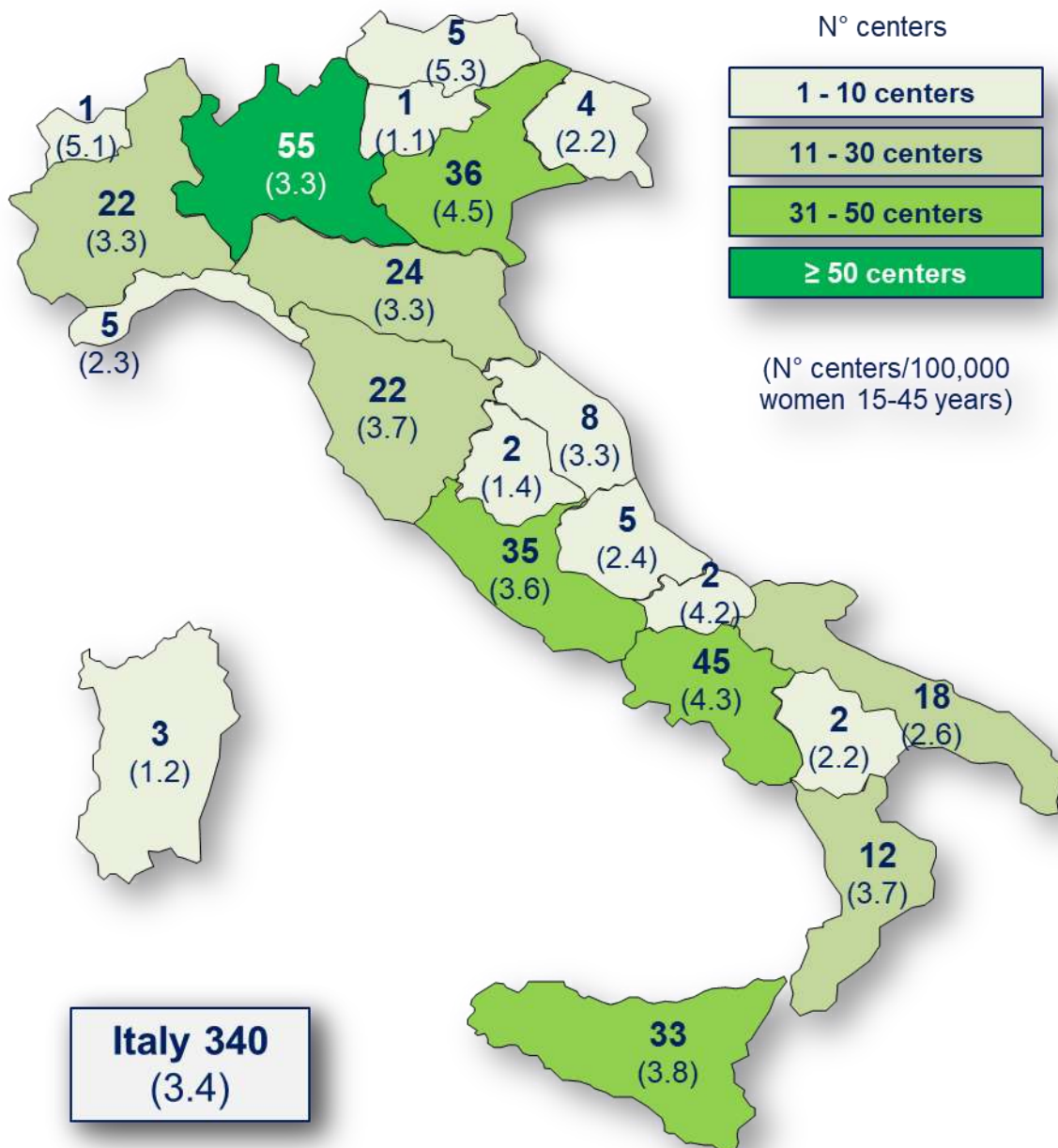
Figure 32. Time-trends of percentage of ART live born babies underweight (<2,500 gr) by gestational order, 2005-2021.

## 4. INTRA-UTERINE INSEMINATION PROCEDURES

## 4.1. Access to Intra-Uterine Insemination service

**Figure 33** shows the regional distribution of the 340 Intra-Uterine Insemination (IUI) authorized centres in 2021, but only 279 performed at least one homologous IUI cycle.

The majority of centres is concentrated in northern Italy (153, 45% of the total) and then in the south (120 centres, 35.3% of the total), irrespective of the amount of activity they performed . Even with some differences the access is almost good in all the regions.



**Figure 33. Regional distribution of IUI + ART authorized centres and in brackets the number of centres per 100,000 women of reproductive age (15-45 years)\*, 2021.**

\*Average resident population in Italy in 2021: Source ISTAT.

As shown in **Table 3**, in 2021 there were 340 authorized centres that perform IUI of which only 119 operating within the National Health System (public and private 35%) and 221 providing private service (65%). Most of public centres that could perform IUI in Italy were in the north: 57 out of 100 centres (57%).

**Table 3. IUI authorized centres distribution by region and type of service, 2021**

Region and geographical area	Total	Type of service					
		public		private covered by NHS		private	
		N	%	N	%	N	%
Piemonte	22	7	31.8	1	4.5	14	63.6
Valle d'Aosta	1	1	100.0	0	0.0	0	0.0
Lombardia	55	16	29.1	9	16.4	30	54.5
Liguria	5	4	80.0	0	0.0	1	20.0
<b>North West</b>	<b>83</b>	<b>28</b>	<b>33.7</b>	<b>10</b>	<b>12.0</b>	<b>45</b>	<b>54.2</b>
P.A. Bolzano	5	3	60.0	0	0.0	2	40.0
P.A. Trento	1	1	100.0	0	0.0	0	0.0
Veneto	36	12	33.3	2	5.6	22	61.1
Friuli Venezia Giulia	4	3	75.0	1	25.0	0	0.0
Emilia Romagna	24	10	41.7	0	0.0	14	58.3
<b>North East</b>	<b>70</b>	<b>29</b>	<b>41.4</b>	<b>3</b>	<b>4.3</b>	<b>38</b>	<b>54.3</b>
Toscana	22	7	31.8	5	22.7	10	45.5
Umbria	2	1	50.0	0	0.0	1	50.0
Marche	8	2	25.0	0	0.0	6	75.0
Lazio	35	5	14.3	1	2.9	29	82.9
<b>Central</b>	<b>67</b>	<b>15</b>	<b>22.4</b>	<b>6</b>	<b>9.0</b>	<b>46</b>	<b>68.7</b>
Abruzzo	5	3	60.0	0	0.0	2	40.0
Molise	2	0	0.0	0	0.0	2	100.0
Campania	45	9	20.0	0	0.0	36	80.0
Puglia	18	4	22.2	0	0.0	14	77.8
Basilicata	2	2	100.0	0	0.0	0	0.0
Calabria	12	3	25.0	0	0.0	9	75.0
Sicilia	33	4	12.1	0	0.0	29	87.9
Sardegna	3	3	100.0	0	0.0	0	0.0
<b>South and islands</b>	<b>120</b>	<b>28</b>	<b>23.3</b>	<b>0</b>	<b>0.0</b>	<b>92</b>	<b>76.7</b>
<b>Italy</b>	<b>340</b>	<b>100</b>	<b>29.4</b>	<b>19</b>	<b>5.6</b>	<b>221</b>	<b>65.0</b>

## 4.2. Efficacy safety and trends of IUI

### 4.2.1. Is the use of IUI-H increasing?

**Intra-Uterine Insemination (IUI)** is a medical procedure in which a laboratory processed sperm is placed into the women’s uterus to attempt a pregnancy<sup>3</sup>. It can be performed using husband semen (**IUI-Homologous**) or with the semen of an anonymous donor (**IUI-Donor**).

As described for ART techniques using donor gametes ([see page 35](#)) the IUI-D procedures have been permitted only after the Italian Constitutional Court sentence in April 2014. For the activity of IUI-D please check on Summary table for trend ([see page 60](#)) for more detailed data.

**Figure 34** shows the use of IUI-H from 2005 to 2021. The number of IUI-H cycles decreased from 26,292 to 14,999 after having reached his maximum of 33,335 cycles in 2009. There were no changes in pregnancy rate from 10.7% in 2005 to 10.5% in 2021. The average age of women is always 35 years.

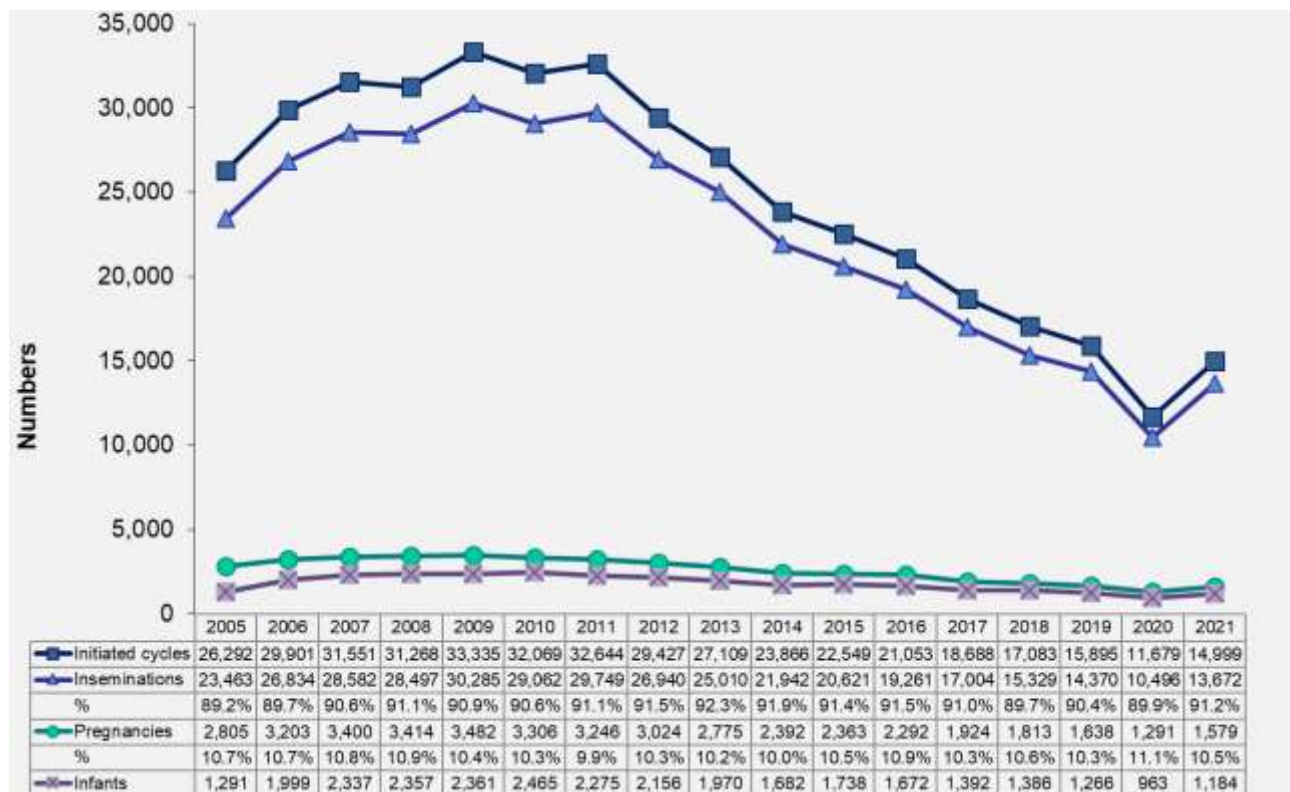


Figure 34. Time-trends of outcomes of IUI-H cycles, 2005-2021.

#### 4.2.2. Do percentages of IUI-H cycles resulting in pregnancies differ among women of different age groups?

Figure 35 shows percentages of insemination cycles for IUI-H that resulted in pregnancies and in deliveries among women of different age groups.

The probability to obtain a pregnancy and to reach a delivery in an IUI-H treatment is highly related to the age of women. The percentage in older women are very low: 3.4% for pregnancy and 1.1% for delivery in over 43.

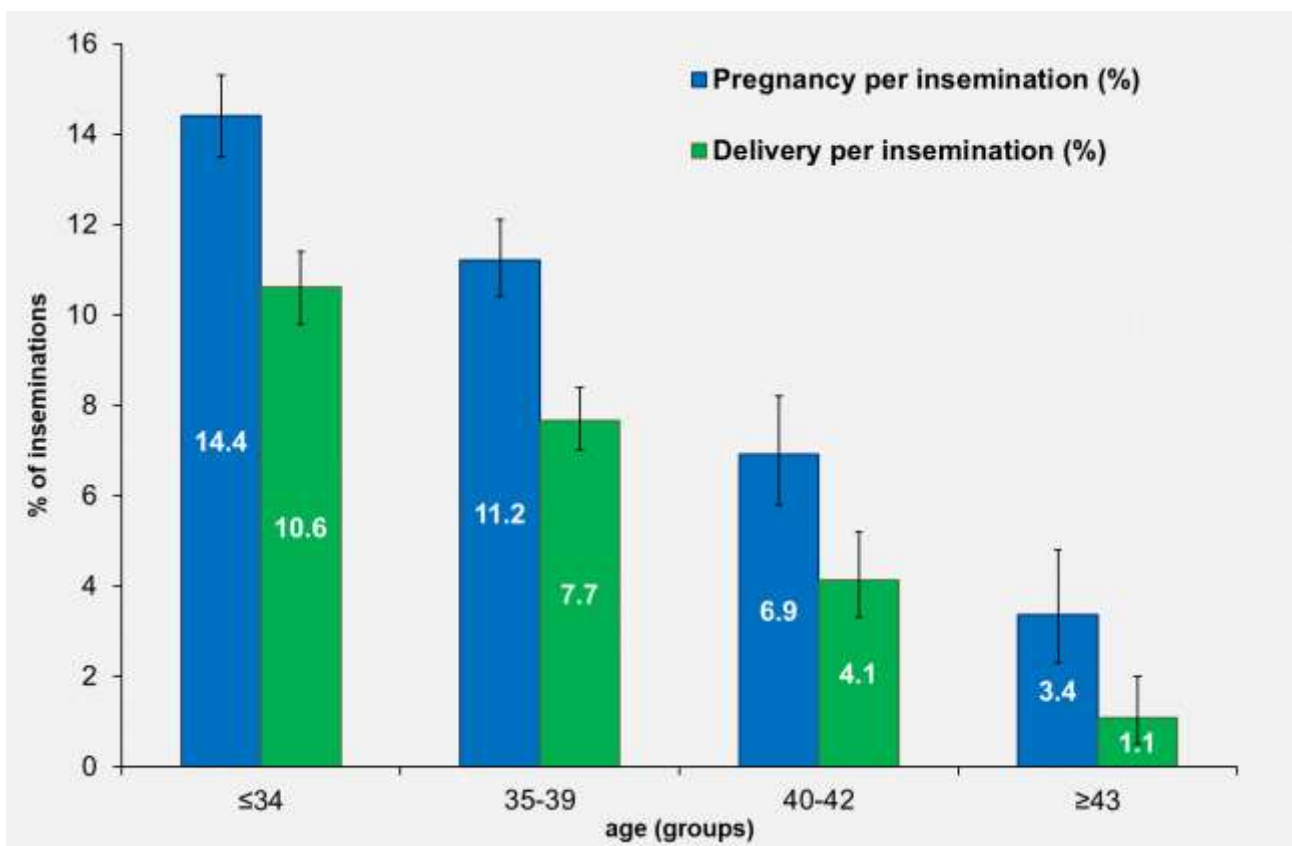


Figure 35. Pregnancy rates and delivery rates per insemination for IUI-H cycles by age groups of female patients, 2021.

#### 4.2.3. What were the outcomes of pregnancies obtained in IUI-H cycles in 2021?

Figure 36 shows the outcomes of the monitored clinical pregnancies obtained from the application of the homologous IUI in Italy in 2021. Of 1,380 monitored pregnancies in homoulogous IUI cycles 6% resulted in multiple deliveries and 18.7% had a miscarriage.

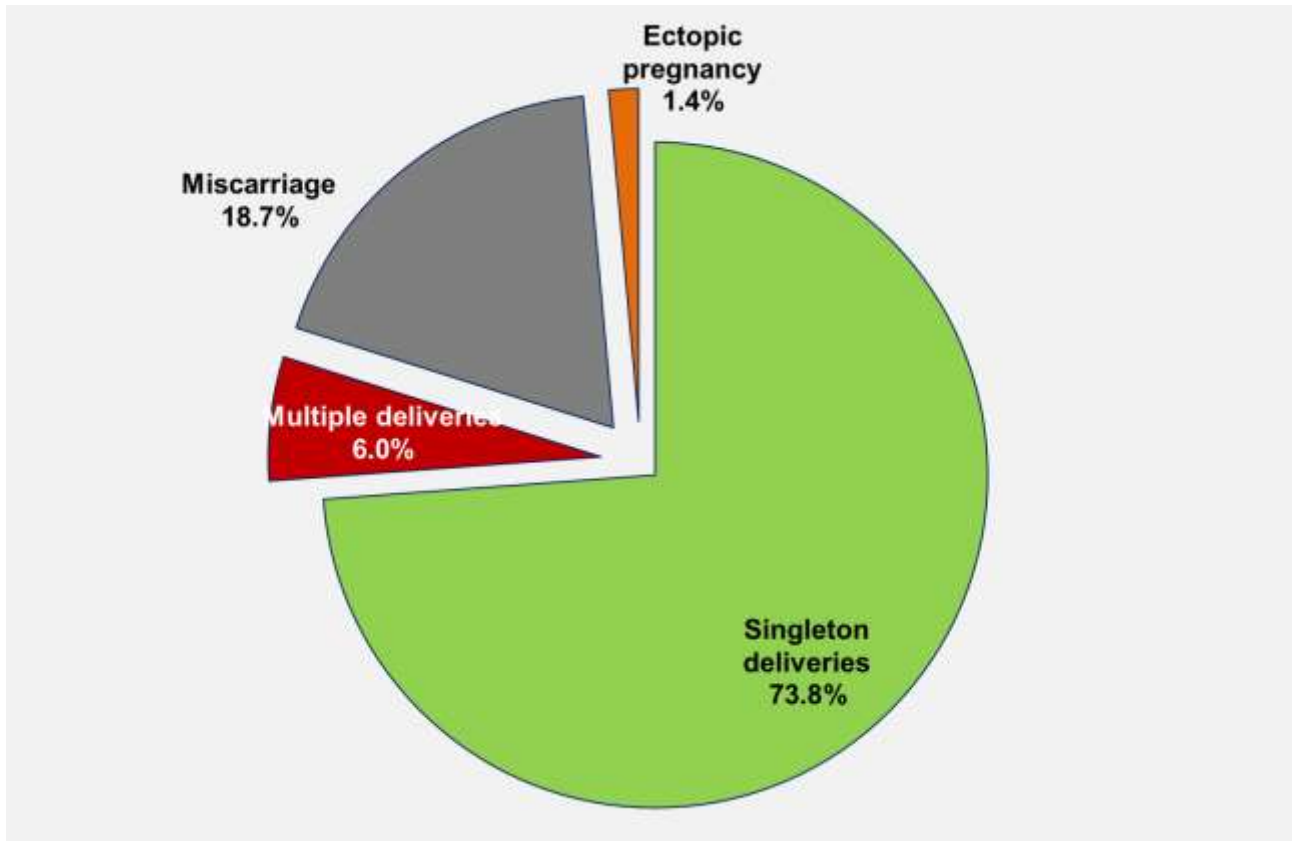


Figure 36. Outcomes of clinical pregnancies that resulted from IUI-H cycles, 2021.

#### 4.2.4. Did the numbers of complications for IUI-H cycles change over time?

Figure 37 shows that complications for OHSS have been decreasing continuously since 2007, going from 42 (0.15% of the inseminations) to 18 (0.13%). Complications for "other reasons" also continue to decrease to 3 (0.02%) but only after reaching their maximum value of 61 (0.21%) in 2011.

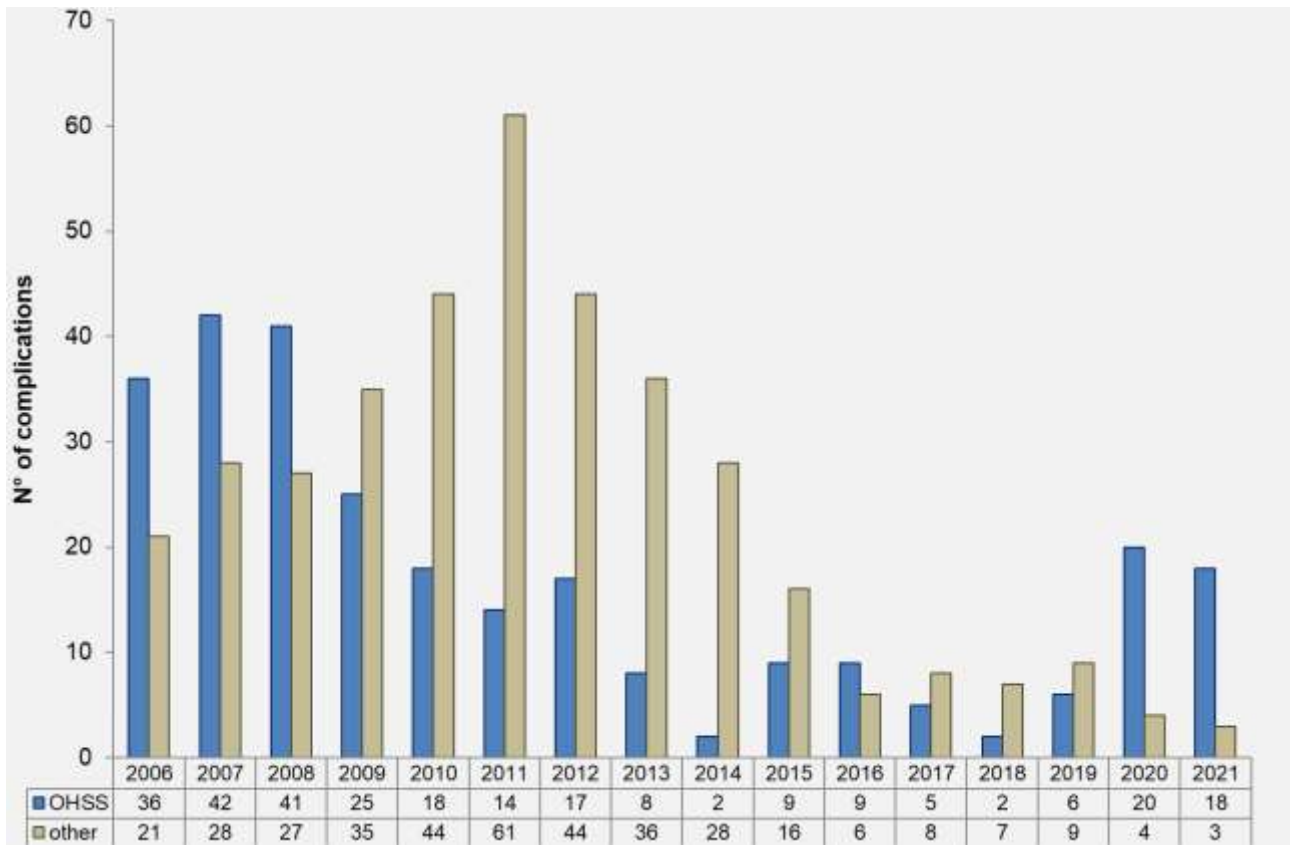
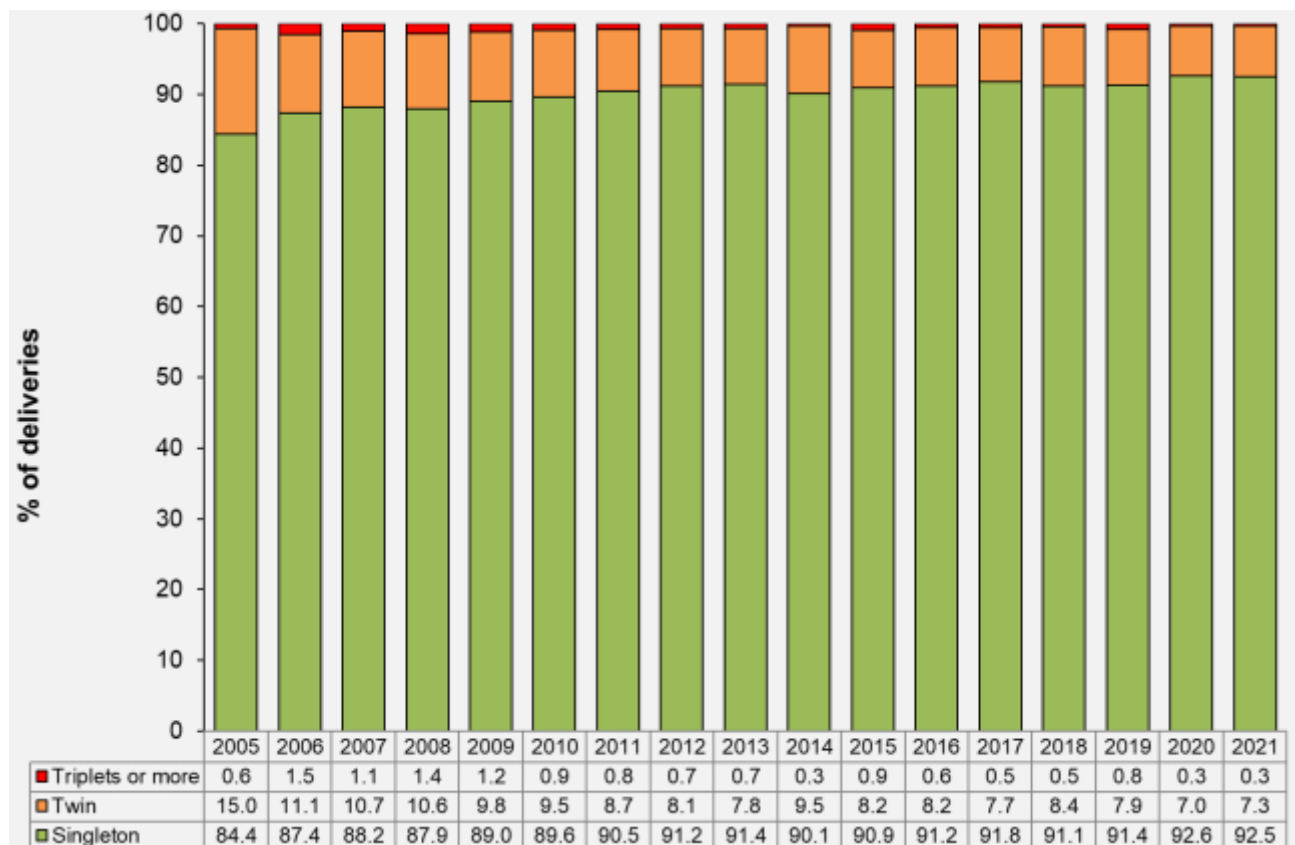


Figure 37. Time-trends of complications in IUI-Homologous treatments, 2006-2021.

#### 4.2.5. Did the percentages of multiple deliveries change over time for homologous intrauterine insemination cycles?

**Figure 38** shows time trends for multiplicity of deliveries in IUI-H cycles. From 2005 to 2021 twin deliveries rates decreased from 15% to 7.3% while percentage of triplets and more deliveries are quite stable. Since 2007, 9 deliveries out of 10 are singleton.



**Figure 38.** Time-trends of deliveries from IUI-H cycles according to gestational order, 2005-2021.

### 4.3. IUI donor cycles

#### 4.3.1. What was the outcome of IUI donor cycles in 2021?

In total 661 initiated cycles using donor sperm in IUI cycle started in 2021, 19.7% resulted in a clinical pregnancy and 15.3% resulted in a delivery. However, most of these cycles (about 80.3%) did not produce a pregnancy while a small proportion (1.8%) resulted in a pregnancy loss (i.e. ectopic pregnancy or miscarriage).

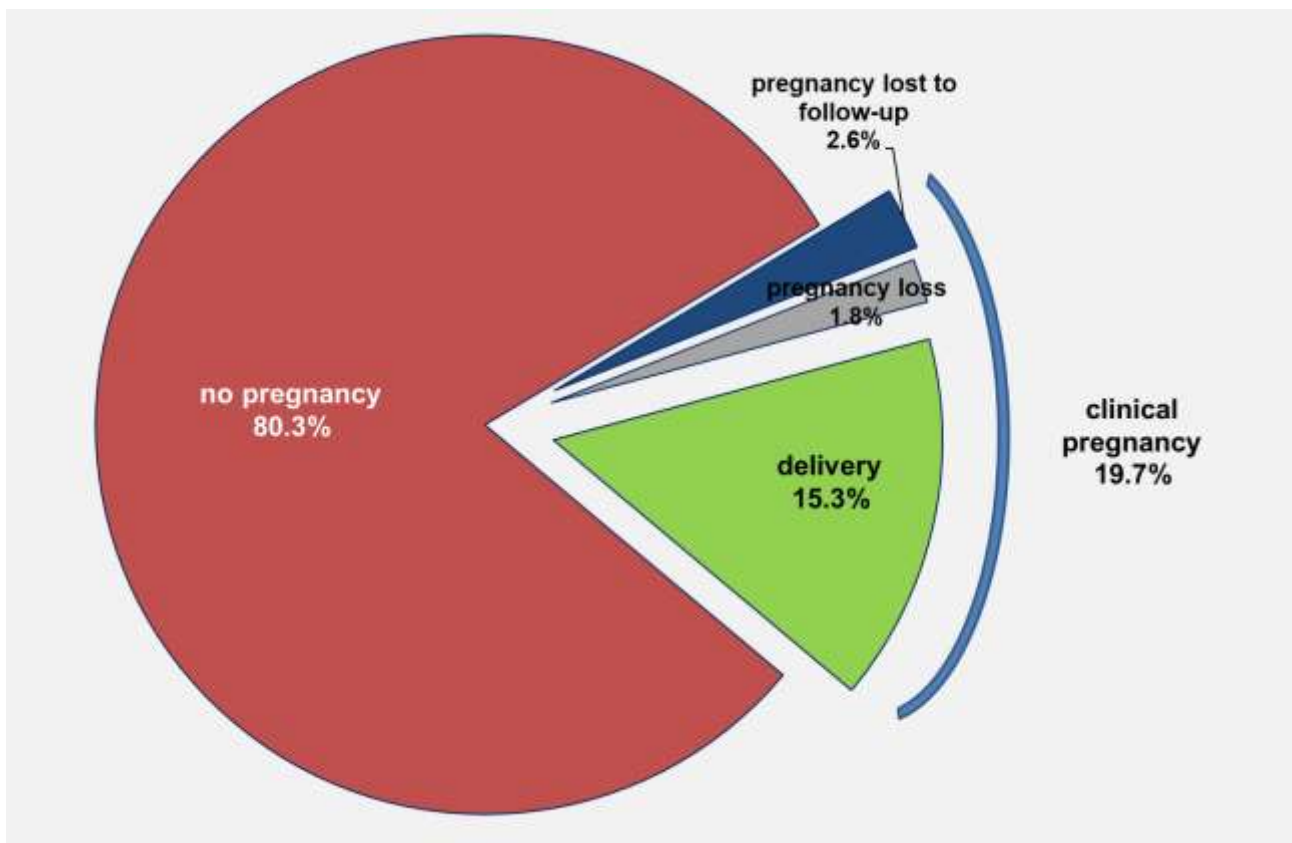


Figure 39. Outcome of IUI-D cycles, 2021 (661 initiated cycles).

APPENDIX

SUMMARY TABLE OF ACTIVITY AND  
OUTCOME OF ART PROCEDURES  
YEARS 2014-2021

## Summary table of activity and outcome of all ART procedures, 2014-2021

	2014	2015	2016	2017	2018	2019	2020	2021
N° Clinics	362	366	360	366	345	346	332	340
Clinics reporting data to ISS (%)	100	100	100	100	100	100	100	100
<b>ALL PROCEDURES (IUI-H, IUI-D, ART Non-donor and Donor)</b>								
N° Patients	70,826	74,292	77,522	78,366	77,509	78,618	57,243	86,090
N° Initiated cycles	90,957	95,110	97,656	97,888	97,509	99,062	76,390	108,067
N° Live born	12,720	12,836	13,582	13,973	14,139	14,162	11,226	16,625
ART infant per national births (%)	2.5	2.6	2.9	3.1	3.2	3.4	2.8	4.2
<b>ART activity (Fresh non-donor, Thawing non-donor, donor)</b>								
N° Patients	55,859	59,747	63,724	65,943	66,083	67,633	57,243	75,856
N° Initiated cycles	67,054	72,048	75,889	78,457	79,735	82,476	67,928	92,407
N° Pregnancies	13,642	14,391	15,405	16,793	17,402	17,787	14,462	21,695
Cumulative Pregnancy Rate per fresh initiated cycle (%)	24.3	24.8	25.4	27.5	28.4	29.3	29.7	33.4
Pregnancies lost to follow-up (%)	10.8	11.3	10.2	11.9	9.7	10.6	10.2	12.7
N° Deliveries	9,252	9,512	10,386	11,094	11,428	11,754	9,635	14,438
N° Live born	11,037	11,029	11,791	12,454	12,646	12,797	10,258	15,330
<b>ART SERVICES AVAILABILITY INDICATORS</b>								
ART Initiated cycles per 1 million women aged 15 and 45	5,860	6,341	6,781	7,106	7,341	7,697	6,525	9,077
ART Initiated cycles per 1 million inhabitants	1,103	1,175	1,237	1,275	1,297	1,341	1,117	1,529
<b>IUI-H and IUI-D activity</b>								
N° Patients	14,967	14,545	13,798	12,423	11,426	10,985	8,462	10,234
N° Initiated cycles	23,903	23,062	21,767	19,431	17,774	16,586	12,171	15,660
N° Pregnancies	2,399	2,466	2,429	2,078	1,952	1,767	1,400	1,709
Pregnancy Rate per cycle (%)	10.0	10.7	11.2	10.7	11.0	10.7	11.5	10.9
Pregnancies lost to follow-up (%)	18.2	16.8	15.0	13.9	11.7	11.2	11.9	12.6
N° Deliveries	1,530	1,649	1,629	1,396	1,369	1,249	968	1,203
N° Live born	1,683	1,807	1,791	1,519	1,493	1,365	1,047	1,295

## Summary table of activity and outcome of ART non-donor procedures, 2014-2021

	2014	2015	2016	2017	2018	2019	2020	2021
<b>FRESH CYCLES (Non-donor)</b>								
N° Patients	45,985	45,689	44,965	44,279	42,090	41,149	32,562	41,172
Average age calculated	36.7	36.7	36.8	36.7	36.7	36.8	36.9	36.8
N° Initiated cycles	55,705	55,329	53,906	53,014	51,087	50,324	38,728	50,297
N° aspirations	50,794	50,214	48,756	47,911	46,387	46,090	34,785	45,817
N° transfers	39,768	37,975	36,038	33,832	30,584	28,731	19,431	24,665
N° Pregnancies	10,834	10,081	9,326	9,310	8,307	7,753	5,197	7,258
Pregnancies rate per cycles (%)	19.4	18.2	17.3	17.6	16.3	15.4	13.4	14.4
Pregnancies rate per cycles without freeze-all strategy (%)	20.7	19.9	19.1	20.0	19.0	18.7	17.1	17.3
Pregnancies rate per aspirations (%)	21.3	20.1	19.1	19.4	17.9	16.8	14.9	15.8
Pregnancies rate per transfers (%)	27.2	26.5	25.9	27.5	27.2	27.0	26.7	29.4
Twin Pregnancies (%)	19.5	17.0	15.6	15.0	13.1	12.3	10.6	10.8
Triplet or more Pregnancies (%)	1.4	0.9	0.6	0.5	0.4	0.5	0.2	0.3
Pregnancies lost to follow-up (%)	11.9	13.1	11.2	13.4	10.9	10.4	12.8	15.1
N° Deliveries	7,277	6,498	6,196	6,029	5,458	5,151	3,327	4,652
N° Live born	8,848	7,695	7,172	6,951	6,186	5,797	3,660	5,156
<b>FROZEN/THAWED EMBRYOS (FER)</b>								
N° Patients	8,139	10,557	12,485	14,441	16,067	17,562	16,029	21,846
Average age calculated	35.4	35.2	35.3	35.3	35.2	35.3	35.3	35.3
N° thawing cycles	9,501	12,903	14,990	17,281	19,587	21,796	19,314	27,204
N° transfers	8,851	11,849	14,328	16,673	19,016	21,078	18,724	26,360
N° Pregnancies	2,448	3,379	4,128	5,059	5,995	6,758	6,096	9,268
Pregnancies rate per thawings (%)	25.8	26.2	27.5	29.3	30.6	31.0	31.6	34.1
Pregnancies rate per transfers (%)	27.7	28.5	28.8	30.3	31.5	32.1	32.6	35.2
Twin Pregnancies (%)	11.2	9.8	9.1	7.7	7.0	5.0	4.8	5.0
Triplet or more Pregnancies (%)	0.4	0.4	0.3	0.1	0.1	0.1	0.1	0.03
Pregnancies lost to follow-up (%)	5.5	5.6	6.7	7.9	6.6	10.2	6.8	11.8
N° Deliveries	1,747	2,403	2,890	3,486	4,127	4,412	4,212	6,158
N° Live born	1,929	2,609	3,104	3,703	4,393	4,637	4,382	6,370
<b>FROZEN/THAWED OOCYTES (FO)</b>								
N° Patients	1,530	1,418	1,341	1,281	1,201	1,248	977	1,254
Average age calculated	35.1	35.2	35.1	35.2	35.4	35.3	35.7	35.3
N° thawing cycles	1,639	1,529	1,460	1,391	1,318	1,361	1,099	1,445
N° transfers	1,295	1,221	1,187	1,146	1,036	1,071	817	1,056
N° Pregnancies	273	254	238	235	223	242	210	278
Pregnancies rate per thawings (%)	16.7	16.6	16.3	16.9	16.9	17.8	19.1	19.2
Pregnancies rate per transfers (%)	21.1	20.8	20.1	20.5	21.5	22.6	25.7	26.3
Twin Pregnancies (%)	12.5	10.6	12.2	12.8	9.9	11.2	10.0	12.1
Triplet or more Pregnancies (%)	0.8	0.4	1.3	0.4	0.0	0.4	0.0	0.6
Pregnancies lost to follow-up (%)	7.0	5.9	4.6	4.7	6.7	7.4	11.9	13.3
N° Deliveries	179	170	154	165	153	149	140	173
N° Live born	199	193	177	190	172	173	153	196

## Summary table of activity and outcome of ART with PGT analysis, 2014-2021

	2014	2015	2016	2017	2018	2019	2020	2021
<b>PGT activity</b>								
N° clinics reporting data (with at least 1 patient treated)	22	33	35	42	46	55	57	66
N° Patients	1,596	1,799	2,247	2,459	2,653	3,625	4,788	4,643
N° Tests performed	1,695	1,894	2,242	2,483	2,447	3,314	3,598	6,349
Patient average age	36.1	36.2	36.0	36.0	36.2	36.3	36.5	36.5
N° Pregnancies	459	617	721	859	850	1,010	1,033	1,587
Pregnancies rate per transfer (%)	45.5	45.1	44.4	43.8	45.0	46.8	44.5	48.4
Pregnancies lost to follow-up (%)	1.5	1.5	2.5	3.3	1.9	18.6	5.0	3.4
N° Deliveries	383	514	582	693	694	665	817	1,291
N° Live born	398	529	599	705	705	677	833	1,293

## Summary table of activity and outcome of ART procedures with gamete donation, 2014-2021

	2014	2015	2016	2017	2018	2019	2020	2021
<b>ART donor activity</b>								
N° clinics reporting data (with at least 1 patient treated)	17	69	83	91	101	96	104	114
N° Patients	205	2,083	4,933	5,941	6,725	7,674	7,675	11,584
N° Initiated cycles	209	2,287	5,533	6,771	7,743	8,995	8,787	13,461
N° Pregnancies	87	677	1,713	2,189	2,517	3,034	2,959	4,891
Pregnancies lost to follow-up (%)	26.4	15.7	13.9	15.5	13.7	12.1	12.8	10.9
N° Deliveries	49	441	1,146	1,414	1,690	2,042	1,956	3,455
N° Live born	61	532	1,338	1,610	1,895	2,190	2,063	3,608
<b>IUI-D activity (sperm donation)</b>								
N° clinics reporting data (with at least 1 patient treated)	13	52	65	62	73	76	65	82
N° Patients	32	379	517	487	488	514	374	469
N° Initiated cycles	37	513	714	743	691	691	492	661
N° Pregnancies	7	103	137	154	139	129	109	130
Pregnancies rate per cycles (%)	18.9	20.1	19.2	20.7	20.1	18.7	22.2	19.7
Pregnancies lost to follow-up (%)	85.7	30.1	16.8	16.9	16.5	12.4	15.6	13.1
N° Deliveries	1	61	98	110	93	90	72	101
N° Live born	1	69	119	127	107	99	84	111

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