human reproduction

# ORIGINAL ARTICLE ESHRE pages

# Assisted reproductive technology in Europe, 2009: results generated from European registers by ESHRE<sup>†</sup>

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**STUDY QUESTION:** The I 3th European *in vitro* fertilization (IVF)-monitoring (EIM) report presents the results of treatments involving assisted reproductive technology (ART) initiated in Europe during 2009: are there any changes in the trends 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 and, while pregnancy rates in 2009 remained similar to those reported in 2008, the number of transfers with multiple embryos (3+) and the multiple delivery rates declined.

**WHAT IS KNOWN ALREADY:** Since 1997, ART data in Europe have been collected and reported in 12 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); cycles started between 1st January and 31st December are collected on a yearly basis; the data are collected by the National Registers, when existing, or on a voluntary basis.

**PARTICIPANTS/MATERIALS SETTING, METHODS:** From 34 countries (-2 compared with 2008), 1005 clinics reported 537 463 treatment cycles including: IVF (135 621), intracytoplasmic sperm injection (ICSI, 266 084), frozen embryo replacement (FER, 104 153), egg donation (ED, 21 604), in vitro maturation (IVM, 1334), preimplantation genetic diagnosis/screening (PGD/PGS, 4389) and frozen oocyte replacements (FOR, 4278). European data on intrauterine insemination using husband/partner's semen (IUI-H) and donor (IUI-D) semen were reported from 21 and 18 countries, respectively. A total of 162 843 IUI-H (+12.7%) and 29 235 IUI-D (+17.3%) cycles were included. Data available from each country are presented in the tables; total values (as numbers and percentages) refer to those countries where all data have been reported.

**MAIN RESULTS AND THE ROLE OF CHANCE:** In 21 countries where all clinics reported to the ART register, a total of 399 020 ART cycles were performed in a population of 373.8 million, corresponding to 1067 cycles per million inhabitants. For IVF, the clinical pregnancy rates per aspiration and per transfer were 28.9 and 32.9%, respectively and for ICSI, the corresponding rates were 28.7 and 32.0%. In FER cycles, the pregnancy rate per thawing was 20.9%; in ED cycles, the pregnancy rate per transfer was 42.3%. The delivery rate after IUI-H was 8.3 and 13.4% after IUI-D. In IVF and ICSI cycles, 1, 2, 3 and 4+ embryos were transferred in 24.2, 57.7, 16.9 and 1.2%, respectively. The proportions of singleton, twin and triplet deliveries after IVF and ICSI (combined) were 79.8, 19.4 and 0.8%, respectively, resulting in a total multiple delivery rate of 20.2%, compared with 21.7% in 2008, 22.3% in 2007, 20.8% in 2006 and 21.8% in 2005. In FER cycles, the multiple delivery rate was 13.0% (12.7% twins and 0.3% triplets). Twin and triplet delivery rates associated with IUI cycles were 10.4/0.7% and 10.3/0.5%, following treatment with husband and donor semen, respectively.

**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.

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†EIM Committee 2011–2013: chairman: A.P.F.; chairman elect: M.K.; past chairman: J.d.M. members: A.N.A. (special advisor), S.B., J.A.C., V.K. and K.E. 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.

**WIDER IMPLICATIONS OF THE FINDINGS:** The I 3th ESHRE report on ART shows a continuing expansion of the number of treatment cycles in Europe, with more than half a million of cycles reported in 2009. The use of ICSI has reached a plateau. Pregnancy and delivery rates after IVF and ICSI remained relatively stable compared with 2008 and 2007. The number of multiple embryo transfers (3+ embryos) and the multiple delivery rate have shown a clear decline.

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

Key words: European society of human reproduction and embryology, Europe, IVF / ICSI, intrauterine insemination, register data

# Introduction

This report is the 13th annual European Society of Human Reproduction and Embryology (ESHRE) publication on European data on assisted reproductive technology (ART). The 12 previous reports, also published in *Human Reproduction* (Nygren and Nyboe Andersen, 2001a,b; Nygren and Nyboe Andersen, 2002; Nyboe Andersen et al., 2004, 2005, 2006, 2007, 2008a, 2009; de Mouzon et al., 2010, 2012; Ferraretti et al., 2012), covered treatment cycles from 1997 to 2008. As in the last report, the printed version contains the four most significant tables. Additional tables are available online, making the whole report consistent with those from previous years. In the published report, these tables will be referred as 'Supplementary data, Tables SI–SXVIII'. The main results of this report were presented at the annual ESHRE congress in Istanbul, July 2012.

# **Materials and Methods**

#### **Data collection**

Data on ART were collected from 34 European countries, covering *in vitro* fertilization (IVF), intracytoplasmic sperm injection (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 (FORs). 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 I January 2009 and 31 December 2009. Data on pregnancy outcomes are derived from follow-up of the cohort treated during this time period.

The method of reporting data in 2009 was similar to that used in the previous year, making almost all tables comparable. A few additional pieces of information were collected regarding the register characteristics (validation process, public access to individual clinical data and financial support) and the number of IVF fresh cycles performed with semen donation or surgically obtained partner's semen. In addition, ED cycles were divided into fresh and frozen replacement categories, and data on embryo donation were also collected. As in 2008, an optional module for data collection on cycles performed for cross-border patients was included. Data were directly entered in ESHRE's computer system by each country co-ordinator, through the software developed by ESHRE. Data analysis was performed in ESHRE's central office by V.G.

As is evident from the tables, the only complete data reported from all countries were on the number of aspirations and the number of clinical pregnancies. The number of transfers was reported from all but a single country (Cyprus), but registers from a number of countries have been unable to provide data on initiated cycles and deliveries; in addition, several countries had a high percentage of pregnancies lost to follow-up. Therefore, complete

outcome data were only available on the pregnancy rate per aspiration, while some of the better indicators of treatment success (clinical pregnancies and deliveries per initiated cycle) cannot be reported correctly and caution should be exercised when comparing outcomes among countries.

Total values (in terms of numbers and percentages) presented in the tables refer to those countries where all data have been reported, as underlined in the footnotes.

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

# Results

# **Participation**

The present report includes data from 34 (Table I) of 47 European countries. In contrast to the 2008 report, four countries were not able to send data: Albania, Bosnia, Estonia (contributing in 2008 with 2603 cycles all together) and Turkey (one of the main contributors in 2008 with 107 clinics and 43 928 cycles). On the other hand, Croatia and Cyprus rejoined the Consortium, reporting 100% of clinics. The proportion of clinics reporting the data was 85.2% (84.5% in 2008) (listed in Supplementary data). In 21 countries (two more compared with 2008), the coverage reached 100% (Supplementary data, Table SI). Switzerland, Ireland and Latvia were able to report data from all but a single centre each. Participation was very low in Greece (8%) and Kazakhstan (20%), and limited in Lithuania (25%) and Bulgaria (40%). Among the countries with the largest populations, the coverage was 100% in Germany, Italy, UK and France, 72% in Russia (74% in 2008) and 66% in Spain (50% in 2008).

# Reporting methods and size of the clinics

Among the 21 countries where reporting was complete (Supplementary data, Table SII), the register was compulsory for 19 (13 held by a National Health Authority and 6 by a Medical Organization) and voluntary for 2 (held by a Medical Organization). Only seven registers were based on individual forms, i.e. cycle-by-cycle data.

In the I3 countries with partial coverage, all the registers were voluntary (three held by a National Health Authority, nine by a Medical Organization and one by personal initiative); only two used individual forms. Fifteen countries (Austria, Belgium, Finland, France, Germany, Hungary, Italy, Montenegro, Poland, Serbia, Slovenia, Spain, Sweden, Switzerland and UK) reported some kind of data validation process. Public access to individual clinic data were available only in nine countries: Hungary, Iceland, Ireland, Latvia, Moldova, Romania, Slovenia, Spain and UK. Public (± industry or professional society) financial support was present in

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	IVF clinic	cs in the	Treatme	nt cycles							Cycles/million <sup>a</sup>	
	Total	Reporting	IVF	ICSI	FER	ED	IVM	PGD	FOR	All	Women 15-45	Population
Austria	26	26	1128	4638	511					6277	3750	765
Belgium	18	18	4377	13 425	8409	1463				27 674	13 173	2574
Bulgaria	17	8	431	1190	124	52	0		0	1797		
Croatia	12	12	1495	2367	218		0		216	4296	4819	957
Cyprus	8	8	303	976	142					1421	5738	1310
Czech Republic	30	30	2990	9640	4443	1883		475	0	19 431	9019	1903
Denmark	19	19	6371	5167	3116	230	0	108	0	14 992	14 160	2726
Finland	19	19	2621	1970	3245	404	2	19	376	8637	8967	1645
France	106	106	21 123	35 111	17 153	641	54	393		74 475	6022	1153
Germany	121	121	11 664	37 772	17913					67 349	4378	823
Greece	50	4	335	1658	210	103	0	4	0	2310		
Hungary	12	12	1230	5088	664	61		25		7068	3437	706
Iceland	1	1	275	188	217	126	0		0	806	12 388	2628
Ireland	7	6	1987	1328	744	6	0	0	0	4065		
Italy	200	200	8407	39 504	1019				3102	52 032	4338	861
Kazakhstan	10	2	691	250	295	214		20	4	1474		
Latvia	4	3	208	287	199	68				762		
Lithuania	4	1	61	54	16					131		
Macedonia	4	4	647	1325	66	27				2065	4531	999
Moldova	1	1	255	370	0	0	0	0	0	625	728	166
Montenegro	3	3	51	397	34					482	3334	717
Norway	11	11	3139	3314	2076		15			8544	9300	1833
Poland	31	25	285	7566	3534	272	96	280	35	12 068		
Portugal	24	24	1475	3405	804	274	11	107	I	6077	2796	568
Romania	12	8	606	323	110	13				1052		
Russia	102	73	19 005	13 755	5456	2190	1088	555	61	42 110		
Serbia	12	9	291	941						1232		
Slovenia	3	3	937	2001	719	14	2	6	1	3680	9002	1835
Spain	166	109	4494	28 734	7901	10 982	10	1706	439	54 266		
Sweden	16	16	5797	5767	4893	140	0	117		16714	9591	1845
Switzerland	26	25	996	4201	3902					9099		
The Netherlands	13	13	8621	8148	5292					22 061	6849	1338
Ukraine	21	15	2858	3057	1323	704		135		8077		

Table I ART in European countries in 2009.

232I ART in Europe, 2009

United Kingdom	70	70	20 467	22 167	9405	1737	26	439	43	54314	4386	876
٩	1179	1005	135 621	266 084	104153	21 604	1334	4389	4278	537 463	5455	1067
Treatment cycles in IVF and ICSI refer to initiated cycles. For Austria, Belgium, France, Germany, Iceland, Kazakhstan and Lithuania, treatr ICSI was performed. For Belgium, there are 754 extra-aspiration cycles for which it is not known whether IVF or ICSI was performed. Treatment cycles in FFR refer to thawinss. For Finland. France, Hungary and The Netherlands, treatment cycles refer to transfers.	and ICSI refer to Belgium, there refer to thawin	Treatment cycles in IVF and ICSI refer to initiated cycles. For Austria, Belgium, France, CISI was performed. For Belgium, there are 754 extra-aspiration cycles for which it Treatment cycles in FER refer to thawinss. For Finland. France, Hunsary and The N	tria, Belgium, Fran on cycles for which Hungary and The	nce, Germany, Icel. thit is not known of Netherlands. Tree	., Germany, Iceland, Kazakhstan and Lithuanië It is not known whether IVF or ICSI was perf Netherlands. treatment cycles refer to transf	and Lithuania, tre CSI was perform efer to transfers.	eatment cycles ned.	refer to aspiratio	ons. For Austria	in 833 cycles and fo	r Germany in 692, it is n	a. treatment cycles refer to aspirations. For Austria in 833 cycles and for Germany in 692, it is not known whether IVF or formed. Fers.

Treatment cycles in ED refer to donation cycles and contain fresh and frozen cycles. For France, Iceland, Kazakhstan and Sweden, fresh ED treatment cycles refer to aspirations. For Iceland, Ineland, Kazakhstan, Slovenia, Spain and the UK, frozen ED For Finland, France, Hungary and The Netherlands, treatment cycles refer to transfers

and aspirations in the frozen cycles. For Kazakhstan, fresh PGD cycles refer to aspirations. For France, frozen PGD treatment cycles refer to cycles in the fresh cycles frozen cycles and refer to initiated

preimplantation genetic diagnosis intracytoplasmic sperm injection; IVM, in vitro maturation; PGD, For Finland, it refers to transfers refer to thawings. frozen embryo replacement; FOR, frozen oocyte replacement; ICSI, to aspirations. Treatment cycles in FOR calculated for the countries with 100% clinics participating. egg donation; per million

25 countries, while in nine countries (Denmark, Germany, Iceland, Ireland, Montenegro, Poland, Portugal, Serbia and Slovenia) all the expenses were covered by the centres.

The distribution of clinics according to the number of cycles varied considerably among the countries (Supplementary data, Table SIII). For instance, small clinics, providing fewer than 100 cycles annually, accounted for 4 of 8 in Romania (50%), 77 of 200 in Italy (38.5%) and 3 of 8 (37.5%) in Cyprus, whereas large clinics performing > 1000 cycles a year constituted 13 of 18 (72.2%) in Belgium, 2 of 3 (66.7%) in Slovenia and 8 of 13 (61.5%) in The Netherlands.

# Number of treatment cycles per technique and availability

In total, 537 463 cycles were reported (Table I), 5203 more than in 2008 (+1.0%) despite the absence of data from a major contributor (Turkey). Among the 30 countries reporting data both in 2008 and 2009, the increase was more noteworthy at 9.5%. Among the 401 705 fresh cycles reported in 2009, 135 621 were IVF (34%) and 266 084 were ICSI (66%). For the first time since 1997, the proportion of ICSI did not increased compared with the previous years (69% in 2008 and 68% in 2007), but this could mainly be due to the absence of Turkish data, where usually ICSI accounted for > 95% of cycles.

Among the fresh aspirations, 19 countries reported 9510 of 263 391 cycles performed with donor semen (3.6%) and 22 countries reported 9442 of 269 699 cycles performed with surgically obtained partner's semen (3.5%).

FER was performed in 32 countries, reporting 104 153 cycles (+7033 compared with 2008). Overall, the proportion in comparison with 'fresh' cycles was 26.0% (24% in 2008), but in some countries the proportion was much higher: 75% in Switzerland, 71% in Finland, 47% in Belgium and Iceland, 42% in Sweden and 40% in Latvia.

The number of ED cycles, reported by 22 countries, was 21 604 (+7995 compared with 2008).

Table I also shows the number of cycles per million women of reproductive age (15-45 years) and per million inhabitants, in the 21 countries where data coverage was 100%. Details are reported in Supplementary data, Table SI.

# 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. Four countries (Czech Republic, Hungary, Latvia and Poland) did not provide data on deliveries. One country (Austria) provided only total cumulative deliveries after IVF and ICSI combined. Thus, the mean pregnancy and delivery rates were computed for countries providing the relevant information. There were significant national variations in clinical outcomes. On average, pregnancy rates were 28.9% (+0.4% compared with 2008) and 28.7% (-0.2%) per aspiration for IVF and ICSI, and 20.9% per thawing for FER (+1.6%). As shown in Supplementary data, Tables SXII and SXIII, several countries experienced difficulties in gathering full pregnancy outcome data. Overall, the pregnancies lost to followup were 12.3% for IVF and ICSI (13 618/110 239) and 9.8% for FER (2113/21547).

The mean delivery rates per aspiration (per thawing for FER) were 20.6, 19.3 and 13.3%, respectively. These figures represent the actual recorded deliveries, even though a number of deliveries may have

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Country	Initiated	IVF			ICSI			FER			ART	ART
	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 (%)	infants <sup>a</sup>	infants per nationa births (%)
Austria	6599	1128	29.1		4638	32.5		511	26.4		1282	1.7
Belgium	20 436	4377	27.1	19.6	13 425	25.8	18.0	8409	17.1	12.1	5002	3.9
Bulgaria	1621	405	34.6	30.4	1174	28.5	24.9	124	18.5	11.3	538	
Croatia	3862	1416	21.0	14.5	1683	23.8	22.6	218	31.7		726	1.7
Cyprus	1279	282	31.9	47.9	920	39.3	30.0	142				
Czech Republic	12 630	2130	23.1		9576	27.6		4443	19.2			
Denmark	11 538	6048	26.0	17.7	5097	27.1	19.4	3116	16.8	10.7	2839	4.5
Finland	4591	2511	29.0	21.7	1913	30.1	23.6			18.1	1920	3.2
France		21 123	23.9	18.9	35	26.4	20.8			13.3	16 074	1.9
Germany	50 128	11 664	26.6	13.4	37 772	26.8	13.6	17913	18.2	9.2	10 073	1.5
Greece	1993	325	31.7	14.5	1578	25.1	10.9	210	33.3	11.0	331	
Hungary	6318	1187	30.5		5028	30.3						
Iceland		275	18.9	14.5	188	29.3	26.1	217	24.4	19.8	169	3.4
Ireland	3315	1599	27.6	22.8	1137	28.9	23.1	744	18.8	15.3	798	1.0
Italy	47 911	7323	24.0	15.6	35 920	22.8	14.7	1019	17.4	11.1	8201	1.4
Kazakhstan		691	35.3	26.5	250	30.8	21.2	295	25.1	18.3	476	
Latvia	495	208	33.7		283	37.5		199	30.2			
Lithuania		61	37.7	24.6	54	40.7	27.8	16	12.5	12.5	76	
Macedonia	1972	615	41.8	31.2	1243	42.5	31.5	66	25.8	19.7	824	3.4
Moldova	625	241	39.4	34.9	355	40.8	34.9				258	0.6
Montenegro	448	48	45.8	45.8	382	33.8	30.1	34	17.6	17.6	176	2.0
Norway	6453	2970	28.9	24.1	3209	27.1	22.9	2076	20.7	17.2	2005	3.1
Poland	7851	273	35.2		7468	36.9		3534	23.2	13.7	2882	
Portugal	4880	1272	35.7	24.5	3151	28.6	22.0	804	21.6	15.4	1498	1.5
Romania	929	598	26.4	4.3	314	29.9	6.4	110	23.6	0.9	66	
Russia	32 760	18 243	34.4	20.4	13418	33.4	19.3	5456	24.9	12.0	9587	
Serbia	1232	271	34.7	28.4	909	34.7	27.7				473	
Slovenia	2938	899	33.3	26.3	1907	33.0	26.1	719	20.4	13.9	974	4.5
Spain	33 228	3947	35.0	20.0	26 364	33.9	19.2	7901	25.8	13.1	12 887	
Sweden	11 564	5362	31.4	24.6	5462	29.1	23.1	4893	26.0	19.7	3851	3.5
Switzerland	5197	916	22.9	17.8	3936	25.4	18.8	3902	19.8	13.6	1686	

2.6		2.0	
4862	2792	15913	109 239
	21.0	<u> 8.</u>	13.3
	27.7	21.0	20.9
	1323	9405	77 799
24.6	27.8	27.4	19.3
32.9	33.0	31.6	28.7
7657	3002	22 127	256 651
20.5	30.0	26.5	20.6
27.8	39.3	30.4	28.9
7896	2766	17723	126793
16 769	5915		348 111
The Netherlands	Ukraine	United Kingdom	Allb

there were 599 deliveries with the unknown outcome. These were accepted as singletons to calculate the ART infants. For FER, there were 48 deliveries with the unknown outcome. These were These were accepted as singletons to calculate the ART infants. Cyprus reported a total of 411 deliveries but no data on multiplicity; these deliveries are not included in the calculation of ART infants. assisted reproductive technology; ED, egg donation; FER, frozen embryo replacement; ICSI, intracytoplasmic sperm injection. were 679 deliveries with the unknown outcome. ED, there For accepted as singletons to calculate the ART infants. For IVF and ICSI, 'ART infants also include ED.

countries where all data were reported for the given technique:

Total rates refer to these

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 data, Table SIV for IVF, Supplementary data, Table SV for ICSI and Supplementary data, Table SVI for FER.

The numbers of documented pregnancy losses (miscarriages) were reported by 29 countries for IVF and ICSI and by 26 countries for FER (Supplementary data, Tables SXII and SXIII). In these countries, the rates varied from 9 to 33% for fresh cycles (mean of 18.5%) and from 0 to 39% for FER (mean of 21.0%). The figures may be an underestimate because of pregnancies lost to follow-up. In the 13 countries with the complete follow-up, the figures were 21.5% for fresh cycles and 18.3% for FER.

ED was reported by 22 countries (Supplementary data, Table SVII). In most of the countries where data were not reported, the technique was illegal. For the first time, the donor cycles (aspirations) and the recipient cycles (transfers) were divided into fresh or frozen/thawed cycles. Frozen/thawed cycles include oocyte or embryo cryopreservation. The mean pregnancy rate was 45.7% in fresh transfers and 31.3% in thawed transfers. In total, 9086 clinical pregnancies resulted from 21 499 embryo transfers with a pregnancy rate of 42.3% per transfer (43.2% in 2008). The mean delivery rates were 30.2% per transfer and 30.0% per donation in the countries reporting deliveries. The pregnancies lost to follow-up were 1323 (15%).

Eleven countries reported data on embryo donation: 963 transfers were performed, with 397 pregnancies (41.2%) and 210 deliveries (21.8%).

In total, 109 239 infants were recorded as having been born as a consequence of IVF, ICSI, FER and ED in the 30 countries where the reporting included newborns (Table II). In the countries with 100% coverage with the relevant data, the percentage of babies conceived through ART on the national births varied from 0.6% in Moldova to 4.5% in Denmark. More details are provided in Supplementary data, Table SI, showing that the percentage of ART babies was > 3.0% in most of the Nordic countries, and between 1.4 and 2.0% in most of the largest European countries (France, Germany, Italy and UK).

Of the 109 239 ART infants, 86 769 (79.4%) were born after IVF/ICSI fresh cycles, 15 126 (13.9%) after FER and 7344 (6.7%) after ED. In Finland, Iceland and Switzerland, one of three ART infants was born after FER.

# Age distribution

The age distribution of women treated with IVF and ICSI varied across countries (Supplementary data, Tables SVIII and SIX). The highest percentages of women aged 40 years or more were found in Greece and Italy, whereas the highest percentages of women aged 34 years or less were found in Czech Republic, Kazakhstan, Lithuania, Poland and Ukraine. As expected, pregnancy rates associated with IVF and ICSI decreased with advancing age. The same trend was seen for delivery rates. FER cycles (Supplementary data, Table SX) included a relatively higher percentage of young women (≤34 years) and, as in fresh cycles, pregnancies and deliveries rates decreased with age. In ED cycles (Supplementary data, Table SXI), the age of the recipient was 40 years or more in 56.2% of cases on average, and few countries reported a figure <40%: Denmark (31.4%), Hungary (24.6%), Macedonia (16.7%), Slovenia (33.3%) and Sweden (10.6%). Pregnancy and delivery rates in oocyte recipients were comparable across different age groups.

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# Number of embryos transferred and multiple births

Table III summarizes the number of embryos transferred after IVF and ICSI combined. In countries with complete data capture, the total proportion of single embryo transfers (SETs) was 24.2% (22.4% in 2008 and 21.4% in 2007). Double embryo transfers (DETs) occurred in 57.7% (53.2% in 2008 and 53.4% in 2007); triple embryo transfers in 16.9% (22.3% in 2008 and 22.7% in 2007) and four or more embryos were transferred in 1.2% (2.1% in 2008 and 2.5% in 2007). Information on numbers of elective single transfers is not yet available. As shown in Table III, major differences were seen between countries. In 2009, three countries reported a SET rate of over 50% (Sweden 70.7%, Finland 65.7% and Norway 53.4%) and three countries over 40% (Belgium 48.9%, Iceland 43.2% and Denmark 42.0%). The proportion of triple embryo transfers ranged from 0 in Sweden and Iceland and < 1% in Finland and Norway to ≥40% in Bulgaria, Greece, Italy, Macedonia, Moldova, Montenegro and Serbia. The transfer of four or more embryos ranged from 0 in 12 countries (and <2% in 5 countries) to 41.2% in Lithuania.

In FER cycles, the proportion of single, double, triple and  $\geq$  4 embryos transfers were 34.3, 54.9, 10.4 and 0.4%, respectively. In ED, the figures were 14.4, 72.4, 12 and 1.2%.

In fresh IVF/ICSI cycles, the percentages of multiple deliveries were 19.4% for twins (20.7% in 2008 and 21.3% in 2007) and 0.8% for triplets (1.0% in 2008 and 2007). After FER, the percentages were 12.7% for twins (13.4% in 2008 and 13.1% in 2007) and 0.3% for triplet deliveries (0.3% in 2008 and 2007). Additional data on pregnancy outcome, singleton and multiple deliveries are provided in Supplementary data, Table SXII (for fresh cycles) and Supplementary data, Table SXIII for FER. In ED, of 5213 deliveries with known data on multiplicity, 1395 were twins (26.8%) and 29 were triplets (0.6%) (data not presented in tables).

# Perinatal risks and complications

Supplementary data, Table SXIV summarizes the risk of preterm deliveries according to the number of newborns. Data were available from 19 countries. These show that the risk of extreme preterm birth (gestational weeks 20-27) increased from 0.9% for a singleton delivery, to 3.0% for twins and 13.6% for triplets. The same trend was noted for very preterm birth (28-32 weeks), from 1.8 to 9.5% and 38.5%, respectively. Term delivery (37+ weeks) rate was 88.6% for singleton, 48.5% for twins and only 10% for triplets.

Ovarian hyperstimulation syndrome (OHSS) was reported in 27 of the 34 countries (Supplementary data, Table SXV). In total, 2137 cases of OHSS were recorded, corresponding to a prevalence of 0.8% of all stimulated cycles in the countries reporting the data. The table also includes data on the incidence of other adverse outcomes, such as bleeding (570 cases), infection (61 cases) and fetal reductions (484 cases).

#### PGD/PGS

PGD/PGS activity, recorded from 15 countries (16 in 2008), involved 4278 cycles, 4048 aspirations, 2994 embryo transfers, 1031 pregnancies (25.5% per aspiration) and 660 deliveries (16.3% per aspiration), the main contributor being Spain with 1706 cycles. More complete data and detailed analysis of PGD/PGS in Europe will be published separately by ESHRE's PGD Consortium (Goossens et al., 2012).

#### In vitro maturation

IVM was recorded in nine countries (Table I). A total of I 334 aspirations (562 in 2008 and 660 in 2007) and 595 transfers were recorded, resulting in I 37 pregnancies and 82 deliveries. Russia accounted for 82% of cycles and 68% of deliveries.

# Frozen oocyte replacement

FOR was recorded by 10 countries, with a total of 4278 thaws, 3416 transfers, 710 pregnancies and 426 deliveries. The majority (72%) was performed in Italy.

#### Intrauterine insemination

The number of IUI laboratories present in the countries was recorded in 2009 for the first time. Only 19 countries reported the figure, with a total of 1000 units, 872 of which (87%) were reporting to the European IVF-monitoring (EIM) Consortium.

Table IV provides data on IUI-H and IUI-D cycles. With regard to insemination with IUI-H's semen, 162 843 cycles (+18334) were reported by 23 countries—the main contributors being France, Italy and Spain. Among the countries reporting deliveries, the mean delivery rate was 8.3% per cycle (-0.8%), with 10.4% of deliveries being twin and 0.7% triplet deliveries. For IUI-D insemination, 29 235 cycles were reported (+4275) by 18 countries, the main contributors being Denmark, France, Spain and UK. The delivery rate was 13.4% per cycle, with multiple delivery rates of 10.3% for twins and 0.5% for triplets.

Data available on outcomes in women below 40 years (upper panel) and 40 years or more (lower panel) are presented in Supplementary data, Table SXVI for IUI-H (and Supplementary data, Table SXVII for IUI-D). The delivery rate associated with IUI-H declined with age (8.0% below 40 versus 3.3% above) and the multiple delivery rate decreased from 11.0 to 4.5% for twins, and from 1.0 to 0.0% for triplets. Similar findings were seen in IUI-D, where delivery rates decreased from 13.7 to 6.0%, twin deliveries from 10.8 to 1.0% and triplets from 0.5 to 0.0%

# **Cumulative delivery rates**

Supplementary data, Table SXVIII gives an estimate of the cumulative delivery rates per initiated stimulated cycle in countries performing FER and reporting deliveries. The calculation, presented as the sum of fresh and FER pregnancies obtained during the same year, is not a true cumulative delivery rate per couple per cycle, but it shows that the delivery rate (fresh versus cumulative) can increase in the countries reporting the relevant data. Overall, the increase after inclusion of FER deliveries was from 19.8 to 23.6% (+19%), but in some countries (Switzerland, Finland, Iceland, Sweden and Belgium) the increment resulted more substantial (+59, +58, +48, +37, +32%, respectively). Additionally, the table shows the rate of multiple deliveries after the 'fresh' cycles and the FER combined. The overall multiple delivery rate was particularly low in Sweden and Finland: 5.8 and 8.7%, respectively, with relatively high cumulative delivery rates (32.7 and 35.8%).

# **Cross-border reproductive care**

Only six countries reported data on cross-border patients: Croatia, Iceland, Ireland, Macedonia, Poland and Spain. A total of 6248 cycles were reported, 75.3% of which involved IVF/ICSI with the couple's

Table III Number of embryos transferred and deliveries after ART in 2009.

Country	IVF + ICSI								FER		
	Transfers	l embryo (%)	2 embryos (%)	3 embryos (%)	4+ embryos (%)	Deliveries	Twin (%)	Triplet (%)	Deliveries	Twin (%)	Triplet (%)
Austria	5875	22.5	68.2	8.6	0.7	1039	21.8	0.8			
Belgium	16 089	48.9	40.7	8.6	1.8	3275	10.3	0.2	1020	11.0	0.2
Bulgaria	1443	9.1	32.3	47.5	10.9	415	12.5	2.7	14	14.3	14.3
Croatia	2774					586	18.4	2.7			
Cyprus						411					
Czech Republic	10 146	19.9	72.8	7.2	0.1						
Denmark	9664	42.0	52.1	6.0	0.0	2056	16.0	0.0	334	17.1	0.0
Finland	3981	65.7	34.1	0.2	0.0	998	8.4	0.1	586	9.2	0.0
France	47 822	27.1	61.8	10.3	0.8	11 292	18.0	0.3	2287	9.9	0.3
Germany	45 476	13.3	68.1	18.7		6717	20.1	0.8	1643	14.9	0.5
Greece	1481	21.7	31.0	40.9	6.4	219	27.6	2.8	23	28.6	9.5
Hungary	5693	14.5	55.7	27.2	2.6						
Iceland	389	43.2	56.8	0.0	0.0	89	14.6	0.0	43	9.3	0.0
Ireland	2487	25.7	65.9	8.3	0.0	627	21.9	1.0	114	8.0	0.0
Italy	37 301	19.0	33.6	44.8	2.6	6409	21.1	2.4	113	12.4	0.0
Kazakhstan	886	13.9	43.5	39.1	3.6	236	36.4	1.7	54	18.5	0.0
Latvia	440	23.0	63.9	13.2	0.0						
Lithuania	114	9.6	13.2	36.0	41.2	30	33.3	6.7	2	0.0	0.0
Macedonia	1703	14.9	29.5	55.6	0.0	584	32.2	1.9	13	7.7	0.0
Moldova	554	8.7	25.1	54.5	11.7	208	21.2	1.4			
Montenegro	398	16.3	29.1	49.5	5.0	137	20.4	1.5	6	16.7	0.0
Norway	5 <b>4</b> 5 I	53.4	45.7	0.9	0.0	1450	11.6	0.1	357	7.9	0.3
Poland	6884	20.7	67.4	11.3	0.6	1866	16.9	0.8	485	15.9	0.0
Portugal	3877	20.6	71.2	7.9	0.3	1006	22.1	0.9	124	15.3	0.8
Romania	875	14.1	39.9	34.3	11.8	46	28.3	4.3	1	0.0	0.0
Russia	29 208	16.4	60.5	19.4	3.6	6308	25.6	1.3	655	15.5	0.6
Serbia	1092	15.7	20.7	42.4	21.2	329	31.0	6.4			
Slovenia	2513	30.4	66.9	2.6	0.0	734	17.6	0.1	100	9.0	0.0
Spain	26 583	15.6	68.2	16.1	0.0	5858	23.3	0.6	1038	17.9	0.5
Sweden	9614	70.7	29.3	0.0	0.0	2580	5.9	0.2	962	5.3	0.0
Switzerland	4170	16.9	64.9	18.2	0.0	903	19.7	0.1	531	13.7	0.2
The Netherlands	13 888					3503	11.2	0.1	883	7.9	0.3
Ukraine	5334	10.6	50.4	35.2	3.7	1667	24.4	1.9	278	21.9	0.4
United Kingdom	36 594	22.7	72.1	5.3	0.0	10 749	22.4	0.4	1703	17.1	0.1
$All^{a}$	340 799	24.2	57.7	16.9	1.2	72 327	19.4	0.8	13 369	12.7	0.3

ART, assisted reproductive technology; FER, frozen embryo replacement; ICSI, intracytoplasmic sperm injection.

<sup>&</sup>lt;sup>a</sup>Totals refer only to these countries where data on the number of transferred embryos and on multiplicity were reported.

Country	IUI-H						IUI-D					
	Cycles	Deliveries	Deliveries (%)	Singleton (%)	Twin (%)	Triplet (%)	Cycles	Deliveries	Deliveries (%)	Singleton (%)	Twin (%)	Triplet (%)
Austria			•••••									
Belgium												
Bulgaria	569	38	6.7	76.3	21.1	2.6	9	1	11.1	100.0	0.0	0.0
Croatia	1746	88	5.0	94.3	4.5	1.1						
Cyprus												
Czech Republic												
Denmark	9982						8912					
Finland	3730	350	9.4	90.6	9.1	0.3	803	107	13.3	95.3	4.7	0.0
France	52 85 1	5044	9.5	89.5	10.2	0.3	3890	612	15.7	88.9	10.8	0.3
Germany												
Greece	319	54	16.9	94.4	5.6	0.0	8	I	12.5	100.0	0.0	0.0
Hungary												
Iceland												
Ireland	1514	138	9.1	92.0	7.2	0.7	232	30	12.9	93.3	3.3	3.3
Italy	33 335	2114	6.3	89.0	9.8	1.2						
Kazakhstan	853	56	6.6	94.6	0.0	3.6	148	9	6.1	100.0	0.0	0.0
Latvia												
Lithuania	200	23	11.5	95.7	4.3	0.0						
Macedonia	710	45	6.3	82.2	17.8	0.0	37	2	5.4	50.0	50.0	0.0
Moldova	171	24	14.0	91.7	8.3	0.0	97	22	22.7	90.9	9.1	0.0
Montenegro	152	19	12.5	100.0	0.0	0.0	344	53	15.4			3.4
Norway	531	40	7.5	83.3	16.7	0.0	1751			96.6	0.0	
Poland	9172						160	32	20.0			0.0
Portugal	1608	158	9.8	84.8	13.9	1.3	235			93.8	6.3	
Romania	1313	20	1.5	95.0	5.0	0.0	2245	322	14.3			0.3
Russia	5774	653	11.3	89.7	10.0	0.3				89.7	10.0	
Serbia	387	24	6.2	91.7	8.3	0.0	10	1	10.0			0.0
Slovenia	659	62	9.4	88.7	8.1	3.2	5927	729	12.3	100.0	0.0	0.7
Spain	25 246	1822	7.2	86.1	12.8	1.2				85.5	13.9	
Sweden												

Table IV IUI-H or IUI-D semen in 2009.

3.4		0.0	0.5	0.5	
		8.9	8.9	10.3	
		1.16	92.7	89.2	
15.4		15.3	1.3	13.4	
53		124	410	2455	
344		810	3617	29 235	
		0.0		0.7	
		1.6		10.4	
		6.06		88.9	
		16.4		8.3	
		1478 243 16.4		11 015	
		1478	10 543	162 843 11 015	
Switzerland	The Netherlands	Ukraine	United Kingdom	$All^{a}$	

celand, a total of 597 IUI cycles were performed resulting in 46 pregnancies and 40 births; Italy, underestimation of deliveries because of the high number of pregnancies which are lost to follow-up. Poland: full data from the only limited number of centres were obtained and not shown in this report.

IUI-H, intrauterine insemination with husband's/partner's semen; IUI-D, intrauterine insemination with donor semen.

reported and mean

data were

where

countries

to these

refers 1

<sup>a</sup>Total

computed on countries with complete information

was

percentage

own gametes, 15.5% were oocyte donations and 9.2% were IUI or IVF with semen donation. Complete information regarding the countries of origin was reported only from Spain, where 63% of the patients were from Italy, 16% from France, 11% from Germany, 4% from UK and 6% from others. The main reason (68%) reported by patients was to seek access to techniques that were not legally available in their home countries.

# **Discussion**

The present report is the 13th, consecutive annual European report on ART data. Taken together, these reports cover treatment cycles from 1997 to 2009.

As shown in the tables, 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. It can be argued that as long as data are incomplete and generated through different methods of collection, results should be interpreted with caution. Nevertheless, the findings reported in this paper reveal important trends in practice and outcomes in Europe and give a clear picture of the differences existing among countries.

In comparison with 2008, the number of countries reporting to the ESHRE's EIM Consortium decreased to 34: Albania, Bosnia, Estonia and Turkey were not able to contribute data, while Croatia and Cyprus re-joined the Consortium. Most of the independent European states that have never contributed data are very small countries (Andorra, Città del Vaticano, Liechtenstein, Luxemburg, Monaco and San Marino). Data have never been available from Malta and the republic of Belarus, but overall, EIM has been collecting data from >80% of the European countries for several years.

In 2009, the coverage was 85.2% of all clinics, a figure similar to 2008 (84.5%) and 2007 (86%). The number of countries with 100% coverage increased to 21 (19 in 2008). As in previous years, the lowest reporting rate was from Greece (4 of 50 clinics).

Overall, the number of reported cycles increased by 1.0% since 2008 (+5203), reaching a total of 537 463 despite fewer countries contributing data. Elsewhere in the world in 2009, 146 244 cycles were reported from the USA (CDC, 2011) and 70 541 cycles from Australia and New Zealand (AlHW, 2011).

As shown in Table I and Supplementary data, Table SI, the average number of treatment cycles per million inhabitants in the countries with 100% coverage was 1067. Huge differences in access exist among countries, with the highest figures from Denmark (2726), Iceland (2628) and Belgium (2574) and the lowest from Moldova (166). A better way to define the availability of ART is to use women of reproductive age (15-49 years) as the denominator, which eliminates the impact of age differences across the countries (Table I and Supplementary data, Table SI). There were also striking differences in access, ranging from 728 cycles in Moldova to 14 160 in Denmark, 13 173 in Belgium and 12388 in Iceland. Countries able to provide over 8000 cycles per million women of reproductive age and over 1700 cycles per million inhabitants were the Czech Republic, Finland, Norway, Slovenia and Sweden. Overall, the highest availability was reported by Nordic countries. Finally, the percentage of newborns conceived through ART varied from 0.6% in Moldova to 4.6% in Denmark (Supplementary data, Table SI).

For the first time, the proportion of ICSI versus conventional IVF procedures showed a marginal decrease compared with data from the

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previous year (66% in 2009 and 69% in 2008), but the figure is likely to have been driven by the absence of data from Turkey, a country with a very high proportion of ICSI cycles (98%) in the previous year. Table I demonstrates a marked variation in the relative proportions of IVF and ICSI within Europe, and the difference seems to have a geographic distribution. In several countries from northern and eastern Europe (Denmark, Finland, Iceland, Ireland, Kazakhstan, Lithuania, Romania, Russia, Sweden and The Netherland), IVF remains the dominant technology; in contrast, in most countries from western and central Europe (Germany, Italy, Spain, Austria and Switzerland) ICSI was used in >75% of cases.

In Australia and New Zealand, 65.6% of all cycles used ICSI in 2009 and in the USA, the corresponding figure was 72.9%, reflecting an uniform 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 similar 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 and fertilization failures (Jain and Gupta, 2007; Nyboe Andersen et al., 2008b). This is, however, unlikely to fully account for the observed differences, which can only be explained by differences in professional strategy and clinical decision-making. In the USA, 53% of ICSI cycles were performed in couples without a diagnosis of male factor infertility (CDC, 2011).

Overall, in 2009, the number of transfers with 3+ embryos (18.1%) was significantly lower compared with 2008 (24.4%), while the mean percentage of SETs increased from 22.4 to 24.2% and the proportion of DET from 53.2 to 57.7%. For the first time since 1997, the proportion of 3+ embryos transfers was <20% and the proportion of SETs was higher than that of triple embryos transfers. The highest proportions of SETs were found in Sweden (70.7%), Norway (53.4%), Belgium (48.9%) and Denmark (42.0%). In contrast, >50% of 3+ embryo transfers were reported in Bulgaria, Greece, Italy, Lithuania, Moldova, Montenegro and Serbia. The EIM reports are unable to discriminate between elective SET (eSET) versus SET in general, but the increase in the number of transfers of one embryo seen in the last years is undoubtedly due to a 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.

Similar observations can be made for the multiple delivery rates. In 2009, the multiple delivery rates (twins + triplets) were marginally lower compared with the previous years: 20.2 versus 21.7% in 2008, 22.3% in 2007 and 20.8% in 2006. Overall, a remarkable reduction in triplet deliveries over the years is seen (3.6% in 1997 and 0.8% in 2009), but major differences are still evident across countries (Table III). Some countries registered a triplet delivery rate of  $>\!2.5\%$  (Bulgaria, Croatia, Greece, Lithuania, Romania and Serbia), while several other countries were able to maintain the triplets deliveries at  $\leq\!0.2\%$  (Belgium, Denmark, Finland, Iceland, Norway, Slovenia, Sweden, Switzerland and The Netherlands). The twin delivery rate ranged from  $<\!10\%$  in Finland and Sweden to  $>\!30\%$  in Lithuania, Macedonia and Serbia.

We have included data describing preterm birth rates according to the number of fetuses in the pregnancy (Supplementary data, Table SXIV), which was completed by 19 countries. The risk of extreme preterm birth ( $<\!28\!$  weeks) was increased 3-fold for twins and 13-fold for triplets. The risk of very preterm (28–32 weeks) birth is increased almost 5-fold for twins and 20-fold for triplets.

Fetal reductions are almost always performed in triplet or higher-order gestations. Thus, when analysing the range of triplet delivery rates in different countries, the number of fetal reductions should also be considered. A total of 484 procedures were reported (90 more than in 2008). However, the number is likely to be an underestimate since several countries, including large countries as Germany and Italy, did not report on this intervention. Without fetal reductions, the proportion of triplet deliveries would have been much higher than the number of recorded triplet deliveries (623 in total).

The pregnancy rate per aspiration remained relatively stable compared with the previous year: 28.9% for IVF and 28.7% for ICSI versus 28.5 and 28.7% in 2008.

Finally, delivery rates per aspiration and per transfer (20.6 and 23.0% for IVF and 19.3 and 21.5% for ICSI, respectively) showed a marginal decline, compared with figures from 2008 (21.2 and 24.3% for IVF and 20.4 and 22.7% for ICSI, respectively), as did the delivery rate per thawing for FER (13.3% in 2009 versus 13.7% in 2008) but this indicator of outcome may be always strongly influenced by the missing data on deliveries.

In comparison with the situation in Europe, data from other registers show that SET was performed in 69.7% of cycles in Australia and New Zealand (AIHW, 2011) and 14% in the USA (CDC, 2011). The delivery rates in Europe remain lower than in the USA, where in fresh non-donor cycles performed in 2008 the delivery rate per aspiration was 33.8% (33.6% in IVF and 33.9% in ICSI) and the delivery rate per transfer was 36.6% (CDC, 2011). However, outcomes were very similar to those achieved in Australia and New Zealand, where the delivery rates in fresh cycles were 23.0% per transfer and 19.7% per aspiration (AIHW, 2011).

Data on deliveries and infants must be considered and compared with some caution because of the difficulties met by several European countries in gathering pregnancy outcome (Supplementary data, Tables SXII and SXIII), while the pregnancy loss to follow-up was close to 0% in the annual reports both in the USA and in Australia/New Zealand.

Figures for multiple-infant birth rate (twins, triplets or more) point to important differences between the USA (31.6%), Europe (20.2%) and Australia/New Zealand (8.2%).

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. In Supplementary data, Table SXVIII, 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 to the delivery rates per cycle: Finland (22.6–35.8%), Belgium (18.4–24.1%), Sweden (23.87–32.7%) and Norway (23.5–29.2%), justifying their transfer and freezing policies.

Regarding direct risks of ART, OHSS was recorded in 0.8% of all stimulated cycles. However, there may be a degree of under-reporting of this complication as the rate varied between 0 and 2.6% in the countries reporting it.

For the eighth consecutive year, the present report includes European data on treatments with IUI-H (162 843 cycles) and IUI-D (29 235), which show an increase compared with 2008 and 2007. Since the inception of IUI data collection, no differences have been noted in terms of delivery rates and in the incidence of multiple pregnancies.

In 2009, the EIM Consortium decided to continue to address the phenomenon of cross-border reproductive care (CBRC). An optional module was added to the data collection sheets asking for the numbers of CBRC patients, the type of treatment requested, main countries of origin and the reason for travelling abroad. A total of 6248 cycles were reported by six countries. As in 2008, the number was much lower compared with the estimation, based on the CBRC study performed recently in Europe (Shenfield et al., 2010): I I 000–I 4 000 patients and 25 000–30 000 cycles per year. In addition, only incomplete information was reported regarding the countries of origin and reasons for travelling. Starting to collect the new data is always difficult. However, because the CBRC phenomenon raises important public health concerns and underlines the need for a detailed evaluation, the Consortium will continue to gather data in the coming years.

In summary, the 13th ESHRE report on ART for Europe shows a continuing expansion in the number of treatment cycles, with more than half a million cycles reported in 2009. The use of ICSI has reached a plateau. Pregnancy and delivery rates after IVF and ICSI remained relatively stable, compared with 2008 and 2007. The number of multiple embryo transfers (3+ embryos) and the multiple delivery rate have shown a clear decline.

# Supplementary data

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

# **Authors' roles**

V.G. performed the calculations. A.P.F. helped with the calculations and 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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