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ART in Europe, 2015: 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 European trends and developments in ART and IUI in 2015 as compared to previous years?

SUMMARY ANSWER: The 19th ESHRE report on ART shows a continuing expansion of treatment numbers in Europe, and this increase, the variability in treatment modalities and the rising contribution to the birth rates in most participating countries all point towards the increasing impact of ART on European society.

WHAT IS KNOWN ALREADY: Since 1997, the ART data generated by national registries have been collected, analysed and reported in 18 manuscripts published in *Human Reproduction*.

STUDY DESIGN, SIZE, DURATION: Collection of European data by the European IVF-Monitoring Consortium (EIM) for ESHRE. The data for treatments performed between 1 January and 31 December 2015 in 38 European countries were provided by national registries or on a voluntary basis by clinics or professional societies.

PARTICIPANTS/MATERIALS, SETTINGS, METHODS: From 1343 institutions in 38 countries offering ART services a total of 849 811 treatment cycles, involving 155 960 with IVF, 385676 with ICSI, 218098 with frozen embryo replacement (FER), 21 041 with preimplantation genetic testing (PGT), 64 477 with egg donation (ED), 265 with IVM and 4294 with FOR were recorded. European data on IUI using husband/partner's semen (IUI-H) and donor semen (IUI-D) were reported from 1352 institutions offering IUI in 25 countries and 21 countries, respectively. A total of 139 050 treatments with IUI-H and 49 001 treatments with IUI-D were included.

MAIN RESULTS AND THE ROLE OF CHANCE: In 18 countries (14 in 2014) with a population of approximately 286 million inhabitants, in which all institutions contributed to their respective national registers, a total of 409 771 treatment cycles were performed, corresponding to 1432 cycles per million inhabitants (range: 727–3068 per million). After IVF the clinical pregnancy rates (PRs) per aspiration and per transfer were slightly lower in 2015 as compared to 2014, at 28.5 and 34.6% versus 29.9 and 35.8%, respectively. After ICSI, the corresponding PR achieved per aspiration and per transfer in 2015 were also slightly lower than those achieved in 2014 (26.2 and 33.2% versus 28.4 and 35.0%, respectively). On the other hand, after FER with own embryos the PR per thawing continued to rise from 27.6% in 2014 to 29.2% in 2015. After ED a slightly lower PR per embryo transfer was achieved: 49.6% per fresh transfer (50.3% in 2014) and 43.4% for FOR (48.7% in 2014). The delivery rates (DRs) after IUI remained stable at 7.8% after IUI-H (8.5% in 2014) and at 12.0% after IUI-D (11.6% in 2014). In IVF and ICSI together, 1, 2, 3 and ≥4 embryos were transferred in 37.7, 53.9, 7.9 and in 0.5% of all treatments, respectively (corresponding to 34.9, 54.5,

†EIM Committee 2017–2019: chairman: C.D.; chairman elect: C.W.; past chairman: C.C-J. members: M.K., E.M., T.M., G.S., J.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. The main results of this report were presented at the annual ESHRE congress in Barcelona, July 2018

9.9 and in 0.7% in 2014). This evolution towards the transfer of fewer embryos in both IVF and ICSI resulted in a proportion of singleton, twin and triplet DR of 83.1, 16.5 and 0.4%, respectively (compared to 82.5, 17.0 and 0.5%, respectively, in 2014). Treatments with FER in 2015 resulted in twin and triplet DR of 12.3 and 0.3%, respectively (versus 12.4 and 0.3% in 2014). Twin and triplet delivery rates after IUI-H were 8.9 and 0.5%, respectively (in 2014: 9.5 and 0.3%), and 7.3 and 0.6% after IUI-D (in 2014: 7.7 and 0.3%).

LIMITATIONS, REASONS FOR CAUTION: The methods of data collection and reporting vary among European countries. The EIM receives aggregated data from various countries with variable levels of completeness. Registries from a number of countries have failed to provide adequate data about the number of initiated cycles and deliveries. As long as incomplete data are provided, the results should be interpreted with caution.

WIDER IMPLICATIONS OF THE FINDINGS: The 19th EIM report on ART shows a continuing expansion of treatment numbers in Europe. The number of treatments reported, the variability in treatment modalities and the rising contribution to the birth rates in most participating countries point towards the increasing impact of ART on reproduction in Europe. Being the largest data collection on ART worldwide, detailed information about ongoing developments in the field is provided.

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

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Key words: IVF/ICSI/IUI using partner's semen or donor semen / egg donation / frozen embryo replacement/insemination / surveillance / vigilance / registry/data collection

Introduction

This is the 19th annual report of the European IVF-monitoring Consortium (EIM) under the umbrella of ESHRE containing the data on ART reported by 38 participating European countries in 2015 (Supplementary Data).

Eighteen previous reports, all published in *Human Reproduction* (https://www.eshre.eu/Data-collection-and-research/Consortia/EIM/Publications.aspx), covered treatment cycles from 1997 to 2014. As in previous reports, the printed version contains the five most relevant tables. Nineteen additional supplementary tables are available online. The settings of the data are consistent with those published in the previous reports, allowing optimal comparisons with earlier trends.

Materials and Methods

Aggregated data on various forms of ART were provided by 38 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). In addition, data on IUI using either 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 in 2015. Data on pregnancies and deliveries are derived from follow-up of the treatments performed in 2015. Each register was informed about the need to obtain signed informed consent prior to the initiation of infertility treatment from each infertile individual for whom data have to be reported to the registry.

For the collection of the data, the national representatives of 43 countries were asked to fill out questionnaires and data were transmitted through an online software package, specially designed for the requirements of this data collection (Dynamic Solutions, Barcelona, Spain). The dataset of 2014 has been extended with an optional module on fertility preservation and now consists of 10 different modules. The software performs all calculations automatically and evaluates the plausibility of all results. If inconsistencies are detected, the administrator of the ESHRE central office (V.G.) contacts the national representative for clarification. The data were assembled similarly as in the previous reports making the results comparable. As usual, footnotes to the tables provide additional information 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 (ICMART) (Zegers-Hochschild *et al.*, 2017).

Results

Participation and data completeness

In Table I, the number of institutions or clinics offering ART services and those performing IUI is listed together with all available treatment modalities. In comparison to the 2014 data (De Geyter *et al.*, 2018) not only has the number of reporting clinics increased (1279) in 2014 to 1343 in 2015, +4.9%), but also the overall number of reported treatments (776 556 in 2014 to 849 811 in 2015, +9.4%). Among the 51 European countries, eight are not members of the EIM Consortium (Supplementary Table SI), most being smaller countries not offering ART services. Georgia became a member of the EIM Consortium but has not yet provided any data to the Consortium. Croatia, Ireland, Slovakia and Turkey failed to deliver data. Of the 43 members, 38 submitted their data (88.4%) and in 18 countries (47.4%) all ART centres reported complete data sets. Currently, 1343 clinics reported their data (90.6% of all known clinics in Europe, 85.4% in 2013). As in 2014, the four European countries with the largest treatment numbers in 2015 were Spain (119 875 treatments), Russia (110723), Germany (96512) and France (93918).

Reporting methods and size of the clinics

There is a large variability in the size of reporting institutions offering ART services, as defined by the number of treatment cycles (Supplementary Table SII). In 2015, clinics with cycle numbers between

Table 1 **Treatment frequencies after ART in European countries in 2015.**

					IVF clinics in the country								Cycles/million*	
Country	**IVF clinics**	**Included IVF clinics**	**IUI labs**	**Included IUI labs**	**IVF**	**ICSI**	**FER**	**PGT**	**ED**	**IVM**	**FOR**	**All**	**Women 15–44**	**Population**
Albania	8	1	8	1		112	50		16			178		
Armenia	5	4	5	4	361	435	490		178		1	1465		
Austria	28	28			1347	5220	2204		7			8778	5331	1011
Belarus	8	6	10	6	1489	1242	196	26	13		3	2969		
Belgium	18	18	32	29	2909	14 239	11 699	580	802		71	30 300	14 272	2684
Bosnia–Herzegovina		2	1	1	93	105	82					280		
Bulgaria	35	35	1	1	933	6624	1643	37	612			9849	7417	1372
Cyprus	6	6	0		264	835	286	34	318			1737	9650	2044
Czech Republic	42	41	0			13 228	10 357	1561	4961			30 107		
Denmark	21	21	56	54	6718	5737	4494	129	360		16	17 454	16 535	3068
Estonia	5	5	5	5	623	1241	911		180			2955	11 913	2247
Finland	19	19	24	24	2567	2062	3839	44	831			9343	9576	1704
France	102	102	186	186	20 477	40 864	30 101	1328	1072	76		93 918	8047	1457
Germany	134	130	0	0	17 382	55 904	23 226					96 512	6809	
Greece	46	46	46	46	2872	13 922	4127	793	5182	5	248	27 149	13 000	2420
Hungary	13	11	0	0	1098	4541	510	12	101			6262		
Iceland	1	1	1	1	198	181	252		108			739	11 029	2238
Italy	201	201	366	366	7985	47 344	12 903	2029	1615		1529	73 405	7199	1234
Kazakhstan	23	6	23	6	1734	1883	667	132	600		4	5020		
Latvia	5	4	5	4	372	769	452	103	441		6	2143		
Lithuania	6	2	7	2	266	389						655		
Macedonia	7	4	0	0	400	1519	157		58	2		2136		
Malta	2	2	2	0		231					80	311	3696	727
Moldova	4	3	3	3	110	747	128		8			993		
Montenegro	5	4	6	4	9	439	58					506		
Norway	11	11	11	11	3316	3140	3868					10 324	10 138	1985
Poland	41	33		27	1050	14 382	9458	416	1031	30	124	26 491		
Portugal	25	25	27	27	2376	3800	1573	104	797		10	8660	4327	831
Romania	18	12	18	12	1196	1641	1021	3	68	1	5	3935		
Russia	188	144	0	0	34 497	41 137	25 397	2913	6270	127	382	110 723		

Continued

Table I Continued

Country	IVF clinics	Included IVF clinics	IUI labs	Included IUI labs	IVF clinics in the country							Cycles/million*		
					IVF	ICSI	FER	PGT	ED	IVM	FOR	All	Women 15–44	Population
Serbia	18	3	18	3	260	205	23					488		
Slovenia	3	3	3	3	986	2355	1271	28	3		6	4649	12255	2241
Spain	250	231	365	280	5786	47893	23692	7045	34176	20	1263	119875		
Sweden	17	17	0	0	5976	6155	5838	323	311			18603	10203	1905
Switzerland	28	27	0	0	947	4604	4487					10038		
The Netherlands	13	13	0	0	6509	7605	11327	695				26136	8388	1543
Ukraine	43	38	18	18	1666	9221	5868	1417	1037		55	19264		
UK	84	84	105	105	21188	23725	15443	1289	3321	4	491	65461	5209	1001
All	1483	1343	1352	1229	155960	385676	218098	21041	64477	265	4294	849811	7795	1432

FER: frozen embryo replacement, PGT: preimplantation genetic testing, ED: egg donation, FOR: frozen oocyte replacement.
Bosnia–Herzegovina consists of two parts: the Federation part and the Republic of Srpska.
Treatment cycles in IVF and ICSI refer to initiated cycles.
For Belgium, France, Iceland and Lithuania, treatment cycles refer to aspirations. For Austria, Belgium and France the total number of initiated cycles was only available for IVF and ICSI together, being 9101, 20050 and 682582, respectively.
For the Czech Republic and Bosnia and Herzegovina, no distinction between IVF and ICSI is made. All cycles are counted as ICSI. For Belgium, there are 881 aspiration cycles for which it is not known whether IVF or ICSI was performed, in 1367 aspirations IVF and ICSI was used.
Treatment cycles in FER refer to thawings.
For Czech Republic, Kazakhstan, Sweden and The Netherlands, treatment cycles refer to transfers.
Treatment cycles in PGD contain both fresh and frozen cycles and refer to initiated cycles in the fresh cycles (except for Finland where it refers to aspirations) and thawings in the frozen cycles (except for The Netherlands where it refers to transfers).
Treatment cycles in ED refer to transfer cycles and contain fresh and frozen cycles.
Treatment cycles in IVM refer to aspirations.
Treatment cycles in FOR refer to thawings.
Women of reproductive age and population were found at the following link: https://population.un.org/wpp/DataQuery/

Table II Number of institutions offering ART services, treatment cycles and infants born after ART in Europe, 1997–2015.

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
total			8 854 745		1 665 994

200 and 499 were the most common (29.9%). When compared to previous EIM reports, the trend towards more large institutions may have stopped (≥1000 cycles, 17.9% in 2015 versus 18.3% in 2014 versus 17.8% in 2013 and 16.9% in 2012).

The motivation for collecting the data may be either voluntary or compulsory (Supplementary Table SIII). Among all participating countries, 19 fulfilled compulsory requirements (50.0%). In another 19 countries, the data collection was based on voluntary initiatives (50.0%). In countries with partial reporting, single personal initiatives continue to play a major role (five countries), as do medical organisations (in 11 countries). In 16 of 20 countries (80.0%) with incomplete data due to partial reporting, a voluntary data collection was present, whereas the data collection was more complete in countries with compulsory data collections (15 of 18 countries, 83.3%).

Aggregate data submission by single ART institutions to the respective national registries was still the most commonly used method (26 countries) in 2015. Individual cycles were reported from 12 countries (Supplementary Table SIII). Aggregate data collection was similarly prevalent in countries with complete and with partial reporting (61.1 versus 75.0%, respectively). Public access to individual clinic data was available only in 12 countries: Bosnia-Herzegovina, Republic of Srpska, Bulgaria, Estonia, Germany, Greece, Hungary, Romania, Slovenia, Spain, Sweden, The Netherlands and the UK. Additional financial support for the national registration was offered by the public, pharmaceutical industries or professional societies in 27 countries. In five countries, the centres covered part of the expenses while in three countries (Germany, Poland and Switzerland) all the expenses were covered by the centres alone. This information is missing in eight countries.

Number of treatment cycles per technique and availability

In 2015, up to a total of 849 811 treatment cycles were reported to EIM (73 255 more than in 2014, +9.4%) (Table I). Since the beginning of its activities, EIM has now recorded more than 8.8 million treatments with ART leading to the birth of more than 1.6 million infants (Table II). In 2015, the most commonly used technique was ICSI (385 676 cycles, 45.4%) followed by FER (218 098, 25.7%) and IVF (155 960, 18.4%). Compared to 2014, all treatment modalities numbers increased, except IVM. The steepest increase in treatment number was observed in FER (+13.6%), in ED (+14.1%) and in PGT (+32.4%). A small number of countries reported fewer treatment cycles (Austria, Belarus and Bosnia-Herzegovina). As in 2014, two countries reported a large increment in treatment numbers (Russia and Spain), both with more participating ART institutions.

Among the total of 541 636 fresh treatments (ICSI+IVF), 71.2% were performed with ICSI, showing a rise of +6.5% compared to 2014. The preponderance of ICSI over conventional IVF still continues to be more pronounced (Fig. 1).

As in previous years, with 218 098 treatments, FER is rapidly gaining ground (+13.6%) but the relative proportion of FER to fresh treatments was stable (40.3% in 2015 and 37.8% in 2014). Switzerland is the country with the highest proportion of FER (44.7% of all treatment modalities) and Serbia with the lowest (4.7%).

Availability of ART in any particular country is calculated by dividing the number of treatment cycles by the number of women of reproductive age (15 to 45 years) (Supplementary Table SIV). Availability can only be calculated in the 18 countries with full coverage, and in those

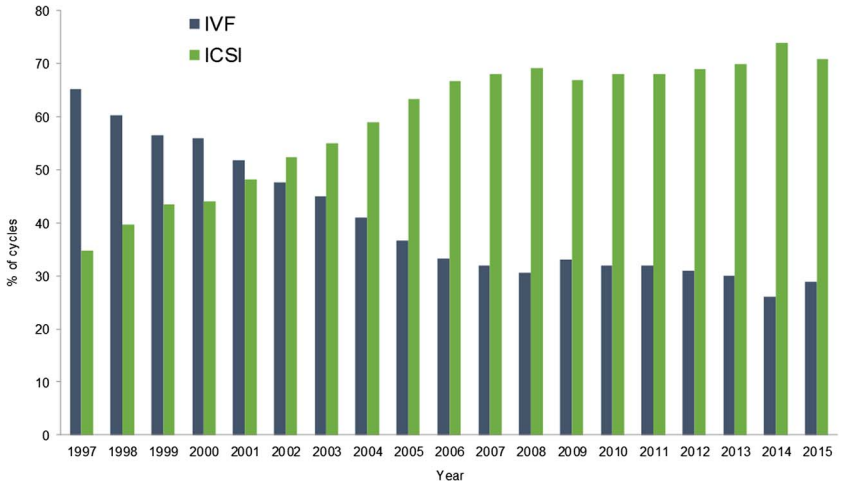

Figure 1 Proportion of IVF versus ICSI in Europe, 1997–2015.

18 countries, a huge variability in availability was observed, ART being most available in Denmark and least available in Malta. As a result, the proportion of newborns resulting from ART born in Denmark was 6.6% of all newborns in that country and 0.6% in Malta.

Pregnancies and deliveries after treatment

Table III lists pregnancy (PR) and delivery rates (DR) after IVF or ICSI and after FER (after both IVF and ICSI). As in previous reports, data on the number of initiated cycles were incomplete. For that reason, we calculated outcome data per aspiration. Among the 38 participating countries, only 34 were able to provide pregnancy and delivery data after aspiration after IVF and ICSI (completeness rate: 89.5%). Six countries failed to provide those after FER (completeness rate: 84.2%). Complete coverage data on both pregnancies and deliveries were provided by 18 countries (Supplementary Table SIV). As in earlier reports, the PR and DR (all treatment modalities included) varied significantly from one country to another, with PR ranging from 19.6 to 44.0%, and DR ranging from 10.2 to 40.0% in fresh cycles after IVF or ICSI. After FER, the DR varied between 12.8 and 37.5% among different countries.

Detailed accounts of cycle numbers, aspirations, transfers, pregnancies, deliveries in IVF, ICSI and FER (after both IVF and ICSI) are given in the Supplementary Tables SV, SVI and SVII. For the second time, information about 'freeze all' cycles was collected (Supplementary Table SV). As in 2014, 'freeze all' was carried out at the oocyte level in six reporting countries (15.8%) and at the embryonic level in 21 reporting countries (55.2%) (46.1%, in 2014: 18 countries).

Whereas in 2014 only 22 countries were able to provide egg/oocyte donation (ED) data, in 2015 the data from 29 of 38 participating countries are available (76.3%) (Supplementary Table SVIII). In most of the other countries, this technology is not being performed for legal reasons. Most donation cycles were carried out in Spain, Russia, the Czech Republic and Greece. Approximately 31511 ED cycles were carried out with freshly collected oocytes, fewer with frozen oocytes (FOR, 13107 cycles). Pregnancy rates were only available per embryo transfer (ET), but were considerably higher with freshly donated oocytes (49.6%) than after thawing of oocytes (40.3%). The differences among countries were considerable, ranging between 16.7 and 58.1% after thawing. A total of 19849 deliveries were counted, which considerably exceeds the 17259 deliveries counted in 2014 (+15.0%). This increment is due to overall higher numbers of reported treatments with ED, regardless of whether eggs were frozen or not.

Age distribution

As in previous reports, the age distribution of women treated with IVF and ICSI varied among different countries (Supplementary Tables SIX and SX). Not all countries were able to provide data on the age distribution in ICSI and in IVF, some because no IVF treatments were carried out. As in 2013 and in 2014, the highest percentage of women aged 40 years and older undergoing aspiration for IVF was found in Greece, whereas the highest percentage of women aged <34 years was found in Montenegro. Also in ICSI, the highest percentage of women aged 40 years and older undergoing aspiration was found in Greece, whereas the highest percentage of women undergoing aspiration aged <34 years was recorded in Albania (as in 2013 and in 2014). Overall, the well-known age-dependent decline of the reported PR and DR was very similar in IVF and ICSI, but the differences among countries were considerable.

Although the age-related decline was present in FER cycles as well (Supplementary Table SXI), the outcome data of FER were generally higher than in the fresh cycles. In contrast, in ED donation cycles (Supplementary Table SXII) age of the recipient women did not impact on PR or on DR.

Number of embryos transferred and multiple births

The number of embryos transferred after IVF and ICSI together is presented in Table IV. Although the specific number of elective single embryo transfers (SET) cannot be identified, the number of transfers of only one embryo per cycle continued to rise (37.7% in 2015, as

Table III Results after ART in 2015.

Country	IVF				ICSI			FER				
	Initiated Cycles IVF + ICSI	Aspirations	Pregnancies per aspiration (%)	Deliveries per aspiration (%)	Aspirations	Pregnancies per aspiration (%)	Deliveries per aspiration (%)	Thawings FER	Pregnancies per thawing (%)	Deliveries per thawing (%)	ART infants	ART infants per national births (%)
Albania	112				110	40.9	32.7	50	34.0	26.0	65	
Armenia	796	361	40.4	33.8	435	37.7	29.2	490	38.0	31.8	597	1.4
Austria	9101	1347	35.5	30.6	5220	30.4	25.9	2204	34.0	29.2	2414	2.9
Belarus	2731	1435	39.2	30.8	1239	39.2	32.0	196	32.1	17.3	1116	0.9
Belgium	20 050	2909	22.3	18.0	14 239	21.0	17.2	11 699	21.1	17.1	5702	4.7
Bosnia–Herzegovina	105	93						82	44.8	24.1	200	0.2
Bulgaria	7557	823	29.4	20.5	5770	26.5	19.1	1643	34.4	20.7	1830	2.8
Cyprus	1099	243	30.0	28.0	799	41.8	39.0	286	24.1	18.9		
Czech Republic	13 228				12 872	25.6	16.3				5590	5
Denmark	12 455	6396	22.3	19.4	5718	24.8	21.9	4494	24.5	21.2	3865	6.6
Estonia	1864	623	27.6	21.3	1241	27.3	19.0	911	19.4	12.8	633	4.5
Finland	4629	2424	26.6	20.2	1982	26.4	20.8	3839	25.7	20.0	1667	3.0
France	68 258	20 477	22.9	18.7	40 864	23.4	19.2	30 101	21.6	16.5	19 181	2.4
Germany	73 286	15 990	26.4	19.4	51 448	26.9	19.7	23 226	25.3	17.1	20 878	2.8
Greece	16 794	2684	27.5	20.5	13 407	26.5	16.3	4127	32.3	20.0	5059	
Hungary	5638	1094	24.7		4539	22.9		510	37.8			
Iceland		198	26.3	17.7	181	24.3	19.9	252	26.2	17.5	149	3.6
Italy	55 329	7107	23.0	15.8	43 107	19.6	12.5	12 903	26.2	18.6	11 275	2.3
Kazakhstan	3617	1734	36.5	24.8	1883	42.8	32.2				1618	0.4
Latvia	1141	372	28.2	22.3	764	30.8	21.7	452	46.0	35.4	634	
Lithuania		266	33.8		389	33.4						
Macedonia	1919	372	41.9	10.2	1378	40.2	34.3	157	29.3	14.6	655	2.8
Malta	231				216						25	0.6
Moldova	857	100	44.0	37.0	707	43.1	40.0	128	31.3	27.3		
Montenegro	448	9	33.3	22.2	432	25.2	17.6	58	36.2	31.0	118	1.6
Norway	6456	3316	26.5	22.4	3140	28.3	23.5	3868	19.3	15.4		
Poland	15 432	1010	29.4	21.4	14 191	27.7	18.4	9458	31.2	19.8	5482	1.5
Portugal	6176	2242	29.9	22.9	3613	26.1	19.3	1573	31.3	21.6	2260	2.6
Romania	2837	1159	36.8	28.8	1598	33.6	27.8	1021	25.2	18.1	1236	0.7
Russia	75 634	33 757	30.9	22.5	40 204	28.3	20.5	25 397	38.7	27.8	30 039	1.6

Continued

Table III Continued

Country	Initiated Cycles IVF + ICSI	IVF Aspirations	IVF Pregnancies per aspiration (%)	IVF Deliveries per aspiration (%)	ICSI Aspirations	ICSI Pregnancies per aspiration (%)	ICSI Deliveries per aspiration (%)	FER Thawings FER	FER Pregnancies per thawing (%)	FER Deliveries per thawing (%)	ART infants	ART infants per national births (%)
Serbia	465	238	33.6	25.6	202	31.7	24.8	23	34.8	34.8	141	0.2
Slovenia	3341	944	34.3	27.9	2274	26.6	20.4	1271	33.8	25.3	1172	5.7
Spain	53 679	5235	28.0	20.0	42 261	25.0	17.6	23 692	33.6	22.1	29 941	7.1
Sweden	12 131	5594	30.7	25.7	5799	26.8	22.7				4790	4.1
Switzerland	5551	852	27.2	20.3	4232	23.3	17.9	4487	20.8	14.3	1836	2.1
The Netherlands	14 114	5687	30.9	22.7	6820	32.0	23.9					
Ukraine	10 887	1626	36.3	26.0	9028	31.1	24.4	5868	44.4	37.5	6795	1.7
UK	44 913	18 535	32.4	28.2	23 592	33.7	29.6	15 443	33.3	28.7	20 599	2.7
All	552 861	147 252	28.5	21.8	365 894	26.2	19.3	189 909	29.2	21.3	187 542	2.3

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 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 FER, 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 PGD, 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.

Table IV Number of embryos transferred after ART and deliveries in 2015.

		IVF + ICSI							FER		
Country	Transfers	1 embryo (%)	2 embryos (%)	3 embryos (%)	4+ embryos (%)	Deliveries	Twin (%)	Triplet (%)	Deliveries	Twin (%)	Triplet (%)
Albania	103	5.8	79.6	13.6	1.0	36	19.4	2.8	13	7.7	0.0
Armenia	651	14.9	62.7	22.4	0.0	249	32.0	4.5	156	21.2	0.0
Austria	5692	62.0	37.5	0.5	0.0	1766			643		
Belarus	2498	13.4	64.3	22.3	0.0	838	25.5	0.6	34	17.6	2.9
Belgium	14 101	59.9	34.3	5.2	0.6	2976	8.8	0.2	2006	6.2	0.2
Bosnia–Herzegovina	476	13.7	45.8	39.5	1.0	128	30.5	1.6	20	25.0	0.0
Bulgaria	4737	21.7	56.3	21.9	0.2	1269			340		
Cyprus											
Czech Republic	10 344	66.3	32.6	1.2	0.0	2092	9.8	0.2	1727	9.8	0.3
Denmark	9760	64.0	34.2	1.9	0.0	2498	8.3	0.1	953	8.2	0.0
Estonia	1618	39.3	53.6	7.0	0.0	369	14.4	0.0	117	18.8	0.9
Finland	3568	82.0	18.0	0.0	0.0	900			767		
France	46 946	42.4	52.1	5.2	0.4	11 678	13.8	0.1	4958	8.4	0.1
Germany	56 112	21.6	69.2	9.2	0.0	13 239	21.5	0.6	3976	15.3	0.6
Greece	11 428	20.6	55.1	19.3	4.9	2743	24.5	0.6	825	18.0	0.8
Hungary	5129	20.8	57.3	18.2	3.8						
Iceland	314	69.7	30.3			71	7.0	0.0	44	9.1	0.0
Italy	37 975	28.8	48.3	21.0	1.9	6498	17.3	0.8	2403	8.7	0.2
Kazakhstan						1036	17.3	1.4	168	9.5	0.0
Latvia	880	33.1	65.7	1.2	0.0	249	16.8	0.8	160	5.8	1.0
Lithuania											
Macedonia	1637	25.8	67.1	7.1	0.0	510	16.5	0.8	23	30.4	0.0
Malta	287					22	13.6	0.0			
Moldova											
Montenegro	394	25.4	36.8	36.8	1.0	78	21.8	0.0	18	27.8	0.0
Norway											
Poland	11 214	63.0	36.6	0.4	0.0	2821	10.6	0.3	1874	8.2	0.2
Portugal	4479	29.9	68.5	1.7	0.0	1212	19.9	0.3	339	17.7	0.3
Romania	2279	16.9	60.0	21.1	2.1	778	25.3	0.7	185	23.9	0.0
Russia	59 934	32.9	61.5	5.5	0.2	15 833	19.1	0.6	7069	14.9	0.3
Serbia	386	20.7	31.6	47.7	0.0	111	23.4	0.0			
Slovenia	2688	44.0	55.5	0.5	0.0	727	10.7	0.0	321	13.1	0.0
Spain	33 039	27.9	67.4	4.7	0.0	8497	19.2	0.2	5237	15.0	0.2
Sweden	9326	81.2	18.8	0.0	0.0	2750	4.4	0.0	1709	2.8	0.1
Switzerland	4043	32.1	58.1	9.7	0.0	929	17.8	0.2	642	15.0	0.0
The Netherlands											
Ukraine	7845	22.8	64.2	12.9	0.2	2630	19.0	0.5	2198	18.4	0.0
UK	37 846	49.9	46.4	3.7	0.0	12 213	12.7	0.2	4434	13.4	0.4
All*	387 729	37.7	53.9	7.9	0.5	97 746	16.5	0.4	43 359	12.3	0.3

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

compared to 34.9% in 2014), whereas the number of transfers of three or more embryos per cycle decreased (Fig. 2). As in 2014, the same eight countries performed more than 50% SET (Austria, Belgium, Czech Republic, Denmark, Finland, Iceland, Poland and Sweden). Only one country with more than 40% of transfers with three embryos remained in 2015, i.e. Serbia. In Greece, 4.9% of all embryo transfers were carried out with four or more embryos.

Additional details about the pregnancy and delivery data are given in Supplementary Tables SXIII and SXIV. The recorded incidence of pregnancy loss was 16.4% after IVF + ICSI (in 2014: 15.5%) and 20.6%

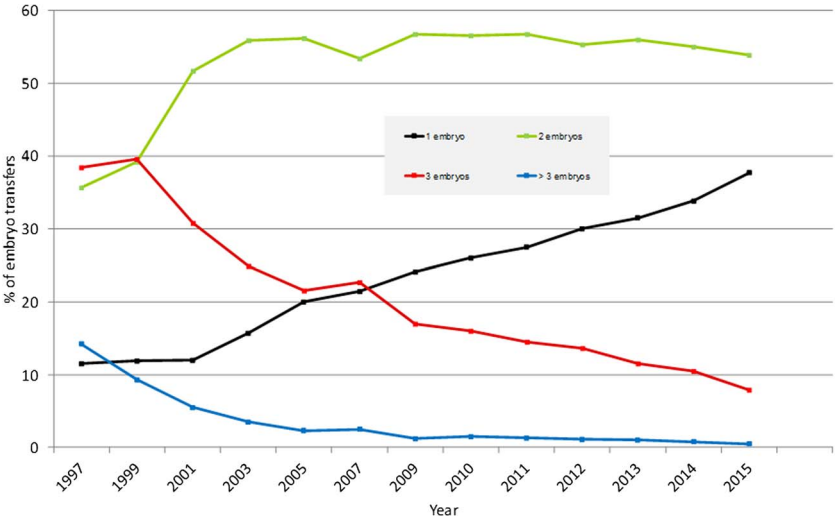

Figure 2 **Number of embryos transferred in IVF and ICSI during fresh cycles in Europe, 1997–2015.**

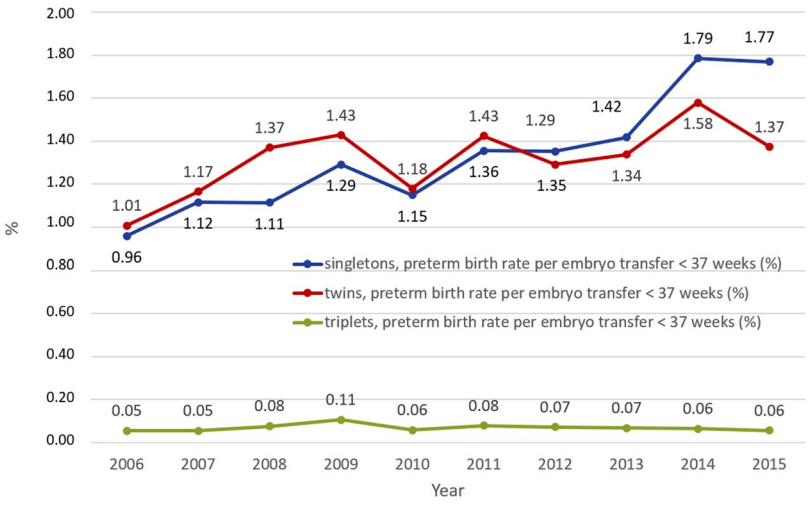

Figure 3 **Proportion of premature deliveries (<37 weeks of gestation in relation to pregnancies ≥37 weeks of gestation) in singleton, twin and triplet pregnancies in Europe, 2006–2015.**

after FER (in 2014: 18.6%). The recorded loss to follow-up was 6.3% after IVF + ICSI (in 2014: 9.9%) and 7.4% after FER (in 2014: 7.3%).

Since the first recorded European data sets, as recorded by EIM, the proportion of both twin and triplet deliveries was found to be declining. Twin and triplet deliveries were similar after IVF + ICSI treatments as after FER. Those countries with the highest proportion of SET also had the lowest twin and triplet delivery rates (the lowest in Sweden, 4.4 and 0%, respectively) after fresh cycles. The countries still proceeding with the transfer of three or more embryos in fresh cycles present with DR of twins ranging between 21.8% (Montenegro) and 32.0% (Bosnia-Herzegovina), and with DR of triplets ranging between 0.6% (Greece) and 4.5% (Armenia). Unfortunately, Finland with the highest SET rate of 82% did not report on multiplicity.

Regarding ED, of 15 178 deliveries with information regarding multiplicity, 3001 were twins (19.8%) and 37 were triplets (0.2%) (data not presented in tables).

Perinatal risks and complications

In 2015, data on premature deliveries were available from 18 European countries (in 2014 from 20 countries). The incidence of premature delivery is listed according to the number of newborns in Supplementary Table SXV. The prematurity data resulting from fresh IVF and ICSI, from FER and from ED, are listed together. The incidence of extreme preterm birth (gestational weeks 20–27) reached 1.3% in singleton pregnancies (0.9% in 2014), 3.7% in twin pregnancies (3.4%

in 2014) and 13.4% in triplet pregnancies (10.0% in 2014). A high incidence of very premature birth rates (gestational weeks 28–32) was found in twin pregnancies: 9.9% (in 2014: 10.7%) and in triplet pregnancies: 39.2% (in 2014: 34.9%). Term delivery (≥37 weeks) was 86.4% in singleton pregnancies, 44.7% in twin pregnancies and 7.5% in triplet pregnancies, all similar to the results achieved in 2014. Interestingly, the premature DR (<37 weeks) of singleton pregnancies calculated per ET is similar to the premature DR of twin pregnancies (Fig. 3).

As in 2014, complications of various steps of ART, such as ovarian hyperstimulation syndrome (OHSS), haemorrhage, infections and maternal deaths, were reported by 31 countries (Supplementary Table SXVI). With 2167 cases, OHSS was the most common reported complication of ART (incidence rate: 0.44% of all reported cycles, compared to 0.3% in 2014 with 2040 cases). Other complications were much rarer, such as haemorrhage (0.11% of all treatment cycles), infections (0.01%) and maternal death (two per 850 000 treatment cycles). The circumstances of the observed maternal deaths were not provided.

Foetal reductions were reported from 26 countries and were performed in 0.06% of all treatment cycles. Most foetal reductions were reported by the UK, Spain and Russia, as in 2014.

PGT-M/SR/PGT-A

PGT-M/SR (for monogenic disorders or structural rearrangements) and PGT-A (for aneuploidy) activities were reported from 23 countries (22 in 2014, 20 in 2013). The number of treatment cycles was 21 041 (2.48% of all ART treatments, Table I), which compared to 2014 represents a drastic rise in treatment numbers. These involved 16 685 fresh cycles and 4356 thawings, resulting in 6696 fresh ET and 4059 FER. In total, 2662 pregnancies (39.7% per transfer) and 2161 deliveries (32.3% per transfer) resulted from fresh cycles. Corresponding figures for FER were 1666 (41.0% per transfer) and 1398 (34.4% per transfer). The main contributor was Spain with 7045 cycles followed by Russia with 2913 cycles. A more detailed survey of PGT activities can be found in the annual reports of the ESHRE PGT Consortium (De Rycke *et al.*, 2017).

IVM

A total of 265 treatments with IVM were reported from eight countries (292 in 2014) (Table I). Most IVM cycles were performed in Russia. A total of 154 transfers resulted in 45 pregnancies and 33 deliveries.

FOR

FOR was reported by 17 countries (16 in 2014), and this accounted for 4294 thawing cycles (3404 in 2014) (Table I), 3478 transfers, 1067 pregnancies and 716 deliveries, Italy and Spain being the largest contributors (1529 and 1263 cycles, respectively).

IUI

Data on IUI-H (Supplementary Table SXVII) and IUI-D (Supplementary Table SXVIII) were collected by 1229 institutions in 26 and 22 countries, respectively (Table V). Spain, Belgium and Denmark were the most active countries in both treatment modalities. Altogether, 189 764 treatments with IUI-H resulted in 14 886 deliveries (7.8%), whereas 49 514 treatments with IUI-D resulted in 5926 deliveries (12.0%). Many more treatment IUI cycles were reported in 2015 than in 2014, but the outcome results are similar to those reported earlier. In all three age groups (≤34, 35–39 and ≥40 years), most pregnancies led to singleton deliveries (90.6% in IUI-H, 92.1% in IUI-D). The twin and triplet DRs for IUI-H and IUI-D were generally low, depending on the age of the treated patient and were similar to those reported in previous years (twin deliveries: 8.9 and 7.3%, respectively; triplet deliveries: 0.5 and 0.6%, respectively).

Sum of fresh and FER ('cumulative') DR

Supplementary Table SXIX provides us with an estimate (not a true rate, as the data set presented here is cross-sectional) of a cumulative DR, calculated from the fresh ET and those carried out after thawing. The data are presented based on the sum of the fresh and FER deliveries and the number of aspirations of the same year as the denominator. As no data on deliveries were available from Hungary, Bosnia and Herzegovina and Lithuania, we were able to calculate cumulative delivery rates for 35 countries (38 countries in 2014). Whereas in all data taken together, the DR after the fresh cycle amounted to 20.0%, the cumulative DR was 28.9%. The countries with the highest benefit resulting from FER were Ukraine (+20.6%), Armenia (+19.6%) and Finland (+17.4). The countries with the lowest benefit resulting from FER were Belarus (+1.3%) and Macedonia (+1.4%).

Cross-border reproductive care

Eleven countries reported data on cross-border patients: Albania, Belarus, Denmark, Iceland, Macedonia, Malta, Poland, Portugal, Slovenia, Spain and Switzerland. A total of 14 273 cycles were reported, 29.4% of which involved IVF/ICSI with the couple's own gametes, 47.1% were oocyte donations and 22.3% were IVF or ICSI with semen donation. Additionally, 7714 IUI with sperm donation were registered. Information regarding the countries of origin was very incomplete and not reliable enough to draw any meaningful conclusions. The main reasons reported by patients were to have access to a technique not legally available in their home countries (41.7%) or to seek a higher quality treatment (16.6%).

Fertility preservation

Twelve countries were able to provide data on fertility preservation: Albania, Belarus, Belgium, the Czech Republic, France, Greece, Italy, Macedonia, Poland, Portugal, Slovenia and Spain. There were 3659 cases with oocyte cryopreservation and 10 590 cases with ejaculated sperm collection and cryopreservation reported. All other forms of preservation were carried out in 614 cases (prepubertal ovarian tissue, postpubertal ovarian tissue, prepubertal testicular tissue, postpubertal testicular tissue and epididymal sperm).

Only four countries report non-medical oocyte cryopreservation, and three countries report non-medical ejaculated semen collection and cryopreservation. In all other cases, preservation is only carried out for medical reasons.

At this moment, too few data were obtained to report on the outcome.

Table V IUI with husband or donor semen in 2015.

	IUI-H						IUI-D					
Country	**Cycles**	**Deliveries**	**Deliveries (%)**	**Singleton (%)**	**Twin (%)**	**Triplet (%)**	**Cycles**	**Deliveries**	**Deliveries (%)**	**Singleton (%)**	**Twin (%)**	**Triplet (%)**
Albania												
Armenia	571	98	17.2	90.8	9.2	0.0	313	60	19.2	91.7	8.3	0.0
Austria												
Belarus	952	107	11.2	99.1	0.9	0.0						
Belgium	13 162	769	5.8	95.3	4.4	0.3	8112	597	7.4	94.5	5.4	0.2
Bosnia–Herzegovina	191	17	8.9	94.2	5.8	0.0						
Bulgaria	2976	171	5.7				590	35	5.9			
Cyprus												
Czech Republic												
Denmark	10 339	1291	12.5	88.9	9.6	1.5	9924	879	8.9	95.2	4.4	0.3
Estonia	139	6	4.3	100.0	0.0	0.0	91	4	4.4	100.0	0.0	0.0
Finland	3126	284	9.1				1171	138	11.8			
France	50 714	5065	10.0	89.7	9.9	0.3	3294	570	17.3	89.6	10.2	0.2
Germany												
Greece	4561	313	6.9	94.2	5.8	0.0	287	41	14.3	95.1	4.9	0.0
Hungary												
Iceland												
Italy	22 549	1588	7.0	90.9	8.2	0.9	513	61	11.9	88.5	9.8	1.6
Kazakhstan	810	25	3.1	100.0	0.0	0.0	125	8	6.4	100.0	0.0	0.0
Latvia	96	10	10.4	85.7	14.3	0.0	53	6	11.3	100.0	0.0	0.0
Lithuania												
Macedonia	1186	62	5.2	100.0	0.0	0.0	29	3	10.3	100.0	0.0	0.0
Malta												
Moldova	102	7	6.9	100.0	0.0	0.0						
Montenegro	222	24	10.8	87.5	12.5	0.0						
Norway	20 708	47	0.2	83.0	17.0	0.0	614	119	19.4	95.8	4.2	0.0
Poland	9036	570	6.3	94.3	5.5	0.2	1729	173	10.0	96.3	3.7	0.0
Portugal	2188	195	8.9	90.3	8.7	1.0	236	50	21.2	88.0	12.0	0.0
Romania	2091	169	8.1	91.7	8.3	0.0	191	21	11.0	90.5	9.5	0.0
Russia	10 013	1181	11.8	93.2	6.7	0.2	4128	574	13.9	90.9	6.3	2.8
Serbia	408	28	6.9	89.3	10.7	0.0						
Slovenia	246	18	7.3	88.9	11.1	0.0	1	0	0.0			
Spain	26 959	2713	10.1	88.9	10.7	0.4	11 944	1747	14.6	88.8	10.8	0.4
Sweden							760	115	15.1	100.0	0.0	0.0
Switzerland												
The Netherlands												
Ukraine	1570	128	8.2	89.6	10.4	0.0	468	53	11.3	92.5	7.5	0.0
UK	4849						4941	672	13.6	94.9	4.6	0.4
All*	189 764	14 886	7.8	90.6	8.9	0.5	49 514	5926	12.0	92.1	7.3	0.6

*Total refers to these countries where data were reported, and mean percentage was computed on countries with complete information.
Iceland 125 IUI with husband semen (IUI-H) and 177 IUI with donor semen (IUI-D) cycles performed without further information.
Italy: underestimation of deliveries because of high number of pregnancies is lost to follow-up.
Slovenia: Data from two clinics only.

Discussion

This is the 19th annual report of the combined activities of the European (national) registries collecting data on ART. From 1997 to 2015, the EIM Consortium of ESHRE has reported on close to 9 million treatments (8860338) leading to the birth of more than 1.6 million infants (1665994).

The present data report summarizes the totality of the data collections provided by 38 European countries (39 in 2014). For the first time, Armenia provided data. Georgia joined the EIM Consortium, but has not yet been able to submit data, nor did Croatia and Ireland for organisational reasons. Azerbaijan, Kosovo and Luxemburg have not yet joined the EIM Consortium. Another group of small European countries have not considered joining the Consortium, such as Andorra, Liechtenstein, Monaco, San Marino and the Vatican, most likely all without ART services. Excluding these eight countries, the level of completeness at the national level amounts to 88.4% and the number of reporting clinics to 90.6%, which is similar to the participation levels achieved in 2014 (92.9%, respectively 87.5%, De Geyter *et al*., 2018). Whereas the tendency towards large ART services with more than 1000 cycles per year seems to have stabilized in recent years, there are now more middle-sized ART institutions with treatment numbers between 200 and 1000 cycles per year (Supplementary Table SII). The level of completeness is highly variable among countries with 18 countries now able to present data with complete coverage (in 2014: 14 countries).

Despite the fluctuating participation of a few countries with high frequency activities in ART, the reported treatment numbers in ART continue to rise (+9.4%, as compared to 2014) together with more children born (+7.3%, as compared to 2014). Although access to ART services is highly variable among European countries, the proportion of children born after ART continues to rise, particularly in those countries with optimal access to ART. In 2015 up to 6.6% of all newborn babies in Denmark (Supplementary Table SIV) were born after ART (in 2014: 6.4%).

When comparing the 2015 with the 2014 data sets, all treatment modalities in ART were used more frequently except IVM and FOR (Table I). Whereas the preponderance of ICSI over IVF seems to be stabilizing (Fig. 1), FER is becoming more and more important over fresh treatments and the treatment numbers of FER now exceed those of IVF. Since 2014, the elective freezing of all oocytes and embryos is being recorded systematically (Supplementary Tables SV and SVI): when comparing the 2014 and the 2015 data sets, the prevalence of freezing all embryos is on the rise, less so is freezing of all oocytes. Other treatment modalities with a rapidly gaining momentum are PGT and ED.

As in previous years, fewer embryos are now being replaced per treatment cycle. More and more treatments are being performed in which only one embryo is transferred, elective or not (37.7%, Fig. 2). Whereas the transfer of three or more embryos is rapidly disappearing in most countries, even the transfer of two embryos has become less prevalent in recent years (Fig. 2). SET is predominantly carried out in a few countries, the same as in previous years, and those countries are the ones with fewer multiple deliveries. Unfortunately, the same goes for the few countries in which three or more embryos are being transferred. Legal and financial constraints may be the main drivers for this practice (Gianaroli *et al*., 2016), but also attitudes among physicians and patients (Stormlund *et al*., 2019).

This impressive shift in the ET strategy has not yet translated into a major change in the number of multiple deliveries (Table IV). Whereas birth rates of triplets have been on the decline ever since the early recordings by the EIM Consortium, the incidence of twin deliveries has dropped to a much lesser extent. The proportion of premature deliveries of twins and triplets remained similar to previous years. The proportion of premature deliveries (<37 weeks) of singletons per ET has risen from 0.96% in 2006 to 1.77% in 2015 (Fig. 3). Singleton pregnancies after ART are prone to a higher risk of obstetric complications, including prematurity (Wennerholm *et al*., 2013; Sunkara *et al*., 2015; Qin *et al*., 2016), but pregnancy outcome does not depend on the number of retrieved oocytes (Magnusson *et al*., 2018).

Two cases of maternal death were reported in 2015, but the exact conditions under which these events occurred were not given (Supplementary Table SXVI). Other complications of ART, such as OHSS, infections and haemorrhage, remain prevalent at low frequencies. Foetal reduction for the prevention of multiple births is reported by 15 countries. All these numbers, however, most likely are under-reported.

Under-reporting of treatment numbers leads to overestimation of the efficacy of outcome of the offered treatments and at the same time to an underestimation of safety. The steady rise in ART activities in all European countries clearly demonstrates that ART has become an integral part of medical care and has a significant and measurable impact on society, and for that reason data on both efficacy and safety should therefore be of interest to all stakeholders, not least to the patients themselves. Data collection can only be optimized in the presence of good governance (De Geyter, 2019). Compulsory data collection systems have been shown previously to be more effective than voluntary systems: countries with voluntary registries provided more incomplete data sets due to partial reporting (Supplementary Table SIII). In addition, modern software systems enable prospective registration of cycle by cycle data sets instead of aggregate data, which are collected retrospectively. Currently, aggregate data submission by single ART institutions to the national registries is still the most commonly used method for reporting (Supplementary Table SIII). Coherent and systematic data registration and monitoring of all treatment outcomes should become mandatory in ART and must be considered as an indicator of excellent quality of care and good governance.

The instalment of prospective data registration is more and more urgent in light of the current rapid expansion of freezing technology, allowing the long-term storage of gametes, embryos and gonadal tissues (De Geyter *et al*., 2016). Infertility treatments are being segmented into small treatment units, for which the outcome cannot be reported within a 1-year period as was done in the past**.** Traditionally, the data collection organized and managed by the EIM Consortium is cross-sectional and based on annual data reporting. A concept for prospective follow-up of infertility treatment outcomes has been elaborated earlier (De Geyter *et al*., 2016). This would require the development of a European data collection software tool including an international coding system, with which the different therapeutic steps of infertile individuals and couples can be traced prospectively, even if they change the treating institution or their country of origin.

The organisation of data collection, as managed by EIM, must be further developed towards real surveillance and vigilance in ART (Kissin *et al*., 2019). Surveillance is defined by the continuous and systematic collection of health data (here related to ART and its outcome) needed for the analysis and interpretation of trends in medical care with a special focus on safety. That goal can best be achieved if data submission to the national registries becomes compulsory.

Practitioners, professional bodies, and national and European political bodies have a duty to realise that such therapies require appro-

priate logistical and financial support to set up national reporting electronic databases, ideally a pan-European centralised data collection (De Geyter *et al.*, 2016), to monitor not only the efficiency and safety of therapy but also the long-term health of children born after treatment. The creation of a unique individual patient European coding system will ensure all aspects of an ever-increasing spectrum of ART care can be measured and analysed thus ensuring full surveillance and vigilance. The concept of evolving the current cross-sectional register towards prospective surveillance and vigilance of care in ART will take years to become a reality and will require top down support from national and supranational health care authorities. Such a concept can only be supported by all stakeholders of ART, including the patients, and should be motivated by the desire to provide care with excellence.

Supplementary data

Supplementary data are available at *Human Reproduction* online.

Authors' roles

V.G. performed the calculations. C.D.G. 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.

Appendix

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