

Assisted reproductive technology in Europe, 2012: results generated from European registers by ESHRE[†]

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

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STUDY QUESTION: The 16th European IVF-monitoring (EIM) report presents the data of the treatments involving assisted reproductive technology (ART) and intrauterine insemination (IUI) initiated in Europe during 2012: are there any changes compared with previous years?

SUMMARY ANSWER: Despite some fluctuations in the number of countries reporting data, the overall number of ART cycles has continued to increase year by year, the pregnancy rates (PRs) in 2012 remained stable compared with those reported in 2011, and the number of transfers with multiple embryos (3+) and the multiple delivery rates were lower than ever before.

WHAT IS KNOWN ALREADY: Since 1997, ART data in Europe have been collected and re-reported in 15 manuscripts, published in *Human Reproduction*.

STUDY DESIGN, SIZE, DURATION: Retrospective data collection of European ART data by the EIM Consortium for the European Society of Human Reproduction and Embryology (ESHRE). Data for cycles between 1 January and 31 December 2012 were collected from National Registers, when existing, or on a voluntary basis by personal information.

PARTICIPANTS/MATERIALS, SETTING, METHODS: From 34 countries (+1 compared with 2011), 1111 clinics reported 640 144 treatment cycles including 139 978 of IVF, 312 600 of ICSI, 139 558 of frozen embryo replacement (FER), 33 605 of egg donation (ED), 421 of *in vitro* maturation, 8433 of preimplantation genetic diagnosis/preimplantation genetic screening and 5549 of frozen oocyte replacements (FOR). European data on intrauterine insemination using husband/partner's semen (IUI-H) and donor semen (IUI-D) were reported from 1126 IUI labs in 24 countries. A total of 175 028 IUI-H and 43 497 IUI-D cycles were included.

MAIN RESULTS AND THE ROLE OF CHANCE: In 18 countries where all clinics reported to their ART register, a total of 369 081 ART cycles were performed in a population of around 295 million inhabitants, corresponding to 1252 cycles per million inhabitants (range 325–2732 cycles per million inhabitants). For all IVF cycles, the clinical PRs per aspiration and per transfer were stable with 29.4 (29.1% in 2011) and 33.8% (33.2% in 2011), respectively. For ICSI, the corresponding rates also were stable with 27.8 (27.9% in 2011) and 32.3% (31.8% in 2011). In FER cycles, the PR per thawing/warming increased to 23.1% (21.3% in 2011). In ED cycles, the PR per fresh transfer increased to 48.4% (45.8% in 2011) and to 35.9% (33.6% in 2011) per thawed transfer, while it was 45.1% for transfers after FOR. The delivery rate after IUI remained stable, at 8.5% (8.3% in 2011) after IUI-H and 12.0% (12.2% in 2011) after IUI-D. In IVF and ICSI cycles, 1, 2, 3 and 4+ embryos were transferred in 30.2, 55.4, 13.3 and 1.1% of the cycles, respectively. The proportions of singleton, twin and triplet deliveries after IVF and ICSI (added together) were 82.1, 17.3 and 0.6%, respectively, resulting in a total multiple delivery rate of 17.9% compared with 19.2% in 2011 and 20.6% in 2010. In FER cycles, the multiple delivery rate was 12.5% (12.2% twins and 0.3% triplets). Twin and triplet delivery rates associated with IUI cycles were 9.0%/0.4% and 7.2%/0.5%, following treatment with husband and donor semen, respectively.

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[‡]EIM Committee 2013–2015: Chairman: C.C.-J.; Chairman elect: C.G.; Past chairman: M.K.; Members: J.d.M., K.E., E.M., T.M., G.S. and C.W.; 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 Lisbon, June 2015.

LIMITATIONS, REASONS FOR CAUTION: The method of reporting varies among countries, and registers from a number of countries have been unable to provide some of the relevant data such as initiated cycles and deliveries. As long as data are incomplete and generated through different methods of collection, results should be interpreted with caution.

WIDER IMPLICATIONS OF THE FINDINGS: The 16th ESHRE report on ART shows a continuing expansion of the number of treatment cycles in Europe, with more than 640 000 cycles reported in 2012 with an increasing contribution to birthrate in many countries. However, the need to improve and standardize the national registries, and to establish validation methodologies remains manifest.

STUDY FUNDING/COMPETING INTERESTS: The study has no external funding; all costs are covered by ESHRE. There are no competing interests.

Key words: IVF / ICSI / intrauterine insemination / egg donation / frozen embryo replacement / Europe / data collection / registry

Introduction

This report is the 16th annual publication of the European IVF-monitoring (EIM) Consortium under the umbrella of the European Society of Human Reproduction and Embryology (ESHRE) on European data on assisted reproductive technology (ART).

The 15 previous reports, also published in *Human Reproduction* (<https://www.eshre.eu/Data-collection-and-research/Consortia/EIM/Publications.aspx>), covered treatment cycles from 1997 to 2011. As in the last four reports, the printed version contains the four most significant tables. In addition, a total of 19 supplementary tables are available online, making this report consistent with those from previous years.

Materials and Methods

Data on ART were collected from 34 European countries, covering IVF, ICSI, frozen embryo replacement (FER), egg donation (ED), *in vitro* maturation (IVM), pooled data on preimplantation genetic diagnosis (PGD) and preimplantation genetic screening (PGS) as well as frozen oocyte replacements (FOR). In addition to ART, data on intrauterine inseminations using husband/partner's semen (IUI-H) and donor semen (IUI-D) were also included. The report includes treatments started between 1 January 2012 and 31 December 2012. Data on pregnancy outcomes are derived from follow-up of the cohort treated during this time period.

The method of collecting data in 2012 was similar to that used in the previous years, making results comparable. Briefly, a questionnaire with six modules (available online) was sent out to the data collection co-ordinator of each participating country (Supplementary data) in April 2014. The data collected, similar to those of the last 3 years, were directly entered in an online ESHRE computer system by each country co-ordinator. Data analysis was performed in ESHRE's central office by V. Goossens. After the first tables had been created, each participating country was asked to correct inconsistencies in the data during the autumn of 2015.

As usual, footnotes of tables provide details on the diversity of data reported by individual countries when applicable.

Definitions used refer to The International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization glossary of ART terminology (Zegers-Hochschild et al., 2009).

Results

As is evident from the tables, the only complete data reported from all countries were on the number of aspirations and the number of centres performing ART. Few registers have been able to provide reliable

data on initiated cycles and some countries did not report deliveries; in addition, several countries show a high percentage of pregnancies that are lost to follow up. Therefore, complete outcome data were only available on the clinical pregnancy rate (PR) per aspiration, while some of the more relevant indicators of treatment success (clinical pregnancies and deliveries per initiated cycle) cannot be reported completely, and consequently comparison of countries should be performed with caution. Due to the diversity of some of the data reported from the different countries, the footnotes in the tables deserve particular attention for data interpretation.

Participation

The present report includes data from 34 of 51 European countries (Supplementary Table SI).

Cyprus was not able to send data (contributing in 2011 with 2046 cycles altogether), but in contrast Croatia and Albania resumed their participation. Former contributors Bosnia, Latvia, Macedonia and Turkey (one of the main contributors in 2008 with 107 clinics and 43 928 cycles of ART) were not able to participate. Malta (a recent EIM member) and Slovakia never contributed to data collection. The largest contributors in 2012 were France (total number of treatments, excluding IUI—85 594), Germany (71 251), Spain (69 699), Italy (64 197), Russia (62 620) and UK (60 151).

The proportion of ART clinics reporting data was 82.1% (81.0% in 2011) (Table I). In 18 countries (17 in 2011 and 16 in 2010), the coverage reached 100% (Table I and Supplementary Table SIV). Among the countries with the largest populations, the countries with more ART clinics participating in the registry were 100% in France, Italy and UK, 98% in Germany, 80% in Russia and only 57% in Spain.

Belarus, Montenegro, Poland and Switzerland were able to report data from all but a single centre each. Participation was low in Albania (17%), Kazakhstan (20%), Bulgaria (23%) and Greece (26%).

Reporting methods and size of the clinics

Among the 18 countries where reporting was complete (Supplementary Tables SIII and SIV), the register was compulsory for 15 (12 held by a National Health Authority and 3 by a Medical Organization) and voluntary for 3–2 held by a Medical Organization and one by a National Health Authority. Six registers were based on individual forms, i.e. cycle-by-cycle data.

In the 16 countries with partial coverage, 13 registers were voluntary, 3 compulsory. Two were held by a National Health Authority, 11 by a

Table I Treatment frequencies of ART in European countries in 2012 (IUI excluded).

Country	IVF units in the country				Treatment cycles								Cycles/million		
	Clinics	IUI labs	Clinics reporting	IUI labs reporting	IVF	ICSI	FER	PGD	ED	IVM	FOR	All	Women 15–45	Population	
Albania	6	6	1	1		216	44			23	6				
Austria	27	0	27	0	920	4919	983				0	6822	4077	801	
Belarus	4	7	3	3	1275	665	127	23	8			2098			
Belgium	18	34	18	29	3996	13 611	9277	647	1005		42	28 578	13 604	2584	
Bulgaria	26	26	6	6	673	5639	587	26	227	0	10	7162			
Croatia	13		13		1397	1655	94				267	3413	3872	762	
Czech Republic	39		39		1799	10 499	5789	754	3875			22 716	10 473	2145	
Denmark	21	64	21	57	6328	5379	3084	134	209	0	8	15 142	14 431	2732	
Estonia	5	5	5	5	613	1193	761	0	148	0	0	2715	10 724	2106	
Finland	19	23	19	23	2584	2201	3319	18	702	0		8824	9044	1632	
France	103	192	103	192	20 995	39 079	23 841	658	954	67		85 594	7032	1304	
Germany	131		129		12 047	39 911	19 293					71 251			
Greece	76	76	20	16	1329	5343	626	291	617	0	1	8207			
Hungary	12		12		920	3502	401	7	44			4874	2400	489	
Iceland	1	1	1	1	199	206	196	0	132	0	0	733	11 128	2287	
Ireland	7	8	4	5	1119	1008	716	0	0	0	0	2843			
Italy	201	355	201	355	8431	47 064	6513				2189	64 197	5480	1048	
Kazakhstan	15	15	3	3	1193	1070	465	57	358			3143			
Lithuania	5	1	2	0	103	46	24	0	0	0	0	173			
Moldova	4	4	4	4	444	686	43		14			1187	1457	325	
Montenegro	4	4	3	3	2	521	17					540			
Norway	11	9	11	9	3295	3025	2655	0		7	0	8982	9069	1789	
Poland	34		33	31	461	10 253	4969	244	713	70	139	16 849			
Portugal	26	27	26	27	2088	3715	1135	93	403	1	9	7444	3510	690	
Romania	22	22	9	10	627	947	338	0	44	0	0	1956			
Russia C.I.S.	138		110	95	21 967	25 751	10 321	760	3521	226	74	62 620			
Serbia	14	8	8		564	1500						2064			
Slovenia	3	3	3	3	1349	2396	817	31	2	0	2	4597	11 803	2302	
Spain	198	314	113	133	3759	31 671	11 736	3161	16 710	21	2641	69 699			
Sweden	16		16		5965	5910	5809	191	405			18 280	10 097	1909	
Switzerland	27		26		832	4526	4188					9546			
The Netherlands	13		13		7959	8789	8063	362				25 173	7943	1505	
Ukraine	38		32	13	3467	5329	2258	132	1081	2	13	12 282			
UK	77	102	77	102	21 278	24 375	11 069	844	2410	21	154	60 151	4918	954	
All	1354	1306	1111	1126	139 978	312 600	139 558	8433	33 605	421	5549	640 144	6525	1253	

ART, assisted reproductive technology; IUI, intrauterine insemination; ED, egg donation; FER, frozen embryo replacement; FOR, frozen oocyte replacement; IVM, *in vitro* maturation.

Treatment cycles in IVF and ICSI refer to initiated cycles.

IVF and ICSI: for Austria, Belgium, France, Germany, Greece, Hungary and Lithuania treatment cycles refer to aspirations.

For Belgium 700 cycles where aspirated without knowing what treatment was performed (IVF or ICSI).

Treatment cycles in FER refer to thawings.

FER: for the Czech republic, Finland, Lithuania 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 and thawings in the frozen cycles.

Treatment cycles in ED refer to transfers and contain fresh and frozen cycles and FOR.

Treatment cycles in IVM refer to aspirations.

Treatment cycles in FOR refer to thawings.

<http://www.census.gov/population/international/data/idb/region.php>.

Medical Organization and 3 by personal initiative; only 4 used individual forms.

Fourteen countries (Austria, Belarus, Belgium, Finland, France, Germany, Italy, Kazakhstan, Poland, Slovenia, Spain, Sweden, Switzerland and UK) reported some kind of data validation process.

Public access to individual clinic data was available only in eight countries: France, Ireland, Kazakhstan, Romania, Slovenia, Spain, Sweden and UK.

Public (\pm industry or professional society) financial support for the national registration effort was present in 20 countries, while in 7 countries (Albania, Germany, Greece, Norway, Portugal, Slovenia, and Switzerland) all the expenses were covered by the centres alone. This information is missing in 6 countries.

The distribution of clinics according to the number of cycles varied considerably among the countries (Supplementary Table SII). For instance, small clinics, providing less than 100 cycles annually, accounted for 2 out of 2 reporting centres in Lithuania, 2 of 4 in Moldova, 68 of 201 (33.8%) in Italy and 11 of 33 (33.3%) in Poland. At the other extreme, large clinics performing > 1000 cycles a year constituted 13 out of 18 (72%) in Belgium, 2 of 3 in Slovenia (66.7%), 8 of 13 (61.5%) in the Netherlands and 8 of 16 (50%) in Sweden.

Number of treatment cycles per technique and availability

In total, 640 144 cycles were reported in 2012 (Table I and Fig. 1), 30 171 more than in 2011 (+4.9%). Compared with 2011 one more country contributed in 2012. Comparing the 32 countries which provided data

in 2011 and 2012 consecutively the amount of IVF + ICSI cycles increased from 433 395 to 450 667 (+4.0%).

Among the 452 578 fresh cycles reported in 2012, 139 978 were IVF (31%) and 312 600 were ICSI (69%). For about 10 years (between 1997 and 2007) an increase in the proportion of ICSI to IVF cycles was described. Since 2008 a plateau seems to have been established (Fig. 2).

Among the fresh aspirations, 24 countries reported 16 944 of 296 066 cycles performed with donor semen (5.7%) and 29 countries reported 11 174 of 356 469 cycles performed with surgically obtained partner's semen (3.1%).

Data on FER were available in all countries but Serbia (Tables I and II and Supplementary SVII). Moreover, data on thawing/warming were not available in four countries (Czech Republic, Finland, Lithuania, the Netherlands), making impossible the calculation of per thawing PR and delivery rate for those countries. A total of 122 363 FER-thawing cycles and 129 360 FER-transfer cycles have been reported in 2012, 10 491 (8.8%) more than in 2011.

Overall, the proportion of FER transfers compared with 'fresh' transfers was 34.5% (32.4% in 2011), but in some countries the proportion was >50%: 87.0% in Switzerland, 81.1% in Finland, 59.5% in the Netherlands, 57.4% in the Czech Republic, 56.4% in Iceland, 54.0% in Sweden, 52.0% in Poland and 50.8% in Belgium. It was <20% in 10 countries.

The number of ED cycles, reported by 23 countries, was 33 605 (in 2011: 22 countries with 30 298 cycles).

Regarding overall availability of ART, the number of cycles per million women of reproductive age (15–45 years) and per million inhabitants in the 18 countries where data coverage was 100% is shown in Table I and Supplementary Table SIV. In those countries, babies born as a result of

year	countries	clinics	cycles	cycle-increase (%)	ART infants
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	+ 7.6	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	1,314	609,973	+ 11.3	134,106
2012	34	1,354	640,144	+4.9	143,844
total			6 547,700		1 158,823

* data only from countries reporting 100% coverage of ART activity

Figure 1 Number of clinics, cycles and assisted reproductive technology infants in Europe 1997–2012.

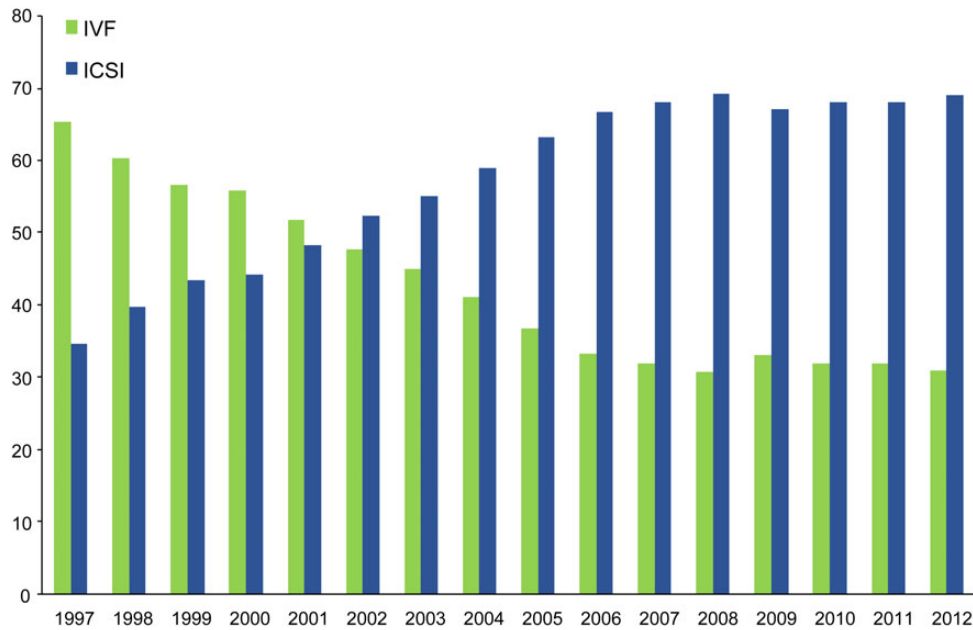


Figure 2 Proportion of IVF/ICSI in Europe 1997–2012.

ART (IUI excluded) varied from 1.3% in Moldova to 6.1% in Denmark. In the Czech Republic, more than 5% of all infants born had been registered by an ART program (5.6%). In contrast, Italy was the other country in which this number was lower than 2% (1.8%).

Pregnancies and deliveries after treatment

Table II shows pregnancy and delivery rates per aspiration for IVF and ICSI, and pregnancy and delivery rates per thawing for FER (regardless of the technique). Mean PR and delivery rate were computed for countries providing the relevant information. Hungary did not register data on deliveries. Austria provided only total deliveries after IVF and ICSI combined.

On average, PRs per aspiration were 29.4% for IVF (+0.3% than in 2011) and 27.8% for ICSI (−0.1% than in 2011). In FER-cycles, the PR per thawing was 23.1% (+1.8% when compared with 2011).

Significant national variations in clinical outcomes were present. In countries reporting 100% of ART activity, the rate of pregnancy per aspiration after IVF ranged from 17.8% in the Czech Republic up to 36.1% in Moldova. For ICSI the variation was from 21.8% in Italy to 38.8% in Moldova. For FER the rate of pregnancy per thawing varied between 15.6% (Estonia) and 33.3% (Croatia).

As shown in [Supplementary Tables SXIII and SXIV](#), several countries experienced difficulties in gathering full pregnancy outcome data. Overall, the pregnancies lost to follow-up were 9.2% (−1.9% than in 2011) for IVF and ICSI, and 9.6% (−1.8% than in 2011) for FER. The mean delivery rates per aspiration for IVF, ICSI and FER (per thawing) were 21.9, 20.1 and 16.0%, respectively (Table II). These figures represent the actual recorded deliveries, even though a number of deliveries may have occurred in the lost to follow-up group.

A detailed account of numbers of cycles, aspirations, transfers, pregnancies, deliveries and the corresponding rates per technique in each

country are reported in [Supplementary Table SV](#) for IVF, [Supplementary Table SVI](#) for ICSI and [Supplementary Table SVII](#) for FER.

The number of documented pregnancy losses was reported by 31 countries for IVF and ICSI and by 29 countries for FER ([Supplementary Tables SXIII and SXIV](#)). In these countries, the rates varied from 8.0 to 26.7% for fresh cycles (mean of 17.0%) and from 12.1 to 37.5% for FER (mean of 20.9%). The figures may be misestimated because of pregnancies lost to follow-up. Moreover, some very high rates may raise the question of the respect of the clinical pregnancy definition. In the eight countries with complete follow-up, the average figures were 16.1% for fresh cycles and 21.1% for FER.

ED (fresh transfer) was reported by 22 countries ([Supplementary Table SVIII](#)). In most of the countries where data were not reported, this technique was not allowed. As in the last three reports, the recipient cycles (transfers) were divided into fresh or frozen/thawed cycles. Similar to the 2011 data report, FOR and FER transfers were considered independently. In total, 14 979 clinical pregnancies resulted from 33 605 embryo transfers.

The mean PR was 48.4% (+2.6% compared with 2011) after 21 354 fresh transfers, 45.1% (45.1% in 2011) after 2696 transfers after FOR (12 countries) and 35.9% (+2.3% than in 2011) after 9555 FER transfers. The overall mean delivery rate per transfer (fresh, FOR and thawed embryos combined) was 28.2%, a value that may be a consequence of a significant loss for follow-up of pregnancies in Spain, by far the main contributor.

Fifteen countries out of the 18 in which embryo donation is allowed reported data on the technique: 3224 transfers were performed, with 1118 pregnancies (34.7% per transfer).

In total, 143 844 infants were born after IVF, ICSI, FER, ED and PGD/PGS in the 33 countries where the reporting included newborns (Table II). A total of 104 269 were born after IVF/ICSI fresh cycles ([Supplementary Table SXIII](#)) and 25 015 were born after FER ([Supplementary Table SXIV](#)).

Table II Results after ART in 2012.

Country	Cycles IVF + ICSI	IVF			ICSI			FER			ART infants (IUI excluded)	ART infants per national births
		Aspirations	Pregnancies per aspiration (%)	Deliveries per aspiration (%)	Aspirations	Pregnancies per aspiration (%)	Deliveries per aspiration (%)	Thawings	Pregnancies per thawing (%)	Deliveries per thawing (%)		
Albania	216				204	41.7	33.8	44	45.5	34.1	104	
Austria		920	34.7		4919	31.3		983	33.6	12.9	2078	2.6
Belarus	1940	1229	39.8	27.3	659	46.7	34.4	127	22.0	11.0	734	0.6
Belgium		3996	28.7	21.1	13 611	25.5	18.4	9277	22.7	16.3	5779	4.6
Bulgaria	6312	593	27.3	17.9	5206	21.4	15.6	587	32.7	25.9	1422	2.1
Croatia	3052	1811	26.7	7.2	2736	24.2	10.5	94	33.0	14.9	466	
Czech Republic	12 298	1739	17.8	14.2	10 147	33.4	24.4		6106	5.6		
Denmark	11 707	5970	25.0	22.1	5278	25.2	22.7	3084	18.8	16.2	3564	6.1
Estonia	1806	606	27.7	22.8	1188	28.7	23.5	761	15.6	10.0	598	4.1
Finland	4785	2475	28.6	22.1	2143	25.7	20.8				1851	3.1
France		20 995	23.8	19.2	39 079	24.0	19.6	23 841	16.7	13.2	17 302	2.1
Germany		12 047	27.2	17.8	39 911	26.6	18.1	19 293	20.1	12.6	14 240	
Greece		1329	32.8	15.7	5343	32.2	17.2	626	60.4	29.6	1971	2.0
Hungary		920	34.5		3502	31.7		401	31.4			
Iceland		199	25.6	18.1	206	22.8	19.9	196	18.9	14.3	145	3.2
Ireland	2127	904	34.4	24.7	922	32.0	24.4	716	23.3	14.1	624	0.9
Italy	55 495	7397	23.9	15.3	42 690	21.8	14.0	6513	18.9	12.1	9594	1.8
Kazakhstan	2263	1188	37.5	24.7	1059	41.8	28.3	465	34.2	22.8	976	0.3
Lithuania		103	41.7	32.0	46	32.6	21.7				66	0.2
Moldova	1130	429	36.1	32.6	667	38.8	36.0	43	23.3	18.6	502	1.3
Montenegro	523	2	50.0	50.0	504	29.4	24.8	17	17.6	17.6	169	2.3
Norway	6320	3131	29.3	23.6	2925	28.0	23.2	2655	19.3	15.3	2026	
Poland	10 714	450	30.0	20.9	10 017	34.7	26.4	4969	26.5	18.7	4560	1.2
Portugal	5803	1838	34.3	26.5	3385	28.4	21.8	1135	20.6	14.3	1866	2.1
Romania	1574	627	40.0	31.9	908	31.6	25.3	338	20.7	11.8	604	0.3
Russia C.I.S.	47 718	21 144	34.1	24.3	25 062	30.1	21.2	10 321	30.7	17.9	16 191	
Serbia	2064	510	35.3	27.1	1386	34.6	28.6				684	
Slovenia	3745	1231	31.8	25.3	2278	25.5	20.5	817	25.0	20.0	1067	4.9
Spain	35 430	3277	33.5	19.4	27 926	31.0	18.1	11 736	29.0	16.4	15 522	
Sweden	11 875	5437	30.8	24.7	5695	30.6	24.9	5809	25.9	20.7	4307	3.8
Switzerland	5358	710	25.8	20.0	4126	22.6	16.6	4188	20.2	15.0	1724	2.1
The Netherlands	16 748	7139	28.2	19.4	8122	29.8	21.8				4759	2.7
Ukraine	8796	3383	41.6	29.9	5116	37.4	29.9	2258	34.9	24.1	4287	0.8
UK	45 653	18 853	31.0	27.0	24 299	31.8	27.8	11 069	25.4	22.0	17 956	2.2
All	305 452	132 582	29.4	21.9	301 265	27.8	20.1	122 363	23.1	16.0	143 844	

For FER there were for France, Greece, Poland, Russia and Spain, respectively, 9, 1, 6, 196 and 38 deliveries with unknown outcome. These were accepted as singletons to calculate the ART infants.

For the Czech Republic, Finland, Lithuania, Moldova, Serbia and the Netherlands no data on the number of thawings were available.

For ED there were for Finland, Greece, Russia and Spain, respectively, 148, 1, 74 and 569 deliveries with unknown outcome. These were accepted as singletons to calculate the ART infants.

For PGD there were for Finland, Greece and Russia, respectively, 2, 1 and 32 deliveries with unknown outcome. These were accepted as singletons to calculate the ART infants.

For Austria only the total number of deliveries for IVF and ICSI together was reported, leading to a delivery rate per aspiration of 28.7%.

Age distribution

The age distribution of women treated with IVF and ICSI varied across countries (Supplementary Tables SIX and SX). The highest percentages of women aged 40 years or more submitted to IVF aspirations were found in Greece, Italy and Denmark, whereas the highest percentages of women aged less than 35 years were found in Belarus, Ukraine and Poland. For ICSI aspirations, countries with the highest proportion of female patients 40 years or more were Greece, Italy and Lithuania; those with more female patients less than 35 years old were Sweden, Belarus and Albania.

As expected, PRs associated with IVF and ICSI decreased with advancing age. The same trend was seen for delivery rates.

For women ≥ 40 years undergoing IVF treatment, the delivery rates vary from 0.8% in the Czech Republic to 17.3% in Ireland (Supplementary Table SIX). For ICSI the delivery rates vary from 4.5% in Croatia to 24.6% in Belarus (Supplementary Table SX).

FER cycles (Supplementary Table SXI) included a relatively higher percentage of young women (≤ 34 years: 48.9%) and, as in fresh cycles, pregnancy and delivery rates decreased with age.

In ED cycles (Supplementary Table SXII), the age of the recipient was 40 years or more in 61.0% of cases on average, and few countries reported a figure $< 40\%$: Belarus (25.0%), Denmark (33.5%), Slovenia (0%) and Sweden (9.4%). Pregnancy and delivery rates in oocyte recipients were comparable across different age groups.

Number of embryos transferred and multiple births

Table III summarizes the number of embryos transferred after IVF and ICSI combined. The total proportion of single embryo transfers (SETs) was 30.2% (27.5% in 2011). Information on numbers of elective single transfers is not available. Double embryo transfers (DET) occurred in 55.4% of the cycles with embryo transfer (56.7% in 2011), triple embryo transfers were reported in 13.3% (14.5% in 2011) and four or more embryos were transferred in 1.1% of the transfers (1.3% in 2011). Figure 3 shows the trends of the numbers of embryos transferred since the first EIM report.

As shown in Table III, major differences were seen between countries concerning the number of embryos transferred. Four countries reported a SET rate of over 50% (Sweden 76.3%, Finland 75.0%, Norway 60.8% and Belgium 51.1%). The proportion of triple embryo transfers ranged from 0% in Finland, Sweden and Iceland to $\geq 40\%$ in Greece, Moldova, Montenegro and Serbia. The transfer of four or more embryos ranged from 0% in 17 countries and over 2% in 7 countries, to 18.6% in Moldova.

In FER cycles, the proportion of single, double, triple and ≥ 4 embryos transfers were 36.0, 45.0, 7.3 and 0.3%, respectively. The missing proportion relates to an unknown number of embryos transferred. In ED, the proportion of single, double, triple and ≥ 4 embryos transfers was 22.4, 61.2, 6.6 and 0.4%, respectively. Also for ED almost 10% of transfers were of a non-disclosed number of embryos.

In fresh IVF/ICSI cycles, the percentages of multiple deliveries were 17.9% in total, ranging from 5.2% in Iceland up to 37.2% in Lithuania, (19.2% in 2011 and 19.6% in 2010), 17.3% twins (18.6% in 2011, 19.6% in 2010) and 0.6% triplets (0.6% in 2011 and 1.0% in 2010) (Table III). After FER, the percentages were 12.2% for twins (12.8% in 2011 and 12.5% in 2010) and 0.3% for triplet deliveries (0.4% in 2011 and 0.3% from 2010 to 2007) (Table III). Additional data on pregnancy

outcome, singleton and multiple deliveries are provided in Supplementary Tables SXIII and SXIV.

In ED, of 8674 deliveries with information regarding multiplicity, 2137 were twins (24.6%) and 49 were triplets (0.6%) (data not presented in tables).

Perinatal risks and complications

Supplementary Table SXV summarizes the risk of preterm deliveries according to the number of new-borns. Data were available from 19 countries. These show that the risk of extreme preterm birth (gestational weeks 20–27) increased from 1.0% (0.9% in 2011 and 1.1% in 2010) for a singleton delivery, to 3.6% (3.7% in 2011 and 3.2% in 2010) for twins and 6.3% (13.5% in 2011 and 12.8% in 2010) for triplets: the same trend was noted for very preterm birth (28–32 weeks), from 2.1 to 10.0 and 37.9%, respectively. Term delivery (37+ weeks) rate was 87.7% for singleton, 47.0% for twins and only 8.1% for triplets.

Ovarian hyperstimulation syndrome (OHSS) was reported in 28 of the 34 countries (Supplementary Table SXVI). In total, 1953 cases of OHSS were recorded, corresponding to a prevalence of 0.6% (0.6% in 2011) of all stimulated cycles in the countries reporting that information. The table also includes data on the incidence of other adverse outcomes, such as bleeding (848 cases), infection (101 cases) and fetal reductions (485 cases). Maternal death was reported in three cases (one case in 2011, two cases in 2010 and one in 2009). The figures on risks may be underestimated because of incomplete reporting.

PGD/PGS

PGD/PGS activity, recorded from 19 countries (16 in 2011) (Table I), involved 7551 fresh cycles and 882 thawings, resulting in 4465 fresh and 671 frozen embryo transfers. A total of 1689 pregnancies (37.8% per transfer) and 1244 deliveries (27.9% per transfer) resulted from fresh cycles, and corresponding figures for FER were 255 (38.0% per transfer) and 181 (27.0% per transfer). The main contributor was Spain with 2744 cycles. More complete data and detailed analysis of PGD/PGS in Europe was published separately by ESHRE's PGD Consortium (De Rycke *et al.*, 2015).

In vitro maturation

IVM was recorded in nine countries (Table I). A total of 421 aspirations (511 in 2011) and 357 transfers were recorded, resulting in 91 pregnancies and 79 deliveries. Russia accounted for 53.7% of immature oocyte aspirations and 62% of deliveries after IVM.

Frozen oocyte replacement (ED not included)

FOR was recorded by 13 countries (Table I), with a total of 5549 thawings (5237 in 2011), 4645 transfers, 1737 pregnancies and 954 deliveries. The vast majority (87%) was performed in Italy and Spain.

Intrauterine insemination

In 2012, 26 countries reported IUI cycles, with a total of 1306 units, 1126 of which (86.2%) were reporting to the EIM (Table I).

Table IV provides data on IUI-H and IUI-D cycles. With regard to insemination with IUI-husband/partner's semen, 175 028 cycles (174 390 in 2011) were reported by 26 countries, the main contributors being France, Italy, Spain, Poland and Belgium. Among the 24 countries reporting deliveries, the mean delivery rate per cycle was 8.5% (8.3% in 2011),

Table III Number of embryos transferred after ART and deliveries in 2012.

Country	IVF + ICSI								FER										
	Transfers	1 embryo	%	2 embryos	%	3 embryos	%	4+ embryos	Deliveries	Twin deliveries	%	Triplet deliveries	%	Deliveries	Twin deliveries	%	Triplet deliveries	%	
Albania	194	26	13.4	136	70.1	32	16.5	0	0.0	69	6	8.7	0	0.0	15	3	20.0	0	0.0
Austria	6349	2953	46.5	3245	51.1	145	2.3	6	0.1	1801	261	14.5	8	0.4					
Belarus	1737	182	10.5	964	55.5	577	33.2	14	0.8	563	122	25.4	11	2.3	14	3	21.4	0	0.0
Belgium	15 730	8028	51.1	6302	40.1	1173	7.5	216	1.4	3342	333	10.0	10	0.3	1512	146	9.7	3	0.2
Bulgaria	3404	636	18.7	1171	34.4	1109	32.6	488	14.3	917	198	21.6	9	1.0	152	41	27.0	0	0.0
Croatia	3359	1089	32.4	1754	52.2	516	15.4	0	0.0	380	44	11.7	2	0.5	30	6	20.0	1	3.3
Czech Republic	10 079	4773	47.4	5004	49.6	287	2.8	15	0.1	2726	424	15.6	4	0.1	1162	200	17.2	2	0.2
Denmark	9445	4332	46.4	4441	47.6	561	6.0	1	0.0	2518	359	14.3	10	0.4	501	68	13.6	0	0.0
Estonia	1615	438	27.1	1076	66.6	101	6.3	0	0.0	417	54	12.9	2	0.5	76	6	7.9	0	0.0
Finland	4093	3070	75.0	1023	25.0	0	0.0	0	0.0	992	74	7.5	2	0.2	597	33	5.5	1	0.2
France	49 269	16 735	34.0	28 873	58.6	3388	6.9	268	0.5	11 666	1882	16.2	28	0.2	3140	262	8.4	6	0.2
Germany	46 905	7606	16.2	32 422	69.2	6843	14.6	0	0.0	9377	1914	20.4	61	0.7	2439	354	14.5	17	0.7
Greece	5582	923	16.5	1672	30.0	2509	45.0	477	8.5	1083	277	25.6	15	1.4	185	39	21.2	2	1.1
Hungary	4171	714	17.1	2437	58.4	919	22.0	101	2.4										
Iceland	330	163	49.4	167	50.6	0	0.0	0	0.0	77	4	5.2	0	0.0	28	1	3.6	0	0.0
Ireland	1624	624	38.4	907	55.8	93	5.7	0	0.0	448	62	13.8	2	0.4	101	9	8.9	0	0.0
Italy	41 822	8657	20.7	18 228	43.6	13 434	32.1	1503	3.6	7112	1396	19.6	98	1.4	790	96	12.2	2	0.3
Kazakhstan	2110	405	19.2	1278	60.6	415	19.7	11	0.5	593	84	14.2	12	2.0	106	11	10.4	1	0.9
Lithuania	144	57	39.6	33	22.9	54	37.5	0	0.0	43	14	32.6	2	4.7	5	0	0.0	0	0.0
Moldova	1071	97	9.1	313	29.2	462	43.1	199	18.6	380	76	20.0	14	3.7	8	1	12.5	0	0.0
Montenegro	462	59	12.8	144	31.2	243	52.6	16	3.5	126	40	31.7			3		0.0		0.0
Norway	5241	3169	60.8	2010	38.6	35	0.7	0	0.0	1418	162	11.4	2	0.1	407	35	8.6	0	0.0
Poland	9106	2251	24.7	6303	69.2	546	6.0	6	0.1	2740	416	15.2	13	0.5	928	100	10.8	1	0.1
Portugal	4454	862	19.4	3412	76.6	179	4.0	1	0.0	1224	239	19.5	5	0.4	162	27	16.7	0	0.0
Romania	1405	128	9.1	667	47.5	502	35.8	106	7.6	430	101	25.4	3	0.8	40	5	12.5	0	0.0
Russia C.I.S.	40 040	8230	23.9	20 346	59.1	5281	15.3	577	1.7	10 459	2027	21.0	94	1.0	1848	260	15.7	9	0.5
Serbia	1794	348	19.4	432	24.1	1014	56.5	0	0.0	510	174	34.1	0	0.0					
Slovenia	3072	1215	39.6	1820	59.2	37	1.2	0	0.0	779	107	13.7	0	0.0	163	12	7.4	1	0.6
Spain	25 696	5042	19.6	18 505	72.0	2149	8.4	0	0.0	5700	1246	21.9	20	0.4	1927	322	17.0	5	0.3
Sweden	9704	7402	76.3	2302	23.7	0	0.0	0	0.0	2761	155	5.6	3	0.1	1202	40	3.3	2	0.2
Switzerland	4247	1024	24.1	2592	61.0	631	14.9	0	0.0	828	150	18.1	8	1.0	627	99	15.8	2	0.3
The Netherlands	13 560							0		3151	232	7.4	4	0.1	1269	61	4.8	1	0.1
Ukraine	7877	1087	13.8	4513	57.3	2219	28.2	58	0.7	2542	580	22.8	20	0.8	545	112	20.6	6	1.1
UK	39 389	15 037	38.2	22 474	57.1	1875	4.8	0	0.0	11 856	1997	16.8	42	0.4	2438	354	14.5	8	0.3
All	375 080	107 362	30.2	196 966	55.4	47 329	13.3	4063	1.1	89 028	15 210	17.3	504	0.6	22 420	2706	12.2	70	0.3

Note: Percentages of transfers of 1, 2, 3 and 4+ embryos are computed after excluding missing data.

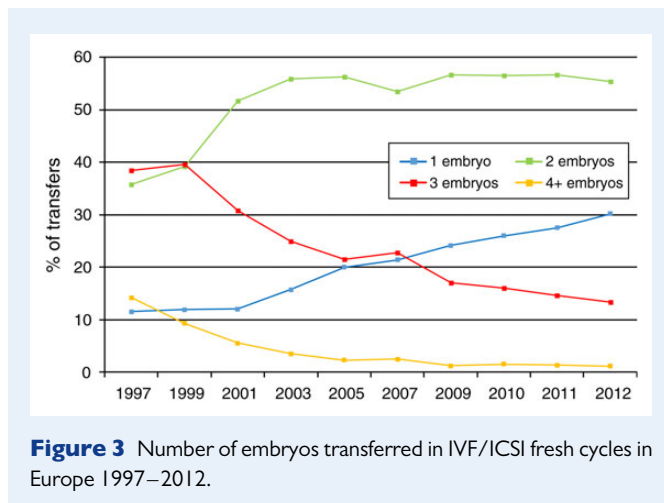


Figure 3 Number of embryos transferred in IVF/ICSI fresh cycles in Europe 1997–2012.

with 9.0% (9.7% in 2011) of deliveries being twin and 0.4% (0.6% in 2011) triplet deliveries.

For IUI-D insemination, 43 497 cycles (41 151 in 2011) were reported by 20 countries, the main contributors being Denmark, Belgium and Spain. The delivery rate per cycle was 12.0% (12.2% in 2011), with multiple delivery rates of 7.2% (7.3% in 2011) for twins and 0.5% (0.3% in 2011) for triplets.

Data available on outcomes in women below 40 years and 40 years or more are presented in [Supplementary Tables SXVII and SXVIII](#). The delivery rate associated with IUI-H declined with age (8.2% below 40 years versus 4.1% above) and the multiple delivery rate decreased from 8.2 to 5.8% for twins, and from 0.5 to 0.0% for triplets. Similar findings were seen in IUI-D, where delivery rates decreased from 12.3 to 6.5%, twin deliveries from 6.8 to 6.0% and triplets from 0.5 to 0.0%.

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

[Supplementary Table SXIX](#) gives an estimate of a cumulative delivery rate in countries performing FER and reporting deliveries.

The calculation is presented as the sum of fresh and FER deliveries as nominator and the number of aspirations of the same year as denominator. So, numbers cannot be considered as a true cumulative delivery rate per couple per aspiration cycle.

Overall, the increase after inclusion of FER deliveries was from 20.7 to 26.0% in the 29 countries providing these data, but, in some countries, the increment in the delivery rate was even more substantial (Switzerland +13.0%, Finland +12.9%, Sweden +10.8%). In 19 of the countries the 'benefit' of using our definition of cumulative delivery rate was more than 3.5%.

Cross-border reproductive care

Eleven countries reported data on cross-border patients: Belarus, Croatia, Denmark, Greece, Iceland, Lithuania, Moldova, Poland, Slovenia, Spain and Switzerland. A total of 6350 cycles were reported, 61.3% of which involved IVF/ICSI with the couple's own gametes, 18.6% were oocyte donations and 17.0% were IVF or ICSI with semen donation. Additionally, 7237 IUI with sperm donation 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 countries (43.8%) or to seek a higher quality treatment (36.7%).

Discussion

The present report is the 16th consecutive, annual European report on ART data. Taken together, these reports cover almost 6.5 million treatment cycles from 1997 to 2012 and 1 159 278 infants.

In spite of some positive changes in the last years, the registry systems remain very much diverse among countries. As a consequence, some data are not reported and a number of countries have been unable to provide some relevant information, such as initiated cycles and deliveries. Another area of concern is the weakness or the absence of data validation methodologies in the vast majority of the European countries. It could be argued that as long as data are incomplete and generated through different methods of collection, results may be questionable. Nevertheless, the findings reported in this paper are extremely relevant because they reveal important trends in practice and outcomes in Europe and give a clear picture of the differences existing among countries.

In spite of several actions trying to overcome the difficulties related to registries of several countries, participation in this effort in 2012 was similar to that in 2011, as the number of countries reporting was 34, one more than in 2011 ([Supplementary Table SI](#)). Bosnia, Cyprus, Latvia, Macedonia, Malta, Slovakia and Turkey are members of the EIM Consortium but were not able to participate. Data are also not available from Azerbaijan, Georgia and Kosovo, as before. Some other independent very small European states have never participated in the EIM registry (Andorra, Armenia, Liechtenstein, Luxemburg, Monaco, San Marino and Vatican City). Overall, the EIM has been collecting data from nearly 80% of the European countries for several years.

In 2012, the proportion of clinics providing ART data was 82.1, slightly higher than in 2011. The lowest reporting rates were from Albania (17%), Kazakhstan (20%), Bulgaria (23%) and Greece (26%).

The number of countries with 100% coverage was 18—close to previous years (17 in 2011 and 2010).

Overall the number of reported cycles of IVF and ICSI increased by 4.9%. Comparing the 32 countries which reported also in 2011, an increase of IVF/ICSI cycles from 433 395 to 452 578 could be demonstrated (4.0%). Some variations were apparent: in Bulgaria 255% more cycles were registered in 2012 compared with 2011; Moldova (+79%), Greece (+52%) and Lithuania (+51%) also reported a relevant increase in number of cycles. On the other hand, nine countries registered a lower activity in 2012 but none decreased by more than 7% regarding the number of cycles.

The reasons for this trend are not clear and a combination of improved registry systems and consequences of the economic situation could be addressed here.

In 2012, the USA ([CDC, 2014](#)) reported 99 665 started IVF/ICSI cycles (101 213 in 2011). For Australia and New Zealand 42 299 initiated cycles were reported (40 696 in 2011) ([Macaldowie et al., 2014](#)).

After a continuous increase until 2008 and a small decrease in 2009 the proportion of ICSI versus conventional IVF procedures showed stable percentages (2012: 69.0%) in recent years ([Fig. 2](#)). The drop from 2008 to 2009 is likely to have been driven by the absence of data from Turkey after 2008, a country with a very high proportion of ICSI cycles (98% in 2008). A marked variation in the relative proportions of IVF and ICSI within Europe is clear, and the difference seems to have a

Table IV Intrauterine insemination with husband (partner) semen (IUI-H) or donor semen (IUI-D) in 2012.

Country	IUI-H									IUI-D								
	Cycles	Deliveries	%	Singleton	%	Twin	%	Triplet	%	Cycles	Deliveries	%	Singleton	%	Twin	%	Triplet	%
Albania	61	6	9.8	5	83.3	1	16.7	0	0.0									
Austria																		
Belarus	543	72	13.3	66	91.7	6	8.3	0	0.0	9	1	11.1	1	100.0				
Belgium	11 919	679	5.7	641	95.4	31	4.6	0	0.0	7345	482	6.6	451	94.9	24	5.1	0	0.0
Bulgaria	1441	118	8.2	103	87.3	15	12.7	0	0.0	353	37	10.5	34	91.9	3	8.1	0	0.0
Croatia	1712	91	5.3	83	91.2	8	8.8	0	0.0									
Czech Republic																		
Denmark	8989	1096	12.2	982	89.6	105	9.6	9	0.8	10 612	1193	11.2	1115	93.5	65	5.4	13	1.1
Estonia	158	11	7.0	11	100.0	0	0.0	0	0.0	135	8	5.9	8	100.0	0	0.0	0	0.0
Finland	3479	305	8.8	285	93.4	20	6.6	0	0.0	1049	129	12.3	124	96.1	5	3.9	0	0.0
France	54 390	5480	10.1	4885	89.3	571	10.4	17	0.3	3870	702	18.1	626	89.2	72	10.3	4	0.6
Germany																		
Greece	1985	105	5.3	96	91.4	9	8.6	0	0.0	99	12	12.1	11	91.7	1	8.3	0	0.0
Hungary																		
Iceland																		
Ireland	726	56	7.7	51	91.1	5	8.9	0	0.0	221	39	17.6	33	84.6	5	12.8	1	2.6
Italy	29 427	1974	6.7	1801	91.2	159	8.1	14	0.7									
Kazakhstan	564	45	8.0	43	95.6	2	4.4	0	0.0	370	27	7.3	27	100.0	0	0.0	0	0.0
Lithuania	276	28	10.1	22	78.6	4	14.3	2	7.1	0	0	0.0	0		0		0	
Moldova	414	46	11.1	45	97.8	1	2.2	0	0.0									
Montenegro	177	18	10.2	18	100.0		0.0		0.0									
Norway	515	45	8.7	40	88.9	5	11.1	0	0.0	383	65	17.0	62	95.4	3	4.6	0	0.0
Poland	12 719	971	7.6	853	93.6	58	6.4	0	0.0	2008	273	13.6	247	94.3	14	5.3	1	0.4
Portugal	2304	197	8.6	179	90.9	18	9.1	0	0.0	239	48	20.1	43	89.6	5	10.4	0	0.0
Romania	1692	121	7.2	102	92.7	8	7.3	0	0.0	201	22	10.9	21	100.0	0	0.0	0	0.0
Russia C.I.S.	8885	956	10.8	880	92.5	67	7.0	4	0.4	3807	670	17.6	624	93.3	43	6.4	2	0.3
Serbia	1800		0.0															
Slovenia	700	52	7.4	47	90.4	4	7.7	1	1.9	2	0	0.0	0		0		0	
Spain	21 561	1559	7.2	1391	89.2	155	9.9	13	0.8	7035	768	10.9	672	87.5	92	12.0	4	0.5
Sweden										867	123	14.2	120	97.6	3	2.4	0	0.0
Switzerland																		
The Netherlands																		
Ukraine	1113	99	8.9	93	93.9	6	6.1	0	0.0	453	49	10.8	48	98.0	1	2.0		0.0
UK	7478									4439	558	12.6	519	93.0	38	6.8	1	0.2
All	175 028	14 130	8.5	12 722	90.6	1257	9.0	60	0.4	43 497	5206	12.0	4786	92.3	374	7.2	26	0.5

For Austria, the Czech Republic, Iceland, the Netherlands and Switzerland: no data on IUI available.

IUI-D not allowed in Italy, Lithuania and Serbia.

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

Sweden: for IUI-H no data available.

UK: for IUI-H only the number of cycles and pregnancies are available.

geographic distribution. In several countries from northern and eastern Europe (Belarus, Denmark, Finland, Iceland, Ireland, Kazakhstan, Lithuania, Norway) IVF remains the dominant technology. In contrast, in most countries from western and central Europe (Bulgaria, Czech Republic, Greece, Italy, Montenegro, Poland, Spain, Switzerland) ICSI was used in a minimum of 80% of cases.

In Australia and New Zealand, 68.2% of all non-donor cycles used ICSI in 2012 and in the USA the corresponding figure was 68%, reflecting a trend throughout the world in performing ICSI in the majority of the cycles.

The marked increase in the use of ICSI cannot be explained by a proportional increase in male infertility but rather by a more liberal use of this technique in cases with mixed infertility, unexplained infertility, mild male factor infertility, low oocyte number and fertilization failures (Jain and Gupta, 2007; Nyboe Andersen *et al.*, 2008b). However, the observed differences among different European countries can only be explained by differences in professional strategy, clinical decision-making and insurance-strategies, since overall results of ICSI treatments have not been better than with IVF in EIM reports.

Availability of ART is a very relevant topic. The cultural and legal conditions, insurance/public funding systems and structure of data-collection can influence not only the amount of treatment cycles per inhabitant but also success rates. This has to be taken into account when comparing different annual reports.

As shown in Table I and Supplementary Table SIV, the average number of treatment cycles per million inhabitants in the countries with 100% reporting coverage was 1252 (1269 in 2011) and 6519 (6559 in 2011) per million females of reproductive age (15–45 years). Huge differences in access (cycles/million females of reproductive age) exist among countries, with the highest figures from Denmark (14 431), Belgium (13 616) and Slovenia (11 803) and the lowest from Moldova (1457).

Some years ago the ESHRE Capri Group estimated that IVF/ICSI services for 1500 couples with current infertility per annum per million inhabitants would be required to fulfil the ART needs of a population (and each couple would need on average more than one cycle of treatment) (The ESHRE Capri Workshop Group, 2001). Out of the 18 countries where that evaluation is possible (those with full coverage of activity reporting), 3 countries reported an accessibility above 1500 cycles/million inhabitants—Denmark (2112), Slovenia (1876) and Belgium (1592). Nine countries reported less than 1000 (Austria, Croatia, Finland, France, Hungary, Italy, Moldova, Portugal and UK) (Table I).

Finally, the percentage of new-borns conceived through ART (not including IUI) varied from 0.2% in Lithuania to 6.1% in Denmark with a total of 5 countries exceeding 4% of ART contribution to national natality.

To report the efficacy of ART is a very difficult issue nowadays. Live birth per initiated cycle seemed the purest way to address this issue. However, the freeze-all policy followed at present by many clinics and the multiple frozen embryo transfers resulting from the same cycle represent important challenges to registries and make this outcome less strong than years ago. It should remain, nevertheless, very relevant information. As stated before, some countries could not provide the number of initiated cycles. Moreover, the very low percentage of cancellations reported in some countries points out the difficulty in getting information on all initiated cycles. Therefore, the outcome that is available for all countries is the PR per aspiration. In the last few years no relevant change has been apparent for IVF, in spite of a positive trend: 29.4% in 2012 (2011: 29.1%, 2010: 29.2%). For ICSI treatment the PR per

aspiration remained stable and was again lower than 28%: 27.8% in 2012 (2011: 27.9%, 2010: 29.8%).

In 2012, delivery rates per aspiration and per transfer for IVF (21.9 and 25.2%, respectively) showed no change, compared with figures from 2011 (21.7 and 24.8%) and previous years (2010: 22.4 and 25.5%). Delivery rates per aspiration and per transfer for ICSI (20.1, 23.4%) also showed similar figures for 2012 compared with 2011 (19.9%, 22.7%), (2010: 21.2 and 23.7%), (2009: 19.3 and 21.5%), (2008: 20.4 and 22.7%). The delivery rate per thawing for FER (16.0%) was in 2012 slightly higher (2011: 14.4%, 2010: 14.3%).

The delivery rates in Europe remain lower than in the USA, where in fresh non-donor cycles performed in 2012 the delivery rate (live birth) per cycle was 29.5% and the delivery rate per transfer was 36.4% (CDC, 2014). The outcomes in Europe were very similar to those achieved in Australia and New Zealand, where the delivery rates (live deliveries) in fresh cycles were 18.3% per aspiration and 22.8% per transfer, with a majority of cycles ending in an elective SET (eSET) (Macaldowie *et al.*, 2014). However, data on deliveries and infants must be considered and compared with some caution because of the difficulties met by several European countries in gathering data on pregnancy outcome, while the pregnancy loss to follow-up was low in the annual reports both in the USA and in Australia/New Zealand.

The number of embryos transferred is generally considered an indicator of quality because of its impact in the proportion of multiple pregnancies (and associated obstetrical and neonatal complications). Overall, in 2012, in fresh non-donor cycles, the number of transfers with 3+ embryos (13.7%) was lower than in 2011 (15.8%) and 2010 (17.5%) while the mean percentage of SETs (intended and not intended) increased to 28.6% (2011: 27.5%, 2010: 22.4%). The proportion of DET decreased to 55.4% (56.7% in 2011) and for the first time since 1997, the proportion of 3+ embryos transfers was < 15% and the proportion of SETs was more than twice that of triple embryo transfers.

The highest proportions of SETs were found in Sweden (76.3%), Finland (75.0%), Norway (60.8%), Belgium (51.1%), Iceland (49.4%), Czech Republic (47.4%), Austria (46.5%) and Denmark (46.4%). In contrast, $\geq 50\%$ of 3+ embryo transfers were reported in Greece, Moldova, Montenegro and Serbia.

The EIM reports are unable to discriminate between elective (intended) SET (eSET) and SET in general (unintended), but the increase in the number of transfers of one embryo seen in the last few years is undoubtedly due to an increase in eSET. Despite huge differences in embryo transfer policy across countries, the overall trend towards transferring fewer embryos seen over the last 10 years seems to continue.

In comparison with the situation in Europe, data from other registers show that SET was performed in 76.3% (2011: 73.2%) of cycles in Australia and New Zealand (Macaldowie *et al.*, 2014) and 19.5% (2011: 17%) in the USA (CDC, 2014).

Similar observations can be made for the multiple delivery rates.

In 2012, the multiple delivery rates (twins + triplets) in IVF and ICSI cycles decreased compared with the previous years: 17.1 and 0.6%, respectively (2011: 18.6 and 0.6%, 2010: 19.6 and 1.0%, 2009: 19.4 and 0.8%). Overall, a remarkable reduction in multiple deliveries over the years is seen in Europe but major differences are still evident across countries. Some countries registered a high triplet delivery rate, like Lithuania (4.7%), Moldova (3.7%) and Belarus (2.3%). Several other countries were able to maintain the triplet deliveries at $\leq 0.2\%$ (Albania, Czech Republic, Finland, France, Iceland, Norway, Serbia, Slovenia, Sweden and

The Netherlands). The twin delivery rate ranged from 5.2% in Iceland to 34.1% in Serbia.

Figures for multiple-infant birth rate (twins, triplets or more) point to important differences between the USA (27.4%), Europe (17.9%) and Australia/New Zealand (6.5%), again in 2012.

We have included data describing preterm birth rates according to the number of fetuses in the pregnancy (Supplementary Table XV), which was completed by 19 countries. The risk of extreme preterm birth (<28 weeks) was increased almost 4-fold for twins and more than 6-fold for triplets (1.06.3%). The risk of very preterm birth (28–32 weeks) is increased almost 5-fold for twins and 19-fold for triplets (2.137.9%).

Fetal reductions are almost always performed in triplet or higher order gestations. Thus, when analysing the figures for triplet delivery rates in different countries, the number of fetal reductions should also be considered. A total of 485 procedures were reported (142 more than in 2011) (Supplementary Table XVI). However, the number is likely to be an underestimate since several countries, including large countries such as Germany and Italy, did not report on this intervention. Without fetal reductions, the proportion of triplet deliveries would have been probably much higher. Still, everything should be done to prevent fetal reduction as a means to decrease high order multiple delivery in ART.

As expected the effect of women's age on treatment outcome is clearly shown again in 2012. The PRs per aspiration in IVF cycles decreased from 29.6% in women aged less than 35 years, to 13.5% in those aged 40 years or more (Supplementary Table SIX). Similar trends were noted for ICSI (from 29.3 to 12.6%, Supplementary Table SX) and FER (from 28.9 to 21.3%, Supplementary Table SXI), but not for ED (Supplementary Table SXI). These supplementary tables also provide delivery rates per aspiration. It is important to consider these tables since they better allow comparisons between the countries, as age is a major prognostic factor that is unequally distributed across the countries.

Regarding ED, for the first year, it is possible to evaluate the outcome of fresh, FER and FOR separately (Supplementary Table SVIII): the PR per transfer was 48.4, 45.1 and 35.9%, respectively. The results of FOR cycles, reported by 11 countries, are very promising as they look close to those of fresh cycles. FER results are clearly lower, a situation that repeats previous years (33.6% in 2011 and 33.3% in 2010) and can raise some concern about a widespread freeze-all policy.

With the noticeable decline in the number of embryos transferred and the increasing proportion of FER cycles, the cumulative delivery rate per started cycle may be the most relevant end-point for ART. However, this figure can only be obtained a few years after the initial oocyte aspiration and not many countries are able to report this information. In Supplementary Table SXIX, the cumulative delivery rate is presented as the sum of fresh and FER pregnancies obtained in the same calendar year. The method of calculation can be methodologically flawed, but the estimate may be close to the actual figure. In several countries, FER deliveries added substantially (more than 6%) to the delivery rates per cycle: Finland (20.7–33.2%), Switzerland (15.5–27.2%), Sweden (23.3–33.4%), Belgium (19.0–27.6%), Czech Republic (22.2–31.6%), Poland (25.6–34.2%), the Netherlands (18.8–26.4%), Iceland (19.0–25.9%) and Albania (31.9–38.9%), justifying their transfer and freezing policies.

Safety is also addressed in the EIM registry. Regarding direct risks of ART, OHSS was recorded only in 0.6% of all stimulated cycles.

However, there may be a degree of under-reporting of this complication as the rate varied between 0 and 1.7% in the countries reporting it. Other complications are extremely rarely reported.

For the 11th consecutive year, the present report includes European data on treatments with IUI-H (175 028 cycles) and IUI-D (43 497), which are similar to 2011.

In spite of increasing numbers of IUI reported since the inception of IUI data collection, no significant differences have been noted in terms of delivery rates and in the incidence of multiple pregnancies.

European countries have very different legal/regulatory frameworks. Cross-border reproductive care is, therefore, a relevant social phenomenon. In this report, the EIM Consortium continues to address this topic using an optional module included in the data collection sheets. A total of 6350 cycles were reported in 2012 by 11 countries. This represents an 81% increase in the number of cycles compared with 2011. However, this number is still much lower than estimated, based on the CBRC study performed in Europe (Shenfield et al., 2010). Regarding the countries of origin and reasons for travelling, only incomplete information could be gathered.

In summary, the 16th ESHRE report on ART for Europe shows a continuing moderate expansion in the number of treatment cycles, with more than 640 000 cycles reported in 2012. The use of ICSI has reached a plateau. Pregnancy and delivery rates after IVF or ICSI remained relatively stable compared with 2011. The number of multiple embryo transfers (3+ embryos) and the multiple delivery rate were the lowest ever.

Supplementary data

Supplementary data are available at <http://humrep.oxfordjournals.org/>.

Authors' roles

V.G. performed the calculations. C.C.-J. wrote the paper. All other co-authors reviewed the document and made appropriate corrections and suggestions for improving the document. Finally, this document represents a fully collaborative work.

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Conflict of interest

None declared.

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