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ORIGINAL ARTICLE ***Reproductive epidemiology***

International Committee for Monitoring Assisted Reproductive Technologies world report: Assisted Reproductive Technology 2006†

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STUDY QUESTION: What are the access, effectiveness and safety of assisted reproductive technology (ART) worldwide in 2006?

SUMMARY ANSWER: ART access, effectiveness and safety vary markedly among countries. Overall, there was an increase in the use of ICSI, single embryo transfer (SET) and frozen embryo transfer (FET). There was a decline in the multiple delivery rate (DR) and preterm birth rate.

WHAT IS KNOWN ALREADY: ART is widely practiced worldwide and there is a need for its continuous monitoring to improve the comprehensiveness and quality of ART data and services.

STUDY DESIGN, SIZE, DURATION: This is a retrospective, cross-sectional survey of ART cycles undertaken worldwide in 2006.

PARTICIPANTS, SETTING, METHODS: A total of 2352 clinics in 56 countries provided data. Data were analyzed at a country and regional level. The forms for data collection were developed by the International Committee Monitoring Assisted Reproductive Technologies (ICMART) and sent to each country or regional ART register.

MAIN RESULTS AND THE ROLE OF CHANCE: A total of >1 050 300 initiated cycles resulted in an estimated >256 668 babies. The overall pregnancy rates (PRs) and DRs per aspiration for IVF were 30.7 and 22.8%, respectively, and for ICSI 29.7 and 20.0%, respectively. The PRs and DRs for FETs were 26.4 and 17.8%, respectively. Multiple DR per PR were 22.2% for twins and 1.5% for triplets following fresh IVF/ICSI and 16.4% for twins and 0.8% for triplets for FETs. Ovarian hyperstimulation syndrome complicated >4585 cycles (0.6%). Access to ART varied from 11 to 3988 cycles per million population. ICSI comprised 66.0% of all initiated cycles, FET 27.4% and SET 20.7%. Perinatal mortality rate was 25.2 per 1000 births for fresh IVF/ICSI and 17.5 per 1000 for FETs.

LIMITATIONS, REASONS FOR CAUTION: 44.6% of the countries provided incomplete data. Quality of data varies among individual countries and is dependant on the policy of the local regulatory authority for monitoring ART clinics. Continuous efforts are needed to improve comprehensiveness and quality of data collected.

WIDER IMPLICATIONS OF THE FINDINGS: Adopting the policy of SET, FET and the cessation of transferring more than two embryos should be widely applied. ICMART will continue helping countries and regions to establish their own ART registries.

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STUDY FUNDING/COMPETING INTEREST(S): ICMART receives financial support from medical societies: European Society for Human Reproduction and Embryology (ESHRE), American Society for Reproduction Medicine (ASRM), Fertility Society of Australia (FSA), Japan Society for Reproductive Medicine (JSRM), Latin American Network for Reproductive Medicine (REDLARA) and Middle East Fertility Society (MEFS) and Society for Assisted Reproductive Technology (SART). All authors have no conflict of interest in relation to this work. We declare no support or financial relationship with any organizations or any activities that could appear to have influenced the submitted work.

Key words: ICSI / IVF / ART / registries / ICMART

Introduction

This is the 12th World Report on assisted reproductive technology (ART) and the seventh prepared by the International Committee Monitoring Assisted Reproductive Technologies (ICMART) (Adamson *et al.*, 2006; de Mouzon *et al.*, 2009; Nygren *et al.*, 2011; Sullivan *et al.*, 2013; Zegers-Hochschild *et al.*, 2013). Data were first collected on the number of ART cycles worldwide in 1989 by the International Working Group for Registers on Assisted Reproduction (IWGROAR) (Cohen *et al.*, 1993; de Mouzon and Lancaster, 1995, 1997; de Mouzon *et al.*, 1998; Adamson *et al.*, 2001). In 2001, ICMART continued this activity. ICMART is a non-governmental organization (NGO) in official relations with the World Health Organization (WHO). The aim of this report is to provide global ART data for the Year 2006 for use in monitoring the access, effectiveness and safety of ART.

Materials and Methods

Data collection

The forms for data collection were developed by ICMART and sent to each country or regional ART register to be completed voluntarily. The 2009 ICMART–WHO revised glossary (Zegers-Hochschild *et al.*, 2009) was used as a reference for terminology. This report covers ART-initiated treatment cycles between 1 January 2006 and the 31 December 2006 and is based on aggregated country data.

Data were supplied to the Uppsala Clinical Research (UCR) Center, Uppsala University, Uppsala, Sweden, where data validation was undertaken, a statistical plan was developed with the investigators, and a statistical report was prepared. The delay in reporting of data is a result of logistical difficulties regarding international data collection.

Data were provided directly from national ART registries or from regional registries. According to regions, data came either from individual clinics to the national register and then to the regional registry, or directly to the regional registry. Finally, in a few countries with no national or regional registers, data came directly from individual clinics. For this report data were received from a total of 56 countries belonging to seven regions. When a specific set of data was unavailable in a certain country, it was registered as not available (NA). The forms for data collection were designed to obtain information on the number of treatments and pregnancies for four reporting categories: (i) IVF, (ii) ICSI, (iii) gamete intra-Fallopian transfer and (iv) frozen embryo transfer (FET: IVF/ICSI) for initiated cycles, aspirations, transfers, pregnancies and deliveries. Data on aspirations, pregnancies and deliveries by woman's age category were also obtained. Data on the number of transferred embryos for fresh transfers and FETs were obtained.

The forms include data on gestational age by treatment and multiple deliveries, neonatal outcome (live birth, stillbirth and neonatal death), preimplantation genetic diagnosis, oocyte donation (OD), treatment complications and congenital anomalies. The forms also collect information on intrauterine insemination from husband (IUI-H), and donors (IUI-D) by women's age, *in vitro* maturation (IVM), surrogacy and multifetal reduction.

Data management

Country and regional data were provided to ICMART. Data management and analysis were undertaken by UCR Center Sweden.

SAS software (version 9.3) was used for data management and to create tables. Graphs were obtained using R (version 2.14.1).

Imputation of missing data

In countries with missing data on the number of initiated cycles, aspirations, pregnancies or deliveries, estimations were made according to certain premises, as published previously (Zegers-Hochschild *et al.*, 2013).

Results

The results are presented in Tables I–IV and Figs 1–3. Tables SI–SX and Figs S1–S9 are available as Supplementary data online.

Access

Data were received from 2352 (84.4%) of known ART clinics in 56 countries. There are 15 fewer clinics and 3 more countries than in 2005. At the regional level Europe had the largest number of clinics providing data ($n = 999$, 42% of total) followed by Asia ($n = 771$, 33%). At a country level, Japan followed by the USA had the highest number of participating clinics (Supplementary data, Table SI). Out of 56 countries included in this report, 31 (55.4%) received data from 100% of the clinics in that country.

Table I shows >1 050 300 treatment cycles estimated in 2006 with no increase from 2005, and with a 10.0% increase in cycles since 2004. The availability of ART varied from 77 cycles per million population in Latin America to 1979 cycles per million population in Australia and New Zealand. Eight countries reported <100 cycles per million (Albania, India, Brazil, Chile, Colombia, Dominican Republic, Peru and Venezuela), and the least access was 11 cycles per million in Dominican Republic. Japan reported the largest number of aspirations (92 063) followed by the USA (75 543) and France (50 776).

On a regional basis, Europe represents the largest proportion (52.7%) of aspirations worldwide. Overall, FETs represented 27.4% of all initiated cycles which was similar to 2005 (28.2%). ICSI comprised 66% of all aspirations, a continued increase from 60.6% in 2004 and 62.9% in 2005. The proportion of ICSI procedures varied according to region: 96% in the Middle East, 81% in Latin America, 70% in North America, 76% in Europe and 56% in Australia and New Zealand (Supplementary data, Table SII).

Effectiveness

Table II reports on the outcomes of ART procedures. Pregnancy rates (PRs) and DRs per aspiration for IVF were 30.7 and 22.8%, respectively, and for ICSI 29.7, and 20.0%, respectively. For FETs, PR and DR per transfer were 26.4 and 17.8%. The PRs and DRs varied greatly among

Table I Reported data and estimations (bold) for Year 2006.

Country name	Fresh						FET				
	IVF and ICSI										
	[b]Aspirations	[c]PR/ Asp (%)	[d]DR/ Asp (%)	[e]DR/Asp Cumul. (%)	[f]Babies/ Asp fresh (%)	[f]Babies/ Asp cumul. (%)	[f]Babies/ FET (%)	[g]Estimated or reported overall total number of cycles	[h]Availability cycles/million	[i k]Total babies reported from participating clinics	[j k]Total babies estimated from all clinics
India	21 408	27.1	NA	NA	27.4	28.9	17.8	**43 877**	**40**	7317	**11 228**
Japan	92 063	17.8	11.1	18.8	NA	NA	NA	**14 019**	**1100**	**22 689**	**22 808**
South Korea	23 721	29.4	**20.7**	**20.7**	NA	2.5	13.7	**44 090**	**903**	632	**1096**
Australia	**24 078**	**27.1**	**21.2**	**31.5**	**24.0**	**35.7**	19.4	**43 891**	**2166**	9097	9097
New Zealand	**2452**	**35.0**	**28.3**	**39.5**	**111.9**	**124.5**	22.6	**4286**	**1051**	3118	3118
Albania	119	40.3	36.1	36.1	57.1	57.1	NA	141	39	78	78
Austria	4778	32.8	**23.1**	**24.1**	NA	NA	NA	5177	632	**1511**	**1511**
Belgium	15 547	27.5	19.0	22.7	21.2	25.6	15.1	22 730	2190	4214	4214
Bulgaria	1202	30.0	23.3	23.9	30.0	30.9	12.8	**2601**	**352**	378	709
Cyprus	1122	35.2	**24.8**	**26.6**	NA	NA	NA	1432	1826	**391**	**391**
Czech Republic	8839	36.1	**25.4**	**31.5**	NA	NA	NA	13 707	1339	**3661**	**3661**
Denmark	9641	26.9	20.7	23.3	24.7	28.4	17.3	12 566	2305	2742	2742
Finland	4655	26.9	21.2	32.9	23.8	36.5	19.3	8749	1672	1819	1819
France	50 776	25.2	19.7	23.3	22.6	26.3	13.6	65 680	1079	13 448	13 448
Germany	38 065	28.5	18.5	22.7	22.5	28.5	16.2	54 695	664	10 846	10 846
Greece	3130	28.3	17.3	19.0	26.5	28.5	21.5	**22 061**	**2064**	1176	**6533**
Hungary	2499	30.1	25.1	27.5	31.4	35.7	17.4	**6560**	**657**	902	**1804**
Iceland	346	30.3	25.1	35.3	28.6	40.5	25.3	530	1770	149	149
Ireland	2179	30.2	25.5	29.2	31.5	36.0	19.1	**3771**	**928**	788	**919**
Italy	32 821	21.2	12.6	12.8	15.9	16.4	16.7	37 771	650	5368	5368
Latvia	168	58.3	**41.1**	**44.6**	NA	NA	NA	280	123	**98**	**98**
Lithuania	**385**	**28.8**	**6.2**	**6.8**	**7.8**	**8.3**	2.9	**717**	**200**	32	**48**
Macedonia	826	23.5	19.4	19.7	27.0	27.5	16.0	911	444	227	227
Montenegro	227	22.5	21.1	21.6	24.7	25.1	33.3	245	NA	57	57
The Netherlands	13 803	31.2	23.8	27.9	27.7	32.2	21.6	17 770	1078	4448	4448
Norway	4847	29.6	24.9	29.8	28.8	34.2	17.2	7115	1543	1660	1660
Poland	4025	35.1	28.8	34.7	34.9	42.1	17.5	**11 701**	**304**	1817	**3420**
Portugal	3090	30.7	24.0	25.8	29.5	31.5	20.0	**4275**	**403**	984	**1088**
Russia	16 677	34.4	21.4	23.7	27.3	30.8	22.2	**23 858**	**167**	5491	**6040**
Serbia	478	32.0	26.2	26.6	40.2	40.6	22.2	**1447**	**134**	247	**679**
Slovenia	2064	28.8	23.9	27.5	28.4	32.5	14.8	2804	1395	671	671

Region	Fresh						FET				
	IVF and ICSI										
	[b]Aspirations	[c]PR/Asp (%)	[d]DR/Asp (%)	[e]DR/Asp Cumul. (%)	[f]Babies/Asp fresh (%)	[f]Babies/Asp cumul. (%)	[f]Babies/FET (%)	[g]Estimated or reported overall total number of cycles	[h]Availability cycles/million	[i k]Total babies reported from participating clinics	[j k]Total babies estimated from all clinics
Spain	29 451	34.1	19.1	22.5	24.0	29.7	25.0	**84 649**	**2095**	11 353	**19 311**
Sweden	9496	31.4	24.7	33.0	26.1	35.6	22.0	14 895	1652	3420	3420
Switzerland	3751	25.9	18.6	28.4	22.4	33.3	14.7	7109	945	1577	1577
Turkey	32 079	37.6	11.5	12.1	NA	NA	NA	37 468	532	5364	5364
Ukraine	4213	34.4	24.9	27.4	32.0	35.2	19.6	**6125**	**131**	1629	**1862**
UK	31 668	29.5	26.1	30.5	32.4	37.8	22.9	43 949	725	12 631	12 631
Argentina	4317	28.5	23.1	25.1	30.9	33.6	16.5	**8994**	**225**	1982	**2874**
Bolivia	44	34.1	31.8	31.8	36.4	36.4	0.0	NA	NA	16	NA
Brazil	10 229	30.9	24.4	26.4	32.1	34.5	17.4	12 871	68	3878	3878
Chile	1011	34.5	27.0	30.6	34.5	39.2	21.8	1418	88	436	436
Colombia	813	27.2	21.4	22.5	27.9	29.0	12.7	**1671**	**38**	347	**501**
Dominican Republic	97	19.6	11.3	11.3	19.6	19.6	NA	102	11	23	23
Ecuador	176	27.3	24.4	27.3	33.0	37.5	25.0	326	24	104	104
Guatemala	82	35.4	35.4	40.2	36.6	41.5	33.3	NA	NA	44	NA
Mexico	2680	30.4	23.2	24.9	30.3	32.3	14.6	NA	NA	1280	NA
Peru	583	27.1	22.6	24.4	28.6	30.5	14.9	1236	44	485	485
Uruguay	236	28.8	23.7	25.8	28.8	30.9	11.9	**660**	**192**	88	**176**
Venezuela	573	33.0	24.8	27.9	30.0	33.2	19.6	909	35	278	278
Egypt	7536	37.7	28.9	30.3	40.4	42.6	17.1	**27 306**	**346**	3208	**10 025**
Lebanon	1192	31.3	25.4	25.7	28.9	29.1	10.0	NA	NA	385	NA
Saudi Arabia	1486	34.2	29.4	31.3	36.7	39.2	18.8	NA	NA	583	NA
[a]Israel	**19 054**	**26.6**	**18.7**	**23.6**	NA	NA	NA	25 333	3988	**5893**	**5893**
Canada	7861	35.7	28.7	35.5	37.9	46.6	25.9	11 779	356	3890	3890
USA	75 543	40.7	32.9	40.3	43.6	52.8	36.8	**15 786**	**529**	50 352	**63 965**
South Africa	1486	34.2	29.4	31.3	36.7	39.2	18.8	NA	NA	583	NA
Asia	1 37 192	21.3	13.0	19.2	27.4	15.0	14.9	2 28 161	179	30 638	35 132
Australia and New Zealand	26 530	27.9	21.9	32.3	32.1	44.0	19.7	48 177	1979	12 215	12 215
Europe	3 32 967	29.6	19.7	23.0	24.5	29.0	18.2	5 23 489	701	99 177	1 16 793
Latin America	20 841	30.4	23.9	26.0	31.4	33.9	17.1	>28 187	77	8961	>8755
Middle East	10 214	36.4	28.6	29.9	38.6	40.5	17.2	>27 306	346	4176	>10 025

Continued

Table I *Continued*

Country name	Fresh						FET				
	IVF and ICSI										
	[b]Aspirations	[c]PR/ Asp (%)	[d]DR/ Asp (%)	[e]DR/Asp Cumul. (%)	[f]Babies/ Asp fresh (%)	[f]Babies/ Asp cumul. (%)	[f]Babies/ FET (%)	[g]Estimated or reported overall total number of cycles	[h]Availability cycles/million	[i k]Total babies reported from participating clinics	[j k]Total babies estimated from all clinics
Middle East (Israel)	19 054	26.6	18.7	23.6	NA	NA	NA	25 333	3988	5893	5893
North America	83 404	40.2	32.5	39.8	43.1	52.2	35.4	1 69 647	512	54 242	67 855
Southern Africa	1486	34.2	29.4	31.3	36.7	39.2	18.8	NA		583	NA
Total	6 31 688	29.2	20.5	25.2	29.2	33.1	21.3	>10 50 300	371	215 885	>256 668

PR, pregnancy rate; DR, delivery rate; Cumul, cumulative rate per aspiration, computed by adding the FET deliveries and babies to those obtained after fresh cycle, the sum being divided by the number of aspirations; NA, not available, the total numbers and numbers by region were calculated only from the countries with complete data (e.g. both number of pregnancies and number of oocyte aspirations).

[a]Countries that did not separate ICSI and IVF.

[b]Imputed by applying the average cancellation rate to the number of initiated cycles when not reported.

[c]Imputed by calculating the number of aspirations from the number of initiated cycles reported when not reported.

[d]Imputed by calculating the mean percentage of deliveries per pregnancy when not reported.

[e]Imputed by calculating the mean percentage of deliveries per pregnancy.

[f]In countries where the sum of singleton, twins and triplets was less than the total number of deliveries, the number of unknown babies and lost-to-follow-up deliveries were estimated by applying distribution of observed deliveries in which this was known.

[g]Initiated cycles overall countries estimation. Step 1: Reported cycles for countries reporting them, or estimation by applying their cancellation rate to the aspiration (Asp) numbers for the countries not reporting them. Step 2: Total of step 1 if 100% of the clinics reported, or estimation by applying the percentage of participating clinics to this total in the other situations.

[h]Total estimated number of cycles in the country divided by its population in 2005 (CIA World Fact Book).

[i]Imputed by multiplying number of deliveries by the average number of babies per delivery category described in form 4.

[j]Total babies reported if 100% of the clinics reported, or estimation by applying the percentage of participating clinics to this total in the other situations.

[k]Total babies also include PGD and OD.

Table II IVF, ICSI and FET [pregnancies (PR) and deliveries (DR)] for Year 2006.

Country name	IVF		ICSI		FET		IVF and ICSI fresh
	PR/Asp (%)	DR/Asp (%)	PR/Asp (%)	DR/Asp (%)	PR/FET (%)	DR/FET (%)	DR/Asp (%)
India	NA	NA	NA	NA	22.1	14.4	NA
Japan	20.2	12.8	15.9	9.6	33.0	19.8	11.1
South Korea	31.4	NA	27.7	NA	33.5	NA	NA
Australia	NA	NA	NA	NA	22.5	17.0	NA
New Zealand	NA	NA	NA	NA	25.6	20.0	NA
Albania	NA	NA	40.3	36.1	NA	NA	36.1
Austria	32.9	NA	32.8	NA	31.4	NA	NA
Belgium	28.3	21.0	27.2	18.4	20.1	12.9	19.0
Bulgaria	29.0	21.3	30.9	25.3	NA	NA	23.3
Cyprus	30.0	NA	37.9	NA	27.2	NA	NA
Czech Republic	31.4	NA	37.6	NA	25.3	NA	NA
Denmark	27.8	21.1	25.9	20.1	19.0	12.5	20.7
Finland	27.0	21.0	26.8	21.6	23.1	17.7	21.2
France	24.2	18.7	25.8	20.3	17.5	13.0	19.7
Germany	29.9	18.8	28.0	18.4	19.0	11.4	18.5
Greece	24.6	17.6	30.5	17.1	23.6	18.3	17.3
Hungary	21.7	17.6	32.0	26.8	18.2	9.7	25.1
Iceland	32.4	25.4	28.3	24.9	29.0	21.6	25.1
Ireland	30.9	26.3	29.1	24.3	22.0	15.9	25.5
Italy	21.4	13.4	21.1	12.3	17.0	9.8	12.6
Latvia	NA	NA	41.3	NA	10.6	NA	NA
Lithuania	NA	NA	NA	NA	11.8	2.9	NA
Macedonia	25.3	21.4	20.9	16.4	16.0	12.0	19.4
Montenegro	18.9	16.2	23.2	22.1	33.3	33.3	21.1
The Netherlands	29.9	22.2	32.9	25.8	25.3	19.2	23.8
Norway	30.6	25.7	28.4	24.1	21.0	15.3	24.9
Poland	34.1	29.9	35.2	28.7	17.6	14.3	28.8
Portugal	34.8	26.3	28.5	22.8	23.2	17.1	24.0
Russia	34.8	22.2	33.7	20.2	23.7	14.6	21.4
Serbia	47.9	38.5	26.9	22.2	33.3	22.2	26.2
Slovenia	31.1	26.0	27.8	22.9	19.6	13.3	23.9
Spain	34.9	30.6	34.0	17.6	26.4	14.8	19.1
Sweden	32.5	25.4	30.2	23.9	26.8	19.2	24.7
Switzerland	24.2	16.6	26.3	19.1	19.4	13.3	18.6
Turkey	47.9	14.5	37.3	11.5	37.4	8.3	11.5
Ukraine	34.1	24.1	35.1	26.7	22.9	15.5	24.9
UK	28.9	25.7	30.1	26.5	21.7	18.9	26.1
Argentina	29.2	21.5	28.3	23.5	21.1	12.6	23.1
Bolivia	33.3	25.0	34.4	34.4	0.0	0.0	31.8
Brazil	24.8	19.1	31.4	24.9	21.7	14.5	24.4
Chile	37.3	28.5	33.4	26.4	23.1	16.7	27.0
Colombia	28.4	24.1	26.6	20.1	15.5	12.7	21.4
Dominican Republic	26.8	17.1	14.3	7.1	NA	NA	11.3
Ecuador	21.4	21.4	29.1	25.4	21.9	15.6	24.4
Guatemala	44.0	44.0	21.9	21.9	33.3	33.3	35.4
Mexico	28.1	22.7	31.6	23.5	27.8	12.4	23.2

Continued

Table II *Continued*

Country name	IVF		ICSI		FET		IVF and ICSI fresh
	PR/Asp (%)	DR/Asp (%)	PR/Asp (%)	DR/Asp (%)	PR/FET (%)	DR/FET (%)	DR/Asp (%)
Peru	28.3	22.9	26.6	22.5	20.3	13.5	22.6
Uruguay	23.8	23.8	29.3	23.7	26.2	11.9	23.7
Venezuela	34.6	26.1	32.0	24.0	29.3	19.6	24.8
Egypt	40.1	35.2	37.6	28.8	24.0	10.9	28.9
Lebanon	26.6	22.0	32.1	26.0	13.3	10.0	25.4
Saudi Arabia	30.0	26.0	34.3	29.5	19.3	14.2	29.4
[a]Israel	NA	NA	NA	NA	23.0	NA	NA
Canada	34.3	27.7	36.5	29.2	26.6	20.3	28.7
USA	42.5	34.6	39.9	32.2	37.5	29.2	32.9
South Africa	30.0	26.0	34.3	29.5	19.3	14.2	29.4
Region	**IVF**		**ICSI**		**FET**		**IVF and ICSI fresh**
	PR/Asp (%)	**DR/Asp (%)**	**PR/Asp (%)**	**DR/Asp (%)**	**PR/FET (%)**	**DR/FET (%)**	**DR/Asp (%)**
Asia	29.3	20.0	18.3	9.6	32.5	19.6	11.1
Australia and New Zealand	NA	NA	NA	NA	22.7	17.3	NA
Europe	28.9	21.5	29.9	18.4	21.7	14.2	19.4
Latin America	28.8	22.6	30.5	24.2	22.5	14.1	23.9
Middle East	32.7	28.1	36.6	28.6	22.9	11.5	28.6
Middle East (Israel)	NA	NA	NA	NA	23.0	NA	NA
North America	41.5	33.8	39.6	32.0	36.2	28.1	32.5
Southern Africa	30.0	26.0	34.3	29.5	19.3	14.2	29.4
Total	30.7	22.8	29.7	20.0	26.4	17.8	20.4

NA, not available.
[a]Countries that did not separate ICSI and IVF.

countries in both fresh IVF/ICSI and FETs (Supplementary data, Figs S1–S3). The cumulative DRs (fresh plus frozen cycles) increased to 25.2% compared with 24.3% in 2004 and 23.9% in 2005. When combining IVF and ICSI fresh cycles, DR per aspiration was 20.4%, which is similar to 20.4% in 2004, and higher than 19.6% in 2005.

The miscarriage rate per clinical pregnancy (Table III) averaged 19.3% in fresh cycles compared with 20.4% in 2004, and 20.8% in 2005. The miscarriage rate for FETs was 24.2% compared with 24.6% in 2004 and 25% in 2005.

A total of 215 885 babies were reported to have been born as a result of ART procedures performed in 2006. When the imputed numbers were added this reached an estimated total number of >256 668 babies (Table I). The estimated total number of babies born was 237 809 in 2004 and 237 315 in 2005. The number of babies estimated in 2006 increased by 7.9% relative to 2004 and 8.9% relative to 2005.

The proportion of older women (age ≥40 years) accessing ART varied among countries and regions (Supplementary data, Table SIII) with the highest in Montenegro (30.6%), Greece (24.2%), Italy (23.8%) and Australia (23.1%). In 10 countries, >60% of the women were ≤34 years old (Bulgaria, Cyprus, Czech Republic, Hungary, Lithuania, Poland, Russia, Ukraine, Guatemala and Egypt; Supplementary data, Table SIII). Overall, the proportion of women aged ≥40 years having ART treatment was 15.5% compared with 14.9% in 2004 and 15.9% in 2005. Overall, the fresh non-donor IVF/ICSI PR and DR in women ≥40 years old were 16.0 and 9.4%, respectively (Supplementary data, Table SIVa), and for FETs 18.2 and 11.1%, respectively (Supplementary data, Table SIVb). Supplementary data, Figure S4 illustrates results according to age group.

Safety

The proportion of single embryo transfers (SETs) increased to 20.7% from 16.4% in 2004 and 17.5% in 2005, with the highest rates in Sweden (69.9%), New Zealand (61.4%), Finland (54.7%) and Australia (53.3%) (Table IV). This increase in the practice of SETs was reflected in the decrease of twin deliveries from 25.1% in 2004 and 23.6% in 2005 to 22.2% in 2006. Moreover, the proportion of triplet deliveries continued to decrease from 2.0% in 2003, to 1.8% in 2004 and 1.5% in each of 2005 and 2006. However, multiple pregnancy rates varied markedly among countries (Table IV, Supplementary data, Fig. S5); considering only countries that reported >2000 cycles, the percentage of twin deliveries was >25% in six countries (Greece, Egypt, USA, Canada, Ukraine and South Korea) and <10% in two countries (Sweden and New Zealand). Triplet and high-order multiple deliveries varied from >3% in four countries (India, Argentina, Brazil and Mexico) to <0.3% in seven countries (Finland, Sweden, Denmark, Belgium, Norway, New Zealand and Slovenia). Figure 1 and Supplementary data, Fig. S6 illustrate the correlation of triplet rate with the mean number of embryos

Table III Pregnancy miscarriages or stillbirths, prematurity and perinatal mortality for Year 2006.

Country name	Aspiration cycles (IVF and ICSI)					FET				
	Pregnancies			Deliveries		Pregnancies			Deliveries	
	Reported (*n*)	[a]Pregnancy outcome reported (*n*)	[b]Early pregnancy losses (%)	[c]Preterm (%)	[d]Perinatal mortality (p1000)	Reported (*n*)	[a]Pregnancy outcome reported (*n*)	[b]Early pregnancy losses (%)	[c]Preterm % (*n*)	[d]Perinatal mortality (p1000)
India	NA	NA	NA	NA	NA	398	397	33.5	NA	NA
Japan	16 410	NA	NA	NA	NA	11 797	NA	NA	NA	NA
South Korea	6971	2376	NA	NA	16.2	1451	442	NA	NA	10.3
Australia	6530	5103	0.0	17.6	19.2	3282	3199	22.3	13.9	16.8
New Zealand	857	857	83.2	15.4	14.3	352	347	21.0	17.2	9.9
Albania	48	48	10.4	39.5	NA	NA	NA	NA	NA	NA
Austria	1568	929	12.4	NA	NA	71	NA	NA	NA	NA
Belgium	4270	3700	22.7	16.6	NA	899	795	28.9	17.0	NA
Bulgaria	360	350	20.0	NA	NA	21	17	58.8	NA	NA
Cyprus	395	NA	NA	NA	NA	31	NA	NA	NA	NA
Czech Republic	3189	NA	NA	NA	NA	829	NA	NA	NA	NA
Denmark	2595	2431	18.0	NA	NA	391	330	22.1	NA	NA
Finland	1253	1253	21.5	13.6	NA	709	709	23.7	11.6	NA
France	12 796	12 258	22.9	NA	NA	2458	2327	27.0	NA	NA
Germany	10 843	9413	25.2	21.0	NA	2696	2335	30.8	18.8	NA
Greece	887	739	16.8	34.1	NA	67	61	21.3	27.3	NA
Hungary	751	726	13.4	NA	NA	114	87	32.2	NA	NA
Iceland	105	105	17.1	16.1	NA	47	47	25.5	14.3	NA
Ireland	657	657	15.5	18.9	NA	112	111	27.0	30.8	NA
Italy	6950	5452	24.3	NA	NA	145	105	20.0	NA	NA
Latvia	98	NA	NA	NA	NA	9	NA	NA	NA	NA
Lithuania	111	28	14.3	12.5	NA	8	3	33.3	100.0	NA
Macedonia	194	194	13.9	34.8	NA	4	4	25.0	33.3	NA
Montenegro	51	51	5.9	12.5	NA	1	1	0.0	0.0	NA
The Netherlands	4312	4312	23.7	NA	NA	740	740	24.2	NA	NA
Norway	1434	1434	15.8	NA	NA	325	325	27.4	NA	NA
Poland	1413	1327	12.7	NA	NA	291	284	16.9	NA	NA
Portugal	948	885	18.5	24.7	NA	73	71	23.9	14.6	NA
Russia	5738	4501	20.7	NA	NA	630	516	24.8	NA	NA

Continued

Table III *Continued*

Country name	Aspiration cycles (IVF and ICSI)					FET				
	Pregnancies			Deliveries		Pregnancies			Deliveries	
	Reported (*n*)	[a]Pregnancy outcome reported (*n*)	[b]Early pregnancy losses (%)	[c]Preterm (%)	[d]Perinatal mortality (p1000)	Reported (*n*)	[a]Pregnancy outcome reported (*n*)	[b]Early pregnancy losses (%)	[c]Preterm % (*n*)	[d]Perinatal mortality (p1000)
Serbia	153	153	19.0	16.5	NA	3	3	33.3	50.0	NA
Slovenia	595	590	16.4	21.1	NA	111	111	32.4	10.8	NA
Spain	10 049	7218	21.9	28.5	NA	1776	1364	27.3	18.9	NA
Sweden	2981	2968	21.3	10.9	NA	1157	1157	26.0	15.2	NA
Switzerland	970	965	28.3	25.0	NA	541	526	31.0	15.7	NA
Turkey	12 068	NA	NA	NA	NA	864	NA	NA	NA	NA
Ukraine	1451	1372	23.6	NA	NA	155	144	27.1	NA	NA
UK	9340	9194	10.0	18.5	NA	1598	1570	11.6	16.6	NA
Argentina	1230	1180	15.4	22.6	19.6	146	118	26.3	23.8	0.0
Bolivia	15	15	6.7	61.5	62.5	0	0	NA	NA	NA
Brazil	3158	3054	18.3	32.7	20.3	310	284	27.1	14.9	13.0
Chile	349	344	20.6	30.0	0.0	50	49	26.5	31.4	21.7
Colombia	221	214	18.7	28.8	22.3	11	11	18.2	11.1	0.0
Dominican Republic	19	16	31.3	54.5	0.0	0	0	NA	NA	NA
Ecuador	48	48	10.4	21.4	35.7	7	6	16.7	20.0	0.0
Guatemala	29	29	0.0	3.4	0.0	4	4	0.0	50.0	0.0
Mexico	814	783	20.6	35.1	13.1	103	68	32.4	40.9	0.0
Peru	158	158	16.5	27.8	31.4	15	15	33.3	25.0	0.0
Uruguay	68	68	17.6	19.6	0.0	11	11	54.5	20.0	0.0
Venezuela	189	188	24.5	16.7	17.6	27	27	33.3	5.6	0.0
Egypt	2840	2503	20.1	36.0	104.1	224	190	46.3	37.4	155.2
Lebanon	373	371	18.3	15.2	91.3	4	4	25.0	NA	NA
Saudi Arabia	508	507	13.8	27.5	27.3	38	38	26.3	37.0	200.0
Israel	5067	NA	NA	NA	NA	1406	NA	NA	NA	NA
Canada	2807	2718	17.1	26.7	20.8	707	690	21.6	20.0	15.0
USA	30 714	30 482	18.7	NA	22.7	7115	7057	21.6	NA	17.3
South Africa	508	507	13.8	27.5	27.3	38	38	26.3	37.0	200.0

Region	Aspiration cycles (IVF and ICSI)					FET				
	Pregnancies			Deliveries		Pregnancies			Deliveries	
	Reported (*n*)	[a]Pregnancy outcome reported (*n*)	[b]Early pregnancy losses (%)	[c]Preterm (%)	[d]Perinatal mortality (p1000)	Reported (*n*)	[a]Pregnancy outcome reported (*n*)	[b]Early pregnancy losses (%)	[c]Preterm % (*n*)	[d]Perinatal mortality (p1000)

Asia	>23 381	>2376	NA	NA	16.2	13 646	>839	33.5	NA	10.3
Australia and New Zealand	7387	5960	12.0	17.3	18.6	3634	3546	22.2	14.2	16.1
Europe	98 573	>73 253	20.5	20.5	NA	>16 876	>13 743	25.4	16.9	NA
Latin America	6298	6097	18.2	29.9	18.3	684	593	28.0	21.3	8.0
Middle East	3721	3381	18.9	32.0	100.0	266	232	42.7	37.3	157.0
Middle East (Israel)	5067	NA	NA	NA	NA	1406	NA	NA	NA	NA
North America	33 521	33 200	18.6	26.7	22.5	7822	7747	21.6	20.0	17.1
Southern Africa	508	507	13.8	27.5	27.3	38	38	26.3	37.0	200.0
Total	>178 456	>124 774	19.3	22.1	25.2	>44 372	>26 738	24.2	16.8	17.5

NA, not available.
[a]Pregnancy outcome reported (pregnancy losses + deliveries total).
[b]Losses = abortions (spontaneous and induced) and ectopic pregnancies.
[c]Preterm: <37 weeks.
[d]Mortality = perinatal mortality (stillbirths + neonatal deaths/stillbirths + live births) × 1000.

transferred ($r = 0.47$, $P = 0.0007$). Twin DR for FETs was 16.4%, which is <17.0% in 2004 and similar to 16.1% in 2005. Triplet DR for FETs was 0.8% in 2006, which is similar to 0.9% in 2005 and <1.0% in 2004 (Supplementary data, Table SV).

The mean number of embryos per transfer in fresh IVF/ICSI was 2.22 with great variations among countries (Supplementary data, Figs S7 and S8). However, it was not correlated with the overall DRs (Fig. 2, Supplementary data, Fig. S9), ($r = 0.10$, $P = 0.50$). There is a trend towards a steady decrease in the mean number of embryos per transfer from 2.37 in 2003, to 2.35 in 2004, to 2.29 in 2005, to 2.22 in 2006. In fresh non-donor cycles the overall DRs per transfer were 27.3 and 27.6% when three or four embryos were transferred, respectively. This was lower than the 29.4% DR per transfer when two embryos were transferred (Supplementary data, Table SVIa). This was not the case in non-donor FETs (Supplementary data, Table SVIb); the DRs per transfer were 19.0, 21.7 and 26.1% when 2, 3 and 4 embryos were transferred, respectively.

The preterm DR in fresh IVF/ICSI cycles (Table III) was 22.1% which is a marked decrease from 33.7% in 2004 and 26.6% in 2005. Preterm DR in FETs was 16.8% in 2006 which is much <26.3% in 2004 and similar to 16.3% in 2005.

The perinatal mortality rate was 25.2 per 1000 babies born from fresh IVF/ICSI, which is similar to 25.8 per 1000 in 2004 and >2005 (23.2 per 1000). The perinatal mortality rate for FETs increased to 17.5 per 1000 babies when compared with 14.2 per 1000 babies in 2004, and 10 per 1000 in 2005. Loss to follow-up and/or absence of data collection systems on perinatal outcome is notably high as 39 countries did not report on perinatal mortality (Table III).

The frequency of ovarian hyperstimulation syndrome (OHSS) was reported to be 0.6%, which is lower than 1.2% reported in 2004 and 1.1% reported in 2005 (Supplementary data, Table SVII).

Special techniques: OD, PGD, IVM, surrogacy, multifetal reduction and IUI

Forty-one countries reported 36 272 OD transfers, an increase from 26 765 in 2004 and 30 861 in 2005 (Supplementary data, Table SVIII). Of these OD transfers, 70.2% were FETs. Three countries reported the majority of OD transfers: USA (36.9%), Spain (18.0%) and India (10.6%). OD cycles represented 20.1% of all initiated cycles in Spain, 18.0% in India and 15.4% in the USA. The average OD DR per transfer (including all transfers, both fresh and FET) was 36.3% with the USA highest at 47.2%. The multiple DR from OD transfer was 31.8%. The number of babies born was 17 400 and 50% of them were born in the USA.

Thirty-two countries reported 11 481 PGD aspiration cycles with PR and DR per aspiration at 33.1% and 21.7%, respectively. The number of babies born following PGD was 2832 (Supplementary data, Table SIX).

Minimal data were reported on IVM, surrogacy and multifetal reduction (Supplementary data, Table SVII). Twenty countries reported 128 408 IUI-H cycles and 18 countries reported 23 225 IUI-D cycles. Data on IUI-H were reported from Europe, while data on IUI-D were reported from Europe, Australia and New Zealand.

The PRs and DRs per cycle for IUI-H were 12.2 and 8.8%, respectively, and for IUI-D 16.5 and 11.5%, respectively (Supplementary data, Table SXa and Supplementary data, Table SXb). It should be noted that some

Table IV Fresh non-donor IVF and ICSI cycles: number of transferred embryos and multiple births for Year 2006.

Country name	Aspirations	Transfers	No. of transferred embryos (%)					Multiple births	
			1	2	3	≥4	Average	Twin (%)	Triplet+ (%)
India	21 408	17 031	8.9	23.0	45.3	22.8	2.87	21.0	4.6
Japan	92 063	61 910	NA	NA	NA	NA	NA	NA	NA
South Korea	23 721	21 790	8.7	13.7	22.6	54.9	3.48	32.5	2.7
Australia	NA	20 821	53.3	45.6	1.1	0.0	1.48	12.5	0.3
New Zealand	NA	2120	61.4	38.1	0.5	0.0	1.39	9.9	0.2
Albania	119	110	4.5	10.0	24.5	60.9	3.42	30.2	14.0
Austria	4778	NA	16.6	71.5	10.9	1.0	1.97	22.0	2.9
Belgium	15 547	14 260	49.2	41.9	8.0	0.8	1.61	15.2	0.1
Bulgaria	1202	1089	9.0	30.2	43.7	17.1	2.72	22.5	3.2
Cyprus	1122	1103	NA	NA	NA	NA	NA	NA	NA
Czech Republic	8839	8009	NA	NA	NA	NA	NA	NA	NA
Denmark	9641	8253	36.4	59.3	4.2	0.0	1.68	19.3	0.1
Finland	4655	4281	54.7	45.0	0.3	0.0	1.46	12.0	0.0
France	50 776	43 766	20.0	63.3	15.2	1.5	1.98	20.1	0.5
Germany	38 065	36 875	12.4	65.8	21.8	0.0	2.09	19.8	0.9
Greece	3130	2784	13.7	26.4	46.3	13.5	2.60	32.4	1.3
Hungary	2499	2313	11.2	45.7	37.3	5.9	2.38	19.9	2.4
Iceland	346	288	35.1	56.6	8.3	0.0	1.73	11.5	1.1
Ireland	2179	2018	9.5	80.7	9.7	0.1	2.00	22.7	0.5
Italy	32 821	28 315	18.7	30.4	50.9	0.0	2.32	21.0	2.8
Latvia	168	164	15.2	52.4	32.3	0.0	2.17	NA	NA
Lithuania	NA	333	8.1	12.0	79.9	0.0	2.72	16.7	4.2
Macedonia	826	665	26.5	23.5	29.9	20.2	2.44	29.9	1.8
Montenegro	227	219	12.8	24.7	34.7	27.9	2.78	16.7	0.0
The Netherlands	13 803	12 169	NA	NA	NA	NA	NA	15.5	0.3
Norway	4847	4404	48.0	51.8	0.2	0.0	1.52	14.9	0.2
Poland	4025	3684	14.0	66.0	19.4	0.6	2.07	19.2	1.0
Portugal	3090	2817	17.0	67.8	14.4	0.7	1.99	22.2	0.3
Russia	16 677	15 609	16.6	59.4	18.6	5.4	2.13	24.5	1.5
Serbia	478	406	16.5	35.8	23.6	24.1	2.71	38.3	3.0
Slovenia	2064	1886	23.6	70.4	5.9	0.0	1.82	18.5	0.2
Spain	29 451	25 975	NA	NA	NA	NA	NA	22.1	1.6
Sweden	9496	8555	69.9	30.1	0.0	0.0	1.30	5.7	0.1
Switzerland	3751	3481	13.1	64.4	22.5	0.0	2.09	18.8	1.0
Turkey	32 079	28 331	NA	NA	NA	NA	NA	NA	NA
Ukraine	4213	3 948 000	9.9	29.8	38.1	22.1	2.80	26.0	1.4
UK	31 668	29 416	11.6	83.6	4.8	0.0	1.93	23.5	0.3
Argentina	4317	3793	13.7	40.3	38.4	7.6	2.40	18.6	7.4
Bolivia	44	40	7.5	40.0	40.0	12.5	2.58	14.3	0.0
Brazil	10 229	9309	9.9	26.0	39.9	24.1	2.81	23.4	4.0
Chile	1011	889	8.2	40.4	45.3	6.1	2.49	24.2	1.8
Colombia	813	746	15.0	31.1	34.0	19.8	2.63	23.6	3.4
Dominican Republic	97	94	16.0	19.1	45.7	19.1	2.68	36.4	18.2
Ecuador	176	161	7.5	27.3	55.3	9.9	2.69	25.6	4.7
Guatemala	82	82	3.7	19.5	52.4	24.4	3.00	3.4	0.0
Mexico	2680	2425	13.1	27.5	35.1	24.4	2.75	22.3	3.9

Continued

Table IV *Continued*

Country name	Aspirations	Transfers	No. of transferred embryos (%)					Multiple births	
			1	2	3	≥4	Average	Twin (%)	Triplet+ (%)
Peru	583	521	12.9	45.7	29.9	11.5	2.41	17.4	3.8
Uruguay	236	218	10.6	39.0	37.2	13.3	2.54	17.9	1.8
Venezuela	573	551	13.2	33.6	46.6	6.5	2.47	16.9	2.1
Egypt	7536	7157	6.2	19.3	55.4	19.1	2.94	28.6	2.3
Lebanon	1192	1083	14.8	40.2	26.3	18.7	2.58	12.9	0.0
Saudi Arabia	1486	1336	3.4	62.2	32.3	2.0	2.33	17.6	3.4
Israel	NA	16 477	NA	NA	NA	NA	NA	NA	NA
Canada	7861	7348	11.5	55.7	23.6	9.2	2.34	28.9	1.5
USA	75 543	69 357	9.9	46.2	27.6	16.2	2.55	29.1	1.8
South Africa	1486	1336	3.4	62.2	32.3	2.0	2.33	17.6	3.4
Region	**Aspirations**	**Transfers**	**No. of transferred embryos (%)**					**Multiple births**	
			1	2	3	≥4	Average	Twin (%)	Triplet+ (%)
Asia	137 192	100 731	8.8	17.7	32.4	41.1	3.22	25.0	3.9
Australia and New Zealand	NA	22 941	56.6	42.5	0.9	0.0	1.44	11.7	0.3
Europe	>332 582	>295 526	22.1	57.3	19.0	1.6	2.00	20.1	0.9
Latin America	20 841	18 829	11.4	30.9	39.1	18.6	2.67	21.9	4.5
Middle East	10 214	9576	6.8	27.7	48.9	16.6	2.81	25.1	2.2
Middle East (Israel)	NA	16 477	NA	NA	NA	NA	NA	NA	NA
North America	83 404	76 705	10.1	47.1	27.2	15.6	2.53	29.0	1.8
Southern Africa	1486	1336	3.4	62.2	32.3	2.0	2.33	17.6	3.4
Total	>585 719	>542 121	20.7	48.5	21.9	9.0	2.22	22.2	1.5

NA, not available.

countries provided only the number of IUI cycles without the numbers of pregnancies or deliveries.

Discussion

Monitoring ART practice, outcomes and complications at an international level is essential to quantifying the access to ART services, determining effectiveness of infertility treatment services, identifying safety issues in ART, and providing an evidence base for use in advocacy, education and policy development on ART. The annual collection of ICMART data is essential to developing comprehensive international statistics on ART.

This ICMART report covers an estimated two-thirds of the world's ART activities in 2006.

Access

ART access, like other medical services, varies greatly among countries according to economic status, cultural characteristics, government policy, regulations, societal financial support, the number of service providers and other known and unknown factors (Adamson, 2009). In some regions (Latin America) ART availability was 77 cycles per million population, while in other regions, such as Australia and New Zealand, it was 1979 cycles per million populations.

For proper evaluation of ART availability we need to measure infertility prevalence. A review of the literature on prevalence studies measuring infertility highlights a lack in consistency of determining prevalence because of use of different definitions of duration of infertility (Gurunath *et al.*, 2011). To measure infertility on a population level, it is best to use the demographic definition of infertility (Mascarenhas *et al.*, 2012). Analysis of 53 surveys representing 26 countries shows the age-standardized prevalence of primary infertility ranging from 0.6 to 3.4% and of secondary infertility from 8.7 to 32.6% (Mascarenhas *et al.*, 2012). In another study examining 25 population surveys, the estimated overall median prevalence of infertility was 9% (Boivin *et al.*, 2007). In 2006 the world population was 6.7 billion (United Nations, 2007). Based on the above two studies we can estimate that 72.4 million women were infertile in 2006. If we assume only 20% of this infertile population will ultimately need ART, this means an estimated 15 million ART cycles were needed worldwide in the Year 2006. The ICMART report estimated 1 million initiated ART cycles were undertaken in 2006. If we consider that the report covered about two-thirds of the world ART activity this suggests that ~1.5 million ART cycles were likely undertaken in 2006. This is a significant mismatch between the need and availability of ART with an estimated 15 million ART cycles needed and only

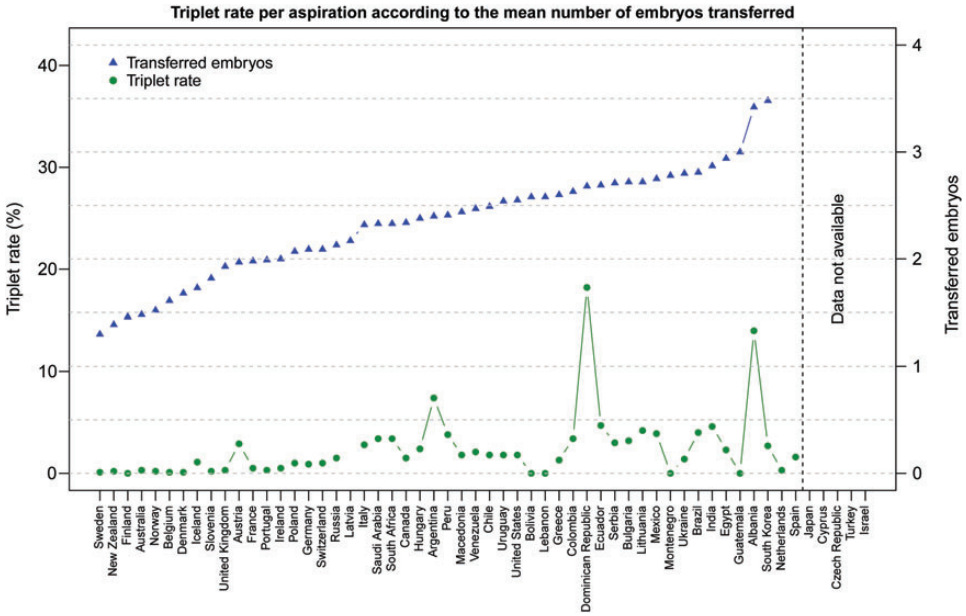

Figure 1 Triplet rate per aspiration according to the mean number of embryos transferred.

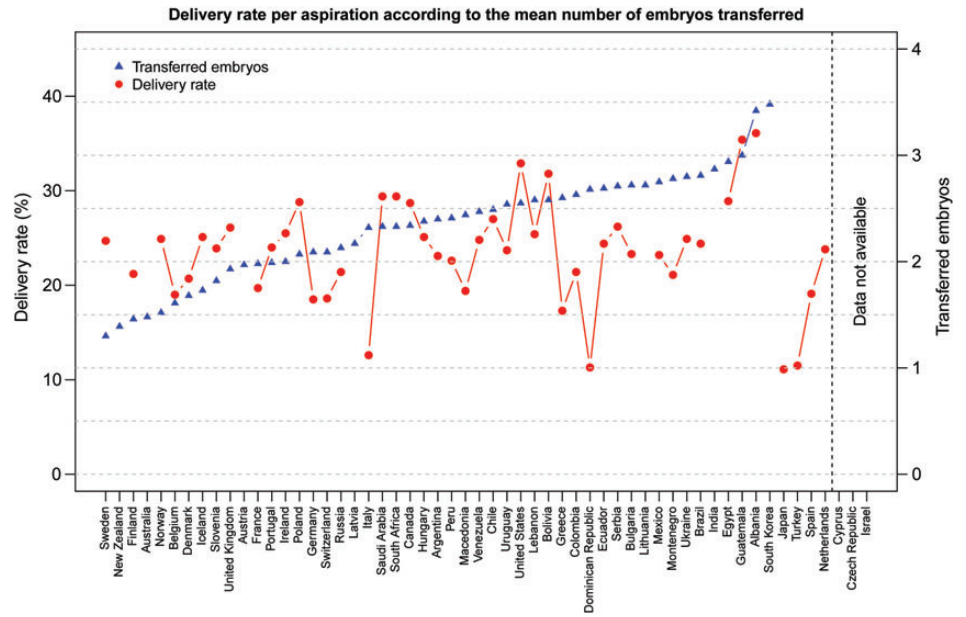

Figure 2 Delivery rate per aspiration according to the mean number of embryos transferred.

1.5 million performed. Therefore, despite ART availability internationally, there was access for only ~10% of those who needed it in 2006. This severe shortfall of ART services to eligible infertile couples is attributable to many factors and most importantly economic ones.

Effectiveness

A reasonable approach to evaluate effectiveness of ART treatment is to combine the results of the fresh cycle transfers plus the FETs with embryos from that cycle to obtain cumulative PRs and DRs. It is not possible to provide confident cumulative data on a worldwide basis since most countries provide summary reports rather than individualized case-by-case reports. In spite of this, cumulative data can be extrapolated as described previously (Zegers-Hochschild *et al.*, 2013). In 2006, the cumulative DR increased to 25.2% compared with 24.3% in 2004 and 23.9% in 2005. The wide use of FETs and the optimization of cryopreservation techniques will ultimately increase the gap between the DRs in the initial fresh cycle transfer and the cumulative DRs when all embryos from

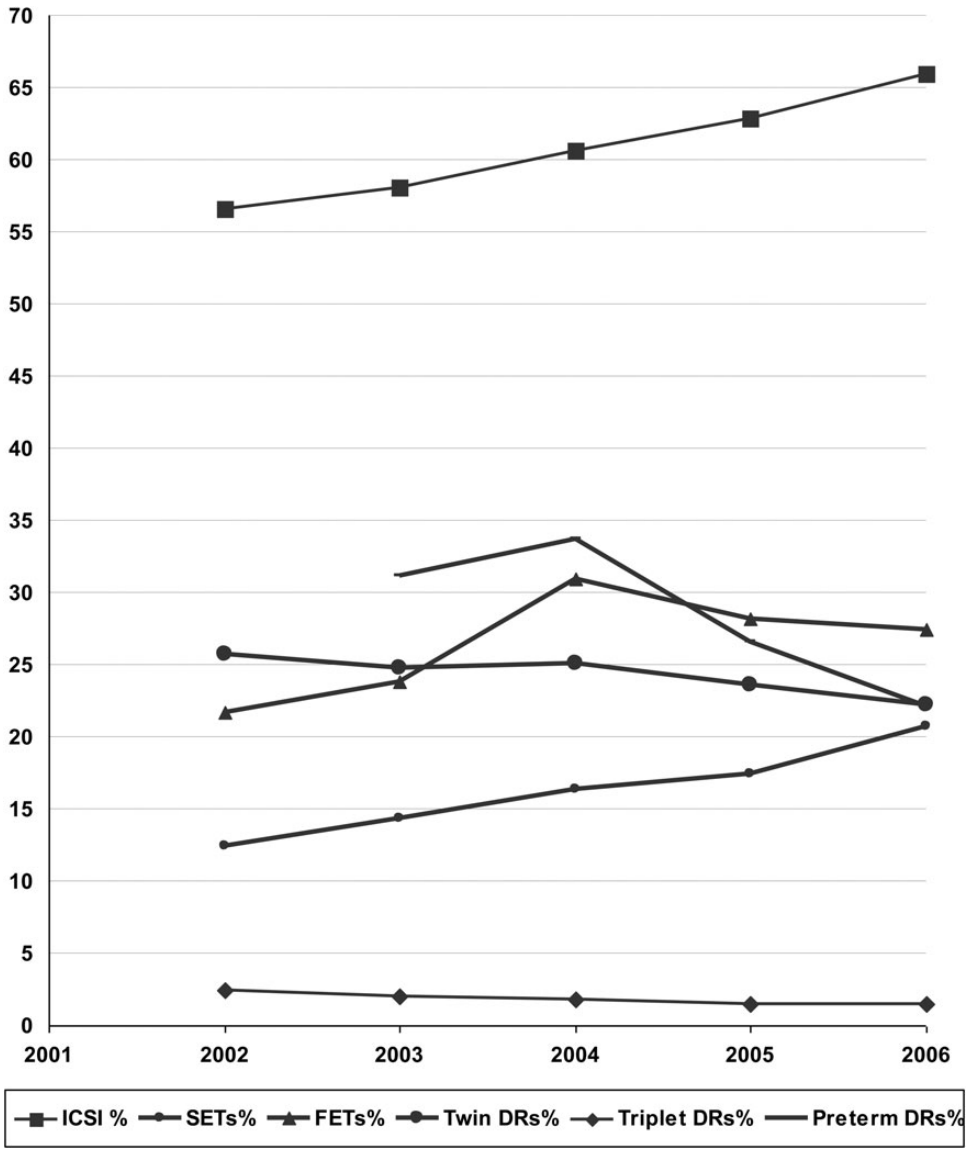

Figure 3 Trends in ART practice in 2002–2006.

a given aspiration cycle are transferred. This is already evident in some countries, such as Australia, New Zealand, Finland, Switzerland and Iceland which have reported >10% increase in the cumulative DRs compared with fresh cycles DRs. There is a wide variation among countries in the DRs for fresh cycles and FETs. The highest cumulative DR (40.3%) was reported by the USA, even though 19.4% of the women were ≥40 years old. It is important to note that the DR per aspiration was not correlated with the mean number of embryos transferred (Fig. 2).

Spontaneous miscarriage occurred more frequently after FETs when compared with fresh cycles, which may be a result of the difference in women's age as well as other unknown factors. Despite this finding, some individual literature reports have shown improved outcomes following FET compared with fresh transfer and so the issue of reproductive outcome of fresh compared with frozen transfer needs further assessment before firm conclusions can be drawn.

Utilization of ICSI continued to rise markedly from 47.6% in 2000 to 66.0% in 2006. The preference of ICSI over conventional IVF as the method of fertilization was seen across all regions, with major variations among countries, reaching 96% in the Middle East when compared with 56% in Asia. The reasons for this increase are not fully understood. Generally, it denotes either an increase in the medical indications for ICSI and/or clinical preference of ICSI as an efficient method of fertilization (Aboulghar *et al.*, 1996). Consequently, it might be the first choice for couples with no medical coverage. The perinatal risks associated with the use of ICSI or IVF have been the focus of many studies. A recent controlled national cohort study demonstrated that children born after ICSI using surgically retrieved sperm have a similar neonatal outcome, including total birth defect rates, as children born after ICSI and IVF using ejaculated sperm (Fedder *et al.*, 2013). However, another large study found an increase in birth defects with ICSI but not with IVF (Davies *et al.*, 2012).

Therefore, further surveillance and research of this complex issue is warranted.

Safety

One of the main concerns in ART is the high multiple DR. The triplet and higher order DRs decreased to 1.5% in 2006 and 2005 compared with 2.0% in 2003, and 1.8% in 2004. However, this triplet rate remains significantly higher than natural conception (1 in 6000–8000) (Guttmacher, 1953). Twin DRs decreased from 25.1% in 2004 to 23.6% in 2005 and 22.2% in 2006, which is still very high when compared with natural conception (1.6%) (ESHRE Capri Workshop, 2000). In the UK, the multiple birth rates after ART in 2006 were 235 twins and 3 triplets per thousand, which is 15 times higher than the rates in natural conception (10.4 and 15.3 per thousand in the Years 1970 and 2006, respectively) (Statistical Bulletin, 2012).

The high multiple DRs after ART is iatrogenic and can be, to a great extent, controlled through limiting the number of embryos per transfer. The mean number of embryos per transfer in 2006 was 2.22 compared with 2.35 in 2004 and 2.29 in 2005. However, it should be noted that there are great variations among countries in the average number of embryos per transfer. In fresh IVF/ICSI the average number of embryos per transfer was <1.5 embryos in three countries (Sweden, New Zealand and Australia) and was >3 embryos in two countries (South Korea, Albania). It should also be noted that the decrease in the triplet DRs in some countries is a reflection of multifetal reduction, rather than a decrease in the average number of embryos per transfer (Mansour *et al.*, 1999). Even though multifetal reduction is a relatively effective technology to avoid the consequences of multiple births, this practice raises significant professional and ethical issues.

The proportion of SETs increased from 16.4% in 2004 to 17.5% in 2005 and 20.7% in 2006, with marked variations among countries. The leading four countries practicing SET were Sweden (69.9%), New Zealand (61.4%), Finland (54.7%) and Australia (53.3%). The ultimate goal is to optimize IVF/ICSI laboratory techniques as well as ovarian stimulation, embryo assessment and embryo transfer techniques in order to be able to transfer one high-quality viable embryo in the appropriately selected patients.

The decrease in multiple DRs was directly reflected in the preterm DRs that declined markedly compared with previous years (33.7% in 2004, 26.6% in 2005 to 22.1% in 2006).

The frequency of OHSS dropped from 1.2% in 2004 to 1.1% in 2005, to 0.6% in 2006. It is important for ART centers to utilize protocols that decrease as much as possible the incidence of OHSS. Another main concern in ART practice is the incidence of congenital malformations, which are usually incompletely reported and, in any event, do not have standardized definitions and reporting even in many developed countries. At the international level this type of detail currently can only be reported in generalities that have very limited utility (Sullivan *et al.*, 2013). Record linkage at a country level with perinatal registers is a better option to compare neonatal outcomes of ART babies with natural conception (Sullivan *et al.*, 2013).

Limitations

This report covers about two-thirds of the world ART activity, which means that approximately one-third of the ART data have not been reported and therefore cannot be collected or analyzed by ICMART. ICMART continues to work at an international level to obtain data from countries that are beginning to collect data including China, Indonesia, Pakistan, the Philippines, Bangladesh and sub-Saharan Africa. Additionally, some countries provide data that are incomplete. Furthermore, the quality of data varies among individual countries and is dependent on the local regulatory authority's policy and ability to monitor ART clinics.

To standardize terminology and improve data reporting, ICMART has published original and revised glossaries in collaboration with WHO (ICMART Glossary, 2002; Zegers-Hochschild *et al.*, 2006, 2009) and has recently published a 'toolkit' to support data collection practices for countries setting up registries to monitor ART (www.icmartivf.org/toolbox/toolbox-main.html). Moreover ICMART, as an NGO in official relations with WHO, has collaboratively organized workshops in different regions and countries to help them establish their own ART registries.

Trends

Despite the wide variability among countries in the practice of ART, and the incomplete reporting, the overall data suggest some important trends. ART data from six consecutive world reports from 2000 to 2006 illustrate the following trends: (i) the practice of ICSI steadily increased from 47.6% in 2000 to 56.6% in 2002 to 66.0% in 2006, (ii) the practice of SET steadily increased from 10.5% in 2000 to 12.4% in 2002 to 20.7% in 2006, (iii) the use of FET increased steadily from 11.1 to 21.7% to 23.8 to 31% from 2000 to 2004, then slightly dropped to 28.2 and 27.4% in 2005 and 2006, respectively, (iv) twin DRs decreased steadily from 26.5% in 2000 to 25.7% in 2002 to 22.2% in 2006, (v) triplet DRs decreased steadily from 2.9% in 2000 to 2.5% in 2002 to 1.5% in 2005 and 2006, (vi) preterm DRs decreased from 33.7 to 26.6% to 22.1% in 2004 to 2006. One of the most remarkable trends is the steady increase in the number of OD cycles from 14 887 in 2000 to 36 272 in 2006. Figure 3 represents trends from 2002 to 2006.

Conclusions

The ICMART report on worldwide ART data in 2006 is the most comprehensive global statistical report to date. It showed marked differences among countries in access, effectiveness and safety of ART. The availability of ART and data reporting need to be improved. ICMART is working diligently with many national organizations, governments and ART practitioners and the WHO to do this. Progress has been and is being made. In general, the practice of ICSI is increasing compared with conventional IVF. The mean number of embryos per transfer has decreased, and the practice of SET has increased compared with previous reports. The multiple DRs, and consequently the preterm DRs, have decreased. OHSS, as the single most serious maternal complication other than multiple pregnancies, has decreased. The total number of babies born in 2006 was estimated to be 256 668. Continuous efforts are needed to improve the comprehensiveness and quality of data collected, and to help countries and regions establish their own ART registries.

Supplementary data

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

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Authors' roles

R.M. was involved in the study design, data interpretation and preparing the manuscript. D.A., K.N., F.Z.-H, E.S., J.M., O.I. and S.D. were involved in study design, method investigation, data interpretation and revising the manuscript. All authors have contributed to data collection and the conducting of the study. The manuscript and the order of authorship have been approved by all authors.

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Conflict of interest

All authors have no conflict of interest in relation to this work. We declare no support or financial relationship with any organizations or any activities that could appear to have influenced the submitted work.

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