

International Committee for Monitoring Assisted Reproductive Technologies (ICMART) world report: assisted reproductive technology 2004[†]

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STUDY QUESTION: Have changes in assisted reproductive technology (ART) practice and outcomes occurred globally between 2003 and 2004?

SUMMARY ANSWER: Globally, ART practice has changed with an increasing prevalence of the use of ICSI rather than conventional IVF. In 2004, a small but increasing number of countries are incorporating single embryo transfer. There remain unacceptably high rates of three or more embryo transfers in select countries resulting in multiple births and adverse perinatal outcomes.

WHAT IS KNOWN ALREADY: World data on the availability, effectiveness and safety of ART have been published since 1989. The number of embryos transferred is a major determinant of the iatrogenic increase in multiple pregnancies and is highly correlated with the likelihood of multiple birth and excess perinatal morbidity and mortality.

STUDY DESIGN, SIZE, DURATION: Cross-sectional survey of countries and regions undertaking surveillance of ART procedures started in 2004 and their corresponding outcomes.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Of total, 2184 clinics from 52 reporting countries and regions. Number of ART clinics, types of cycles and procedures, pregnancy, delivery and multiple birth rates and perinatal outcomes.

MAIN RESULTS AND THE ROLE OF CHANCE: A total of 954 743 initiated cycles resulted in an estimated 237 809 babies born. This was a 2.3% increase in the number of reported cycles from 2003. The availability of ART varied by country and ranged from 14 to 3844 treatment cycles per million population. Over one-third (37.2%) of ART clinics performed < 100 cycles per year with only 19.9% performing ≥ 500 cycles per year. Of all cycles, 60.6% were ICSI. Frozen embryo transfers (FETs) represented 31% of the initiated cycles. The overall delivery rate per fresh aspiration for IVF and ICSI was 20.2% compared with 16.6% per FET. The average number of embryos transferred was 2.35. Single (16.3%) and double embryo transfers accounted for 73.2% of cycles. The overall proportion of deliveries with twins and triplets from IVF and ICSI was 25.1 and 1.8%, respectively, but varied widely by country and region. The proportion of premature deliveries per fresh aspiration for IVF and ICSI was 33.7% compared with 26.3% per FET. The perinatal death rate was 25.8 per 1000 births for fresh aspiration for IVF and ICSI compared with 14.2 per 1000 births per FET.

LIMITATIONS, REASONS FOR CAUTION: Data are incomplete with seven countries not providing data to the International Committee for Monitoring Assisted Reproductive Technologies (ICMART) in 2004 that had in 2003. The validity of data reflects current data collection practice. In 2004, 79.3% of the clinics in participating countries reported to their national or regional registries and to ICMART. In addition, the number of ART cycles per million population is a measure which is affected by a country's government policy,

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regulation, funding and the number of service providers.

WIDER IMPLICATIONS OF THE FINDINGS: ART practice, effectiveness and outcomes vary markedly internationally. Notably, the increasing proportion of cycles that are FET, the change in practice to single embryo transfer and the cessation of the transfer of three or more embryos in some countries has resulted in improved perinatal outcomes with minimal impact on pregnancy rates.

STUDY FUNDING/COMPETING INTEREST(S): ICMART receives financial support from ASRM, ESHRE, FSA, Japan Society for Reproductive Medicine, REDLARA, MEFS and SART.

Key words: assisted reproductive technology / registries / outcomes / multiple pregnancies / public health

Introduction

This is the Tenth World Report on assisted reproductive technology (ART) and the fifth prepared by the International Committee for Monitoring Assisted Reproductive Technologies (ICMART) since 2006 (IWGROAR, 2001; Adamson *et al.*, 2006; ICMART, 2009; Nygren *et al.*, 2011). The aim of this report is to provide international information on availability, effectiveness and perinatal outcomes of ART treatment cycles for 2004 and to allow benchmarking of ART practice.

Materials and Methods

The data for ART treatment cycles in 2004 were collected from five regional ART registries compiled from national registry data in Europe, North America and Australia/New Zealand, from individual ART clinics in Latin America and the Middle East, and from national registries directly reporting to ICMART in Asia and Israel. Ethics approval (2011-7-12) for this report was granted from the University of New South Wales.

The ICMART data collection uses forms describing the organization of each country's register, the practice of ART and the results of IVF, ICSI and frozen embryo transfer (FET) and includes initiated cycles, aspirations, transfers, clinical pregnancies, deliveries and newborns. These variables are further classified according to the fertilization technique, woman's age, number of embryos transferred and gestational age at delivery. Other forms describe preimplantation genetic diagnosis (PGD), oocyte donation (OD), immediate complications for women and congenital anomalies detected during the perinatal period.

The 2002 ICMART-World Health Organization (WHO) glossary (Vayena *et al.*, 2002) was used as a reference for terminology. This report covers ART-initiated treatment cycles between 1 January 2004 and the 31 December 2004 and is based on aggregated country data. Data were supplied to the Uppsala Clinical Research Center, Uppsala University, Uppsala, Sweden, where data validation were 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 as well as implementation of ICMART's revised data collection and analysis processes.

Data are presented by country and region. Where data were incomplete the methods used previously for the 2003 report were employed (Nygren *et al.*, 2011). When the number of initiated cycles was unavailable in a national or regional register, an estimation of this number was made by using the average cancellation rate. For national registries with incomplete coverage, the number of initiated cycles per country was estimated by using the reported clinical pregnancy rate (PR), average miscarriage rate and multiple live birth rate in the countries that reported all of these variables. There was variability in the reporting of maternal complications, fetal reduction and maternal surrogacy; this limited the generalizability of these data. There was variability in the quality and reporting of perinatal

outcomes, particularly congenital anomalies data, and these data are not reported. There are no data on causes of perinatal deaths.

Lastly, the estimated total number of babies born worldwide from ART procedures in 2004 was calculated using the hypothesis that the missing countries, mostly in Asia, Africa, Oceania and West Indies, performed between 10 and 20% of the world activity in ART. Availability is expressed as the number of cycles (estimated) per million inhabitants in 2004 (The World Factbook, 2005). A cumulative delivery rate (DR) per aspiration was estimated by adding the FET deliveries to those obtained from fresh cycles and dividing the sum by the number of aspirations.

Results

The results are presented in Tables I–IV and Figs. 1–3. Additional results are provided in [Supplementary data, Tables SI–SVI and Supplementary data, Figs SI–S3](#), which are available online.

Availability

Data were received from 2184 clinics in 52 countries, representing 475 more clinics and 2 fewer countries than in 2003 (Nygren *et al.*, 2011). These clinics represented 79.3% of all registered clinics in those countries. Europe was the region with the largest number of clinics providing data to ICMART ($n = 785/1121$; 70.0%) ([Supplementary data, Table SI](#)). At a country level, Japan followed by the USA had the highest number of participating clinics at 620 ($n = 627$, 98.9%) and 349 ($n = 463$, 80.6%). Twenty-four countries could provide data on >95% of cycles that were performed in their country. The number of cycles completed per year by reporting clinics varied markedly by geographic location. Clinics reporting <100 cycles were mainly located in Asia (61.6%) and Latin America (42.2%) and large-volume clinics (>1000 cycles, 100% participating clinics) were located in Slovenia (66.7%), The Netherlands (61.5%), Belgium (44.4%), Australia (36.0%), Israel (29.2%) and New Zealand (25.0%).

Table I reports an estimated 954 743 treatment cycles from participating clinics, which represented a 2.3% increase in cycles since 2003. The availability of ART varied from 14 treatment cycles per million population in Ecuador to 3844 per million population in Israel. Japan reported the largest number of aspirations, followed by the USA and then France. On a regional basis, Europe made the largest contribution (55.1%) of aspirations worldwide. FETs represented 31% of the initiated cycles (23.8% in 2003). ICSI represented 60.6% of fertilization procedures, an increase from 58.1% in 2003, and varied according to regions. The proportion of ICSI procedures ranged from 59.9% in Europe to 76.5% in Latin America to 98.2% in the Middle East.

Table I General data: distribution of procedures for year 2004.

Country/ region	Non-donation cycles					FET cycles ^c Thaw cycles	Transfer cycles	PGD cycles transfer cycles	OD transfer cycles	Estimated overall total cycle ^d	Availability, cycles/million ^e
	Fresh cycles ^c										
	Initiated cycles ^b	Aspiration cycles									
	Total ^b	IVF	ICSI	GIFT							
India ^a	14 483	NA	NA	NA	NA	1809	1275	NA	NA	20 306	19
Japan	86 317	83 284	39 556	43 628	100	30 193	24 342	NA	NA	117 825	925
South Korea	14 709	13 683	6873	6808	2	2653	2577	NA	386	36 861	758
Taiwan	5629	5598	2962	2624	12	395	390	NA	141	6165	271
Australia	NA	NA	NA	NA	0	13 210	12 240	796	1272	36 921	1854
New Zealand	NA	NA	NA	NA	0	1026	929	32	123	3020	756
Albania	129	110	51	59	NA	NA	NA	0	0	258	73
Austria	NA	4504	1220	3284	NA	NA	NA	NA	NA	4889	598
Belgium	NA	13 794	4053	9741	NA	4324	3825	NA	477	19 775	1911
Bulgaria	928	785	467	318	NA	51	45	0	21	2000	266
Denmark	9598	9214	5299	3915	NA	1565	1384	NA	58	11 221	2073
Finland	4761	4647	2849	1798	NA	3434	3037	NA	820	9015	1729
France	55 217	50 192	21 749	28 443	NA	13 648	12 072	196	231	69 292	1147
Germany	NA	38 824	12 211	26 613	NA	19 269	17 043	NA	NA	61 413	745
Greece	7577	7851	2662	5189	NA	1222	1081	96	269	NA	NA
Hungary	2593	2498	639	1859	NA	280	248	1	28	5320	530
Iceland	NA	234	107	127	NA	83	73	0	8	345	1174
Ireland	2114	1837	1079	758	NA	459	406	NA	0	3002	756
Italy	23 711	20 968	6233	14 735	NA	2488	2201	NA	NA	42 943	740
Latvia	138	134	85	49	NA	50	44	0	2	570	247
Lithuania	NA	83	45	38	NA	8	7	0	0	294	81
Macedonia	521	489	283	206	NA	1	1	0	NA	NA	NA
Netherlands	15 297	13 959	8273	5686	NA	2287	2023	69	NA	17 653	1082
Norway	5136	4952	2692	2260	NA	937	829	0	NA	6073	1328
Poland	3675	3592	550	3042	NA	1317	1165	0	100	7638	198
Portugal	NA	2491	848	1643	NA	374	331	NA	21	3464	329
Russia	12 052	11 656	8281	3375	NA	1768	1564	87	910	16 299	113
Serbia	181	160	11	149	NA	NA	NA	NA	2	732	68
Slovenia	2100	2016	656	1360	NA	601	532	5	17	2723	1354
Spain	27 481	24 315	4537	19 778	NA	5059	4475	1362	4219	82 596	2051
Sweden	9593	8982	4490	4492	NA	2980	2636	NA	97	12 670	1410
Switzerland	3145	2924	645	2279	NA	2722	2408	NA	NA	6176	829
Turkey	3472	3277	23	3254	NA	73	65	36	0	69 830	1014
Ukraine	1505	1439	1023	416	NA	33	29	30	57	2216	46

Continued

Table I Continued

Country/ region	Non-donation cycles						FET cycles ^c Thaw cycles	PGD cycles transfer cycles	OD transfer cycles	Estimated overall total cycle ^d	Availability, cycles/million ^e
	Fresh cycles ^c					Transfer cycles					
	Initiated cycles ^b	Aspiration cycles		ICSI	GIFT						
	Total ^b	IVF									
UK	30 375	28 173	14 898	13 275	NA	7420	6563	107	1959	39 561	661
Argentina	3964	3665	964	2687	14	553	489	NA	662	7152	183
Brazil	9126	8462	1059	7397	6	982	869	NA	815	10 923	59
Chile	906	824	372	421	31	234	207	NA	90	1406	89
Colombia	817	792	306	485	1	77	68	NA	217	1605	38
Ecuador	109	92	10	82	0	18	16	NA	52	179	14
Guatemala	22	22	16	6	0	1	1	NA	7	NA	NA
Mexico	2692	2474	877	1597	0	374	331	NA	747	NA	NA
Peru	591	566	217	285	64	66	58	NA	398	1055	38
Uruguay	355	330	143	187	0	41	36	NA	31	854	251
Venezuela	730	562	193	369	0	97	86	NA	102	929	37
Egypt	8218	7696	119	7577	0	952	912	5	NA	30 583	402
Jordan	2933	2676	0	2676	NA	184	129	265	NA	NA	NA
Lebanon	703	663	101	562	0	11	10	NA	28	NA	NA
Saudi Arabia	1120	1060	0	1060	0	120	92	NA	NA	NA	NA
Israel ^a	17 486	NA	NA	NA	NA	6342	5917	NA	NA	23 828	3844
Canada	7983	7104	2977	4124	3	2352	2228	NA	523	10 858	334
USA	87 177	75 801	26 150	49 571	80	16 883	16 296	NA	11 875	146 005	498
Total	>487 369	>479 454	>188 854	>290 287	>313	>151 026	>133 585	>3087	>26 765	>954 743	345
Region											
Asia	121 138	>102 565	>49 391	>53 060	>114	35 050	28 584	NA	>527	181 157	143
Australia/New Zealand	NA	NA	NA	NA	0	14 236	13 169	828	1395	39 941	1671
Europe	>221 299	264 100	105 959	158 141	NA	>72 453	>64 087	>1989	>9296	>498 268	690
Latin America	19 312	17 789	4157	13 516	116	2443	2161	NA	3121	>24 103	69
Middle East	12 974	12 095	220	11 875	NA	1267	1143	>270	>28	>30 583	402
Middle East (Israel)	17 486	NA	NA	NA	NA	6342	5917	NA	NA	23 828	3844
North America	95 160	82 905	29 127	53 695	83	19 235	18 524	NA	12 398	156 863	482

GIFT, gamete intra-Fallopian transfer; FET, frozen embryo transfers.

Note: NA $\frac{1}{4}$ not available.

^aCountries that did not separate ICSI and IVF.

^bReported in the registries.

^cExcluding PGD and OD cycles.

^dOverall initiated cycles estimation: step 1: reported cycles for countries reporting them, or estimation by applying their cancellation rate to the aspiration numbers for the non-reporting countries; step 2: total of step 1 if 100% of the clinics reported, or estimation by applying the percentage of participating clinics to this total if <100% of the clinics reported.

^eTotal estimated number of cycles in the country divided by its population in 2003 (CIA World Fact Book).

Table II IVF, ICSI and FET results for year 2004.

Country/ region	IVF		ICSI		FET		IVF and ICSI				Total babies reported (n) ^{c,e}	Total babies est (n) ^{d,e}	
	PR/Asp (%)	DR/Asp (%)	PR/Asp (%)	DR/Asp (%)	PR/FET (%)	DR/FET (%)	DR/Asp fresh (%)	DR/Asp cum (%) ^{f,g}	Babies/Asp fresh (%)	Babies/Asp cum (%) ^b			
India ^a	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Japan	21.6	14.2	17.8	11.5	31.2	19.9	12.8	18.6	NA	NA	20422 ³	20 653	
South Korea	31.7	NA	28.2	NA	35.0	NA	NA	26.2 ¹	30.3	36.2	5013	10 412	
Taiwan	43.3	32.1	40.1	29.6	36.4	26.9	30.9	32.8	44.1	46.4	2667	2667	
Australia	NA	NA	NA	NA	20.0	15.3	NA	NA	NA	NA	7081	7081	
New Zealand	NA	NA	NA	NA	25.7	20.3	NA	NA	NA	NA	905	905	
Albania	21.6	7.8	23.7	10.2	NA	NA	9.1	9.1	11.8	11.8	13	26	
Austria	30.1	19.1	29.0	NA	NA	NA	NA	21.2 ¹	NA	NA	1255 ³	1255	
Belgium	21.5	13.5	20.0	12.9	13.3	10.3	13.1	15.9	14.5	17.7	2654	2654	
Bulgaria	23.1	16.3	46.5	42.5	17.8	8.9	26.9	27.4	35.8	36.4	289	578	
Denmark	27.9	21.6	27.7	21.4	18.5	11.4	21.5	23.2	26.2	28.7	2661	2661	
Finland	23.7	18.6	25.4	19.8	23.5	17.1	19.1	30.2	21.7	34.2	1596	1596	
France	22.7	17.3	23.8	18.3	16.4	11.8	17.9	20.7	22.0	25.2	12 719	12 719	
Germany	25.7	16.4	26.7	17.6	17.3	10.3	17.3	21.8	21.2	27.6	10 699	10 699	
Greece	32.4	15.6	32.1	15.8	30.9	16.8	15.7	18.0	21.0	25.1	2100	6431	
Hungary	31.5	22.7	32.0	24.7	31.5	23.4	24.2	26.5	33.7	36.5	928	1701	
Iceland	26.2	21.5	27.6	23.6	21.9	12.3	22.6	26.5	28.6	33.3	81	81	
Ireland	27.6	24.1	27.8	19.9	25.9	17.5	22.4	26.2	27.7	32.1	590	688	
Italy	22.4	13.9	23.3	14.5	18.5	11.8	14.3	15.6	18.0	19.6	4119	6751	
Latvia	36.5	16.5	40.8	16.3	15.9	11.4	16.4	20.1	20.9	26.1	35	105	
Lithuania	24.4	11.1	26.3	13.2	14.3	0.0	12.0	13.3	18.1	18.1	15	45	
Macedonia	26.5	16.3	12.6	6.3	0.0	0.0	12.1	12.1	16.0	16.0	78	78	
Netherlands	29.6	NA	31.7	NA	21.0	NA	NA	24.1 ¹	NA	NA	4432 ³	4432	
Norway	29.5	24.3	25.1	19.7	19.8	15.0	22.2	24.7	27.5	30.5	1512	1512	
Poland	33.1	17.1	33.0	24.6	17.9	9.5	23.4	26.5	29.1	34.2	1248	1872	
Portugal	29.0	19.8	24.7	18.8	17.5	8.8	19.1	20.3	24.2	26.2	666	744	
Russia	31.9	18.4	31.3	17.3	21.5	12.4	18.1	19.8	23.3	25.4	3210	3531	
Serbia	18.2	NA	29.5	NA	NA	NA	NA	20.6 ¹	NA	NA	43 ³	172	
Slovenia	27.6	21.6	27.6	22.2	17.3	14.3	22.0	25.8	26.1	30.3	613	613	
Spain	31.8	14.5	32.5	16.0	27.5	12.0	15.7	17.9	20.2	24.9	7827	16 959	
Sweden	30.2	23.8	27.0	21.3	26.0	18.9	22.6	28.1	23.9	29.9	2711	2711	
Switzerland	26.2	19.2	24.7	17.7	18.5	13.2	18.1	28.9	22.3	35.7	1043	1098	
Turkey	47.8	47.8	40.8	17.2	49.2	3.1	17.4	17.5	24.7	24.9	821	16 010	
Ukraine	25.5	20.0	27.4	23.8	37.9	37.9	21.1	21.9	29.2	30.0	484	660	
UK	26.8	23.5	27.4	24.5	19.0	16.3	23.9	27.8	29.8	34.4	10 335	10 335	
Argentina	26.5	21.8	23.1	18.4	19.4	14.7	19.3	21.3	30.7	32.9	1473	2034	

Continued

Table II Continued

Country/ region	IVF		ICSI		FET		IVF and ICSI				Total babies reported (n) ^{c,e}	Total babies est (n) ^{d,e}
	PR/Asp (%)	DR/Asp (%)	PR/Asp (%)	DR/Asp (%)	PR/FET (%)	DR/FET (%)	DR/Asp fresh (%)	DR/Asp cum (%) ^{f,g}	Babies/Asp fresh (%)	Babies/Asp cum (%) ^b		
Brazil	33.1	19.7	32.3	23.9	18.1	12.5	23.4	24.7	58.0	59.6	5350	5350
Chile	30.4	24.2	29.2	24.7	17.9	13.0	24.5	27.9	52.3	56.7	477	545
Colombia	30.1	24.5	30.1	22.7	29.4	25.0	23.4	25.5	41.2	43.7	451	651
Ecuador	20.0	20.0	34.1	26.8	50.0	43.8	26.1	33.7	60.9	68.5	87	87
Guatemala	50.0	31.3	16.7	16.7	0.0	0.0	27.3	27.3	68.2	68.2	16	NA
Mexico	30.2	22.6	28.9	23.0	22.7	17.8	22.8	25.2	36.3	39.4	1338	NA
Peru	27.6	18.9	31.6	19.3	20.7	8.6	19.1	20.1	30.3	31.5	401	401
Uruguay	29.4	24.5	21.4	16.6	22.2	13.9	20.0	21.5	26.4	27.9	101	202
Venezuela	35.2	26.9	27.4	21.1	24.4	17.4	23.1	25.8	57.8	60.5	382	382
Egypt	39.5	27.7	38.7	29.7	23.6	14.7	29.7	31.4	41.2	43.9	3334	11 273
Jordan	NA	NA	24.6	12.5	14.0	7.0	12.5	12.8	24.5	25.3	698	NA
Lebanon	32.7	27.7	34.0	29.2	10.0	10.0	29.0	29.1	29.3	29.9	215	NA
Saudi Arabia	NA	NA	29.2	26.9	20.7	14.1	26.9	28.1	30.4	31.7	336	NA
Israel ^a	NA	NA	NA	NA	20.2	15.7	NA	NA	NA	NA	5812 ³	5812
Canada	36.5	28.6	35.2	26.0	25.0	18.0	27.1	32.7	35.0	42.7	3238	3238
USA	40.5	33.6	37.2	30.8	35.4	28.2	31.7	37.8	42.8	50.5	45 578	57 399
Total	28.2	20.4	28.2	20.1	24.1	16.6	20.2	24.3	29.1	33.9	>180 206	>237 809
Region												
Asia	24.3	15.4	20.2	12.6	31.6	20.1	13.9	20.4	34.3	39.2	>28 102	>33 732
Australia/ New Zealand	NA	NA	NA	NA	20.4	15.6	NA	NA	NA	NA	7986	7986
Europe	26.6	18.7	27.2	18.1	19.2	12.6	18.3	21.6	22.6	26.8	71 777	108 717
Latin America	30.2	22.1	29.6	22.4	20.0	14.6	22.3	24.1	47.0	49.1	10 076	>9652
Middle East	36.4	27.7	34.5	25.6	22.1	13.7	25.6	26.9	36.3	38.0	4583	>11 273
Middle East (Israel)	NA	NA	NA	NA	20.2	15.7	NA	NA	NA	NA	5812	5812
North America	40.1	33.1	37.1	30.4	34.2	26.9	31.3	37.4	42.1	49.8	48 816	60 637

PR, pregnancy rate; DR, delivery rate.

Note: The total numbers and numbers by region were calculated only from the countries with complete data (i.e. both number of pregnancies and number of aspirations). Cum $\frac{1}{4}$ cumulative rate per aspiration, computed by adding the FET deliveries and babies, respectively, to those obtained after fresh cycles, the sum being divided by the number of aspirations; NA $\frac{1}{4}$ not available.

^aCountries that did not separate ICSI and IVF.

^bIn countries in which the sum of singleton, twins and triplets were less than the total number of deliveries, the numbers of unknown babies and lost-to-follow-up deliveries were estimated by applying the distribution of reported deliveries in these countries.

^cImputed by multiplying the number of deliveries by the average number of babies per delivery.

^dTotal babies reported if 100% of the clinics reported. If < 100% of clinics reported, this number was estimated by using the percentage of participating clinics to calculate the total number of babies as if all clinics in these countries had reported.

^eTotal babies also includes PGD and OD.

^fImputed by calculating the mean percentage of deliveries per pregnancy.

^gNumber of aspirations was imputed.

Table III IVF and ICSI cycles: number of transferred embryos, effectiveness and multiplicity for year 2004.

Country/region	Aspirations	Transfers ^c	No. of transferred embryos (%)					Effectiveness			Multiplicity	
			1	2	3	≥4	Average	PR/Asp (%)	DR/Asp (%)	Babies/Asp (%) ^b	Twin (%)	Triplet + (%)
India	13 342 ^a	13 268	8.9	20.3	41.2	29.6	2.99	NA	NA	NA	NA	NA
Japan	83 184	58 936	NA	NA	NA	NA	NA	19.6	12.8	NA	NA	NA
South Korea	13 681	15 722	9.6	16.1	24.9	49.3	3.36	30.0	21.6 ^e	30.3	16.7	1.1
Taiwan	5586	5548	8.0	15.4	22.5	54.0	3.46	41.8	30.9	44.1	38.8	1.7
Australia	NA	17 309	37.8	58.1	3.7	0.4	1.67	NA	NA	NA	17.5	0.4
New Zealand	NA	1482	28.4	67.7	3.6	0.2	1.76	NA	NA	NA	20.1	0.4
Albania	110	102	9.8	21.6	21.6	47.1	3.06	22.7	9.1	11.8	30.0	0.0
Austria	4504	4315	14.6	63.6	20.3	1.4	2.09	29.3	21.2 ^e	NA	27.9	1.3
Belgium	13 794	12 787	48.9	42.1	7.6	1.5	1.62	20.4	13.1	14.5	10.2	0.2
Bulgaria	785	855	7.5	28.1	49.0	15.4	2.72	32.6	26.9	35.8	25.6	3.8
Denmark	9214	7795	27.4	67.5	5.2	0.0	1.78	27.8	21.5	26.2	21.0	0.4
Finland	4647	4176	47.0	52.7	0.3	0.0	1.53	24.4	19.1	21.7	12.9	0.5
France	50 192	43 821	17.5	59.1	18.7	4.7	2.10	23.3	17.9	22.0	22.0	0.5
Germany	38 824	35 951	11.6	61.3	27.1	0.0	2.15	26.4	17.3	21.2	20.7	1.1
Greece	7851	6953	14.5	23.6	40.1	21.9	2.69	32.2	15.7	21.0	30.6	1.5
Hungary	2498	2334	7.5	27.9	45.2	19.4	2.77	31.8	24.2	33.7	32.9	3.1
Iceland	234	201	20.9	65.7	13.4	0.0	1.93	26.9	22.6	28.6	18.9	3.8
Ireland	1837	1705	7.9	78.0	12.8	1.3	2.08	27.7	22.4	27.7	22.1	0.7
Italy	20 968	18 521	18.3	32.3	48.5	0.9	2.32	23.0	14.3	18.0	21.3	2.0
Latvia	134	120	19.2	53.3	27.5	0.0	2.08	38.1	16.4	20.9	27.3	0.0
Lithuania	83	76	11.8	17.1	50.0	21.1	2.80	25.3	12.0	18.1	30.0	10.0
Macedonia	489	407	21.1	30.5	37.1	11.3	2.39	20.7	12.1	16.0	25.4	3.4
Netherlands	139 59	12 474	NA	NA	NA	NA	NA	30.5	22.0 ^e	NA	NA	NA
Norway	4952	4564	25.5	74.2	0.4	0.0	1.75	27.5	22.2	27.5	23.4	0.4
Poland	3592	3344	12.9	64.9	19.8	2.4	2.12	33.0	23.4	29.1	21.5	1.3
Portugal	2491	2257	14.9	56.5	26.7	1.9	2.16	26.1	19.1	24.2	23.7	1.3
Russia	11 656	10 904	13.2	47.7	28.0	11.1	2.37	31.7	18.1	23.3	24.9	2.0
Serbia	160	126	23.0	14.3	25.4	37.3	2.77	28.8	20.6 ^e	NA	NA	NA
Slovenia	2016	1787	26.5	61.0	12.5	0.0	1.86	27.6	22.0	26.1	17.3	0.7
Spain	24 315	21 085	13.3	49.8	36.9	0.0	2.24	32.4	15.7	20.2	25.1	1.8
Sweden	8982	8137	67.4	32.5	0.1	0.0	1.33	28.6	22.6	23.9	5.6	0.0
Switzerland	2924	2752	13.0	67.1	19.8	0.1	2.07	25.0	18.1	22.3	21.2	1.1
Turkey	3277	3015	9.2	18.3	39.3	33.2	2.97	40.9	17.4	24.7	36.3	3.0

Continued

Table III Continued

Country/region	Aspirations	Transfers ^c	No. of transferred embryos (%)					Effectiveness			Multiplicity	
			1	2	3	≥4	Average	PR/Asp (%)	DR/Asp (%)	Babies/Asp (%) ^b	Twin (%)	Triplet + (%)
Ukraine	1439	1352	17.4	21.1	29.6	31.9	2.76	26.1	21.1	29.2	34.9	1.6
UK	28 173	26 192	9.4	85.1	5.5	0.0	1.96	27.1	23.9	29.8	23.9	0.3
Argentina	3651	3266	14.5	31.5	41.9	12.1	2.53	24.0	19.3	30.7	33.0	10.1
Brazil	8456	7727	8.1	19.3	32.2	40.5	3.16	32.4	23.4	58.0	39.9	16.0
Chile	793	697	8.2	32.4	52.9	6.5	2.58	29.8	24.5	52.3	42.1	5.5
Colombia	791	736	12.0	25.4	36.0	26.6	2.87	30.1	23.4	41.2	35.5	8.4
Ecuador	92	81	7.4	30.9	45.7	16.0	2.72	32.6	26.1	60.9	33.3	11.1
Guatemala	22	21	14.3	42.9	33.3	9.5	2.38	40.9	27.3	68.2	28.6	42.9
Mexico	2474	2226	9.2	19.5	40.9	30.5	2.98	29.3	22.8	36.3	30.3	10.3
Peru	502	462	7.8	23.6	53.9	14.7	2.79	29.9	19.1	30.3	48.2	0.0
Uruguay	330	291	12.7	25.1	42.6	19.6	2.71	24.8	20.0	26.4	37.5	0.0
Venezuela	562	550	11.8	40.1	34.4	13.5	2.50	30.1	23.1	57.8	31.5	15.5
Egypt	7696	7226	7.4	16.0	53.7	23.0	2.99	38.8	29.7	41.2	28.6	2.3
Jordan	2676	2406	12.3	15.0	35.0	37.7	3.06	24.6	12.5	24.5	24.3	5.7
Lebanon	663	646	2.5	75.8	21.7	0.0	2.19	33.8	29.0	29.3	2.5	0.0
Saudi Arabia	1060	1026	3.6	44.2	49.1	3.1	2.50	29.2	26.9	30.4	9.1	1.8
Israel	16 108 ^a	15 162	NA	NA	NA	NA	NA	25.6 ^d	21.6 ^e	NA	NA	NA
Canada	7101	6689	9.7	56.6	24.8	8.9	2.35	35.7	27.1	35.0	26.2	1.6
USA	75 721	70 141	8.3	39.5	31.7	20.5	2.71	38.4	31.7	42.8	30.4	1.1
Total	>508 591	469 726	16.3	46.9	25.1	11.6	2.35	28.1	20.4	29.1	25.1	1.8
Region												
Asia	1 15 793	93 474	9.1	17.6	30.8	42.5	3.23	22.2	15.0	34.3	24.0	1.3
Australia/New Zealand	NA	18 791	37.1	58.9	3.7	0.4	1.67	NA	NA	NA	17.8	0.4
Europe	264 100	238 108	19.2	55.4	22.1	3.3	2.10	27.0	18.5	22.6	21.7	1.0
Latin America	17 673	16 057	9.9	23.7	37.4	29.0	2.92	29.7	22.3	47.0	37.4	13.2
Middle East	12 095	11 304	7.7	19.3	46.7	23.0	2.85	34.5	25.6	35.9	25.5	2.5
Middle East (Israel)	16 108	15 162	NA	NA	NA	NA	NA	25.6	21.6	NA	NA	NA
North America	82 822	76 830	8.4	40.9	31.1	19.5	2.68	38.1	31.3	42.1	30.1	1.2

^aImputed by applying the average cancellation rate to the number of initiated cycles.

^bIn countries in which the sum of singleton, twins and triplets was less than the total number of deliveries, the numbers of unknown babies and lost-to-follow-up deliveries were estimated by applying the distribution of reported deliveries in these countries.

^cReported directly in the International Committee for Monitoring Assisted Reproductive Technologies (ICMART) registry forms.

^dImputed by calculating the number of aspirations from the number of initiated cycles reported.

^eImputed by calculating the mean percentage of deliveries per pregnancy.

Table IV Pregnancy losses, prematurity and perinatal mortality for year 2004.

Country/region	Aspiration cycles (IVF and ICSI)					FET cycles				
	Pregnancies			Deliveries		Pregnancies			Deliveries	
	Reported (n)	Outcome (n) ^a	Losses (%)	Preterm (%) ^b	Mortality (per 1000) ^c	Reported (n)	Issue (n) ^a	Losses (%)	Preterm (%) ^b	Mortality (per 1000)
India	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Japan	16 302	NA	NA	NA	12.9	7595	NA	NA	NA	9.0
South Korea	4101	599	100.0	NA	NA	901	NA	NA	NA	NA
Taiwan	2335	2327	25.7	35.6	45.0	142	142	26.1	22.9	0.0
Australia	4862	4797	20.5	19.6	14.3	2450	2407	22.3	14.5	8.1
New Zealand	653	634	19.2	18.9	8.1	239	230	17.8	10.6	4.7
Albania	25	13	23.1	NA	NA	0	NA	NA	NA	NA
Austria	1320	233	0.0	NA	NA	NA	NA	NA	NA	NA
Belgium	2814	1802	0.0	NA	NA	510	394	NA	NA	NA
Bulgaria	256	247	14.6	NA	NA	8	6	33.3	NA	NA
Denmark	2563	2318	14.6	NA	NA	256	218	27.5	NA	NA
Finland	1133	1131	21.7	NA	NA	715	709	26.9	NA	NA
France	11 696	11 660	23.5	NA	NA	1983	1973	28.3	NA	NA
Germany	10 252	9121	26.6	NA	NA	2947	2577	31.7	NA	NA
Greece	2526	1514	18.5	NA	NA	334	227	19.8	NA	NA
Hungary	795	764	20.9	NA	NA	78	78	25.6	NA	NA
Iceland	63	63	15.9	NA	NA	16	16	50.0	NA	NA
Ireland	509	509	22.8	NA	NA	105	100	29.0	NA	NA
Italy	4826	3954	24.0	NA	NA	407	359	27.6	NA	NA
Latvia	51	29	24.1	NA	NA	7	6	16.7	NA	NA
Lithuania	21	16	37.5	NA	NA	1	1	100.0	NA	NA
Macedonia	101	83	28.9	NA	NA	0	NA	NA	NA	NA
Netherlands	4251	0	NA	NA	NA	425	NA	NA	NA	NA
Norway	1362	1341	18.3	NA	NA	164	164	24.4	NA	NA
Poland	1187	984	14.4	NA	NA	209	155	28.4	NA	NA
Portugal	651	619	22.9	NA	NA	58	50	42.0	NA	NA
Russia	3698	2712	22.2	NA	NA	337	266	27.1	NA	NA
Serbia	46	0	NA	NA	NA	NA	NA	NA	NA	NA
Slovenia	557	531	16.4	NA	NA	92	90	15.6	NA	NA
Spain	7866	5101	25.2	NA	NA	1229	828	35.1	NA	NA
Sweden	2566	2553	20.6	NA	NA	686	285	27.3	NA	NA
Switzerland	732	683	22.7	NA	NA	446	422	24.9	NA	NA
Turkey	1339	736	22.6	NA	NA	32	5	60.0	NA	NA

Continued

Table IV Continued

Country/region	Aspiration cycles (IVF and ICSI)					FET cycles				
	Pregnancies			Deliveries		Pregnancies			Deliveries	
	Reported (n)	Outcome (n) ^a	Losses (%)	Preterm (%) ^b	Mortality (per 1000) ^c	Reported (n)	Issue (n) ^a	Losses (%)	Preterm (%) ^b	Mortality (per 1000)
Ukraine	375	373	18.5	NA	NA	11	11	0.0	NA	NA
UK	7633	7526	10.4	NA	NA	1244	1218	12.0	NA	NA
Argentina	877	731	NA	16.4	28.8	95	66	24.2	8.1	0.0
Brazil	2740	2740	NA	32.6	22.3	157	151	291.	23.8	7.6
Chile	236	236	NA	30.9	14.9	37	36	25.0	24.0	0.0
Colombia	238	214	NA	21.0	32.4	20	7	0.0	14.3	0.0
Ecuador	30	30	NA	4.8	0.0	8	0	NA	0.0	0.0
Guatemala	9	7	NA	0.0	0.0	0	0	NA	NA	NA
Mexico	726	595	NA	33.8	17.2	76	25	32.0	32.8	39.5
Peru	150	83	NA	35.8	94.5	12	8	50.0	20.0	0.0
Uruguay	82	32	NA	19.4	11.6	8	3	33.3	20.0	0.0
Venezuela	169	196	NA	17.1	11.3	21	18	27.8	7.7	0.0
Egypt	2983	2856	20.0	31.5	100.2	215	208	35.6	26.1	136.4
Jordan	658	458	27.1	40.1	35.2	18	11	18.2	86.7	NA
Lebanon	224	111	28.8	91.1		1	NA	NA	NA	NA
Saudi Arabia	310	310	8.1	20.7	21.7	19	19	31.6	38.5	NA
Israel	4123	NA	NA	NA	NA	1195	NA	NA	NA	NA
Canada	2538	2379	19.2	24.0	26.5	558	528	23.9	21.3	9.8
USA	29 048	28 984	18.5	37.5	21.1	5809	5765	20.8	32.5	16.2
Total	>144 608	>104 908	20.4	33.7	25.8	>31 876	>20 182	24.6	26.3	14.2
Region										
Asia	>22 738	>2926	40.9	35.6	24.5	>8638	>142	26.1	22.9	8.5
Australia/New Zealand	5515	2431	20.3	19.5	13.5	2689	2637	21.9	14.2	7.8
Europe	71 214	56 616	20.4	NA	NA	>12 300	>10 558	27.1	NA	NA
Latin America	5257	4837	NA	28.9	23.8	434	314	27.7	20.3	10.6
Middle East	4175	3735	20.1	33.0	85.8	253	>238	34.5	32.7	136.4
Middle East (Israel)	4123	NA	NA	NA	NA	1195	NA	NA	NA	NA
North America	31 586	31 363	18.6	36.6	21.5	6367	6293	21.0	31.6	15.7

^aPregnancies with known outcome (i.e. both pregnancy losses and live births).

^bPreterm $\frac{1}{4}$ <37 weeks.

^cMortality $\frac{1}{4}$ perinatal mortality (stillbirths \pm neonatal deaths/stillbirths \pm live births)_1000.

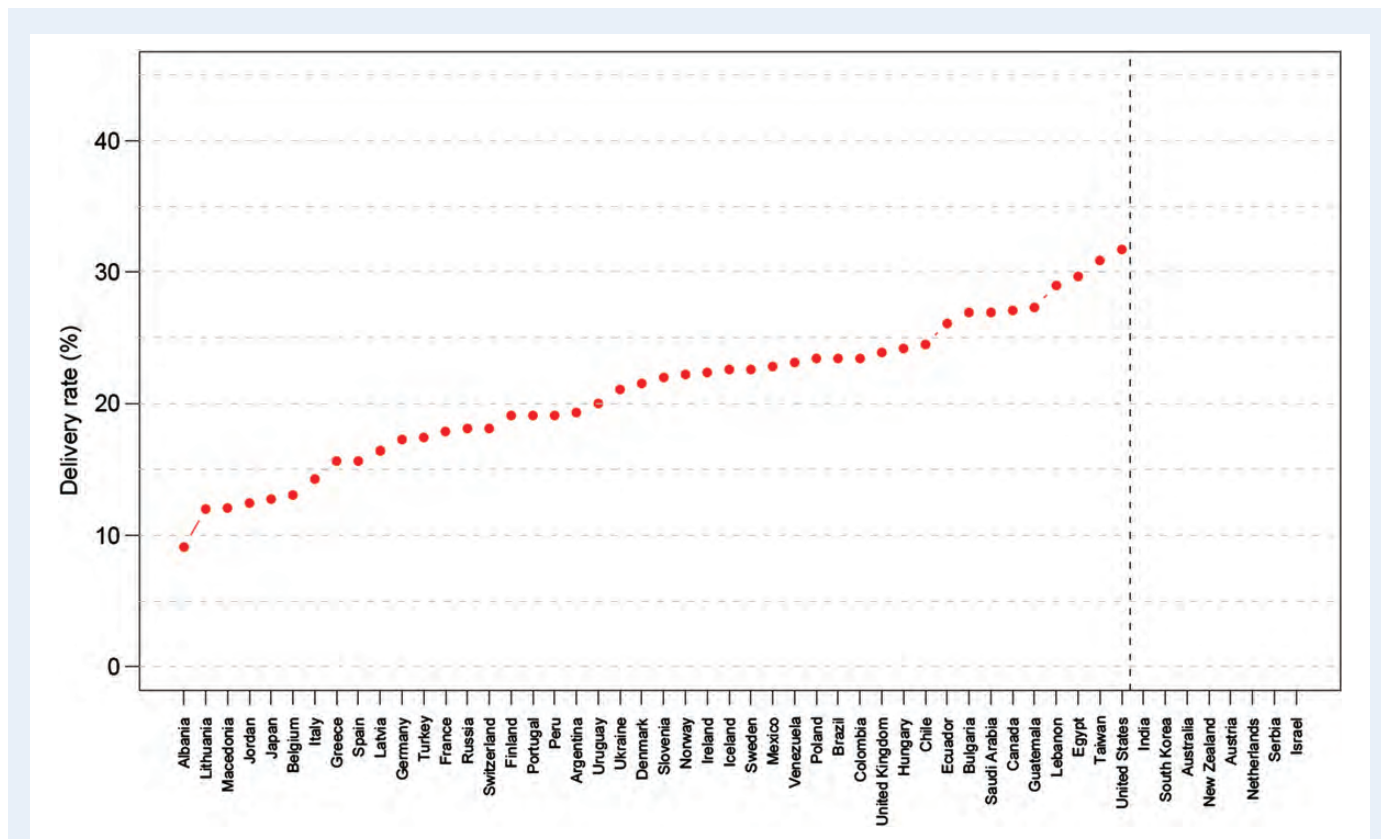


Figure 1 Delivery rate (DR) per aspiration.

Effectiveness

Table II reports on the outcomes of ART procedures. PRs and DRs per aspiration were similar in IVF and ICSI: PR 28.2 versus 28.2% and DR 20.4 versus 20.1%, respectively. For FET cycles, the number of transferred embryos, effectiveness and multiplicity are reported in [Supplementary data, Table SII](#). Since 2003, the DR for FET cycles declined from 17.1 to 16.6%. The DR per aspiration varied among countries (Figs 1 and 2). The cumulative DR per aspiration varied among countries, with the highest in North America (37.4%). When combining IVF and ICSI fresh cycles (Table III), DR per aspiration decreased to 20.4% compared with 23.1% in 2003, and the cumulative DR (fresh plus frozen cycles) decreased to 24.3% compared with 26.3% in 2003. The miscarriage rate per clinical pregnancies (Table IV) averaged 20.4% in fresh cycles, a slight decrease from 2003, with both large differences among countries and higher proportions in FET pregnancies (24.6%).

A total of 237 809 babies (Table II) were reported to have been born in 2004, an increase of 4829 (2.0%) from the estimated number of babies born in 2003 of 232 980.

Overall, the proportion of women aged ≥ 40 years having ART treatment cycles was 14.9% compared with 14.6% in 2003. The proportion of older women accessing ART varied among countries and regions, with Italy, Greece, Australia and Serbia having more than one in five cycles to women aged ≥ 40 years ([Supplementary data, Table SIII](#)).

Safety and quality

The proportion of single embryo transfers (SETs) increased from 14.7% in 2003 to 16.3%, with the highest levels reported by Sweden (67.4%), Belgium (48.9%) and then Finland (47.0%) (Table III). The proportion of twin deliveries marginally increased from 24.8% in 2003 to 25.1%, while the proportion of triplet deliveries continued to decrease, from 2.0% to 1.8%. However, these rates differed largely among countries; the percentage of twin births ranged from 5.6% in Sweden to 48.2% in Peru, and births of triplet and higher order multiples from $< 1\%$ in several countries (including Sweden, Belgium, Australia, New Zealand, Norway, Denmark and France) to $> 10\%$ in Lithuania and six Latin American countries (Argentina, Brazil, Ecuador, Guatemala, Mexico and Venezuela) ([Supplementary data, Fig. S1](#)). Similar rates of multiple deliveries were seen for FET in 2003 and 2004, with twins at 17.0% and triplets or higher at 1.0% ([Supplementary data, Table SII](#)). The percentage of transfers with four or more embryos in fresh cycles increased slightly, to 11.6% from 10.8% in 2003, but with major differences among and within regions (Table III). The lowest proportion of ≥ 4 fresh embryo transfers was reported from Australia/New Zealand at 0.4% then Europe at 3.3% and the highest from Asia at 42.5% with the Nordic countries reporting no embryo transfer cycles of ≥ 4 . The mean number of embryos transferred was lowest from Australia and New Zealand, 1.67 and 1.76, respectively (Table III). Figure 3 shows the DR per aspiration varied by both individual country and mean number of embryos transferred. The mean number of embryos

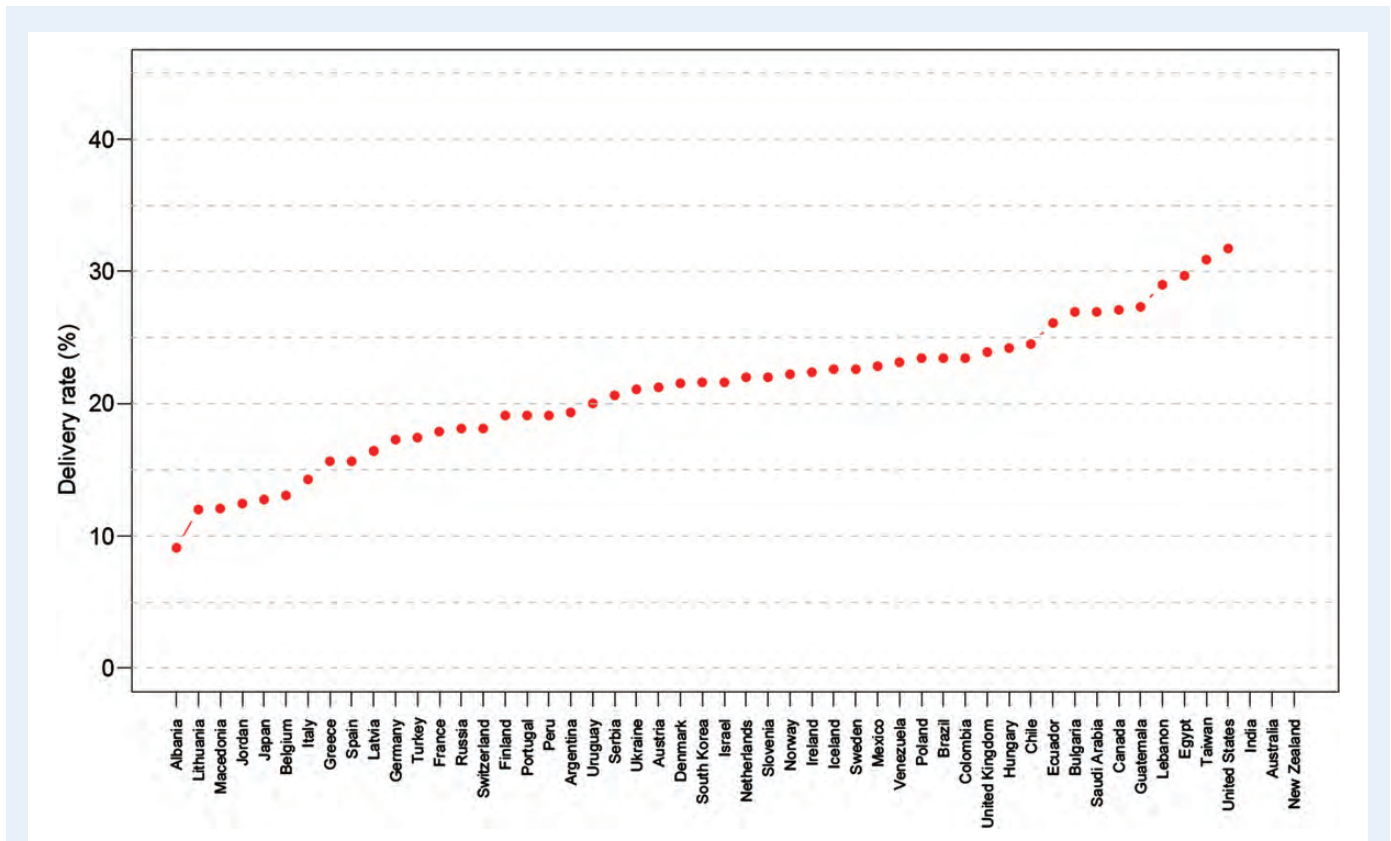


Figure 2 DR per aspiration (imputed when complete data not available).

transferred was not correlated with the overall DR (Supplementary data, Fig. S2; $r = 0.11$, NS) or triplet rate (Supplementary data, Fig. S3 $r = 0.24$, NS).

The proportion of premature delivery per fresh aspiration for IVF and ICSI was 33.7% compared with 26.3% per FET, which had increased from 19.9% in 2003 to 26.3% in 2004. The perinatal death rate was 25.8 per 1000 births for fresh aspiration for IVF and ICSI compared with 14.2 per 1000 births for FET (Table IV). These data must be interpreted with caution as no data from European countries were available on these birth outcomes and this may bias the results. The frequency of ovarian hyperstimulation syndrome (OHSS) was reported as 1.2%, with a regional range of 0.2–7.5% (Supplementary data, Table SIV). Three countries (Taiwan, Portugal and Slovenia) reported >10% of cycles resulted in OHSS.

Special techniques—ovum donation, PGD, *in vitro* maturation, surrogacy and multifetal reduction

There were 26 765 ovum donation (OD) transfers, an increase from 23 664 in 2003 (Supplementary data, Table SV). Of these transfers, 44.4% were performed in the USA and 72.2% were fresh embryos transfers. DRs per transfer (fresh plus FET) was 34.1%, with the USA highest at 44.7%. The multiple DR from OD transfers was 34.6%. Of the 12 334 babies reported from OD, 60% were born in the USA. Eighteen countries reported 2739 PGD aspiration cycles, with PR and DR per aspiration at 21.9 and 15.9%, respectively

(Supplementary data, Table SVI). Very few data were reported on *in vitro* maturation, surrogacy and multifetal reduction.

Discussion

The 2004 ICMART world report is the most comprehensive global statistical report on ART practice and includes measures of effectiveness, safety and quality of services. In 2004 an estimated 954 743 ART cycles were reported by 2184 clinics resulting in 237 809 babies, an increase of 2.0% on 2003 births. To contextualize the significance of this number of births, it is equivalent to 5.9% of an estimated 4023, 572 babies born in the European Union and Norway for 2004 (EURO-PERISTAT, 2008).

Monitoring of ART practice, effectiveness and outcomes at an international level is central to improving fertility services and outcomes worldwide and to monitoring the impact of policy initiatives, such as SET, over time. It is important to monitor ART to determine availability and access to fertility services, the benefits and risks of new technology and the changes in practice as well as to benchmark treatment and perinatal outcomes. The latter is critical to developing comprehensive statistics to inform policy and planning of ART-related health care and to provide an evidence base on ART for populations seeking fertility treatment.

Availability

One way of measuring access to ART is the number of countries that provides ART services. In 2004, there remained enormous variability

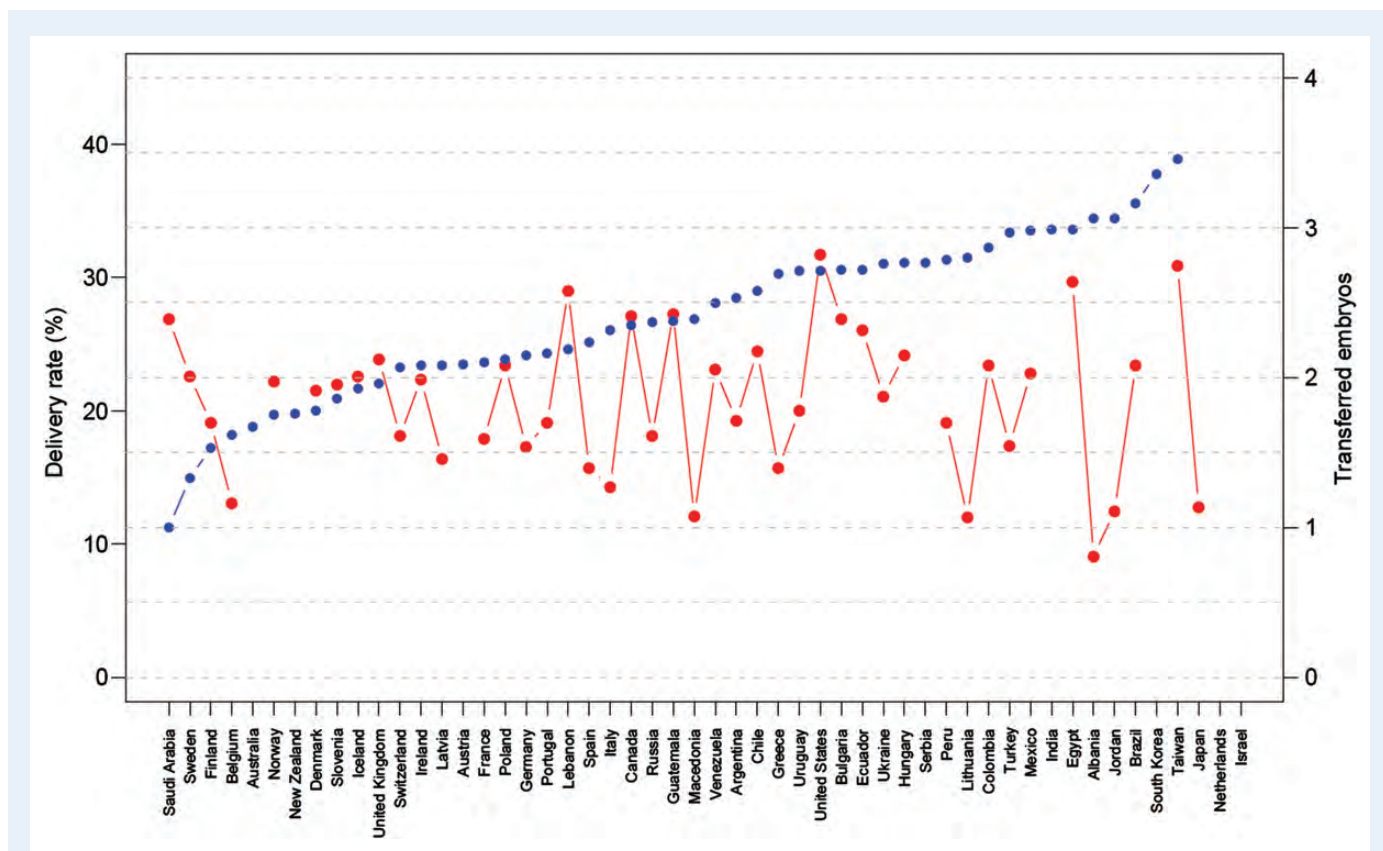


Figure 3 DR per aspiration (red) according to the mean number of embryos transferred.

and incomplete information on service provision with only 52 of 193 countries internationally providing information to ICMART (United Nations, 2011). Although this is an under-estimation of the worldwide provision of ART services, it provides robust information on North and South America, Europe, Australasia, India and Japan. In 2004 four countries (Croatia, Bolivia, Dominican Republic and Tunisia) who had previously supplied information to ICMART did not while two other countries (Albania and Turkey) provided information. Croatia, Bolivia, Dominican Republic and Tunisia are continuing to offer ART services as well as many countries in East Asia, such as China and Thailand and sub-Saharan Africa, such as South Africa. Notably, the new South African Register of Assisted Reproductive Techniques was established in South Africa in 2009 and was based on the Latin American Network for Reproductive Medicine (REDLARA) programme. Preliminary work continues with other countries regarding establishment of national registers.

A second crude population measure of availability is the number of ART cycles per million population. This measure is inherently unstable, affected by a country's government policy, regulation, funding and the number of service providers, and has continued to fluctuate with each ICMART report. Interpretation of this measure needs to be contextualized to the local legislative frameworks that countries operate under for the practice of ART. Notably, there is enormous variability internationally with the majority of countries having either mandatory governmental regulations or voluntary guidelines promulgated by professional societies, the latter often having significant involvement in the regulation and licensing of ART clinics. In contrast, in 2004 Canada,

Finland and a number of countries from South America did not have guidelines or regulations in place (IFFS, 2004). In 2004, availability ranged from <100 cycles per million population in several Latin American countries to a pro-natalist high of 3844 cycles per million population in Israel: the latter reflects both the policy framework and the availability of public or third-party payment for ART cycles. In 2004, Israel had a policy of full financial coverage for ART (for 2 children), while Australia (1854 cycles per million population) had a mixed model of partial public sector, private health insurance coverage with a varying amount of patient's out of pocket payments. In contrast, the USA and Canada had partial coverage from private health insurance (498 per million) and no coverage (334 per million) and this is reflected in their level of availability (IFFS, 2004). These proxy measures do not replace the need for better information on the proportion of women/couples with infertility accessing ART treatment, as well as an internationally accepted measure of cost and affordability of ART treatment.

Practice change

The trend of an increasing proportion of ICSI continued in 2004 with 60.6% of all cycles being ICSI compared with 56.6% in 2002 and 47.6% in 2000. This trend in the increase of ICSI versus conventional fertilization was seen across all regions. Notably, four countries (Saudi Arabia, Jordan, Turkey and Egypt) reported that 98% or more fresh non-donor aspirations were ICSI. In contrast, only three countries (Russia, Ukraine and Guatemala) reported <30% of fresh non-donor aspirations were ICSI. At a regional level the use of ICSI varied from

60% in Europe to 76% in Latin America. This provides confirmation of the adoption of ICSI as the preferred fertilization practice for ART internationally. This practice change is evidence based for male factor and for combined male/female factor infertility but may require further justification for other causes of infertility (Nangia et al., 2011; Halliday, 2012). There is a lack of international agreement of the overall benefit of using ICSI where conventional fertilization traditionally would have been the first-line management.

A number of studies report differential perinatal risks associated with the use of either IVF or ICSI (Bonduelle et al., 2002; Lie et al., 2005; Al-Fifi et al., 2009; Davies et al., 2012) while others have found no marked difference (Källén et al., 2005, 2010; Romundstad et al., 2008). The development of additional data items on the indication for ICSI or IVF and origin of sperm would be a first step in monitoring this change in practice and allow evaluation of its impact on pregnancy and perinatal outcomes. Additionally, gamete intra-Fallopian transfer (GIFT) is no longer usual practice and is no longer available or monitored in the majority of countries and its exclusion from future world reports should be considered.

Safety and quality

The number of embryos transferred per ART cycle varied among countries. The average number of embryos transferred overall has decreased from 2.47 in 2002 to 2.35 in 2004 reflecting the five percentage point increase in single and double embryo transfers from 67.6% in 2002 to 73.2% in 2004. Positively, triple and quadruple embryo transfers decreased between 2002 and 2004 from 28.6 to 25.1% and 13.7 to 11.6%, respectively, and this has contributed to the decline in the trend of multiple deliveries following ART. However, this practice was not uniform with only the Australia and New Zealand region reporting an overall proportion of <5% for embryo transfers ≥ 3 . Twelve countries, primarily from Europe, reported no embryo transfers ≥ 4 in contrast to 15 countries who reported 20% or more embryo transfers ≥ 4 , peaking at 54%. Taiwan had three quarters of its embryo transfers ≥ 3 and reported 35.6% of deliveries were preterm with a perinatal mortality of 45.0 per 1000 births for fresh non-donor cycles. In contrast, New Zealand had only 3.8% embryo transfers ≥ 3 and reported fewer adverse perinatal outcomes with 18.9% of deliveries preterm and a perinatal mortality of 8.1 per 1000 births for fresh non-donor cycles. Comparatively, three countries (Sweden, Finland and Norway) reported <1% of triple embryo transfers versus 30 countries who reported 20% or more of triple embryo transfers. The variability in practice demonstrated by these findings continues to provide stark evidence that the most modifiable, preventable risk factor to prevent multiple pregnancy and its known sequelae is the number of embryos transferred per procedure.

The European Perinatal Health Report used data from 2004 for all births from 25 European countries belonging to the European Union in addition to Norway (EURO-PERISTAT, 2008). In these European countries, the multiple birth rate (per 1000 women giving birth) for twins ranged from 11 to 23 and for triplets from 0.1 to 1.6 (EURO-PERISTAT, 2008). Comparatively, for women giving birth following ART, the estimated multiple birth rate (per 1000 women giving birth after ART) for twins ranged from 178 in the Australia and New Zealand region, to 217 for Europe, to 374 for Latin America and for

triplets from 4 in the Australia and New Zealand region, to 10 in Europe and to 13 for Latin America. Notably, the proportion of higher order multiples has markedly declined since 1998 but major differences persist among regions with only selected Nordic countries and Australia and New Zealand approaching spontaneous conception population rates of higher order multiples of <1 per 1000 women giving birth (IWGROAR, 2001; Adamson et al., 2006; ICMART, 2009; Nygren et al., 2011).

Effectiveness

Most change in practice was to SET with the mean percentage increasing by almost four percentage points to 16.3%. This reflects the change in practice to SET for a number of countries, predominantly from Europe. Three European countries reported SET in over 45% of cycles: Sweden 67.4% (increased from 30.6% in 2002), Belgium 48.9% (increased from 16.5% in 2002) and Finland 47.0% (increased from 38.7% in 2002). In parallel, the overall proportion of FET cycles increased to 31%. This seven percentage point increase in FET cycles would have likely impacted the cumulative PR with an overall lower pregnancy (24.1) and DR (16.6) than for fresh transfer cycles. Interestingly, the DR for fresh IVF and ICSI combined fell three percentage points to 20.4%, while the cumulative DR (fresh plus frozen cycles) decreased two percentage points to 24.3%.

Effectiveness remains difficult to measure using cycle rather than women-based data because cumulative PRs cannot be calculated directly but can only be indirectly estimated. The measure of effectiveness is further limited by the incomplete data on access and outcomes of ART, and standard populations to compare ART with spontaneously conceived infants. At an international level, this type of detail is not feasible or warranted. Instead, record linkage at a country level with perinatal registers has been used successfully to measure effectiveness and to demonstrate improving neonatal outcomes for ART babies when compared with spontaneously conceived babies (Romundstad et al., 2008; Källén et al., 2010). Higher incidences of congenital anomalies and of both autosomal and sex-chromosome abnormalities specifically have been reported in both IVF and ICSI compared with spontaneously conceived infants (Bonduelle et al., 2002; Al-Fifi et al. 2009; Finnström et al., 2011; Davies et al., 2012). The variable quality and limited international data for congenital anomalies limits monitoring of the short- and medium-term outcomes of babies and evaluation of the risks of new technology and changes in practice.

Limitations

The quality and completeness of data reflect local data collection practice. This varies by individual country and region and is dependent upon the local regulatory environment and whether data supply to the national or regional registries is voluntary or mandatory. Although many countries submitted incomplete data, the major outcomes (procedures, pregnancies, deliveries and babies) are largely comparable across registries. The promotion of data standards and common terminology internationally has strengthened since 2002 with the development of the original and then revised ICMART glossaries (Vayena et al., 2002; Zegers-Hochschild et al., 2006a,b; Zegers-Hochschild et al., 2009a,b); and more recently with the publication of the ICMART toolkit which is designed to support data collection practice

for countries setting up registries to monitor ART. However, there may still be discrepancies in the use of the ICMART glossary and the data available in countries and these data need to be interpreted with caution.

In 2004, one-fifth of the clinics in participating countries did not report information on ART treatment and outcomes to their national and/or regional registries. This may reflect the local regulatory environment for ART practice including requirements for national reporting. Critically, factors such as whether the collection is mandatory or voluntary, has leadership and support from the country's leading professional fertility organization, and its funding model, e.g. government, patient or private sector funded, underpin the sustainability of the collection and quality of monitoring at the country level. The value of the world report is its capacity to benchmark practice internationally; the limitation is that this benchmarking is only as valid as the data supplied. The most significant gaps in the data remain a number of populous countries, including China, Pakistan, Bangladesh, Indonesia, Philippines and regional sub-Saharan Africa, which do not have registries.

Conclusion

In conclusion, this world report has shown a continued increase in the number of reporting clinics and ART treatment cycles worldwide. However, there remains significant variability in ART practice and outcomes. Of note is the continuing rise in ICSI worldwide and the slow but steady adoption SET as the first-line management for selected women/couples. These changes in practice are already differentially impacting the multiple birth rate and perinatal outcomes of countries, with Australia and New Zealand, Europe and North America continuing to reduce the proportion of multiple births, particularly higher order multiple births, in contrast to increases in Asia and the Middle East.

List of contributors

Australian and New Zealand Assisted Reproduction Database (ANZARD), Fertility Society of Australia, European IVF Monitoring (EIM) Consortium, Japan Society of Obstetrics and Gynecology, Latin American Network for Reproductive Medicine (REDLARA), Society for Assisted Reproductive Technology (SART)/Centers for Disease Control (CDC), Middle East IVF registry and all of the participating individual countries.

Supplementary data

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

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Authors' roles

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

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Conflict of interest

All authors have no conflict of interest in relation to this work. There is a financial relationship between the University of New South Wales and the Fertility Society of Australia. The Fertility Society of Australia funds the Perinatal and Reproductive Epidemiology Research Unit to manage ANZARD and conduct national reporting of ART in Australia and New Zealand. Elizabeth A. Sullivan is Director, Perinatal and Reproductive Epidemiology Research Unit, University of New South Wales. The Fertility Society of Australia did not provide research funding for the study. We declare no support from any organizations for the submitted work, no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years and no other relationships or activities that could appear to have influenced the submitted work.

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