

ART in Europe, 2018: results generated from European registries by ESHRE[†]

The European IVF Monitoring Consortium (EIM)[‡], for the European Society of Human Reproduction and Embryology (ESHRE)

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STUDY QUESTION: What are the data and trends on ART and IUI cycle numbers and their outcomes, and on fertility preservation (FP) interventions, reported in 2018 as compared to previous years?

SUMMARY ANSWER: The 22nd ESHRE report shows a continued increase in reported numbers of ART treatment cycles and children born in Europe, a decrease in transfers with more than one embryo with a further reduction of twin delivery rates (DRs) as compared to 2017, higher DRs per transfer after fresh IVF or ICSI cycles (without considering freeze-all cycles) than after frozen embryo transfer (FET) with higher pregnancy rates (PRs) after FET and the number of reported IUI cycles decreased while their PR and DR remained stable.

WHAT IS KNOWN ALREADY: ART aggregated data generated by national registries, clinics or professional societies have been gathered and analysed by the European IVF-monitoring Consortium (EIM) since 1997 and reported in 21 manuscripts published in *Human Reproduction* and *Human Reproduction Open*.

STUDY DESIGN, SIZE, DURATION: Data on medically assisted reproduction (MAR) from European countries are collected by EIM for ESHRE on a yearly basis. The data on treatment cycles performed between 1 January and 31 December 2018 were provided by either national registries or registries based on initiatives of medical associations and scientific organizations or committed persons of 39 countries.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Overall, 1422 clinics offering ART services in 39 countries reported a total of more than 1 million (1 007 598) treatment cycles for the first time, including 162 837 with IVF, 400 375 with ICSI, 309 475 with FET, 48 294 with preimplantation genetic testing, 80 641 with egg donation (ED), 532 with IVM of oocytes and 5444 cycles with frozen oocyte replacement (FOR). A total of 1271 institutions reported data on IUI cycles using either husband/partner's semen (IUI-H; n = 148 143) or donor semen (IUI-D; n = 50 609) in 31 countries and 25 countries, respectively. Sixteen countries reported 20 994 interventions in pre- and post-pubertal patients for FP including oocyte, ovarian tissue, semen and testicular tissue banking.

MAIN RESULTS AND THE ROLE OF CHANCE: In 21 countries (21 in 2017) in which all ART clinics reported to the registry, 410 190 treatment cycles were registered for a total population of ~ 300 million inhabitants, allowing a best estimate of a mean of 1433 cycles performed per million inhabitants (range: 641–3549). Among the 39 reporting countries, for IVF, the clinical PR per aspiration slightly decreased while the PR per transfer remained similar compared to 2017 (25.5% and 34.1% in 2018 versus 26.8% and 34.3% in 2017). In ICSI, the corresponding rates showed similar evolutions in 2018 compared to 2017 (22.5% and 32.1% in 2018 versus 24.0% and 33.5% in 2017). When freeze-all cycles were not considered for the calculations, the clinical PRs per aspiration were 28.8% (29.4% in 2017) and

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27.3% (27.3% in 2017) for IVF and ICSI, respectively. After FET with embryos originating from own eggs, the PR per thawing was 33.4% (versus 30.2% in 2017), and with embryos originating from donated eggs 41.8% (41.1% in 2017). After ED, the PR per fresh embryo transfer was 49.6% (49.2% in 2017) and per FOR 44.9% (43.3% in 2017). In IVF and ICSI together, the trend towards the transfer of fewer embryos continues with the transfer of 1, 2, 3 and ≥ 4 embryos in 50.7%, 45.1%, 3.9% and 0.3% of all treatments, respectively (corresponding to 46.0%, 49.2%, 4.5% and 0.3% in 2017). This resulted in a reduced proportion of twin DRs of 12.4% (14.2% in 2017) and similar triplet DR of 0.2%. Treatments with FET in 2018 resulted in twin and triplet DRs of 9.4% and 0.1%, respectively (versus 11.2% and 0.2%, respectively in 2017). After IUI, the DRs remained similar at 8.8% after IUI-H (8.7% in 2017) and at 12.6% after IUI-D (12.4% in 2017). Twin and triplet DRs after IUI-H were 8.4% and 0.3%, respectively (in 2017: 8.1% and 0.3%), and 6.4% and 0.2% after IUI-D (in 2017: 6.9% and 0.2%). Among 20 994 FP interventions in 16 countries (18 888 in 13 countries in 2017), cryopreservation of ejaculated sperm ($n = 10\,503$, versus 11 112 in 2017) and of oocytes ($n = 9123$ versus 6588 in 2017) were the most frequently reported.

LIMITATIONS, REASONS FOR CAUTION: The results should be interpreted with caution as data collection systems and completeness of reporting vary among European countries. Some countries were unable to deliver data about the number of initiated cycles and/or deliveries.

WIDER IMPLICATIONS OF THE FINDINGS: The 22nd ESHRE data collection on ART, IUI and FP interventions shows a continuous increase of reported treatment numbers and MAR-derived livebirths in Europe. Although it is the largest data collection on MAR in Europe, further efforts towards optimization of both the collection and reporting, with the aim of improving surveillance and vigilance in the field of reproductive medicine, are awaited.

STUDY FUNDING/COMPETING INTEREST(S): The study has received no external funding and all costs are covered by ESHRE. There are no competing interests.

Key words: IVF / ICSI / IUI / egg donation / frozen embryo transfer / surveillance / vigilance / registry / data collection / fertility preservation

Introduction

This is the 22nd annual report of the European IVF-monitoring Consortium (EIM) under the umbrella of ESHRE, assembling the data on ART, IUI and fertility preservation (FP) as reported by 39 participating European countries in 2018 ([Supplementary Table S1](#) and [Supplementary Data](#)).

Eighteen previous annual reports published in *Human Reproduction* (<https://www.eshre.eu/Data-collection-and-research/Consortia/EIM/Publications.aspx>) and three in *Human Reproduction Open* ([De Geyter et al., 2020a](#); [Wyns et al., 2020, 2021](#)) covered data on treatment cycles collected on a yearly basis from 1997 to 2017. As in previous reports, the printed version contains the five most relevant tables. Twenty additional [supplementary tables](#) ([Supplementary Tables S1–SXX](#)) are available online on the publisher's homepage. To allow easy comparison and assessment of trends, the presentation of the data is consistent with previous reports. For the third consecutive year, data on FP were collected and added to this report.

Materials and methods

Data were collected on an aggregate basis and were provided by 39 European countries, covering treatments with IVF, ICSI, frozen embryo transfer (FET), egg donation (ED), IVM, preimplantation genetic testing (PGT; pooled data), frozen oocyte replacement (FOR), IUI with husband's/partner's semen (IUI-H) and with donor semen (IUI-D). The report includes treatments started between 1 January and 31 December in 2018. Data on pregnancies and deliveries represent the outcomes of treatments performed in 2018. Aggregated data on FP include numbers and types of cryopreserved material and interventions

for use of cryostored material between 1 January and 31 December in 2018.

The national representatives of the 44 countries that are members of the EIM consortium were asked to fill out the survey with the same data requirements as in 2017. A total of 10 modules on specific topics/questions were sent using software designed for the requirements of this data collection (Dynamic Solutions, Barcelona, Spain). Any identified inconsistency was clarified through direct contacts between the administrator of the ESHRE central office (V.G.) and the national representative.

The data were analysed and presented similarly to previous reports. Footnotes to the tables were added to clarify some results reported by individual countries, when applicable.

The terminology used was based on the glossary of The International Committee for Monitoring Assisted Reproductive Technology ([Zegers-Hochschild et al., 2017](#)).

Results

Participation and data completeness

[Table 1](#) shows the number of clinics providing ART services with the different treatment modalities they offer and institutions performing IUI (IUI-H and IUI-D). Compared to 2017, the total number of reporting clinics (1422 versus 1381 in 2017) and number of reported treatments (1 007 598 versus 940 503 in 2017, +7.1%) increased. Among the 51 European countries, 44 are EIM members including 28 that were members of the European Union (EU) at that time and 39 (39 in 2017) provided data ([Supplementary Table S1](#)). Non-EIM members are mainly small countries not offering ART services. Croatia, Cyprus,

Table 1 Treatment frequencies after ART in European countries in 2018.

| Country | IVF clinics in the country | | | | | | | | | | | Cycles/million* | | |
|-------------------------------------|----------------------------|----------------------|----------|-------------------|--------|--------|--------|------|------|-----|------|-----------------|-------------|------------|
| | IVF clinics | Included IVF clinics | IUI labs | Included IUI labs | IVF | ICSI | FET | PGT | ED | IVM | FOR | All | Women 15–45 | Population |
| Albania | 8 | 1 | 10 | 1 | 0 | 86 | 69 | 21 | 24 | 0 | 2 | 202 | | |
| Armenia | 7 | 6 | 10 | 6 | 786 | 967 | 2156 | 24 | 815 | | | 4748 | | |
| Austria | 30 | 30 | 0 | 0 | 1701 | 5703 | 3161 | 0 | 61 | | | 10 626 | 6611 | 1209 |
| Belarus | 8 | 7 | 10 | 7 | 1253 | 2039 | 992 | 69 | 115 | | 1 | 4469 | | |
| Belgium | 18 | 18 | 28 | 28 | 2554 | 13 783 | 13 821 | 1397 | 1603 | 167 | 91 | 33 416 | 15 449 | 2891 |
| Bosnia-Herzegovina, Federation part | 10 | 1 | 10 | 1 | 0 | 111 | 58 | 0 | 0 | | | 169 | | |
| Bulgaria | 37 | 37 | 38 | 38 | 1078 | 8404 | 2469 | 0 | 1140 | | | 13 091 | 10 580 | 1855 |
| Czech Republic | 48 | 48 | 0 | 0 | 1954 | 13 481 | 14 749 | 0 | 5007 | | | 35 191 | 18 310 | 3294 |
| Denmark | 19 | 19 | 54 | 52 | 6479 | 5536 | 6912 | 536 | 1120 | 0 | 33 | 20 616 | 19 181 | 3549 |
| Estonia | 6 | 6 | 6 | 6 | 672 | 1394 | 1044 | 0 | 212 | 0 | 4 | 3326 | 15 948 | 2674 |
| Finland | 16 | 16 | 20 | 20 | 2538 | 1834 | 3736 | 279 | 714 | | | 9101 | 9241 | 1643 |
| France | 103 | 102 | 180 | 179 | 20 821 | 41 021 | 41 258 | 1646 | 1532 | 127 | 479 | 106 884 | | |
| Germany | 140 | 134 | 0 | 0 | 21 007 | 54 719 | 29 334 | | 0 | | 268 | 105 328 | | |
| Greece | 43 | 33 | 0 | 31 | 2111 | 14 174 | 5623 | 575 | 4875 | 20 | 76 | 27 454 | | |
| Hungary | 14 | 11 | 21 | 13 | | 7819 | 1186 | | 0 | | | 9005 | | |
| Iceland | 1 | 1 | 1 | 1 | 301 | 188 | 307 | 0 | 101 | 0 | 1 | 898 | 12 910 | 2614 |
| Ireland | 9 | 2 | 2 | 1 | 291 | 316 | 408 | 609 | 2 | 0 | 3 | 1629 | | |
| Italy | 202 | 202 | 345 | 345 | 7871 | 43 215 | 19 587 | 3441 | 5947 | | 1318 | 81 379 | 7650 | 1309 |
| Kazakhstan | 8 | 8 | 0 | 0 | 1555 | 4955 | 3489 | 829 | 1187 | | | 12 015 | 2878 | 641 |
| Latvia | 6 | 3 | 6 | 3 | 143 | 439 | 359 | 46 | 83 | 0 | 1 | 1071 | | |
| Lithuania | 6 | 6 | 6 | 6 | 472 | 405 | 201 | 7 | 3 | 0 | 0 | 1088 | 2335 | 389 |
| Luxembourg | 1 | 1 | 0 | 0 | 175 | 560 | 397 | | 0 | 0 | 0 | 1132 | 8760 | 1868 |
| Malta | 2 | 2 | 2 | 0 | 0 | 249 | 2 | 0 | 0 | 0 | 73 | 324 | 3769 | 722 |
| Moldova | 4 | 3 | 5 | 3 | 0 | 1248 | 210 | | 0 | | | 1458 | | |
| Montenegro | 5 | 4 | 5 | 4 | 0 | 586 | 57 | | 0 | | | 643 | | |
| North-Macedonia | 7 | 5 | 1 | 0 | 438 | 2199 | 411 | 0 | 151 | 0 | 0 | 3199 | | |
| Norway | 11 | 11 | 11 | 11 | 4208 | 3161 | 4178 | 0 | 0 | | | 11 547 | 11 109 | 2150 |
| Poland | 45 | 45 | 0 | 42 | 263 | 16 221 | 12 423 | 1545 | 1489 | 7 | 375 | 32 323 | 4365 | 841 |
| Portugal | 25 | 25 | 27 | 27 | 2476 | 3740 | 2725 | 436 | 1496 | 9 | 80 | 10 962 | 5890 | 1060 |
| Romania | 20 | 12 | 20 | 12 | 1696 | 2303 | 2174 | 20 | 0 | | 20 | 6213 | | |
| Russia | 230 | 182 | 0 | 0 | 38 937 | 53 609 | 43 996 | 8783 | 9804 | 87 | 733 | 155 949 | | |

(continued)

Table 1 Continued

| Country | IVF clinics in the country | | | | | | | | | | | Cycles/million* | | |
|-----------------|----------------------------|----------------------|----------|-------------------|--------|--------|--------|--------|--------|-----|------|-----------------|-------------|------------|
| | IVF clinics | Included IVF clinics | IUI labs | Included IUI labs | IVF | ICSI | FET | PGT | ED | IVM | FOR | All | Women 15–45 | Population |
| Serbia | 18 | 1 | 18 | 1 | 102 | 48 | 16 | 0 | 0 | 0 | 2 | 168 | | |
| Slovenia | 3 | 3 | 2 | 2 | 1213 | 2181 | 1568 | 85 | 4 | 0 | 10 | 5061 | 14622 | 2408 |
| Spain | 247 | 245 | 366 | 313 | 6352 | 42 773 | 31 894 | 20 783 | 37 618 | 9 | 1069 | 140 498 | | |
| Sweden | 18 | 18 | 0 | 0 | 5990 | 5733 | 7167 | 509 | 346 | | | 19 745 | 10 621 | 1968 |
| Switzerland | 28 | 28 | 0 | 0 | 920 | 5450 | 4871 | 356 | 0 | | | 11 597 | 7351 | 1399 |
| The Netherlands | 15 | 15 | 0 | 0 | 6363 | 7082 | 13 342 | 414 | 0 | | | 27 201 | 8721 | 1587 |
| Ukraine | 48 | 45 | 17 | 17 | 628 | 11 410 | 10 620 | 4098 | 1552 | | 13 | 28 321 | | |
| UK | 86 | 86 | 101 | 101 | 19 489 | 21 233 | 22 505 | 1786 | 3640 | 106 | 792 | 69 551 | 5728 | 1069 |
| All | 1552 | 1422 | 1322 | 1271 | 162837 | 400375 | 309475 | 48294 | 80641 | 532 | 5444 | 1007598 | 7581 | 1402 |

Treatment cycles in IVF and ICSI refer to initiated cycles.

For Austria, Belgium, Denmark and France, treatment cycles refer to aspirations. For Austria and Belgium, the total number of initiated cycles was only available for IVF and ICSI together, being 10 828 and 19 032. For Hungary and Malta, the number refers to aspiration cycles for IVF + ICSI.

For Belgium, there were 875 extra aspiration cycles for which it is not known whether IVF or ICSI was performed. From these, only one had a transfer without pregnancy.

Treatment cycles in frozen embryo transfer (FET) refer to thawings.

For Finland, Hungary, Kazakhstan, Luxembourg, Moldova, Sweden and the Netherlands, treatment cycles refer to transfers.

Treatment cycles in PGT contain both fresh and frozen cycles and refer to initiated cycles in the fresh cycles and thawings in the frozen cycles.

For Finland, it refers to initiated cycles and transfers; for France, it refers to aspirations and thawings. Kazakhstan and Lithuania only reported fresh, initiated cycles.

Treatment cycles in egg donation (ED) refer to donation cycles and contain fresh and frozen cycles.

Treatment cycles in IVM refer to aspirations.

Treatment cycles in frozen oocyte replacement (FOR) refer to thawings.

PGT, preimplantation genetic testing.

Georgia, Slovakia and Turkey did not deliver data in 2018 (11.4% of EIM members, as in 2017, but with Croatia failing to provide data and Ireland sending data). In 21 countries (53.8% of reporting countries as in 2017), all ART clinics participated in the reporting. Among 1552 known IVF clinics in Europe, 1422 clinics reported data sets (91.6% versus 90.1% in 2017). As in 2017, the four European countries with the largest treatment numbers in 2018 were Russia (155 949; 137 211 in 2017), Spain (140 498; 125 592 in 2017), France (106 884; 108 820 in 2017) and Germany (105 328; 99 466 in 2017).

Size of the clinics and reporting methods

The size of reporting clinics, as calculated based on the number of cycles per year, was highly variable among and within countries, as seen in previous years (Supplementary Table SII). In 2018, clinics with cycle numbers between 200 and 499 and 500–999 were the most common (27.3% and 26.3%). These numbers were comparable with the numbers reported in 2017 (25.9% and 26.3%). The proportion of clinics performing more than 1000 treatment cycles per year was slightly higher than in 2017 (21% versus 19% in 2017). Small clinics with <100 treatment cycles per year were present in 21 countries (24 countries in 2017).

Country-specific requirements of registries and reporting methods are shown in Supplementary Table SIII. Data collection was either voluntary (16 out of 39 countries) or compulsory. Twenty-two countries

reported all or a part of the treatment cycles to the national health authority. Among 18 countries with only partial reporting, the data were mainly provided on a voluntary basis (12 countries) to medical organizations (7 countries), to the national health authority (8 countries) or as a single person who took the initiative (3 countries).

In contrast, complete reporting was most often achieved when data collection was compulsory (17/21 countries) with data communication to the national health authority (all but 4 countries). Transfer of the data was mainly done on an aggregate basis (25 countries/39).

Number of treatment cycles per technique and availability

In 2018, 1 007 598 treatment cycles were reported to EIM (67 095 more than in 2017, +7.1%). Since 1997, increasing numbers of clinics reported to EIM to reach a total 11 726 598 treatment cycles and the birth of more than 2 275 585 infants (Table II). As seen in Table I, 11 countries reported fewer treatment cycles than in 2017. Furthermore, the largest increments in reported treatment numbers were observed for Russia (+ 18 738, +23 clinics) and Spain (+14 906, +6 clinics). Table I shows the numbers of treatment cycles per technique in 2018: ICSI remains the most used (400 375, 39.7% of all treatment cycles versus 391 379, 41.6% in 2017). Cycles of IVF, FET, ED, FOR, PGT and IVM represented 16.2%, 30.7%, 8%, 0.5%, 4.8% and 0.0005% of all cycles, respectively. The distribution of the available techniques

Table II Number of institutions offering ART services, treatment cycles and infants born after ART in Europe, 1997–2018.

| Year | No. of countries | No. of centres | No. of cycles | Cycle increase (%) | No. of infants born |
|--------------|------------------|----------------|---------------|--------------------|---------------------|
| 1997 | 18 | 482 | 203 225 | | 35 314 |
| 1998 | 18 | 521 | 232 225 | +14.3 | 21 433 |
| 1999 | 21 | 537 | 249 624 | +7.5 | 26 212 |
| 2000 | 22 | 569 | 275 187 | +10.2 | 17 887 |
| 2001 | 23 | 579 | 289 690 | +5.3 | 24 963 |
| 2002 | 25 | 631 | 324 238 | +11.9 | 24 283 |
| 2003 | 28 | 725 | 365 103 | +12.6 | 68 931 |
| 2004 | 29 | 785 | 367 056 | +0.5 | 67 973 |
| 2005 | 30 | 923 | 419 037 | +14.2 | 72 184 |
| 2006 | 32 | 998 | 458 759 | +9.5 | 87 705 |
| 2007 | 33 | 1029 | 493 420 | +7.7 | 96 690 |
| 2008 | 36 | 1051 | 532 260 | +7.9 | 107 383 |
| 2009 | 34 | 1005 | 537 463 | +1.0 | 109 239 |
| 2010 | 31 | 991 | 550 296 | +2.4 | 120 676 |
| 2011 | 33 | 1314 | 609 973 | +11.3 | 134 106 |
| 2012 | 34 | 1354 | 640 144 | +4.9 | 143 844 |
| 2013 | 38 | 1169 | 686 271 | +7.2 | 149 466 |
| 2014 | 39 | 1279 | 776 556 | +13.1 | 170 163 |
| 2015 | 38 | 1343 | 849 811 | +10.2 | 187 542 |
| 2016 | 40 | 1347 | 918 159 | +8.0 | 195 766 |
| 2017 | 39 | 1382 | 940 503 | +2.4 | 198 215 |
| 2018 | 39 | 1422 | 1 007 598 | +7.1 | 215 610 |
| Total | | | 11 726 598 | | 2 275 585 |

remained similar to 2017 (respectively, 17.6%, 28.9%, 7.4%, 0.5%, 4% and 0.0004% for IVF, FET, ED, FOR, PGT and IVM); however, reported cycle numbers increased for ICSI, FET, ED, PGT, IVM and FOR, and decreased for IVF (−1.5%).

The steepest rise in treatment numbers was observed for FET (+14%; +8.2% in 2017), ED (+16.2%; −6.1% in 2017) and PGT (+29.5%; +37.8% in 2017).

Figure 1A shows the evolution and continuing preponderance of ICSI over conventional IVF. Among a total of 563 212 fresh treatments (ICSI + IVF), 71.1% (70.3% in 2017) were done with ICSI.

The highest proportions of FET treatments (calculated as FET/(FET + ICSI + IVF)) were reached in Armenia (+55.1%), The Netherlands

(49.8%), Czech Republic (48.9%), Ukraine (46.9%), Finland (46.1%), Belgium (45.8%), Albania (44.5%), Switzerland (43.3%) and Poland (43%), with an overall proportion of 35.5% and comparable to 32.6% in 2017 (Fig. 1B).

The number of cycles per million women of reproductive age and per million inhabitants is shown in Table 1 and Supplementary Table SIV. Availability of ART treatments was calculated for the 21 countries with full coverage (Supplementary Table SIV) showing a huge variability in availability when all techniques are considered (range per million women aged 15–45 years: 2335 in Lithuania to 19181 in Denmark); corresponding proportions of newborns resulting from ART were 0.9% and 5.7% of all newborns in these countries. Among other

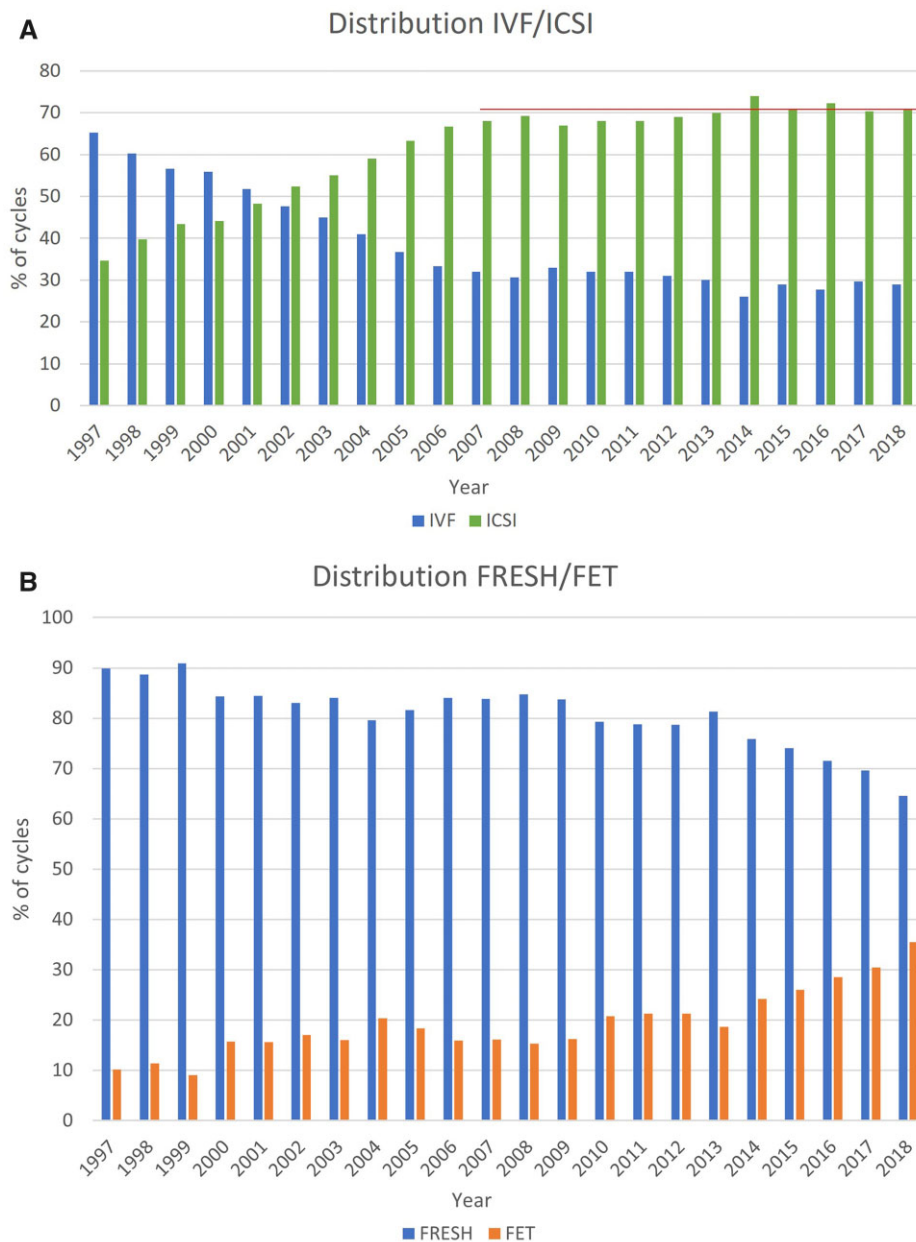


Figure 1. Distribution of treatments in Europe, 1997–2018. (A) Proportion of IVF versus ICSI cycles. (B) Proportion of fresh versus frozen cycles.

countries with complete reporting to the national registry, proportions of ART infants above 5% were calculated for Austria, Czech Republic, Iceland and Slovenia.

Pregnancies and deliveries after treatment

Table III shows pregnancy and delivery rates after IVF or ICSI and after FET (after both IVF and ICSI). Outcome data were calculated per aspiration rather than per initiated cycle as the numbers of initiated cycles have often been incompletely reported.

Among the 39 reporting countries, 36 were able to provide both pregnancy and delivery rates per aspiration after IVF ($n=33$) and/or ICSI ($n=36$). For FET when considering thawing cycles, 32 countries were able to report pregnancy and delivery rates (28 in 2017). Supplementary Table SIV shows the numbers of deliveries for the 21 countries with full coverage of the reporting.

Significant variation for pregnancy and delivery rates (for all types of treatment cycles) was observed between countries as in previous years.

Per aspiration, total pregnancy rates are shown in Fig. 2A and ranged from 7.8% to 47.2%. The total delivery rates per aspiration are shown in Fig. 2B and ranged from 6.3% to 31.3% in fresh cycles after IVF or ICSI (including the freeze-all cycles whether performed or not by the countries) (Table III). For FET, the pregnancy and delivery rates per thawing varied between 24.4% and 49.5% and between 17.8% and 40.6%, respectively. Overall, while higher pregnancy and delivery rates were recorded for FET cycles (per thawing) than for both fresh IVF and ICSI cycles (per aspiration) (Table III; Supplementary Table SVII), the pregnancy rates per transfer in fresh cycles remained at the same level (34.1% for IVF and 32.1% for ICSI; Fig. 3A) as in FET cycles (34.3%), as did delivery rates per transfer (26.1% for IVF, 23.9% for ICSI and 24.9% for FET), as in 2017 (Supplementary Tables SV–SVII; Fig. 3B).

When considering the stage of replaced embryos, the data showed pregnancy rates for blastocyst transfers to be higher (40.0% versus 28.5% for cleavage stage embryos for fresh IVF and ICSI cycles together, and 38.6% versus 27.2% for cleavage stage embryos for FET).

Cycle numbers, aspirations, transfers, pregnancies, deliveries in IVF, ICSI and FET (after both IVF and ICSI) by country are presented in Supplementary Tables SV–SVII.

For the fifth time, freeze-all cycles were collected (Supplementary Tables SV and SVI) including either freezing of all oocytes reported by 11 countries for IVF (10 in 2017 and 10 in 2016) and 17 countries for ICSI (17 in 2017 and 15 in 2016), or of all embryos by 23 countries for IVF (22 in 2017 and 22 in 2016) and 25 countries for ICSI (27 in 2017 and 22 in 2016). The highest proportions of freeze-all cycles per aspiration (oocytes and embryos together) were 29.8% (5.4% in 2017) and 41.7% (49.1% in 2017), respectively, for IVF and ICSI.

ED cycle numbers were available for 23 countries (21 in 2017) although 27 (26 in 2017) provided outcome data (Supplementary Table SVIII). The highest numbers of ED cycles were reported from Spain, the Czech Republic and Russia, as in 2017. The number of aspirations of donated oocytes was 36 938 (34 545 in 2017) that led to 24 148 fresh transfers (26 447 in 2017), while the replacements of frozen oocytes (FOR) were 16 130 (14 129 in 2017). The pregnancy rates per fresh embryo transfer were 49.6% (49.2% in 2017) for freshly donated oocytes and 44.9% (41.1% in 2017) for thawed oocytes. A high

variability was seen between countries, ranging from 31.2% to 83.3% for fresh oocytes and from 24.8% to 57.1% for thawed oocytes, as in previous years. Overall (including also the replacements of frozen embryos), 25 760 deliveries were reported with donated eggs (21 312 in 2017 and 22 497 in 2016). Compared to cycles using own oocytes, pregnancy and delivery rates per transfer were higher for fresh (IVF and ICSI) and FET cycles together.

Age distribution

Supplementary Tables SIX and SX showed that age distributions of women treated with IVF and ICSI varied between countries. Some countries were not able to provide age categories (eight for IVF and four for ICSI). The highest percentage of women aged 40 years and older undergoing aspiration for IVF was reported by Greece (as in 2017), whereas the highest percentage of women aged <34 years was reported by Ukraine (as in 2017). For ICSI, the highest percentage of women aged 40 years and older undergoing aspiration was also reported by Greece (as in 2017), whereas the highest percentage of women undergoing aspiration aged <34 years was recorded in Sweden (Albania in 2017). An age-dependent decrease of pregnancy and delivery rates for IVF and ICSI cycles was reported, as expected. Pregnancy and delivery rates in women aged 40 years and older ranged between 5.3% and 32.3%, and 0% and 22%, respectively. The age-related decline was also visible in FET cycles (Supplementary Table SXI) with recorded pregnancies and delivery rates among women aged 40 years and older ranging from 0 to 49.1% and 0 to 40%, respectively.

As seen in Supplementary Table SXII, the age of the recipient women had no influence on outcomes of ED cycles.

Numbers of embryos transferred and multiple births

The number of embryos replaced per transfer procedure after IVF and ICSI together as well as multiple birth rates per subgroups defined by the number of embryos replaced are presented in Table IV.

Four countries did not report either on the number of replaced embryos or on multiplicity. For the first time, most transfers involved the replacement of one embryo (elective or not) (50.7% of cycles versus 46% with single embryo replacement in 2017). The evolution of the proportions of replacements of one, two and three or more embryos is shown in Fig. 4A.

Eighteen countries reported more than 50% of single embryo transfers (13 in 2017) with six reporting more than 75% of single embryo transfers. For the second year, none of the reporting countries carried out more than 50% of their transfers with three embryos. Among five countries recording transfers of four or more embryos, the highest proportion was recorded in Greece (5.5% versus 4% in 2017). For the third consecutive year, data on the embryo stage at transfer was collected. Taking into account that the embryo stage at transfer was unknown for 20.8% of the fresh (IVF + ICSI) cycles, 50.1% (44.1% in 2017) of the transfers were performed at the blastocyst stage. The corresponding figure for FET was 73.9% (64.1% in 2017). Such information was not available for each of the subgroups for numbers of embryos replaced.

Table III Results after ART in 2018.

| Country | IVF | | | ICSI | | | FET | | | ART infants [†] | ART infants per national births (%) | |
|-------------------------------------|-----------------------------|-------------|--------------------------------|-------------------------------|-------------|--------------------------------|-------------------------------|--------------|-----------------------------|--------------------------|-------------------------------------|----------------------------|
| | Initiated cycles IVF + ICSI | Aspirations | Pregnancies per aspiration (%) | Deliveries per aspiration (%) | Aspirations | Pregnancies per aspiration (%) | Deliveries per aspiration (%) | Thawings FET | Pregnancies per thawing (%) | | | Deliveries per thawing (%) |
| Albania | 86 | | | | 86 | 30.2 | 18.6 | 69 | 33.3 | 27.5 | 62 | |
| Armenia | 1753 | 783 | 25.3 | 24.1 | 954 | 18.8 | 17.5 | 2156 | 38.8 | 31.2 | 1412 | 3.4 |
| Austria | 10 828 | 1701 | 28.7 | 24.0 | 5703 | 27.1 | 22.5 | 3161 | 33.2 | 28.4 | 5372 | 6.3 |
| Belarus | 3292 | 1223 | 32.2 | 20.9 | 1884 | 29.4 | 17.9 | 992 | 35.9 | 21.0 | 945 | 1.1 |
| Belgium | 19 032 | 2554 | 21.3 | 15.3 | 13 783 | 21.8 | 15.6 | 13 821 | 27.8 | 19.2 | 5973 | 5.0 |
| Bosnia-Herzegovina, Federation part | 111 | | | | 98 | 32.7 | 22.4 | 58 | 48.3 | 27.6 | 41 | |
| Bulgaria | 9482 | 1078 | 12.2 | 7.7 | 8404 | 14.7 | 11.3 | 2469 | 30.8 | 23.0 | | |
| Czech Republic | 15 435 | 1426 | 7.8 | 6.3 | 13 446 | 22.2 | 13.8 | 14 749 | 30.7 | 18.0 | 6281 | 5.5 |
| Denmark | | 6479 | 19.4 | 12.7 | 5536 | 19.2 | 15.4 | 6912 | 28.5 | 21.9 | 3534 | 5.7 |
| Estonia | 2066 | 638 | 24.0 | 19.0 | 1325 | 24.4 | 18.8 | 1044 | 29.0 | 19.0 | 702 | 4.9 |
| Finland | 4372 | 2371 | 22.9 | 18.0 | 1741 | 21.0 | 16.8 | | | | 1791 | 3.7 |
| France | | 20 821 | 19.7 | 16.7 | 41 021 | 19.9 | 17.0 | 41 258 | 24.4 | 20.3 | 21 125 | 2.8 |
| Germany | 75 726 | 19 347 | 25.5 | 18.9 | 50 350 | 25.1 | 18.6 | 29 334 | 27.4 | 19.0 | 21 924 | |
| Greece | 16 285 | 2111 | 20.5 | 14.0 | 14 174 | 13.8 | 8.7 | 5623 | 38.6 | 17.8 | 5022 | 5.8 |
| Hungary | | | | | | | | | | | 1734 | 2.0 |
| Iceland | 489 | 272 | 25.7 | 19.5 | 183 | 31.1 | 27.3 | 307 | 41.4 | 31.9 | 236 | 5.6 |
| Ireland | 607 | 239 | 30.1 | 23.8 | 287 | 33.4 | 24.0 | 408 | 37.5 | 24.0 | 317 | 0.5 |
| Italy | 51 086 | 7160 | 20.9 | 14.2 | 39 227 | 17.4 | 11.3 | 19 587 | 30.6 | 21.1 | 12 949 | 2.9 |
| Kazakhstan | 6510 | 1555 | 29.6 | 21.2 | 4955 | 18.5 | 15.7 | | | | 3140 | |
| Latvia | 582 | 143 | 17.5 | 13.3 | 439 | 21.0 | 13.7 | 359 | 42.9 | 29.2 | 219 | |
| Lithuania | 877 | 472 | 47.2 | 22.2 | 405 | 37.3 | 14.1 | 201 | 30.3 | 23.9 | 255 | 0.9 |
| Luxembourg | 735 | 160 | 28.1 | 21.9 | 516 | 26.0 | 18.4 | | | | 211 | 3.4 |
| Malta | | | | | | | | 2 | | | 58 | 1.3 |
| Moldova | 1248 | | | | 1055 | 36.5 | 31.3 | | | | | |
| Montenegro | 586 | | | | 569 | 26.2 | 21.8 | 57 | 29.8 | 24.6 | 174 | 2.4 |
| North-Macedonia | 2637 | 332 | 41.3 | 13.3 | 2012 | 28.7 | 23.7 | 411 | 32.8 | 26.3 | 818 | 3.8 |
| Norway | 7369 | 3975 | 26.3 | 22.8 | 3056 | 25.6 | 21.6 | 4178 | 25.7 | 21.4 | | |

(continued)

Table III Continued

| Country | IVF | | | ICSI | | | FET | | | ART infants [†] | ART infants per national births (%) | |
|-----------------|-----------------------------|----------------|--------------------------------|-------------------------------|----------------|--------------------------------|-------------------------------|----------------|-----------------------------|--------------------------|-------------------------------------|----------------------------|
| | Initiated cycles IVF + ICSI | Aspirations | Pregnancies per aspiration (%) | Deliveries per aspiration (%) | Aspirations | Pregnancies per aspiration (%) | Deliveries per aspiration (%) | Thawings FET | Pregnancies per thawing (%) | | | Deliveries per thawing (%) |
| Poland | 16 484 | 262 | 27.5 | 21.4 | 15 989 | 22.5 | 13.9 | 12 423 | 36.6 | 23.1 | 6177 | 1.6 |
| Portugal | 6216 | 2351 | 23.5 | 17.6 | 3457 | 19.4 | 14.7 | 2725 | 33.9 | 23.9 | 2453 | 2.8 |
| Romania | 3999 | 1632 | 30.4 | 23.1 | 2233 | 27.6 | 17.9 | 2174 | 39.7 | 28.8 | 1581 | |
| Russia | 92 546 | 37 516 | 27.7 | 20.1 | 52 093 | 25.3 | 17.6 | 43 996 | 41.4 | 28.7 | 37 987 | 2.4 |
| Serbia | 150 | 102 | 31.4 | 18.6 | 48 | 25.0 | 20.8 | 16 | 37.5 | 37.5 | 46 | 0.1 |
| Slovenia | 3394 | 1158 | 29.8 | 22.5 | 2112 | 23.9 | 19.5 | 1568 | 33.3 | 24.5 | 1161 | 6.0 |
| Spain | 49 125 | 5925 | 25.0 | 18.4 | 38 706 | 19.9 | 14.4 | 31 894 | 37.5 | 26.3 | 34 541 | 9.3 |
| Sweden | 11 723 | 5611 | 27.1 | 21.9 | 5365 | 25.9 | 22.0 | | | | 5108 | 4.3 |
| Switzerland | 6370 | 838 | 24.3 | 17.3 | 5027 | 21.1 | 16.1 | 4871 | 31.1 | 21.5 | 2161 | 2.5 |
| The Netherlands | 13 445 | 5541 | 29.9 | 21.3 | 6398 | 32.3 | 23.7 | | | | | |
| Ukraine | 12 038 | 598 | 31.4 | 26.9 | | | | 10 620 | 49.5 | 40.6 | 8792 | 2.7 |
| UK | 40 722 | 17 274 | 31.5 | 27.8 | 20 974 | 31.7 | 27.9 | 22 505 | 35.5 | 31.0 | 21 312 | 2.9 |
| All | 487 406 | 153 648 | 25.5 | 19.6 | 36 3611 | 22.5 | 16.7 | 279 948 | 33.4 | 24.2 | 215 614 | 3.5 |

Total rates refer to these countries were all data were reported for the given technique.

[†]ART infants also include egg donation (ED).

For IVF and ICSI, there were for France, Greece, Ireland, Kazakhstan, Russia and Spain, respectively 177, 46, 1, 8, 543 and 27 deliveries with unknown outcome. These were accepted as singletons to calculate the ART infants.

For frozen embryo transfer (FET), there were for France, Greece, Kazakhstan, Russia and Spain, respectively, 41, 4, 2, 8 and 4 deliveries with unknown outcome. These were accepted as singletons to calculate the ART infants.

For the Netherlands, no data on the number of thawings were available.

For ED, there were for France, Greece, Kazakhstan, Poland, Russia, Spain and Ukraine, respectively, 1, 2, 1, 1, 23, 8 and 9 deliveries with unknown outcome. These were accepted as singletons to calculate the ART infants.

For PGT, there was for Russia one delivery with unknown outcome. This one was accepted as singleton to calculate the ART infants.

In the Czech Republic, IVF and ICSI were reported together, no details on pregnancies and deliveries.

PGT, preimplantation genetic testing.

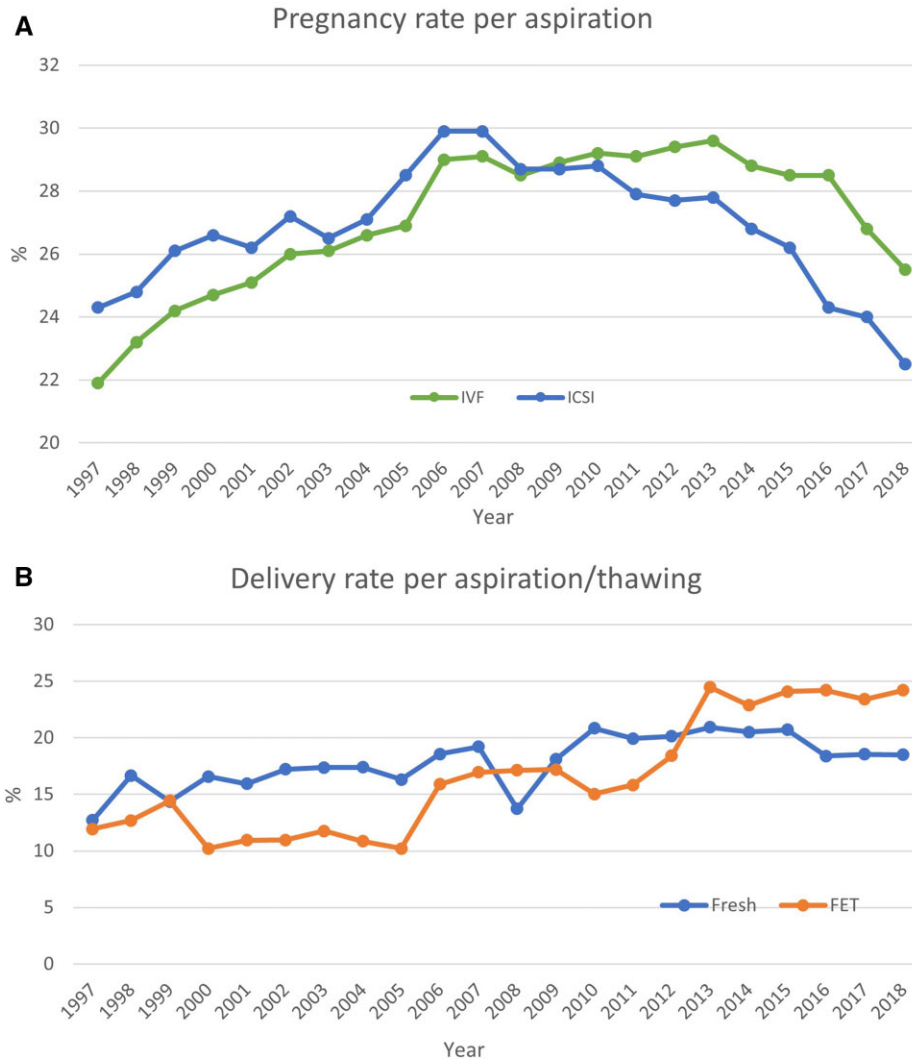


Figure 2. Pregnancy and delivery rates per aspiration in Europe, 1997–2018. (A) Pregnancy rates for IVF versus ICSI cycles. **(B)** Delivery rates for fresh versus frozen cycles.

As a result of decreasing numbers of embryos replaced per transfer, the global proportion of twin and triplet deliveries continued to decrease (Fig. 4B). Twin and triplet rates for fresh IVF and ICSI cycles together were 12.4% (range: 1.9–27.4) and 0.2% (range: 0–4.2), respectively; corresponding results for FET were 9.4% and 0.1%. Two countries reported rates of single embryo replacement above 90% in fresh cycles (98.4% for Iceland, 94.3% for Finland) and twin rates were as low as 1.9% (for Iceland, not available for Finland).

Supplementary Tables SXIII and SXIV provide additional information on pregnancies and deliveries. The reported incidence of pregnancy loss was 19.3% after removing countries where no pregnancy loss was documented (16.6% in 2017) after IVF + ICSI, and 21.4% (18.3% in 2017) after FET. The proportion of recorded lost to follow-up was 7.2% after IVF + ICSI (7.5% in 2017) and 7.2% after FET (8.1% in 2017).

Perinatal risks and complications

Data on premature deliveries were available from 21 countries (19 countries in 2017). Premature delivery rates (for fresh IVF and ICSI, FET and ED together) according to multiplicity are presented in Supplementary Table SXV. The incidence of extreme preterm birth (20–27 gestational weeks at delivery) was 1% in singletons (1.1% in 2017), 3.1% in twins (3.4% in 2017) and 6% in triplets (10.7% in 2017). Very premature birth rates (28–32 gestational weeks at delivery) were recorded in 2.2% of singletons (2.4% in 2017), 9.7% of twin pregnancies (10.3% in 2017) and 37.9% in triplet pregnancies (21.7% in 2017). The evolution of the proportions of premature deliveries (before 37 weeks) over the years according to multiplicity is shown in Fig. 5. Term deliveries (≥ 37 weeks) were achieved in 83.1% (86.6% in 2017) of singleton pregnancies, 43.6% (45.2% in 2017) of twin pregnancies and 8.1% (27% in 2017) of triplet pregnancies.

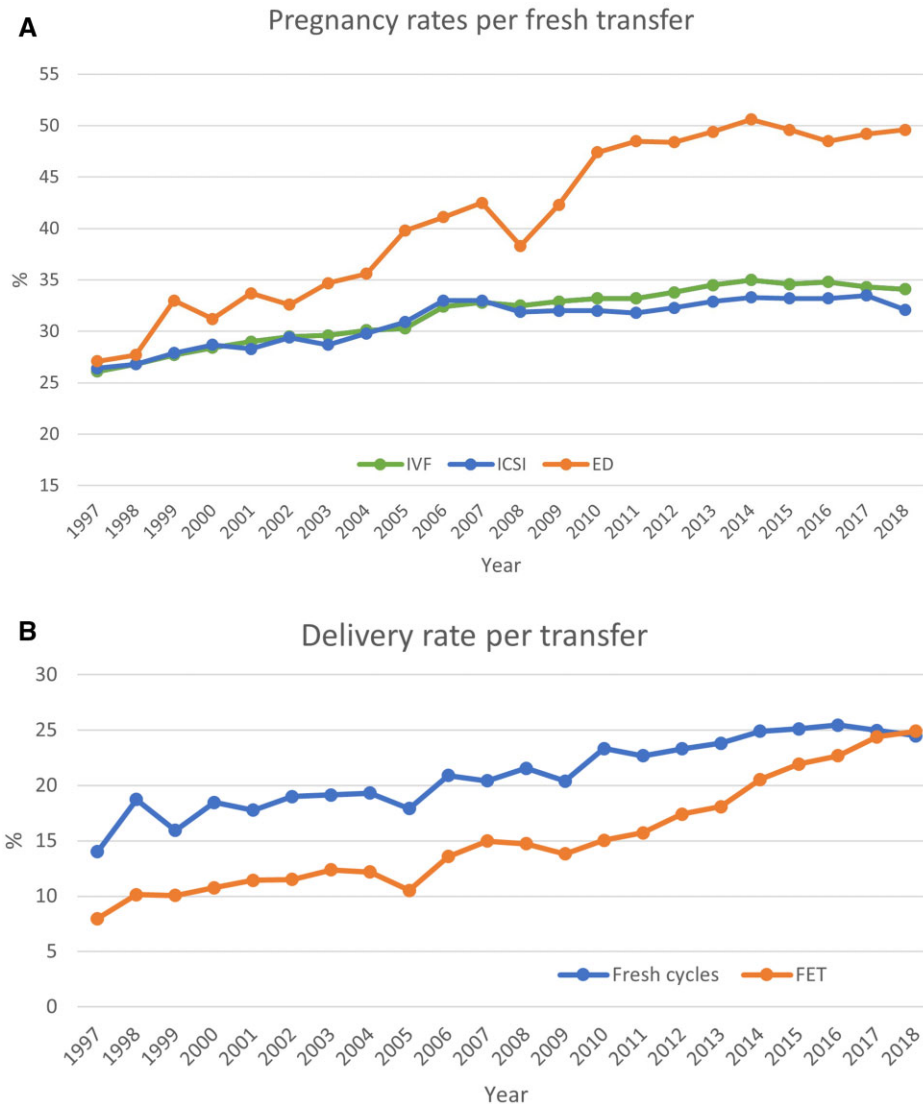


Figure 3. Pregnancy and delivery rates per transfer in Europe, 1997–2018. (A) Pregnancy rates for IVF versus ICSI and ED cycles. (B) Delivery rates for fresh versus frozen cycles. ED, egg donation.

Complications related to ART procedures were reported by 34 countries (32 in 2017) and foetal reductions by 34 countries (24 in 2017); one country (Albania) only reported foetal reductions but no other complications (Supplementary Table SXVI). The main reported complication was ovarian hyperstimulation syndrome (OHSS) (Grades 3–5) with a total reported number of 1719 (1839 in 2017) corresponding to an incidence rate of 0.17% (0.20% in 2017). Other complications (1379; 1484 cases in 2017) were reported with a total incidence of 0.14% (0.16% in 2017) and bleeding being the most recorded (0.1%, identical to 2017). Three maternal deaths were reported (one in 2017). After inquiry, no details on a potential link with ART were obtained for two of these. One maternal death was caused by massive bilateral pulmonary embolism in a patient without identified risk factors. The causal link to the ART procedure itself

could not be established with certainty. Foetal reductions were reported in 509 cases (599 in 2017), the majority from the UK, Belgium and Spain, as in 2017.

Preimplantation genetic testing

Table 1 includes PGT for monogenic disorders and structural rearrangements (PGT-M/SR) and PGT for aneuploidies (PGT-A) activities, which were reported from 24 countries (25 in 2017). The main contributors were Spain, Russia, Ukraine and Italy. The total number of treatment cycles was 48 294 representing 7.1% of initiated IVF + ICSI and FET cycles together (37 303; 4.3% in 2017). More details on PGT/PGT-A activities can be found in the annual reports of the ESHRE PGT consortium (Van Montfoort et al., 2021).

Table IV Number of embryos transferred after ART and deliveries in 2018.

| Country | IVF + ICSI | | | | | | | | FET | | |
|-------------------------------------|------------|----------------|-----------------|-------------------|-------------------|------------|----------|-------------|------------|----------|-------------|
| | Transfers | One embryo (%) | Two embryos (%) | Three embryos (%) | Four+ embryos (%) | Deliveries | Twin (%) | Triplet (%) | Deliveries | Twin (%) | Triplet (%) |
| Albania | 69 | 14.5 | 85.5 | 0.0 | 0.0 | 16 | 25.0 | 0.0 | 19 | 15.8 | 0.0 |
| Armenia | 936 | 27.8 | 48.4 | 23.8 | 0.0 | 356 | 9.8 | 0.8 | 673 | 5.5 | 0.4 |
| Austria | 9074 | 72.9 | 26.9 | 0.2 | 0.0 | 5174 | 3.6 | 0.1 | | | |
| Belarus | 2480 | 30.4 | 61.6 | 8.0 | 0.0 | 593 | 21.7 | 0.0 | 208 | 10.6 | 1.0 |
| Belgium | 12 135 | 70.4 | 26.1 | 3.2 | 0.3 | 2543 | 6.1 | 0.2 | 2660 | 5.0 | 0.0 |
| Bosnia-Herzegovina, Federation part | 83 | 54.2 | 41.0 | 4.8 | 0.0 | 22 | 13.6 | 0.0 | 16 | 0.0 | 0.0 |
| Bulgaria | | | | | | | | | | | |
| Czech Republic | 10 500 | 76.7 | 22.9 | 0.4 | 0.0 | 1942 | 5.3 | 0.1 | 2660 | 6.9 | 0.1 |
| Denmark | 8580 | 80.6 | 19.1 | 0.3 | 0.0 | 1678 | 2.3 | 0.1 | 1512 | 2.5 | 0.0 |
| Estonia | 1529 | 53.1 | 44.4 | 2.5 | 0.0 | 370 | 11.6 | 0.5 | 198 | 9.1 | 0.0 |
| Finland | 2855 | 94.3 | 5.7 | 0.0 | 0.0 | 719 | | | 878 | | |
| France | 41 180 | 55.4 | 41.2 | 3.1 | 0.2 | 10 465 | 10.3 | 0.2 | 8356 | 6.6 | 0.1 |
| Germany | 54 531 | 30.5 | 65.3 | 4.2 | 0.0 | 13 034 | 19.3 | 0.4 | 5562 | 12.5 | 0.3 |
| Greece | 15 265 | 20.7 | 54.8 | 19.0 | 5.5 | 1529 | 20.3 | 0.5 | 1003 | 24.3 | 0.2 |
| Hungary | 6355 | 0.0 | 0.0 | 0.0 | 0.0 | 1241 | 19.3 | 0.6 | 208 | 14.4 | 0.5 |
| Iceland | 321 | 98.4 | 1.6 | 0.0 | 0.0 | 103 | 1.9 | 0.0 | 98 | 1.0 | 0.0 |
| Ireland | 402 | 71.1 | 28.9 | 0.0 | 0.0 | 129 | 2.3 | 0.0 | 99 | 5.1 | 1.0 |
| Italy | 30 584 | 39.1 | 49.4 | 10.9 | 0.6 | 5458 | 13.6 | 0.3 | 4127 | 6.7 | 0.1 |
| Kazakhstan | 3489 | 46.2 | 50.4 | 3.4 | 0.0 | 1106 | 16.6 | 0.1 | 1203 | 17.5 | 0.3 |
| Latvia | 313 | 80.5 | 18.5 | 1.0 | 0.0 | 79 | 2.9 | 0.0 | 105 | 4.4 | 0.0 |
| Lithuania | 701 | 23.5 | 38.8 | 37.8 | 0.0 | 162 | 24.0 | 4.2 | 48 | 25.0 | 0.0 |
| Luxembourg | 503 | 50.5 | 49.5 | 0.0 | 0.0 | 130 | 3.8 | 0.0 | 73 | 4.1 | 0.0 |
| Malta | 212 | 15.1 | 67.5 | 17.5 | 0.0 | 46 | 21.7 | 2.2 | | | |
| Moldova | | | | | | | | | | | |
| Montenegro | 423 | 22.7 | 40.9 | 36.4 | 0.0 | 124 | 27.4 | 0.0 | 14 | 14.3 | 0.0 |
| North-Macedonia | 1851 | 32.6 | 60.5 | 6.9 | 0.0 | 521 | 21.1 | 0.0 | 108 | 13.9 | 0.0 |
| Norway | | | | | | | | | | | |
| Poland | 9767 | 62.9 | 36.8 | 0.3 | 0.0 | 2277 | 8.0 | 0.0 | 2865 | 5.7 | 0.0 |
| Portugal | 3663 | 44.0 | 55.7 | 0.3 | 0.0 | 921 | 13.0 | 0.2 | 652 | 10.5 | 0.3 |
| Romania | 2478 | 39.3 | 52.1 | 8.1 | 0.5 | 776 | 13.3 | 0.1 | 626 | 11.9 | 0.0 |
| Russia | 64 968 | 52.3 | 46.9 | 0.7 | 0.0 | 16 688 | 13.7 | 0.3 | 12 606 | 12.8 | 0.2 |
| Serbia | 117 | 28.2 | 29.1 | 42.7 | 0.0 | 29 | 24.1 | 3.4 | 6 | 33.3 | 0.0 |
| Slovenia | 2610 | 56.8 | 43.1 | 0.2 | 0.0 | 672 | 9.2 | 0.0 | 384 | 7.0 | 0.0 |
| Spain | 25 693 | 41.7 | 56.7 | 1.7 | 0.0 | 6671 | 13.6 | 0.1 | 8388 | 10.2 | 0.1 |
| Sweden | 8590 | 87.3 | 12.7 | 0.0 | 0.0 | 2409 | 2.7 | 0.0 | 2392 | 2.3 | 0.0 |
| Switzerland | 3705 | 64.5 | 33.6 | 1.9 | 0.0 | 956 | 9.4 | 0.0 | 1047 | 6.3 | 0.1 |
| The Netherlands | | | | | | | | | | | |
| Ukraine | 5493 | 40.2 | 53.0 | 6.8 | 0.0 | 1828 | 16.0 | 0.1 | 4312 | 14.9 | 0.1 |
| United Kingdom | 33 119 | 64.5 | 33.3 | 2.1 | 0.0 | 10 660 | 8.1 | 0.1 | 6979 | 8.8 | 0.2 |
| All* | 364 574 | 50.7 | 45.1 | 3.9 | 0.3 | 91 427 | 12.4 | 0.2 | 70 085 | 9.4 | 0.1 |

*Totals refer only to these countries where data on number of transferred embryos and on multiplicity were reported.

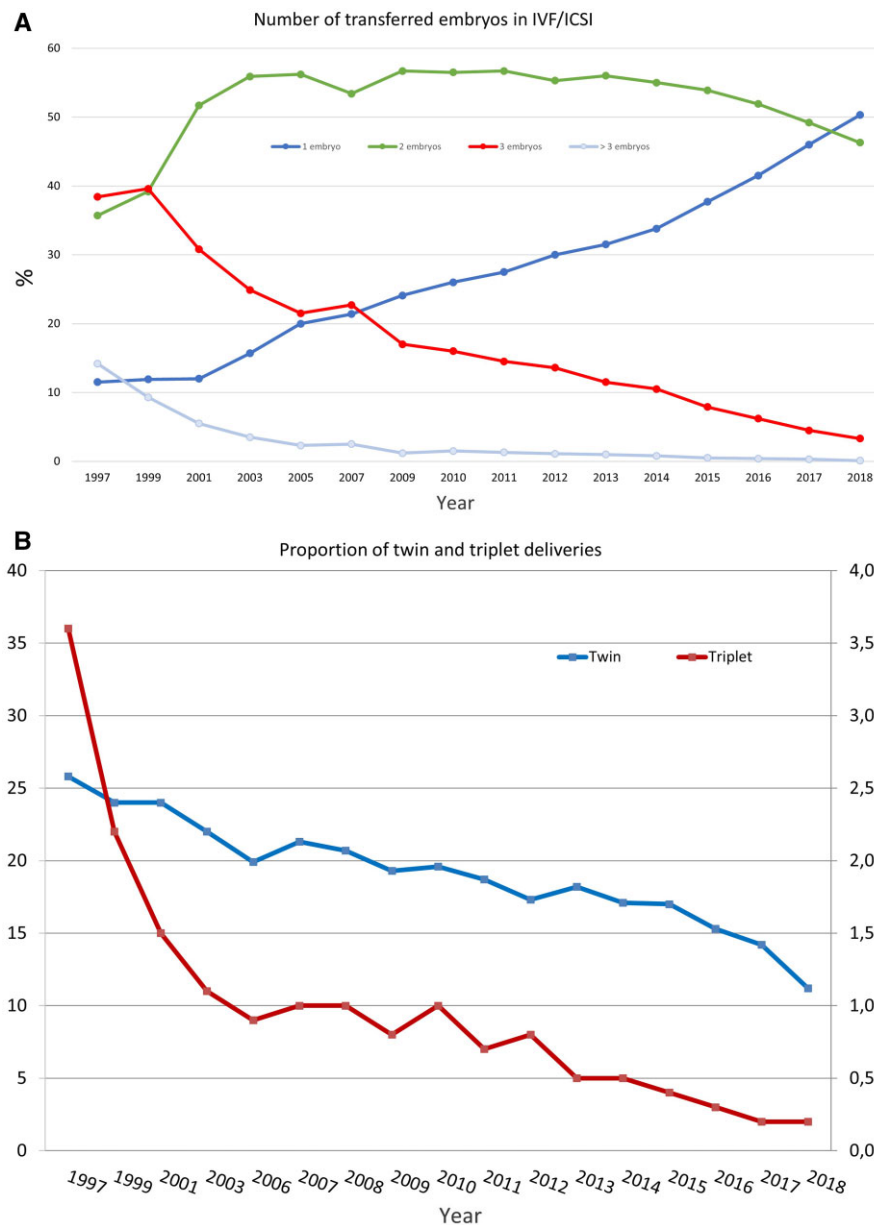


Figure 4. Embryo transfer and multiple births in Europe, 1997–2018. (A) Number of embryos transferred in IVF and ICSI during fresh cycles. **(B)** Percentages of twin and triplet deliveries.

IVM

A total of 532 treatments with IVM were reported from eight countries (378 treatments from the same eight countries in 2017) (Table I). Most IVM cycles were recorded in Belgium, as in 2017. A total of 254 transfers resulted in 49 pregnancies (19.3% per transfer) and 36 deliveries (14.2% per transfer).

Frozen oocyte replacement

A total number of 5444 thawing cycles were reported by 22 countries (5210 from 21 countries in 2017) (Table I) with Italy and Spain being the largest contributors (1318 and 1069 cycles, respectively). Among

3993 transfers, 1178 resulted in pregnancies (29.5%; 27.5% in 2017) and 867 in deliveries (21.7%; 21% in 2017).

IUI

Data on IUI-H or IUI-D were collected by a total of 1271 institutions (1273 in 2017) in 30 and 25 countries, respectively, as in 2017 (Table V). Amongst 148 143 IUI-H (155 794 in 2017) and 50 609 IUI-D (51 402 in 2017) reported cycles, the numbers were the highest for IUI-H in France, Spain, Italy and Belgium, and for IUI-D in Spain, Belgium, Denmark and the UK (Supplementary Tables SXVII and SXVIII).

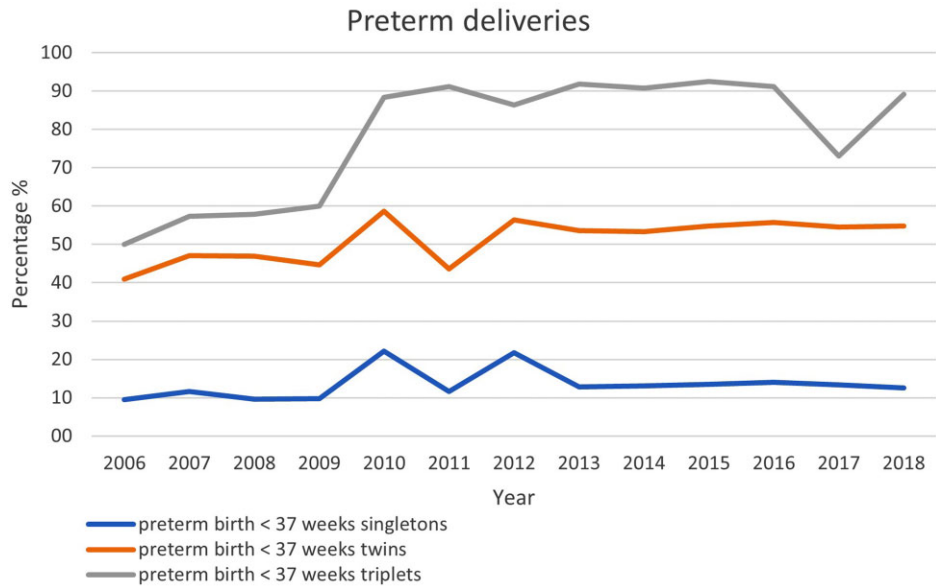


Figure 5. Proportion of premature deliveries (<37 weeks of gestation in relation to pregnancies ≥37 week of gestation) in singleton, in twin and in triplet pregnancies in Europe, 2006–2018.

Delivery rates could be calculated for 144 697 IUI-H cycles (8.9%; 8.9% in 2017) and 50 609 for IUI-D cycles (12.6% versus 12.4% in 2017). Singleton deliveries were the most frequent regardless of the age group with an overall rate of 91.2% for IUI-H and 93.4% for IUI-D (91.6% in IUI-H, 92.9% in IUI-D in 2017). Twin and triplet rates were 8.4% and 0.3% for IUI-H, and 6.4% and 0.2% for IUI-D, respectively (in 2017: 8.1% and 0.3% for IUI-H and 6.9% and 0.2% respectively for IUI-D).

Sum of fresh and FET ('cumulative') delivery rates

Supplementary Table SXIX provides an estimate of a cumulative delivery rate. It was calculated as the ratio between the total number of deliveries from fresh embryo transfers and FET performed during a year (numerator) and the number of aspirations during the same year (denominator) and is thus different from a true cumulative delivery rate, which is based on all transfers resulting from one aspiration. The calculation was based on data from 36 countries (34 countries in 2017), where an overall rate of 32.3% (30.8% in 2017) was recorded. The cumulative increase resulting from additional FET (over delivery rates from fresh embryo transfers) was 14.4% (12.3% in 2017), with the highest benefits reported by Armenia (+38.7%), Albania (+22.1%), Sweden (+21.8%), Iceland (+21.6%) and Finland (+21.3%), and the lowest reported by Montenegro (+2.5%), Serbia (4%), North-Macedonia (+4.6%) and Moldova (+4.7%).

Cross-border reproductive care

Twelve countries reported data on cross-border reproductive care: Albania, Belarus, Bosnia-Herzegovina (Federation Part), Denmark, Greece, Iceland, Lithuania, Poland, Portugal, Slovenia, Spain and

Switzerland. A total of 21 792 cycles (16 733 in 2017) were reported, 21.5% (16.9% in 2017) of which involved IVF/ICSI with the couple's own gametes, 52.6% (50.1% in 2017) were oocyte donations and 20.6% (25.8% in 2017) were IVF or ICSI with semen donation. Additionally, 6791 IUI with sperm donation (7298 in 2017) were registered. Information regarding the countries of origin was very incomplete and not reliable enough to obtain any conclusive information. The main reason reported by patients for crossing the borders was to seek a higher quality treatment (42.3%; 25.7% in 2017). However, cross-border reproductive care was also reported to be performed because the treatment was not legal (21.1%; 41.9% in 2017) or too expensive in the home country (25%; 19% in 2017), or because the waiting list was too long (11.5%; 8% in 2017).

Fertility preservation

For the third year, data on FP were reported. Sixteen countries (14 in 2017 and 11 in 2016) provided data on a total number of 20 994 interventions (18 888 in 2017; 13 689 in 2016) (Supplementary Table SXX) both for medical and non-medical reasons in pre- and post-pubertal patients. The majority of interventions consisted of the cryopreservation of ejaculated sperm ($n=10\,503$ from 14 countries; 11 112 from 13 countries in 2017) and the cryopreservation of oocytes ($n=9123$ from 16 countries; 6588 from 13 countries in 2017). Ovarian tissue cryopreservation was reported by 2 (3 in 2017) and 11 (10 in 2017) countries, respectively, for pre- and post-pubertal patients with use of post-pubertal tissue through transplantation reported in four countries (Greece, Italy, Poland and Spain). Testicular tissue cryopreservation in post-pubertal patients and pre-pubertal boys was reported from eight (8 in 2017) countries and from one country (4 in 2017), respectively.

Table V IUI with husband (IUI-H) or donor (IUI-D) semen in 2018.

| Country | IUI-H | | | | | | IUI-D | | | | | |
|-------------------------------------|----------------|--------------|----------------|---------------|------------|-------------|--------------|-------------|----------------|---------------|------------|-------------|
| | Cycles | Deliveries | Deliveries (%) | Singleton (%) | Twin (%) | Triplet (%) | Cycles | Deliveries | Deliveries (%) | Singleton (%) | Twin (%) | Triplet (%) |
| Albania | 61 | 7 | 11.5 | 57.1 | 42.9 | 0.0 | | | | | | |
| Armenia | 906 | 124 | 13.7 | 82.3 | 17.7 | 0.0 | 108 | 17 | 15.7 | 100.0 | 0.0 | 0.0 |
| Austria | | | | | | | | | | | | |
| Belarus | 1098 | 115 | 10.5 | 92.2 | 7.8 | 0.0 | 45 | 8 | 17.8 | 100.0 | 0.0 | 0.0 |
| Belgium | 12 382 | 880 | 7.1 | 95.8 | 4.0 | 0.2 | 9296 | 1026 | 11.0 | 96.9 | 3.1 | 0.0 |
| Bosnia-Herzegovina, Federation part | 130 | 11 | 8.5 | 100.0 | 0.0 | 0.0 | | | | | | |
| Bulgaria | | | | | | | | | | | | |
| Czech Republic | | | | | | | | | | | | |
| Denmark | 10 108 | 1030 | 10.2 | 90.4 | 9.6 | 0.0 | 8453 | 556 | 6.6 | 95.7 | 4.3 | 0.0 |
| Estonia | 140 | 9 | 6.4 | 100.0 | 0.0 | 0.0 | 170 | 26 | 15.3 | 100.0 | 0.0 | 0.0 |
| Finland | 2570 | 211 | 8.2 | | | | 968 | 133 | 13.7 | | | |
| France | 44 390 | 4568 | 10.3 | 91.3 | 8.4 | 0.3 | 2789 | 526 | 18.9 | 91.8 | 8.0 | 0.2 |
| Germany | | | | | | | | | | | | |
| Greece | 2715 | 213 | 7.8 | 96.2 | 3.8 | 0.0 | 373 | 65 | 17.4 | 93.8 | 6.2 | 0.0 |
| Hungary | 2786 | 158 | 5.7 | 90.5 | 9.5 | 0.0 | | | | | | |
| Iceland | 19 | 6 | 31.6 | 100.0 | 0.0 | 0.0 | 182 | 32 | 17.6 | 100.0 | 0.0 | 0.0 |
| Ireland | 141 | 14 | 9.9 | 92.3 | 0.0 | 7.7 | 90 | 11 | 12.2 | 100.0 | 0.0 | 0.0 |
| Italy | 17 083 | 1276 | 7.5 | 91.1 | 8.4 | 0.5 | 667 | 93 | 13.9 | 86.0 | 11.8 | 2.2 |
| Kazakhstan | 485 | 50 | 10.3 | 80.0 | 18.0 | 2.0 | 51 | 16 | 31.4 | 50.0 | 50.0 | 0.0 |
| Latvia | 63 | 7 | 11.1 | 71.4 | 28.6 | 0.0 | 50 | 4 | 8.0 | 100.0 | 0.0 | 0.0 |
| Lithuania | 382 | 29 | 7.6 | 92.3 | 7.7 | 0.0 | 7 | 2 | 28.6 | 100.0 | 0.0 | 0.0 |
| Luxembourg | 249 | 24 | 9.6 | 83.3 | 16.7 | 0.0 | 78 | 13 | 16.7 | 76.9 | 23.1 | 0.0 |
| Malta | | | | | | | | | | | | |
| Moldova | 87 | | | | | | | | | | | |
| Montenegro | 202 | 25 | 12.4 | 96.0 | 4.0 | 0.0 | | | | | | |
| North-Macedonia | 796 | 26 | 3.3 | 100.0 | 0.0 | 0.0 | 31 | 1 | 3.2 | 100.0 | 0.0 | 0.0 |
| Norway | 276 | 31 | 11.2 | 86.7 | 13.3 | 0.0 | 815 | 109 | 13.4 | 95.4 | 4.6 | 0.0 |
| Poland | 11 918 | 700 | 5.9 | 94.6 | 5.3 | 0.1 | 1863 | 222 | 11.9 | 94.8 | 4.7 | 0.5 |
| Portugal | 2137 | 180 | 8.4 | 90.6 | 8.9 | 0.6 | 426 | 72 | 16.9 | 87.5 | 12.5 | 0.0 |
| Romania | 1625 | 90 | 5.5 | 93.3 | 6.7 | 0.0 | 144 | 18 | 12.5 | 77.8 | 22.2 | 0.0 |
| Russia | 8486 | 861 | 10.1 | 92.5 | 6.6 | 0.8 | 3279 | 413 | 12.6 | 95.4 | 4.6 | 0.0 |
| Serbia | 432 | 28 | 6.5 | 92.9 | 3.6 | 3.6 | | | | | | |
| Slovenia | 594 | 53 | 8.9 | 86.8 | 11.3 | 1.9 | | | | | | |
| Spain | 21 467 | 2183 | 10.2 | 88.9 | 10.9 | 0.2 | 12633 | 1837 | 14.5 | 89.7 | 10.0 | 0.3 |
| Sweden | | | | | | | 2120 | 329 | 15.5 | 98.2 | 1.8 | 0.0 |
| Switzerland | | | | | | | | | | | | |
| The Netherlands | | | | | | | | | | | | |
| Ukraine | 1056 | 75 | 7.1 | 93.3 | 6.7 | 0.0 | 315 | 52 | 16.5 | 96.2 | 3.8 | 0.0 |
| UK | 3359 | | | | | | 5656 | 798 | 14.1 | 94.9 | 4.6 | 0.5 |
| All* | 148 143 | 12984 | 8.9 | 91.2 | 8.4 | 0.3 | 50609 | 6379 | 12.6 | 93.4 | 6.4 | 0.2 |

*Total refers to these countries where data were reported and mean percentage were computed on countries with complete information.

Italy, Spain: underestimation of deliveries because of high number of pregnancies is lost to follow up.

Macedonia: data from two clinics only.

Poland: for IUI with husband sperm (IUI-H) and IUI with donor sperm (IUI-D), there were, respectively, 282 and 63 pregnancies with unknown outcome.

Discussion

From 1997 to 2018, the EIM Consortium of ESHRE has registered more than 11 million treatments cycles (11 726 598) that have led to the birth of over 2 million infants.

This 22nd annual report summarizes and analyses data on ART, IUI and FP activities collected from European compulsory or voluntary registries of 39 European countries (as in 2017). For the first time, more than 1 million treatment cycles in 1 year have been reported. Only a few countries did not participate (5 of 44 EIM members, 7 non-EIM members including Azerbaijan, Kosovo and 5 countries not offering ART services). Only three member states of the EU were not able to deliver data (Croatia, Cyprus and Slovakia). Based on a survey on medically assisted reproduction (MAR) activities (Calhaz-Jorge et al., 2020), the most likely reasons for not being able to send data are either economic at the centre and/or country level, regulatory or political.

Overall, while the number of European countries participating has remained quite stable over the last few years, with only slight fluctuations in some countries, the reported treatment cycle numbers continue to rise (+7.1% as compared to 2017), as do the number of infants born from ART (+8.8% as compared to 2017).

Awareness of the crucial role of registries on MAR activities is growing fast. Indeed, efforts of EIM and the collaboration of the EU affairs committee of ESHRE with the EU Directorate General for Health and Food Safety (DG SANTE), led to a broad reflection on the future of registries in the field of reproductive care; knowing that they are key to improving clinical care based on both outcome parameters and safety in MAR treatments (De Geyter et al., 2016; Kissin et al., 2019). Registries in MAR should aim at reaching the highest level of completeness and harmonization of European data, and joined competences should lead to a flexible common IT solution for data collection from all participating countries. EIM data are also included in the annual report of the world IVF register of ICMART (Chambers et al., 2021).

Despite well-known challenges linked to heterogeneous systems and lack of harmonization of indicators, the participation rate at the country level is as high as 86.3% of all European countries (88.6% of EIM members) after exclusion of those countries where ART is not provided. However, only 21 countries (47.7% of EIM members as in 2017) were able to send data from all institutions offering IVF services, resulting in a proportion of 91.6% of all IVF institutions sending in their data (versus 90.1% in 2017; Wyns et al., 2021). Therefore, next efforts should first focus on reaching the collection of complete data sets within countries.

Further progress towards a higher quality of the data from participating countries is expected through achieving a prospective cycle-by-cycle data collection (ongoing for 14 countries in 2018) with harmonized indicators. In this regard, as a first step, a minimum core data set on outcome parameters with definitions of collected items was established (<https://www.eshre.eu/Data-collection-and-research/Consortia/EIM>). Until higher quality data, including harmonization of collection systems among countries and registration of indicators taking into account centre/country-specific practices (e.g. freeze-all cycles, embryo transfer policy, PGT-A, etc.), become available, the interpretation of the data should remain cautious.

Besides the current EU objective of installing better vigilance in MAR, increased transparency on access to reproductive care and

cross-border treatments for all stakeholders is also of importance. Over the years, EIM has constantly recorded a high variability in access to treatment between countries, ranging per million women aged 15–45 years from 2335 in Lithuania to 19 181 in Denmark, and per million inhabitants from 389 in Lithuania to 3549 in Denmark.

While such data are unique in Europe, interpretation becomes more difficult as the historical estimated threshold of 1500 fresh ART cycles needed for infertility care per million inhabitants is becoming obsolete owing to numerous technological developments in the field. Cross-border patients also matter when best estimates of thresholds for sufficiency need to be established. Unfortunately, data on cross-border care were available for only 12 countries in 2018 (8 in 2017).

Concerning treatment modalities, ICSI remains the most applied with a trend to stabilization of its use during the last years (Table I; Fig. 1). FET is the second most used technique. Over the years, higher proportions of FET treatment cycles (FET/(FET + ICSI + IVF)) (32.6% in 2017 and 35.5% in 2018) were recorded. However, the proportion of FET cycles varies considerably among countries with complete data sets (ranging from 0.8% to 99.2%) reflecting the high variability in practices. This is also observed for freeze-all cycles (Supplementary Tables SV and SVI) that have been increasingly reported since 2014 and which reach proportions per aspiration (oocytes and embryos together) of up to 29.8% (5.4% in 2017) and 41.7% (49.1% in 2017), respectively for IVF and ICSI.

Such variability should be considered when interpreting data, especially regarding the evolution of pregnancy and delivery rates for fresh IVF and ICSI cycles (per aspiration) and for FET cycles (per thawing) over the years (Table III; Figs 2A and B and 3A and B). Indeed, the higher success rates recorded for FET (per thawing) compared to fresh IVF and ICSI (per aspiration), although kept here for comparison with previous reports, is misleading and different factors that may influence outcomes should not be neglected. First, patients who benefit from embryo cryopreservation may have a better prognosis. Second, inequalities in denominators are also of importance as the average proportion of aspirations that will result in embryo transfer is most likely different from the proportion of thawings that will lead to an embryo replacement. It is also of note that recorded delivery rates per transfer were lower for FET than for both IVF and ICSI cycles. Such observations in large data collection sets are key to pinpoint research questions towards potential causes, among others the influence of hormonal support on miscarriage rates in FET cycles.

Cumulative delivery rates per cycle or per aspiration are better outcome indicators to assess treatment effectiveness (De Neubourg et al., 2016) but, so far, true cumulative delivery and livebirth rates cannot be calculated by the EIM consortium as only aggregated data are collected. The addition of outcomes of fresh and FET during the same calendar year is therefore used as a proxy-indicator until a European cycle-by-cycle registry is established. When including data from 36 countries (34 countries in 2017) a 'cumulative' delivery rate during the 1-year period of 32.3% (30.8% in 2017) was recorded. Gains taken from additional FET (over delivery rates from fresh embryo transfers) were also highly variable, ranging from 2.5% to 38.7%, reflecting most likely differences in freezing policies and indications.

Trends are important to inform the field on uptake of data driven from registries and analyse subsequent modification of practices (Ferraretti et al., 2017; De Geyter et al., 2020b). For instance, dissemination of EIM data sets increased awareness among professionals on

the benefit of reducing the number of embryos replaced per transfer (Fig. 4A) to diminish multiple births (Fig. 4B). As a result, for the first time, most transfers involved the replacement of one embryo (elective or not) (50.7% of cycles versus 46% with single embryo replacement in 2017). In parallel to the evolution of the number of replaced embryos, the proportion of both twin and triplet deliveries continued to decrease (Fig. 4B) with twin and triplet rates for fresh IVF and ICSI cycles together being 12.4% (range: 1.9–27.4) and 0.2% (range: 0–4.2), respectively.

In the future, it is expected that efforts will lead to the ultimate goal of the birth of one healthy child (Land and Evers, 2003) per embryo transfer and thus to the concomitant reduction of prematurity associated with multiple births (Fig. 5).

Aiming at promoting singleton pregnancies by elective single embryo transfer but also at a reduced time to pregnancy, embryo culture is often prolonged up to the blastocyst stage. However, while the benefit of blastocyst stage transfers on ART outcomes is still a matter of debate (Glujovsky *et al.*, 2016; Practice Committee of the American Society for Reproductive Medicine and Practice Committee of the Society for Assisted Reproductive Technology, 2018), data showed pregnancy rates for blastocyst transfers to be higher than for cleavage stage embryos (40.0% versus 28.5% for fresh IVF and ICSI cycles together, and 38.6% versus 27.2% for FET). However, one should remember that while blastocyst transfer results in higher pregnancy and live birth rates per transfer, it also results in lower numbers of embryos available for transfer, pointing to the importance of true cumulative outcome parameters. Unfortunately, such data that would also allow the assessment of the time to pregnancy were not available.

Besides multiplicity and prematurity, other safety aspects of ART most likely remain underreported, with the highest rate of complications for OHSS (0.17%, similar to 0.2% in 2017) and an incidence of all other complications being registered at 0.14% (0.16% in 2017). Reports on maternal deaths related to ART are even scarcer, with a reported best estimate of six maternal deaths directly related to IVF per 100 000 IVF treatments in a national cohort from The Netherlands, where OHSS and sepsis were the major causes (Braat *et al.*, 2010). It is noticeable that three maternal deaths after ART were registered in 2018 (Supplementary Table SXVI) although the link with the ART procedure was either not communicated or not established with certainty.

Furthermore, although the age of recipients in ED cycles did not modify the outcome of the cycle, risks associated with pregnancies in aging women should not be neglected as a potential additional safety aspect of the treatment. Indeed, a survey on the legislation and reimbursement aspects has shown that some countries do not have age limitations for recipients in ED cycles (Calhaz-Jorge *et al.* 2020).

Allowing for reliable comparisons of practices and identifying the safest and most efficient care should be the objective of MAR registries. This will only be obtained by upscaling the quality of collected data towards complete and harmonized data throughout Europe. Besides the establishment of clear definitions of registered items, providing the countries and competent authorities with an adapted IT solution should be the next priority. Future developments in MAR registries could be guided and enforced by new requirements established at the EU level. Collaborative work between the EU, national competent authorities and EIM experts will be of the utmost importance to

eventually respond to expectations in terms of vigilance, quality of care and transparency in ART. The same new collaborative methodology would be extended to non-EU countries.

Supplementary data

Supplementary data are available at *Human Reproduction Open* online.

Data availability

All data are incorporated into the article and its online [supplementary material](#).

Authors' roles

C.W. drafted the manuscript and was responsible for final editing of the manuscript. C.D.G., C.C.-J., M.S.K., T.M., J.S., C.B., A.T.-S. and I.A.R. edited the manuscript. V.G. was responsible for the data collection and edited the manuscript. V.G. was responsible for raw data curation, contributed to the tables, contributed to the figures and edited the manuscript. All authors revised and approved the final manuscript.

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Conflict of interest

There are no competing interests.

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