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ART in Europe, 2016: 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 reported data on cycles in ART, IUI and fertility preservation (FP) interventions in 2016 as compared to previous years, as well as the main trends over the years?

SUMMARY ANSWER: The 20th ESHRE report on ART and IUI shows a progressive increase in reported treatment cycle numbers in Europe, with a decrease in the number of transfers with more than one embryo causing a reduction of multiple delivery rates (DR), as well as higher pregnancy rates and DR after frozen embryo replacement (FER) compared to fresh IVF and ICSI cycles, while the outcomes for IUI cycles remained stable.

WHAT IS KNOWN ALREADY: Since 1997, ART aggregated data generated by national registries, clinics or professional societies have been collected, analysed by the European IVF-monitoring Consortium (EIM) and reported in 19 manuscripts published in *Human Reproduction* and *Human Reproduction Open*.

STUDY DESIGN, SIZE, DURATION: Yearly collection of European medically assisted reproduction (MAR) data by EIM for ESHRE. The data on treatments performed between 1 January and 31 December 2016 in 40 European countries were provided by either National Registries or registries based on personal initiatives of medical associations and scientific organizations.

PARTICIPANTS/MATERIALS, SETTING, METHODS: In all, 1347 clinics offering ART services in 40 countries reported a total of 918 159 treatment cycles, involving 156 002 with IVF, 407 222 with ICSI, 248 407 with FER, 27 069 with preimplantation genetic testing, 73 927 with egg donation (ED), 654 with IVM of oocytes and 4878 cycles with frozen oocyte replacement (FOR). European data on IUI using husband/partner's semen (IUI-H) and donor semen (IUI-D) were reported from 1197 institutions offering IUI in 29 and 24 countries, respectively. A total of 162 948 treatments with IUI-H and 50 467 treatments with IUI-D were included. A total of 13 689 FP interventions from 11 countries including oocyte, ovarian tissue, semen and testicular tissue banking in pre-and postpubertal patients were reported.

MAIN RESULTS AND THE ROLE OF CHANCE: In 20 countries (18 in 2015) with a total population of approximately 325 million inhabitants, in which all ART clinics reported to the registry, a total of 461 401 treatment cycles were performed, corresponding to a mean of 1410 cycles per million inhabitants (range 82–3088 per million inhabitants). In the 40 reporting countries, after IVF the clinical pregnancy rates (PR) per aspiration and per transfer in 2016 were similar to those observed in 2015 (28.0% and 34.8% vs 28.5% and

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‡EIM Committee 2019–2021: chairman: C.W.; chairman elect: J.S.; past chairman: C.D. members: C.B., C.C.-J., M.K., T.M., A.R., A.T.-S. and S.V., V.G. is a science manager at ESHRE Central Office, Brussels. See also Appendix for contributing centres and contact persons representing the data collection programmes in the participating European countries.

34.6%, respectively). After ICSI, the corresponding rates were also similar to those achieved in 2015 (25% and 33.2% vs 26.2% and 33.2%). After FER with own embryos, the PR per thawing is still on the rise, from 29.2% in 2015 to 30.9% in 2016. After ED, the PR per fresh embryo transfer was 49.4% (49.6% in 2015) and per FOR 43.6% (43.4% in 2015). 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 41.5%, 51.9%, 6.2% and 0.4% of all treatments, respectively (corresponding to 37.7%, 53.9%, 7.9% and 0.5% in 2015). This resulted in a proportion of singleton, twin and triplet DRs of 84.8%, 14.9% and 0.3%, respectively (compared to 83.1%, 16.5% and 0.4%, respectively in 2015). Treatments with FER in 2016 resulted in twin and triplet DR of 11.9% and 0.2%, respectively (vs 12.3% and 0.3% in 2015). After IUI, the DRs remained similar at 8.9% after IUI-H (7.8% in 2015) and at 12.4% after IUI-D (12.0% in 2015). Twin and triplet DRs after IUI-H were 8.8% and 0.3%, respectively (in 2015: 8.9% and 0.5%) and 7.7% and 0.4% after IUI-D (in 2015: 7.3% and 0.6%). The majority of FP interventions included the cryopreservation of ejaculated sperm ($n = 7877$ from 11 countries) and of oocytes ($n = 4907$ from eight countries).

LIMITATIONS, REASONS FOR CAUTION: As the methods of data collection and levels of completeness of reported data vary among European countries, the results should be interpreted with caution. A number of countries failed to provide adequate data about the number of initiated cycles and deliveries.

WIDER IMPLICATIONS OF THE FINDINGS: The 20th ESHRE report on ART and IUI shows a continuous increase of reported treatment numbers and MAR-derived livebirths in Europe. Being already the largest data collection on MAR in Europe, continuous efforts to stimulate data collection and reporting strive for future quality control of the data, transparency and vigilance in the field of reproductive medicine.

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

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

Introduction

This is the 20th annual report of the European IVF-monitoring Consortium (EIM) under the umbrella of ESHRE containing the data on ART, IUI and fertility preservation (FP) as reported by 40 participating European countries in 2016 (Supplementary Data).

Eighteen previous reports published in *Human Reproduction* (https://www.eshre.eu/Data-collection-and-research/Consortia/EIM/Publications.aspx) and one in *Human Reproduction Open* (De Geyter *et al.*, 2020) covered treatment cycles from 1997 to 2015. As in previous reports, the printed version contains the five most relevant tables. Twenty additional supplementary tables (Supplementary Tables SI–SXX) are available online. The settings of the data are consistent with those published in the previous reports, aiming at easier comparison and assessment of trends. For the first time, an additional set of data dealing with FP was collected and added to this report.

Material and methods

Data collected on an aggregate basis were provided by 40 European countries, covering the following treatment modalities: IVF, ICSI, frozen embryo replacement (FER), egg donation (ED), IVM, pooled data on preimplantation genetic testing (PGT) and frozen oocyte replacement (FOR). With regards to IUI, split data for use of husband's/partner's semen (IUI-H) and donor semen (IUI-D) were included. The report includes treatments started between 1 January and 31 December 2016. Data on pregnancies and deliveries were derived from follow-up of treatments performed in 2016. In addition, data on FP, including numbers and types of cryostored material and interventions for use of stored material between 1 January and 31 December 2016, were provided by 11 countries and reported as aggregated data of events that occurred during a 1-year period.

The national representatives of 44 countries were asked to fill out questionnaires, with other involved stakeholders when applicable. The same data sets as in 2015 and additional data on FP for a total of 10 specific modules were sent using software designed for the specific requirements of this data collection (Dynamic Solutions, Barcelona, Spain). Besides evaluation of the plausibility of the results by the software, other detected inconsistencies were clarified through 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 (although with some additional subgroups of interventions) and footnotes to the tables were added for clarification on diverging 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 I shows the number of institutions or clinics offering ART services with all available treatment modalities and those performing IUI (IUI-H and IUI-D). In comparison to the 2015 data, both the total number of reporting clinics (1343 in 2015 to 1347 in 2016) and the overall number of reported treatments (849 811 in 2015 to 918 159 in 2016, +8.0%) increased. Among the 51 European countries, 44 are EIM members including 28 that are members of the European Union (Supplementary Table SI). Non-EIM members are mainly smaller

Table I Treatment frequencies after ART in European countries in 2016.

Country	IVF clinics in the country												Cycles/million*	
	IVF clinics	Included IVF clinics	IUI labs	Included IUI labs	IVF	ICSI	FER	PGT	ED	IVM	FOR	All	Women aged 15–45 years	Population
Albania	10	1			0	83	63	0	29	0	0	175		
Armenia	5	2	6	2	66	112	107		61			346		
Austria	26	26			1459	5600	2662		0			9721	5886	1110
Belarus	8	7	10	7	1310	1394	270	7	16	0	0	2997		
Belgium	18	18	29	29	2715	13 628	12 052	1100	1163	176	95	30 929	14 136	2738
Bosnia-Herzegovina, Federation part	6	1			0	89	46					135		
Bulgaria	35	35	1	1	920	6879	1813	379	1018			11 009	7153	1544
Cyprus	6	6			158	942	325	31	271			1727	9089	2020
Czech Republic	41	40			0	15 020	12 258		5265			32 543		
Denmark	19	19	35	33	6319	5703	5059	112	484	0	19	17 696	15 917	3088
Estonia	6	6	6	6	641	1184	927	2	191	0	7	2952	11 515	2245
Finland	17	17	22	22	2756	1970	3661	73	731	0		9191	9116	1673
France	102	102	181	181	22 773	45 214	33 792	1422	1158	70	344	104 773	9066	1619
Germany	134	128			17 594	56 587	25 045					99 226		
Greece	39	39	39	39	2304	15 121	4785	1251	4462	2	51	27 976	13 922	2603
Hungary	13	11			1049	3902	632		25			5608		
Iceland	1	1	1	1	199	162	229	0	54	0	0	644	9248	1928
Ireland		1			215	231	260					706		
Italy	200	200	360	360	7584	46 322	14 990	2844	4359		1460	77 559	7014	1280
Kazakhstan	10	5			994	1671	958	154	683			4460		
Latvia	6	3	6	3	352	527	515	7	127			1528		
Lithuania	6	5	6	5	295	371	92			0	0	758		
Luxembourg	1	1	5	0	312	354	314	0	0	0	0	980		1684
Malta	2	2	2	0	7	273	0	0	0	0	79	359	3624	822
Moldova	4	3	5	3	0	739	181		14			934		
Montenegro	5	4	5	4	7	501	58					566		
North Macedonia	7	5	0	0	420	2100	288	0	122	0	4	2934		
Norway	11	11	11	11	3587	3330	3363			0	0	10 280	10 101	1963
Poland	39	39	0	38	881	16 984	11 375	692	1085	33	299	31 349		816
Portugal	24	24	26	26	2462	3751	2008	127	988	1	28	9365	1726	907
Romania	19	11	19	11	1445	2034	1495	6	29			5009		
Russia	199	151			34 058	43 766	31 051	4420	7122	260	558	121 235		
Serbia	12	3	12	3	170	93	23	0	0	0	0	286		
Slovenia	3	3	3	3	1017	2268	1389	37	7	0	7	4725	12 717	2288
Spain	247	240	366	291	5624	56 640	27 559	10 238	39 530	41	1277	140 909		
Sweden	18	17		0	6235	6088	6080	304	282			18 989		
Switzerland	27	27			1042	5059	4859					10 960	10 329	1309
The Nederlands	13	13	90	0	6781	7803	12 545	772				27 901	5403	1639
Ukraine	46	38	17	17	1167	9454	6967	1658	1157		8	20 411		
UK	82	82	101	101	21 084	23 273	18 311	1433	3494	71	642	68 308	5240	1041
All	1467	1347	1364	1197	156 002	407 222	248 407	27 069	73 927	654	4878	918 159	7794	1410

Treatment cycles in IVF and ICSI refer to initiated cycles.
For Austria, Belgium, Iceland, Lithuania and Malta, treatment cycles IVF refer to aspirations. For Austria, Belgium, Iceland and Lithuania, treatment cycles ICSI refer to aspirations. For Austria and Belgium, the total number of initiated cycles was only available for IVF and ICSI together, being 10 097 and 19 163, respectively.
For the Czech Republic, no distinction between IVF and ICSI is made. All cycles are counted as ICSI. For Belgium, there are 824 extra aspiration cycles for which it is not known whether IVF or ICSI was performed.
Treatment cycles in frozen embryo replacement (FER) refer to thawings.
For Finland, Hungary, Kazakhstan, Sweden and the Netherlands, treatment cycles refer to transfers.
Treatment cycles in preimplantation genetic testing (PGT) contain both fresh and frozen cycles and refer to initiated cycles in the fresh cycles and aspirations in the frozen cycles.
Treatment cycles in egg donation (ED) refer to donation cycles and contain fresh and frozen cycles.
ED fresh: for France and Iceland, treatment cycles refer to aspirations. ED frozen: for France, Iceland, Kazakhstan, Spain, Sweden and the UK, treatment cycles refer to aspirations.
Treatment cycles in IVM refer to aspirations.
Treatment cycles in frozen oocyte replacement (FOR) refer to thawings.

countries not offering ART services. In 2016, 40 countries delivered data to EIM with Luxemburg providing data as a new EIM member. Croatia, Georgia, Slovakia and Turkey failed to deliver data (9.1% of EIM members, 11.6% in 2015). In 18 countries (45% of reporting countries), all of the ART clinics within the country reported data sets. Currently, 1347 clinics reported their data (91.8% of all known clinics in Europe, 90.6% in 2015). As in 2015, the four European countries with the largest treatment numbers in 2016 were Spain (140 909), Russia (121 232), France (104 773) and Germany (99 226).

Size of the clinics and reporting methods

The size of reporting clinics, defined by the number of treatment cycles, remains highly variable between and inside countries (Supplementary Table SII). In 2016, clinics with cycle numbers between 200 and 499 were the most common (29.5% vs 29.9%). Small clinics providing less than 100 treatments cycles per year were present in 16 countries (40% of the countries) and the proportion of clinics performing more than 1000 treatment cycles per year seems on a slight rise over the years with 19.4% in 2016, 17.9% in 2015, 18.3% in 2014, 17.8% in 2013 and 16.9% in 2012.

Country-specific requirements and reporting methods are presented in Supplementary Table SIII. Data collection was either voluntary (19 out of 40 countries) or compulsory. Twenty countries had only a partial reporting and provided the data mainly on a voluntary basis (16/20 countries) to medical organizations/professional societies (10 countries), based on a single person's initiatives (five countries) or to the national health authority (one country).

By contrast, complete reporting was achieved mainly when data collection was compulsory (17/20 countries) with subsequent data communication to the national health authority (all but two countries).

Transfer of data was mostly done on an aggregate basis (26 countries/40 in 2016, as in 2015).

Number of treatment cycles per technique and availability

In 2016, 918 159 treatment cycles were reported to EIM (68 348 more than in 2015, +8.0%). Since 1997 increasing numbers of clinics reported to EIM, which so far recorded more than 9 772 904 treatments cycles and the birth of more than 1 861 760 infants (Table II). As shown in Table I, compared to 2015, 10 countries reported fewer treatment cycles, but Ireland and Luxemburg were now able to provide data. Furthermore, the largest increment in reported treatment numbers was recorded in Spain (+21 034, +9 clinics), France (+10 855, same number of clinics) and Russia (+10 512, +7 clinics). The numbers of treatment cycles per technique in 2016 are presented in Table I: ICSI was the most used (407 222, 44.4% of treatment cycles vs 45.4% in 2015). Cycles of IVF, FER, ED, FOR, PGT and IVM represented 17%, 27%, 8.1%, 0.5%, 2.9% and 0.0007% of all cycles, respectively. While the distribution of the available techniques remained similar to 2015 (IVF, FER, ED, FOR, PGT and IVM, respectively 18.4%, 25.7%, 7.6%, 0.5%, 2.5% and 0.0003%), for each single technique higher cycle numbers were registered. The steepest rise in treatment numbers was observed in FER (+13.9%), in ED (+14.7%), in FOR (+13.6%), in PGT (+27.4%) and IVM (+246.8%). The proportion of FER relative to fresh treatments (IVF + ICSI) is still on the rise (44.1% vs 40.3% in 2015 and 37.8% in 2014). The highest proportions were reached in Armenia (75.9%), Belgium (73.7%), Czech Republic (81.6%), Finland (77.5%), Switzerland (79.6%) and The Netherlands (86.0%). No FER were reported/performed in Malta according to their legislation.

Table II Number of institutions offering ART services, treatment cycles and infants born after ART in Europe, 1997–2016.

Year	Countries	Clinics	Cycles	Cycle increase (%)	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
Total			9 772 904		1 861 760

Among the total of 563 224 fresh treatments (ICSI + IVF), 72.3% were performed with ICSI, showing a rise of +1.2% compared to 2015. Figure 1 shows the evolution and continuing preponderance of ICSI over conventional IVF and the increase in the proportion of FER cycles relative to fresh cycles (IVF + ICSI).

The number of cycles per million women of reproductive age and per million inhabitants is shown in Table I and Supplementary Table SIV. Availability of ART was calculated for the 20 countries with full coverage (Supplementary Table SIV). While there is a huge variability in availability (range 1726–15 917 per million women aged 15–45 years), ART was most available in Denmark and least available in Portugal. Consequently, the proportion of newborns resulting from ART born in Denmark was 5.1% of all newborns in that country. Other countries that reported high proportions were Austria (6.2%) and Slovenia (5.5%).

Pregnancies and deliveries after treatment

Table III shows PR and delivery rates (DR) after IVF or ICSI and after FER (after both IVF and ICSI). Because, as in previous years, data on

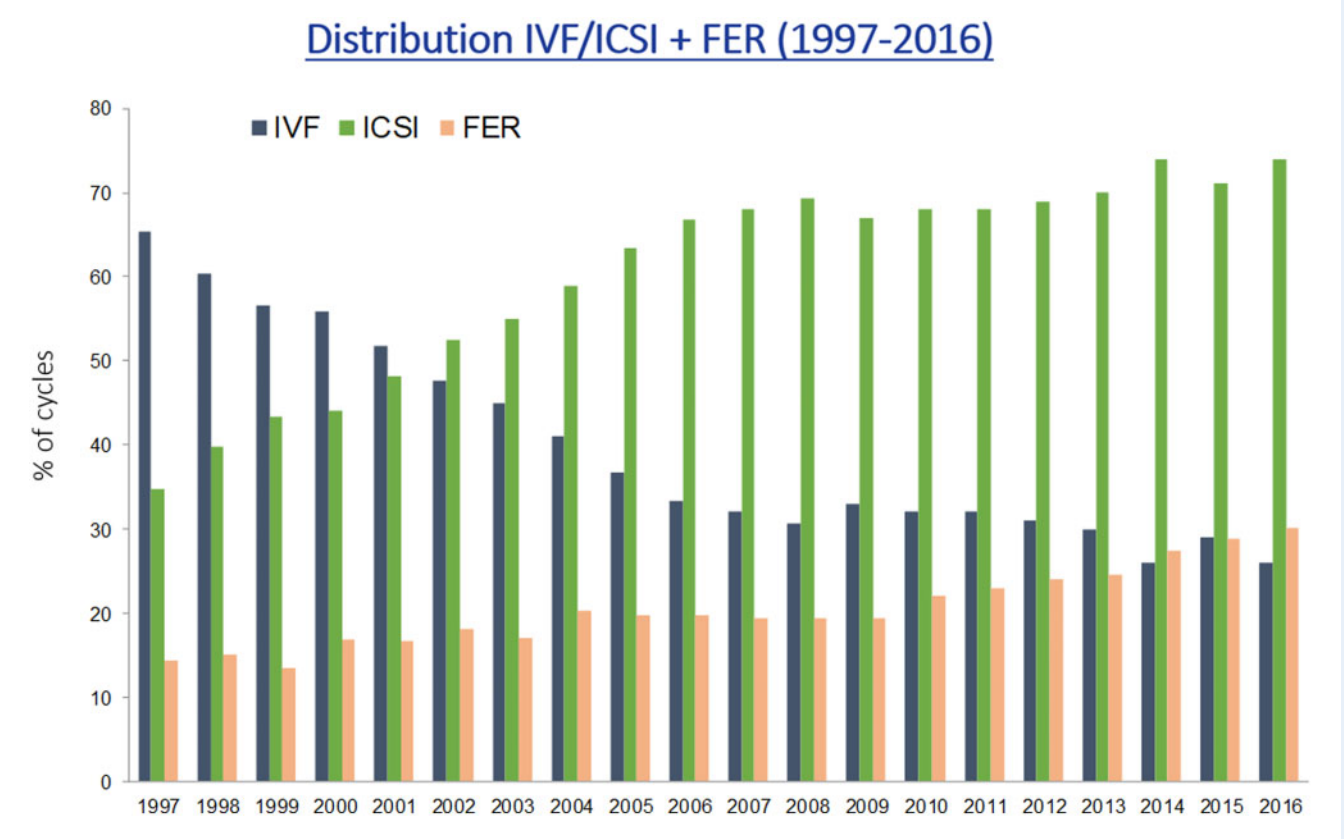

Figure 1. Proportion of IVF versus ICSI and frozen embryo replacement (FER) in Europe, 1997–2016.

numbers of initiated cycles were incomplete, the outcome data were calculated per aspiration.

Among the 40 reporting countries, 33 were able to provide both pregnancy and delivery data per aspiration after IVF and ICSI and per thawing for FER (completeness rate for both: 82.5%). In Supplementary Table SIV, the numbers of deliveries for the 20 countries that had full coverage of the reporting are presented.

As in all previous reports, the PR and DR (for all types of treatment cycles) varied significantly from one country to another. Per aspiration, PR ranged from 13.2% to 57.1% and DR from 12.3% to 46.5% in fresh cycles after IVF or ICSI (excluding Lithuania where DR was not available for two of the five centres reporting pregnancies). After FER per thawing, the PR were between 21.4% and 51.9% and the DR varied between 13% and 45.3%. Overall, PR and DR were higher for FER cycles (per thawing) than for both fresh IVF and ICSI cycles (per aspiration) (Table III).

For the third time, «freeze all» cycles were collected (Supplementary Table SV) including cryopreservation of all oocytes reported by 10 countries (six in 2015 and 2014) and of all embryos by 22 countries (21 in 2015 and 2014). The highest proportions of freeze all cycles per aspiration were 3.5% at the oocyte and 17.3% at the embryo level.

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

As in 2015, ED cycle numbers were available for 26 countries although 29 provided outcome data (Supplementary Table SVIII). Most donation cycles were carried out in Spain, Russia, the Czech Republic and Greece. Freshly collected oocytes were used in 33 406 ED cycles and frozen oocytes (FOR) in 11 757 ED cycles. PR were only available per embryo transfer for freshly donated oocytes (49.4%, in 2015 49.6%) and for thawed oocytes (41%, in 2015 40.3%). Outcomes for the different countries show a high variability ranging between 9.7% and 66.5%% for fresh oocytes and between 29.5% and 67.4% for thawed oocytes. A total of 22 497 deliveries were reported (19 849 in 2015 and 17 259 in 2014) representing a further increase of +13.3%.

Age distribution

As seen in Supplementary Tables SIX and SX, age distributions of women treated with IVF and ICSI varied between countries. Not all countries were able to provide data on the age distribution in ICSI (six missing) and in IVF (seven missing), some because no IVF treatments were carried out. The highest percentage of women aged40 years and older undergoing aspiration for IVF was found in Greece (as in 2015), whereas the highest percentage of women aged <34 years was found in Montenegro (as in 2015) followed by Ukraine. For ICSI, the highest percentage of women aged 40 years and older undergoing aspiration was found in Greece (as in 2015), whereas the highest percentage of women undergoing aspiration aged <34 years was recorded in

Table III Results after ART in 2016.

Country	IVF				ICSI			FER				
	Initiated cycles IVF + ICSI	Aspirations	Pregnancies per aspiration (%)	Deliveries per aspiration (%)	Aspirations	Pregnancies per aspiration (%)	Deliveries per aspiration (%)	Thawings	Pregnancies per thawing (%)	Deliveries per thawing (%)	ART infants †	ART infants per national births (%)
Albania	83				83	41.0	33.7	63	41.3	23.8	70	
Armemia	178	66	24.2	21.2	112	25.9	21.4	107	36.4	28.0	114	0.3
Austria	10 097	1459	33.9		5600	28.5	46.5	2662	34.3		5479	6.2
Belarus	2704	1241	35.9	27.2	1328	34.7	24.9	270	25.9	14.8	798	0.7
Belgium	19 163	2715	27.8	20.3	13 628	24.2	16.0	12 052	27.8	17.1	5566	4.6
Bosnia-Herzegovina, Federation part	89				80	33.8	26.3	46	23.9	13.0	31	
Bulgaria	7799	868	21.7	13.6	5660	26.3	19.7	1813	32.2	25.0		
Cyprus	1100	146	39.0	33.6	813	39.1	37.4	325	40.6	33.5		
Czech Republic	15 020				14 661	22.5	15.0	12 258	30.2	18.9	6278	5.6
Denmark	12 022	6309	20.9	14.1	5701	22.5	17.7	5059	24.7	19.9	3157	5.1
Estonia	1825	635	25.2	19.2	1184	28.0	20.9	927	22.8	15.6	664	4.7
Finland	4726	2573	23.8	18.3	1879	23.8	18.3				1607	3.0
France	67 987	20 058	21.1	18.3	41 587	21.4	18.8	33 792	21.4	18.3	20 187	2.6
Germany	74 181	16 234	28.8	19.4	52 235	27.0	18.2	25 045	27.6	17.4	20 540	
Greece	17 425	2256	26.9	18.6	13 082	23.0	15.3	4785	36.7	23.9	6346	
Hungary	4951	1043	31.4		3871	32.3						
Iceland		199	25.6	23.1	162	30.2	25.3	229	29.3	20.1	155	3.8
Ireland	446	183	40.4	33.9	214	38.8	30.4	260	38.8	30.0	213	
Italy	53 906	6857	21.6	15.1	41 899	18.7	12.3	14 990	27.5	19.3	12 053	2.5
Kazakhstan	2665	974	40.1	26.4	1648	38.3	25.9				1497	0.4
Latvia	879	352	36.9	22.2	527	27.5	15.2	515	40.2	28.3	366	
Lithuania		295	52.9	7.1	371	42.6	1.6	92	23.9		38	0.1
Luxembourg	666	296	13.2	9.8	319	19.7	16.9	314	25.8	17.2	155	2.6
Malta	273	7			187						40	0.9
Moldova	739				731	41.9	34.7	181	51.9	45.3		
Montenegro	508	7	57.1	28.6	496	27.0	21.4	58	31.0	27.6	156	2.1
Norway	6917	3412	28.8	24.2	3172	29.6	24.8	3363	23.5	18.6		

(continued)

Table III Continued

Country	IVF				ICSI			FER				
	Initiated cycles IVF + ICSI	Aspirations	Pregnancies per aspiration (%)	Deliveries per aspiration (%)	Aspirations	Pregnancies per aspiration (%)	Deliveries per aspiration (%)	Thawings	Pregnancies per thawing (%)	Deliveries per thawing (%)	ART infants †	ART infants per national births (%)
North Macedonia	2520	390	33.8	10.5	2068	35.5	18.9	288	34.4	21.2	628	3.4
Poland	17 865	873	28.6	23.1	16 935	25.8	15.6	11 375	35.9	23.6	6336	
Portugal	6213	2279	29.4	22.6	3676	23.0	17.4	2008	30.9	22.8	2333	2.7
Romania	3479	1399	31.6	23.4	1954	28.3	22.7	1495	30.6	19.7	1288	0.7
Russia	77 824	33 129	29.9	21.8	42 542	25.9	18.4	31 051	38.5	27.5	30 770	1.7
Serbia	263	166	25.9	21.7	87	41.4	37.9	23	39.1	39.1	100	0.2
Slovenia	3285	916	33.0	25.8	2220	25.8	20.7	1389	31.3	23.0	1116	5.5
Spain	62 264	5229	26.3	19.1	45 373	22.4	16.3	27 559	34.4	22.9	31 715	7.7
Sweden	12 323	5803	29.3	24.3	5744	27.4	23.2				4923	4.1
Switzerland	6101	958	24.3	17.8	4621	24.5	19.1	4859	23.4	16.6	2160	2.5
The Nederlands	14 584	5819	31.0	22.2	7038	32.9	24.6					
Ukraine	10 621	1141	36.8	25.7	9243	30.1	24.6	6967	46.0	38.6	7622	1.9
UK	44 357	18 483	32.8	28.5	23 097	33.1	28.8	18 311	34.2	29.5	21 265	2.7
All	568 048	144 770	28.0	20.8	375 828	25.0	18.5	224 531	30.9	22.0	195 766	2.9

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

†ART infants also include ED.

For IVF and ICSI, there were for Austria, Czech Republic, Finland, France, Greece, Kazakhstan, Latvia, Poland, Portugal, Russia, Serbia, Spain and Sweden, respectively 2650, 3, 810, 14, 254, 43, 13, 319, 4, 817, 1, 345 and 4 deliveries with unknown outcome. These were accepted as singletons to calculate the ART infants.

For FER, there were for Czech Republic, Finland, France, Greece, Kazakhstan, Latvia, Poland, Russia, Spain and Sweden, respectively 1, 797, 8, 42, 4, 15, 228, 471, 89 and 2 deliveries with unknown outcome. These were accepted as singletons to calculate the ART infants.

For ED, there were for Germany, Italy, Kazakhstan, Romania and Slovenia, respectively 3, 17, 14, 222 and 7582 deliveries with unknown outcome. These were accepted as singletons to calculate the ART infants.

For PGD, there were for Finland, Germany and Romania, respectively 1, 1 and 154 deliveries with unknown outcome. These were accepted as singleton to calculate the ART infants.

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

Kazakhstan (in Albania in 2015 and 2014). As expected, there was an age-dependent decline of the reported PR and DR for IVF and ICSI treatment cycles with DR in women aged 40 years and older, ranging between 0% and 13.1%, and 0% and 42.9% (on small numbers), respectively. With regard to FER (Supplementary Table SXI), the age-related decline was also visible and DR among women aged 40 years and older ranged between 0% and 34.3%.

In ED cycles (Supplementary Table SXII), the age of the recipient women did not influence outcome data and overall PR and DR were higher than in fresh and FER cycles (in partner donation).

Numbers of embryos transferred and multiple births

The subgroups defined by the number of embryos transferred after IVF and ICSI together as well as multiple births are presented in Table IV. Five countries did not report on either the number of replaced embryos per treatment cycle or on multiplicity. While overall most transfers involved the replacement of two embryos (51.9% of the transfer cycles), the proportion of transfers of only one embryo per cycle continued to rise (41.5% vs 37.7% in 2015), and the number of transfers of three or more embryos continued to decrease (Fig. 2). The number of countries reporting more than 50% of single embryo transfers (elective or not) increased to 10 (same eight as in 2015 plus Slovenia and UK). As in 2015, only Serbia reported more than 50% of transfers with three embryos. The highest proportion of transfers of four or more embryos was recorded in Greece (4.2% vs 4.9% in 2015). Information on the type of embryos (cleavage or blastocyst) transferred was not available for each of the subgroups but, for the first time, the embryo stage at the transfer was collected. Taking into account that the embryo stage at transfer was unknown for 44.5% of the fresh (IVF+ICSI) cycles, 41.9% of the transfers were performed at the blastocyst stage and the corresponding figure for FER was 62.2%.

As a result of decreasing numbers of embryos replaced per transfer, the proportion of both twin and triplet deliveries continued to decline. In 2016, twin and triplet rates for fresh IVF and ICSI cycles together were 14.9% (range 1.1–35.7) and 0.3% (range 0–4.4), respectively. Corresponding results for FER were 11.9% and 0.2%. In the two countries with the highest rates of single embryo replacement in fresh cycles (84.3% for Iceland and 82.5% for Sweden), twin rates were as low as 1.1% and 3%, respectively.

Additional information on pregnancy and delivery data are provided in Supplementary Tables SXIII and SXIV. The reported incidence of pregnancy loss was 16.4% after IVF + ICSI (in 2015: 16.4%) and 18.6% after FER (in 2015: 20.6%). The proportion of lost to follow-up was 7.8% after IVF+ICSI (in 2015: 6.3%) and 7.5% after FER (in 2015: 7.4%).

Perinatal risks and complications

In 2016, data on premature deliveries were available from 18 countries (18 countries in 2015). Premature DR based on multiplicity are presented in Supplementary Table SXV. Data from fresh IVF and ICSI, FER and ED are pooled. The incidence of extreme preterm birth (20–27 gestational weeks at delivery) was 1.1% in singletons (1.3% in 2015), 3.3% in twins (3.7% in 2015) and 8.4% in triplets (13.4% in 2015). Very premature birth rates (28–32 gestational weeks at delivery) were recorded in 2.2% of singletons, 10.5% of twin pregnancies (in 2015: 9.9%) and 45% in triplet pregnancies (in 2015: 39.2%). The evolution of the proportion of premature deliveries before 37 weeks per embryo transfer according to multiplicity is shown in Fig. 3. Term deliveries (≥37 weeks) were achieved in 85.9% (86.4% in 2015) of singleton pregnancies, 44.1% (44.7% in 2015) of twin pregnancies and 8.8% (7.5% in 2015) of triplet pregnancies.

Complications related to oocyte retrievals were reported by 33 countries (31 in 2015) and foetal reductions by 35 countries (26 in 2015) (Supplementary Table SXVI). The total number of reported cases of ovarian hyperstimulation syndrome (OHSS) (grades 3 to 5) was 1928, corresponding to a reported incidence of 0.21% (2167 cases in 2015; 0.25%). Other complications were less frequent (1471 cases) with a total reported incidence of 0.2% including 0.1% and 0.001% for bleeding and infection, respectively. No maternal death was reported in 2016 (2 out of 850 000 treatment cycles in 2015). A total of 553 foetal reductions were reported, the majority from UK, Belgium and Spain, as in 2015.

PGT/PGT-A

Table I includes PGT and PGT-A activities, which were reported from 22 countries (23 in 2015, 22 in 2014). The main contributors were Spain, Russia and Italy. The number of treatment cycles amounted to 27 069 representing 3.3% of initiated IVF + ICSI and FER cycles together (21 041; 2.8% in 2015). More details on PGT/PGT-A activities can be found in the annual reports of the ESHRE PGT consortium (De Rycke *et al.*, 2017)

These treatments involved 19 461 fresh cycles and 7242 thawings, resulting in 5776 fresh and 6434 FER. In total, 2418 pregnancies (41.9% per transfer) and 1875 deliveries (32.5% per transfer) resulted from fresh cycles. Corresponding figures for FER were 2811 (43.7% per transfer) and 2259 (35.1% per transfer).

IVM

A total of 654 treatments with IVM were reported from eight countries (265 from eight countries in 2015) (Table I). Most IVM cycles were reported from Russia, as in 2015. A total of 391 transfers resulted in 103 pregnancies (26.3% per transfer) and 43 deliveries (11% per transfer).

FOR

A total number of 4878 thawing cycles were reported by 15 countries (4294 from 17 countries in 2015) (Table I) with Italy and Spain being the largest contributors (1460 and 1277 cycles, respectively). Among 3854 transfers, 1138 resulted in pregnancies (29.5%; 30.7% in 2015) and 808 in deliveries (21%; 20.6% in 2015).

IUI

For each participating country, the institutions performing and collecting data on IUI are listed in Table V. Data on IUI with husband semen (IUI-H, Supplementary Table SXVII) or using donors' semen (IUI-D, Supplementary Table SXVIII) were collected by a total of 1197 institutions in 28 and 23 countries (25 and 21 in 2015, respectively. Among 113 450 IUI-H (139 050 in 2015) and 46 883 IUI-D (49 001 in 2015)

Table IV Number of embryos transferred after ART and deliveries in 2016.

Country	IVF + ICSI													FER		
	Fresh transfers total	Fresh transfers cleavage stage	Fresh transfers blastocyst stage	Fresh transfers unkown stage	% Fresh transfers cleavage stage**	% Fresh transfers blastocyst stage**	1 embryo (%)	2 embryos (%)	3 embryos (%)	4+ embryos (%)	Deliveries	Twin (%)	Triplet (%)	Deliveries	Twin (%)	Triplet (%)
Albania	74	72	2	0	97.3	2.7	9.5	90.5	0.0	0.0	28	35.7	0.0	15	20.0	0.0
Armemia	114	99	15	0	86.8	13.2	11.4	83.3	5.3	0.0	38	15.8	0.0	30	10.0	0.0
Austria	8702	2484	6219	0	28.5	71.5	65.7	34.0	0.3	0.0	5210	10.2	0.1			
Belarus	2300	1462	838	0	63.6	36.4	18.2	73.1	8.7	0.0	668	10.5	0.3	40	15.0	0.0
Belgium	13 081	8856	4225	0	67.7	32.3	62.8	31.9	4.7	0.6	2734	9.2	0.1	2055	7.4	0.0
Bosnia-Herzegovina, Federation part	67	31	36	0	46.3	53.7	46.3	50.7	3.0	0.0	21	14.3	0.0	6	16.7	0.0
Bulgaria																
Cyprus																
Czech Republic	10 727			10 727			70.0	29.4	0.6	0.0	2199	7.7	0.1	2313	9.0	0.2
Denmark	9567	4832	2300	2435	67.8	32.2	71.0	28.7	0.2	0.0	1895	4.9	0.0	1008	4.4	0.0
Estonia	1549	976	573	0	630.	37.0	44.7	48.9	6.3	0.0	370	14.3	0.3	145	16.6	0.0
Finland	3396			3396			85.7	14.3	0.0	0.0	810			797		
France	45 534			45 534			46.5	48.7	4.5	0.3	11 506	13.1	0.1	6189	7.8	0.1
Germany	56 413	39 850	16 563	0	70.6	29.4	21.6	69.2	9.2	0.0	12 688	21.0	0.5	4352	15.2	0.4
Greece	9494	6367	3127	0	67.1	32.9	22.5	59.3	14.0	4.2	2415	22.4	0.3	1146	23.6	0.0
Hungary	4505			4505			22.9	56.4	18.1	2.6						
Iceland	287			287			84.3	15.7	0.0	0.0	87	1.1	0.0	46	4.3	0.0
Ireland	338	338	0		100.0	0.0					127	4.7	0.0	78	2.6	0.0
Italy	36 038			36 038			30.2	50.3	17.9	1.6	6196	15.6	0.4	2890	7.4	0.2
Kazakhstan	2238	2238	0	0	100.0	0.0					674	11.3	0.0	405	32.9	0.0
Latvia	630	428	182	10	69.0	29.4	48.4	51.3	0.3	0.0	158	13.1	0.7	146	7.6	0.8
Lithuania	661	78	30	553	72.2	27.8	13.0	52.8	34.3	0.0	27	33.3	3.7			
Luxembourg	424	416	8	0	98.1	1.9	38.4	61.6	0.0	0.0	83	15.7	0.0	54	9.3	0.0
Malta	181	181	0	0	100.0	0.0	0.0	0.0	0.0	0.0	34	17.6	0.0			

(continued)

Table IV Continued

Country	IVF + ICSI													FER		
	Fresh transfers total	Fresh transfers cleavage stage	Fresh transfers blastocyst stage	Fresh transfers unkown stage	% Fresh transfers cleavage stage**	% Fresh transfers blastocyst stage**	1 embryo (%)	2 embryos (%)	3 embryos (%)	4+ embryos (%)	Deliveries	Twin (%)	Triplet (%)	Deliveries	Twin (%)	Triplet (%)
Moldova																
Montenegro	448	377	71	0	84.2	15.8	16.7	43.8	39.1	0.4	108	25.9	0.0	16	25.0	0.0
Norway																
North Macedonia	2059	1650	409	0	80.1	19.9	25.6	66.1	8.2	0.0	432	16.2	0.7	61	14.8	0.0
Poland	12 345	7104	5241	0	57.5	42.5	52.8	46.6	0.6	0.0	2848	7.6	0.1	2686	7.1	0.0
Portugal	4382	3382	1000	0	77.2	22.8	32.6	66.1	1.3	0.0	1155	19.4	0.3	457	13.6	0.0
Romania	2376	967	1408	1	40.7	59.3	22.5	60.0	17.1	0.4	771	21.3	0.1	294	16.7	0.7
Russia	57 621	15 612	30 092	11 917	34.2	65.8	40.1	56.8	3.0	0.1	15 044	17.7	0.4	8529	14.7	0.2
Serbia	227	223	4	0	98.2	1.8	12.8	26.9	60.4	0.0	69	23.5	4.4	9	0.0	0.0
Slovenia	2582	1362	1220	0	52.7	47.3	53.1	46.5	0.4	0.0	695	9.2	0.0	319	8.8	0.0
Spain	32 982	26 354	5385	1243	83.0	17.0	31.5	65.0	3.5	0.0	8378	17.0	0.2	6319	13.7	0.1
Sweden	9482	7065	2417	0	74.5	25.5	82.5	17.5	0.0	0.0	2746	3.0	0.1	1909	2.6	0.1
Switzerland	4253	3274	979	0	77.0	23.0	31.0	62.0	7.0	0.0	1053	15.6	0.5	808	15.0	0.2
The Nederlands																
Ukraine	6861	1863	4998	0	27.2	72.8	27.7	60.7	11.5	0.0	2571	21.9	0.2	2691	20.6	0.0
UK	36 986	15 572	21 414	0	42.1	57.9	54.7	42.0	3.3	0.0	11 927	11.2	0.2	5406	11.0	0.2
All*	376 348	153 513	108 756	116 646	59.1	41.9	41.5	51.9	6.2	0.4	95 765	14.9	0.3	51 219	11.9	0.2

*Totals refer only to these countries where data on number of transferred embryos and on multiplicity were reported.
**Percentages of cleavage and blastocyst stage transfers are calculated on the proportion of transfers where the day of transfer is known.
The day of transfer is unknown in 25.5%, 1.6%, 83.7%, 0.05%, 20.7% and 3.8% of all transfers in Denmark, Latvia, Lithuania, Romania, Russia and Spain, respectively.

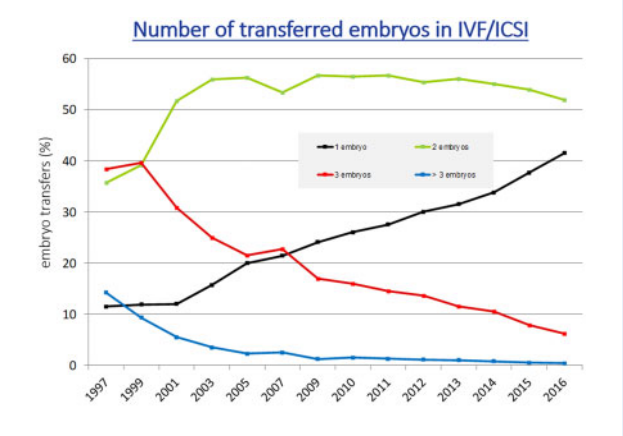

Figure 2. Number of embryos transferred in IVF and ICSI during fresh cycles in Europe, 1997–2016.

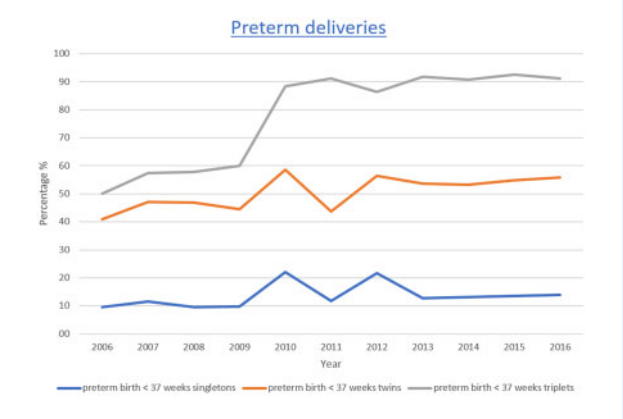

Figure 3. Proportion of premature deliveries (<37 weeks of gestation in relation to pregnancies ≥37 week of gestation) in singleton, in twin and in triplet pregnancies in Europe, 2006–2016.

reported cycles, the numbers were the highest for IUI-H in Spain, Italy and Belgium, and for IUI-D in Spain, Denmark and Belgium.

DR could be calculated for 109 399 IUI-H cycles (8.5% vs 7.8% in 2015) and 46 883 for IUI-D cycles (12% vs 12% in 2015).

Singleton deliveries were the most frequent regardless of the age group with an overall rate of 91.3% for IUI-H and 92% for IUI-D (90.6% in IUI-H, 92.1% in IUI-D in 2015). Twin and triplet rates were 8.4% and 0.3%, respectively for IUI-H, and 7.5% and 0.4% for IUI-D, respectively (in 2015: 8.9% and 0.5%, respectively for IUI-H and 7.3% and 0.6%, respectively for IUI-D).

Sum of fresh and FER ('cumulative') DR

Supplementary Table SXIX provides an estimate of a cumulative DR (different from a true cumulative DR including outcomes of all transfers performed from one aspiration). It was calculated as the ratio between the total number of deliveries from fresh embryo transfers and FER performed during a year (numerator) and the number of aspirations during the same year (denominator). The calculation included data from 38 countries (35 countries in 2015) where an overall rate of 29.6% was recorded. The benefit taken from additional FER (over the DR from fresh embryo transfers) was 10.5%, with the highest benefits recorded for Ukraine (+26.1%), Ireland (+19.6%), Finland and Albania (for both +18.1%) and the lowest for North Macedonia (+2.5%), Belarus (+1.6%) and Lithuania (0%).

Cross-border reproductive care

Ten countries reported data on cross-border patients: Albania, Belarus, Denmark, Greece, Montenegro, Portugal, Serbia, Slovenia, Spain and Switzerland. A total of 19 239 cycles (14 273 in 2015) were reported, 22.1% (29.4% in 2015) of which involved IVF/ICSI with the couple's own gametes, 46.6% (47.1% in 2015) were oocyte donations and 21.8% (22.3% in 2015) were IVF or ICSI with semen donation. In addition, 7062 IUI with sperm donation (7714 in 2015) were registered. Information regarding the countries of origin was very incomplete and not reliable enough to obtain any conclusive information. The main reasons reported by patients were to have access to a technique not legally available in their home country (39.1%; 41.7% in 2015) or to seek a higher quality treatment (23.6%; 16.6% in 2015). In 13 291 cycles (mainly from Spain), there was another, not specified, reason to go abroad.

FP

For the first time data on FP are reported here. Eleven countries were able to provide data on a total number of 13 689 interventions (Supplementary Table SXX) in pre- and postpubertal patients, both for medical and non-medical reasons. The majority of interventions consisted of the cryopreservation of ejaculated sperm ($n = 7877$ from 11 countries) and the cryopreservation of oocytes ($n = 4907$ from eight countries). Ovarian tissue cryopreservation was reported by two and seven countries, respectively, for pre- and postpubertal patients with use of postpubertal tissue through transplantation reported in three countries (Greece, Portugal and Spain). Testicular tissue cryopreservation in postpubertal patients and prepubertal boys was reported from six countries and from France only ($n = 124$), respectively.

Discussion

This is the 20th annual report of the activity collected by EIM from European registries on ART, IUI and for the first time also on FP. From 1997 to 2016, the EIM of ESHRE has reported close to 10 million treatments cycles (9 772 904) that have led to the birth of more than 1.8 million infants.

Despite difficulties caused by the data collection system in a number of countries, the number of participating countries has increased over the years. The current report presents the analysis of data collected in 2016 from 40 European countries (38 in 2015) with Luxemburg providing data for the first time as a new EIM member. Non-EIM members are mainly smaller countries not offering ART services ($n = 5$), except for Azerbaijan and Kosovo. Amongst EIM members, Croatia, Georgia, Slovakia and Turkey did not deliver data most likely due to

Table V IUI with husband (IUI-H) or donor (IUI-D) semen in 2016.

Country	IUI-H						IUI-D					
	Cycles	Deliveries	Deliveries (%)	Singleton (%)	Twin (%)	Triplet (%)	Cycles	Deliveries	Deliveries (%)	Singleton (%)	Twin (%)	Triplet (%)
Albania												
Armemia	275	68	24.7	79.6	20.4	0.0	48	11	22.9	88.9	11.1	0.0
Austria												
Belarus	1017	102	10.0	91.1	8.9	0.0	18	8	44.4	100.0	0.0	0.0
Belgium	12 296	904	7.4	95.2	4.6	0.1	8444	896	10.6	96.3	3.7	0.0
Bosnia-Herzegovina, Federation part	77	4	5.2	100.0	0.0	0.0						
Bulgaria	2515	219	8.7	90.0	10.0	0.0	554	59	10.6	94.9	5.1	0.0
Cyprus												
Czech Republic												
Denmark	9977	1118	11.2	90.0	9.8	0.2	9390	569	6.1	94.4	5.5	0.2
Estonia	90	2	2.2	100.0	0.0	0.0	122	11	9.0	100.0	0.0	0.0
Finland	2936	249	8.5				1125	134	11.9			
France	49 498	5254	10.6	90.4	9.4	0.2	2870	544	19.0	89.9	9.7	0.4
Georgia												
Germany												
Greece	3266	210	6.4	93.7	6.3	0.0	309	42	13.6	91.9	5.4	2.7
Hungary												
Iceland	69	6	8.7	100.0	0.0	0.0	167	21	12.6	100.0	0.0	0.0
Ireland	81	8	9.9	100.0	0.0	0.0						
Italy	21 053	1531	7.3	91.2	8.2	0.6	714	98	13.7	83.7	11.2	5.1
Kazakhstan	2622	23	0.9	100.0	0.0	0.0						
Latvia	103	13	12.6	100.0	0.0	0.0	64	5	7.8	100.0	0.0	0.0
Lithuania	246	15	6.1	100.0	0.0	0.0						
Luxembourg	264	34	12.9	94.1	5.9	0.0	84	10	11.9	100.0	0.0	0.0
Malta												
Moldova	81	9	11.1	100.0	0.0	0.0						
Montenegro							193	19	9.8	89.5	10.5	0.0
Norway	325	47	14.5	83.0	17.0	0.0	614	119	19.4	95.8	4.2	0.0
North Macedonia	1108	23	2.1	95.7	4.3	0.0	79	4	5.1	100.0	0.0	0.0
Poland	11 149	751	6.7	94.5	5.1	0.4	2053	225	11.0	91.7	7.9	0.5
Portugal	2095	190	9.1	85.7	13.8	0.5	185	42	22.7	92.9	7.1	0.0
Romania	2542	143	5.6	66.2	33.8	0.0	278	27	9.7	77.8	22.2	0.0
Russia	9106	1002	11.0	93.1	6.6	0.3	3897	545	14.0	93.4	6.3	0.4
Serbia	393	32	8.1	96.9	3.1	0.0						
Slovenia	551	43	7.8	88.4	11.6	0.0						
Spain	24 130	2404	10.0	90.5	9.2	0.3	12 333	1914	15.5	88.3	11.2	0.5
Sweden							1168	196	16.8	96.9	3.1	0.0
Switzerland												
The Nederlands												
Ukraine	1032	91	8.8	95.6	4.4	0.0	360	43	11.9	97.7	2.3	0.0
UK	4051						5398	707	13.1	92.6	6.8	0.6
All*	162 948	14 495	8.9	91.0	8.8	0.3	50 467	6249	12.4	91.9	7.7	0.4

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

organizational problems or local regulatory problems (Calhaz-Jorge *et al.*, 2020).

Excluding the five small European countries in which ART is not available, the rate of participation at the country level is as high as 87% of European countries (90.9% of EIM members) while at the level of IVF clinics, the proportion of those reporting data sets is 91.8% (vs 90.6% in 2015; De Geyter et al., 2020). Although the participation of some of the countries fluctuated over time, reported ART treatment numbers are on a continuous rise (+8% as compared to 2015) as are the infants born from ART (+4.4% compared to 2015).

Moreover, although the level of completeness is highly variable among countries, 20 countries were able to present data from all IVF clinics (in 2015: 18 and in 2014: 14 countries). Efforts to achieve increased participation and higher completeness of the data aim at an improved transparency and vigilance in reproductive care. However, because of the variety in collection systems, absence or limited presence of data validation methods, differences in definitions of collected items and country-specific practices (e.g. freeze all cycles, embryo transfer policy) that may, among other reasons, be influenced by economic issues, interpretation of the data should remain cautious. Progress towards harmonization of data collections could prove helpful in the future to achieve a higher quality of outcome data for professionals but also for other stakeholders involved in societal, political and economic decisions in medically assisted reproduction (MAR), as well as tissue and cell banking for FP.

Access to care is one of the important and very relevant pieces of information generated by the EIM. Considering that it was estimated that 1500 ART cycles per million inhabitants per year should cover the needs in infertility care (The ESHRE Capri Workshop group, 2008), we noticed that 60% of the countries in which complete data sets were available (12 out of 20) reached this level of access in 2016 (vs 55.6% in 2012, 64.3% in 2014 and 61.1% in 2015). Using the number of women of reproductive age as the denominator and eliminating thereby the impact of age differences among countries, access to care (based on all types of cycles) appeared highly variable, ranging from 1726 to 15 917 cycles per women aged 15–45 years. As the population needs in ART were estimated at a time when FER was not current practice (2001), any interpretation of treatment availability should be cautious. Indeed, FER cycles were included in the calculation on availability and represent a quite high proportion of ART cycles nowadays (in 2016, 44.1% of ART cycles when fresh IVF+ICSI cycles are used as the denominator). Moreover, considering that cross-border care may have an impact on accessibility in some countries, data interpretation will remain difficult before full traceability of all MAR procedures becomes available.

Considering the different treatment modalities, ICSI remains the most used and seems to have stabilized in recent years (Table I; Fig. 1), whereas FER is the second most used technique with a progressive increase over the years in the proportion of FER relative to fresh IVF and ICSI cycles (37.8% in 2014, 40.3% in 2015 and 44% in 2016). Changes in ART practices with higher numbers of freeze all cycles, a reduced number of embryos replaced per transfer and higher survival rates of cryopreserved embryos with the implementation of vitrification (Rienzi *et al.*, 2017) may all explain this evolution. While freeze all cycles have been registered since 2014, showing a 42% increase in reported cycles in 2016 compared to 2015 (Supplementary Table SV), the distinction between techniques of cryopreservation could not be registered by EIM. Enhanced reporting of IVM, PGT, ED and FOR in 2016 may be a reflection of the increased use of these treatment modalities. Expanding the data collection in large registries such as EIM for techniques like IVM and PGT-A, or to other new techniques or laboratory adjuncts (Harper *et al.*, 2017), could help to underscore analysis of their efficacy and safety in the future.

Owing to segmentation of treatments (i.e. treatment is not always a continuous sequence of single procedures but may, for example, include several oocyte retrievals for one transfer or several transfers for frozen cycles), such as for freeze all cycles, and the implementation of new technologies in ART, the cumulative DR per cycle or per aspiration will become the most important outcome indicator of treatment effectiveness. To date, the EIM has gathered data on an aggregate basis precluding thereby the calculation of true cumulative livebirths rates. Hence, as a surrogate indicator or proxy of true cumulative rates, fresh and FER during the same calendar year have been considered. Based on data from 38 countries, cumulative DR reached 29.6% during a 1-year period with a multiple DR of 13.8% and a rate of single embryo transfers of 41.5% in 2016. The absence of a link between cryopreserved embryos and their original cycle, and the limited observation period of 1 year where an unknown number of ART cycles was performed, do not allow comparisons with other registries. However, after seven consecutive ART cycles (fresh and frozen-thawed embryo transfer cycles counted consecutively) the 2011 data registered by the National Perinatal Epidemiology and Statistics Unit for Australia–New Zealand, including 73.2% single embryo transfers, showed a cumulative livebirth rate of 41.1% and a multiple DR of only 6.9% (National Perinatal Epidemiology and Statistics Unit, https://npesu.unsw.edu.au).

Besides local regulations and economic issues that may restrict treatment strategies, the improved awareness of ART outcomes by patients and physicians should guide future decisions. In this regard, the reduction in the number of embryos replaced in a cycle is a main trend that has been recorded by the EIM registry over the years (Fig. 2). While the transfer of two embryos remains the most frequently performed approach (51.9% of the transfers), single embryo transfers (whether elective or not) represented 41.5% of the transfers in 2016 and were carried out in the majority of treatment cycles for 10 of the countries. Transfers of four or more embryos were performed in very few countries and represent only 0.4% of all transfers. The evolution of the transfer policies in clinics often parallels the implementation of embryo culture to the blastocyst stage. However, the quality of evidence to support blastocyst transfers is still low (Glujovsky *et al.*, 2016). For the first time in 2016, EIM data collection allowed separate analysis of blastocyst and cleavage stage embryo transfers, showing that the majority of embryos were transferred at the blastocyst stage (41.9% for fresh IVF + ICSI and 62.2% for FER). Although figures are not available for DR yet, PR per transfer were the highest for blastocysts (39.7% vs 28.3% for cleavage stage embryos). Keeping in mind that the objective of an IVF/ICSI treatment is the delivery of a single healthy child, with a twin pregnancy being regarded as a complication (Land and Evers, 2003), further progress towards a reduction of prematurity associated with multiple births should be obtained at the expense of a reduced proportion of double embryo transfers. Indeed, whereas triplet rates remain low after a significant drop over the years (Ferraretti et al., 2017), twin rates did not follow the same decreasing slope and the resulting prematurity (≤37 weeks) was still observed in more than half of the deliveries.

Compared to singleton deliveries the risk of extreme prematurity was increased by 3-fold and of very preterm birth by nearly 5-fold for twin deliveries. Rates of twins and triplets were slightly lower after FER than after fresh IVF + ICSI treatments, which could also contribute to the decreasing multiple deliveries recorded in the recent years. Furthermore, the practice of foetal reduction for the prevention of multiple births was reported by 35 countries. However, it is not known which of these approaches is having the real impact on the reduction of multiples.

Regarding other safety aspects, no maternal death after ART was reported in 2016 (Supplementary Table SXVI) and the proportions of OHSS, infections and haemorrhage were low and quite stable over time although it is assumed that the complications of ART remain generally underreported.

The future of MAR registries should focus on the health of infants as an increasing number of children are born after ART, with incidences as high as 5.1% of all newborns in Denmark and 7.7% in Spain in 2016. Moreover, considering the increasing use of ED, FOR and the extension of using FP measures for medical reasons to non-medical indications, including planned postponement of motherhood, we may expect ART to contribute more and more to demography. Hence, transparency and vigilance in ART will more than ever be essential to all stakeholders with, as a main requirement, the need to level up the quality of collected data. Prospective compulsory registration systems, including an international coding system to follow gametes and embryos across country borders, should therefore become available to countries rather than the current retrospective aggregate data registration (De Geyter *et al.*, 2016; Kissin *et al.*, 2019).

Supplementary data

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

Authors' roles

V.G. performed the calculations. C.W. wrote the manuscript. All other co-authors reviewed the final manuscript and made appropriate corrections and suggestions to improve it. In all, this document represents a fully collaborative work.

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Conflict of interest

There are no competing interests.

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