Human Reproduction, Vol.35, No.8, pp. 1900–1913, 2020
Advance Access Publication on July 23, 2020 doi:10.1093/humrep/deaa090

human reproduction

ORIGINAL ARTICLE *Reproductive epidemiology*

International Committee for Monitoring Assisted Reproductive Technologies world report: assisted reproductive technology 2012†

Jacques de Mouzon[1,*], Georgina M. Chambers[2], Fernando Zegers-Hochschild[3], Ragaa Mansour[4], Osamu Ishihara[5], Manish Banker[6], Silke Dyer[7,8], Markus Kupka[9], and G. David Adamson[10,11,12]

[1]Epidémiology, Research and Development, Paris, France [2]National Perinatal Epidemiology and Statistics Unit, Centre for Big Data Research in Health, School of Women's and Children's Health, University of New South Wales, Sydney, Australia [3]Clinica las Condes and Program of Ethics and Public Policies in Human Reproduction, University Diego Portales, Santiago, Chile [4]Egyptian IVF-ET Center, Cairo, Egypt [5]Department of Obstetrics and Gynaecology, Saitama Medical University, Moroyama, Japan [6]Nova IVI Fertility, India [7]Department of Obstetrics & Gynaecology, Groote Schuur Hospital, South Africa [8]Faculty of Health Sciences, University of Cape Town, South Africa [9]Fertility Centre, Gynaecologikum Hamburg, Germany [10]Equal3 Fertility, Cupertino, CA, USA [11]Stanford University School of Medicine, Palo Alto, CA, USA [12]University of California School of Medicine, San Francisco, CA, USA

*Correspondence address: Epidémiology, Research and Development, 15 rue Guilleminot, 75014 Paris, France. Tel: ±33 6 62 06 22 74; E-mail: jacques.de.mouzon@gmail.com

Submitted on March 11, 2020; editorial decision on April 2, 2020

STUDY QUESTION: What was the utilization, effectiveness and safety of practices in ART globally in 2012 and what global trends could be observed?

SUMMARY ANSWER: The total number of ART cycles increased by almost 20% since 2011 and the main trends were an increase in frozen embryo transfers (FET), oocyte donation, preimplantation genetic testing and single embryo transfers (SET), whereas pregnancy and delivery rates (PR, DR) remained stable, and multiple deliveries decreased.

WHAT IS KNOWN ALREADY: ART is widely practiced throughout the world, but continues to be characterized by significant disparities in utilization, availability, practice, effectiveness and safety. The International Committee for Monitoring Assisted Reproductive Technologies (ICMART) annual world report provides a major tool for tracking trends in ART treatment for over 25 years and gives important data to ART professionals, public health authorities, patients and the general public.

STUDY DESIGN, SIZE, DURATION: A retrospective, cross-sectional survey on the utilization, effectiveness and safety of ART procedures performed globally during 2012 was carried out.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Sixty-nine countries and 2600 ART clinics submitted data on ART cycles performed during the year 2012, and their pregnancy outcome, through national and regional ART registries. ART cycles and outcomes are described at country, regional and global levels. Aggregate country data were processed and analyzed based on methods developed by ICMART.

MAIN RESULTS AND ROLE OF CHANCE: A total of 1 149 817 ART cycles were reported for the treatment year 2012. After imputing data for missing values and non-reporting clinics in reporting countries, 1 948 898 cycles (an increase of 18.6% from 2011) resulted in >465 286 babies (+17.9%) in reporting countries. China did not report and is not included in this estimate. The best estimate of global utilization including China is ~2.8 million cycles and 0.9 million babies. From 2011 to 2012, the number of reported aspirations and FET cycles increased by 6.9% and 16.0%, respectively. The proportion of women aged 40 years or older undergoing non-donor ART increased from 24.0% in 2011 to 25.2% in 2012. ICSI, as a percentage of non-donor aspiration cycles, increased from 66.5% in 2011 to 68.9% in 2012. The IVF/ICSI combined delivery rates per fresh aspiration and FET cycles were 19.8% and 22.1%, respectively. In fresh non-donor cycles, SET increased from 31.4% in 2011 to 33.7% in 2012, while the average number of transferred embryos decreased from 1.91 to

†This manuscript has not been externally peer reviewed.

1.88, respectively—but with wide country variation. The rates of twin deliveries following fresh non-donor transfers decreased from 19.6% in 2011 to 18.0% in 2012, and the triplet rate decreased from 0.9% to 0.8%. In FET non-donor cycles, SET was 54.8%, with an average of 1.54 embryos transferred and twin and triplet rates of 11.1% and 0.4%, respectively. The cumulative DR per aspiration increased from 28.0% in 2011 to 28.9% in 2012. The overall perinatal mortality rate per 1000 births was 21.4 following fresh IVF/ICSI and 15.9 per 1000 following FET.

LIMITATIONS, REASONS FOR CAUTION: The data presented depend on the quality and completeness of data submitted by individual countries to ICMART directly or through regional registries. This report covers approximately two-thirds of world ART activity, with a major missing country, China. Continued efforts to improve the quality and consistency of reporting ART data by registries are still needed, including the use of internationally agreed standard definitions (International Glossary of Infertility and Fertility Care).

WIDER IMPLICATIONS OF THE FINDINGS: The ICMART world reports provide the most comprehensive global statistical census and review of ART utilization, effectiveness, safety and quality. While ART treatment continues to increase globally, the wide disparities in access to treatment, procedures performed and embryo transfer practices warrant attention by clinicians and policy makers. With the increasing practice of SET and of freeze all and resulting increased proportion of FET cycles, it is clear that PR and DR per aspiration in fresh cycles do not give an overall accurate estimation of ART efficiency. It is time to use cumulative live birth rate per aspiration, combining the outcomes of FET cycles with the associated fresh cycle from which the embryos were obtained, and to obtain global consensus on this approach.

STUDY FUNDING/COMPETING INTEREST(S): The authors declare no conflict of interest and no specific support from any organizations in relation to this manuscript. ICMART gratefully acknowledges financial support from the following organizations: American Society for Reproductive Medicine; European Society for Human Reproduction and Embryology; Fertility Society of Australia; Japan Society for Reproductive Medicine; Japan Society of Fertilization and Implantation; Red Latinoamericana de Reproduccion Asistida; Society for Assisted Reproductive Technology; Ferring Pharmaceuticals and Abbott (both providing ICMART unrestricted grants unrelated to world reports).

TRIAL REGISTRATION NUMBER: NA.

Key words: assisted reproductive technology / registry / ICMART / IVF/ICSI outcome / multiple births / frozen embryo transfer / cumulative live birth rate

Introduction

This is the 17th world report on ART, and the 12th produced by the International Committee for Monitoring Assisted Reproductive Technologies (ICMART). ICMART has generated annual world reports since 1989 (Lancaster, 1996; Adamson *et al.*, 2018). The current report presents data on ART performed in 2012, including country, region and global estimates of ART utilization, effectiveness and safety. Information on global ART practice, IUI and pregnancy and neonatal outcomes is also included.

Materials and methods

The process of data collection and analysis has been described in detail (Zegers-Hochschild *et al.*, 2014). Briefly, data of ART treatments conducted during 2012 were collected from regional or national ART registries or directly from individual clinics in a small number of countries where registries do not exist. Standardized forms, available in the ICMART Tool Box for ART (www.icmartivf.org), were used to collect information on the number of ART clinics, and on procedure- and outcome-related information pertaining to IVF, ICSI, oocyte donation (OD), frozen embryo transfer (FET), preimplantation genetic testing (PGT) and IUI (with husband/partner and with donor sperm). Stratification by woman's age and number of transferred embryos was also provided. All data were provided at an aggregated country level and did not include any individual patient information. Collected data were transferred by ICMART to the Clinical Research Center at Uppsala University, Sweden, for further processing and analysis. Data were checked for inconsistencies, and a statistical report with tables and graphs was generated using SAS statistical software package (version 9.4) (Cary, NC, USA) and R (version 3.1.1).

The terminology used in this report is based on the 2009 ICMART and World Health Organization Revised Glossary on ART (Zegers-Hochschild *et al.*, 2009) because this was the Glossary in use in 2012. Future reports will refer to the updated International Glossary on Infertility and Fertility Care, led by ICMART in Partnership with the American Society for Reproductive Medicine, ESHRE, International Federation of Fertility Societies, March of Dimes, American Fertility Society, Groupe interafricain d'étude, de recherche et d'application sur la fertilité, Asia Pacific Initiative on Reproduction, Middle East Fertility Society, Red Latinoamericana de Reproduccion Asistida and International Federation of Gynecology and Obstetrics (Zegers-Hochschild *et al.*, 2019). Data are presented by country, region and globally. The Middle East region is separated for the purpose of data presentation into 'Middle East' and 'Middle East (Israel)'. The proportion of cycles using ICSI for fertilization included data only from countries reporting data for both conventional IVF and ICSI.

Most of presented data were directly reported by countries and registries. However, in a limited number of countries, some missing fields needed to be estimated from other complementary fields in order to obtain a more realistic perspective. All imputations are described in notes beneath the relevant tables.

No Institutional Review Board approval was requested by ICMART since relevant approvals were obtained at country level.

Results

Key findings are summarized in Tables I and II and Figs 1 and 2. Additional results are available online (Supplementary Tables SI–SXVI and Figs S1–S8).

ART utilization

Sixty-nine countries submitted data for treatments performed in 2012 (Table I), compared to 65 in 2011 and 60 countries in 2010. More specifically, compared to 2011, in 2012 there were seven new countries (Ghana, Nigeria, Albania, Croatia, Bolivia, Dominican Republic and Saudi Arabia) and three missing countries (Ivory Coast, Taiwan and Cyprus). The number of clinics participating was 2600 and the global participation rate (calculated as all participating clinics divided by total number of clinics in reporting countries) was 72.6% (Supplementary Table SI). Of the countries reporting, participation rates >80% were recorded in 39 countries and, globally, in four regions (Australia/New Zealand; Europe; Middle East (Israel); North America). Thirty-five countries and three regions (Australia/New Zealand; Middle East (Israel); North America) reached participation rates ≥95% (Supplementary Table SI). Europe had the highest number of participating clinics globally (1111 representing 42.7% of all participating clinics), followed by Asia (31.7%) and North America (15.8%). At a country level, Japan accounted for 22.7% of all participating clinics followed by the USA (14.6%). In total, 24.6% of clinics performed fewer than 100 cycles (Supplementary Table SI), mostly in Asia, whereas 13.7% of clinics performed more than 1000 cycles, 45.8% of clinics in Israel and 45.7% in Australia/New Zealand.

Based on both reported and estimated numbers for the countries providing data, a total of >1 948 898 ART cycles were initiated in 2012 (Table II), 304 986 more than in 2011 (+18.6%). ART utilization, expressed as the global number of estimated initiated cycles per million population increased in 2012 (520) compared to 2011 (477) and 2010 (474) (Dyer et al., 2016; Adamson et al., 2018). It ranged from 11 cycles per million inhabitants in Mali and Dominican Republic to 5218 in Israel (Table II). Sub-Saharan Africa reported the lowest regional utilization (73), followed by Latin America (179), Asia (329), the Middle East (510), North America (520), Europe (1062) and Australia/New Zealand (2567). Globally, the number of reported fresh non-donor aspirations increased by 6.9% from 818 444 in 2011 to 874 861 in 2012 (Table I). Japan conducted 22.9% of all aspirations in 2012, followed by the USA (9.0%) and France (6.9%). The reported number of non-donor FET cycles was 344 396, 16.0% higher than in 2011. Japan and the USA, followed by France, conducted the largest number of FET cycles (Table I). The percentage of FET among the total number of fresh and frozen transfers increased from 31.2% in 2011 to 33.6% in 2012 (Supplementary Table SII). The percentage of cycles fertilized by ICSI increased, from 66.5% in 2011 to 68.9% in 2012 (Table I), but there is no real trend since 2007. Moreover, the use of ICSI and FET varied considerably by country and region.

Finally, 18 700 PGT cycles and 71 347 OD transfers cycles were reported in 2012, an increase of 35.1% and 14.0%, respectively, compared to 2011.

In total, 1 117 333 embryo transfers were reported (682 890 for fresh IVF/ICSI, 344 396 for non-donor FET, 71 347 for OD and 11 723 for PGT) (Table I and Supplementary Tables SIII and SXIII).

ART effectiveness

The global pregnancy rate (PR) and delivery rate (DR) per aspiration for fresh non-donor IVF was 24.4% and 17.6%, respectively (Supplementary Table SII), close to the rates observed in 2011 (24.0% and 17.6%, respectively). For fresh ICSI, PR and DR were slightly decreased in 2012 (24.8% and 18.0% versus 26.2% and 19.0% in 2011, respectively). For FET, PR and DR per transfer were slightly increased in 2012 (31.5% and 22.1% versus 30.1% and 21.4%, respectively).

Supplementary Fig. S1 shows the overall DR per aspiration for countries reporting it and Fig. 2 shows the same, including six countries in which DR was estimated because this was not reported. Those figures show very large variations, from <10% to almost 60%, which would require a large specific study for a scientific explanation.

The 2012 estimated cumulative DR per aspiration resulting from fresh and frozen transfers after IVF/ICSI was 28.9%, slightly higher than in 2011 (28.0%), and ranging from 9.2% in Croatia to 50.1% in USA (Table II).

In 2012, the rate of early pregnancy loss was 19.5% following fresh embryo transfer, compared to 23.7% following FET. Both rates showed wide regional and national variation (Supplementary Table SV).

Globally, participating clinics reported 322 800 babies born—an increase of 8.7% over 2011 (297 026) (Table II). Estimations that include non-reporting clinics from participating countries, thus excluding China, suggest an estimated total of 465 286 babies were born from ART performed in 2012—an increase of 17.9% (394 662) compared to 2011. The best estimate for China in 2012, according to the Ministry of Health 2013 statistics (Wahlberg, 2016), gives 487 000 ART cycles, which resulted in ~116 000 babies. The estimated total number of babies born in 2012 globally then, including China, would be ~581 000 babies.

The proportion of women aged 40 years or older who underwent aspiration in IVF/ICSI cycles increased from 23.2% in 2010 and 24.0% in 2011, to 25.2% in 2012. Africa had the lowest proportion at 14.3% and Asia the highest at 37.6% (Supplementary Table SVI). The PR and DR in this age group decreased from 10.9% and 6.1% in 2011 to 9.9% and 5.4%, respectively, in 2012 (Supplementary Table SVII; Fig. 1). For non-donor FET cycles, the proportion of women aged ≥40 years increased from 18.7% in 2010 and 20.1% in 2011 to 21.6% in 2012. PR and DR for those women increased from 21.4% and 12.4%, respectively, in 2011, to 24.8% and 14.4%, respectively, in 2012 (Supplementary Table SVIII).

ART safety

The average number of embryos transferred in fresh non-donor IVF/ICSI cycles in 2012 was 1.88 (Supplementary Table SIII), slightly lower than the number observed in 2011 (1.91). In those cycles, the global rate of single embryo transfer (SET) increased from 31.4% in 2011 to 33.7% in 2012, while the transfer of three embryos dropped from 15.5% to 14.8%; and that of four or more embryos decreased from 3.3% to 3.1% (Supplementary Table SIII). The highest regional rate of SET was reported by Australia/New Zealand (71.3%) and the lowest by Africa (13.9%) and Latin America (15.5%), those regions showing the highest proportion for the transfer of three or more embryos. Considering individual countries, SET percentage was at more than 70% in only four countries (Japan, Australia, Finland and Sweden).

Table I Number of procedures by type of procedure for year 2012.

	Non-donation cycles[2]								
	Fresh cycles[3]					FET cycles[3]			
	Initiated cycles	Aspiration cycles				Thaw cycles	Transfer cycles	PGT cycles[2]	Oocyte donation transfer cycles[2]
Country	Total	Total	IVF	ICSI	GIFT	Total	Total	Total	Total
Benin	117	101	9	92	0	0	0	NA	NA
Cameroon	412	406	204	202	NA	NA	NA	NA	18
Egypt	9715	7848	0	7848	0	2089	1819	19	NA
Ghana	NA	27	18	9	0	0	0	NA	17
Mali	NA	154	53	101	0	23	23	NA	NA
Morocco	NA	559	126	433	NA	NA	NA	NA	NA
Nigeria	NA	1393	272	1121	0	NA	54	31	435
South Africa	NA	3417	994	2423	NA	562	541	NA	876
Togo	119	73	20	53	0	5	5	NA	46
Tunisia	NA	3959	378	3581	0	NA	757	NA	NA
India[1]	NA	23 881	NA	NA	NA	NA	4959	NA	6631
Indonesia	NA	3154	519	2635	NA	427	427	NA	NA
Japan	205 101	200 360	77 370	122 962	28	117 946	116 023	NA	NA
South Korea	NA	32 260	10 980	21 280	NA	NA	10 441	335	480
Australia[1]	37 728	34 418	NA	NA	NA	21 278	20 181	2260	1513
New Zealand[1]	3120	2874	NA	NA	NA	1674	1572	38	177
Albania	216	204	0	204	NA	44	39	0	23
Austria	7196	5839	920	4919	NA	983	955	0	0
Belarus	1940	1888	1229	659	NA	127	107	23	8
Belgium	NA	17 607	3996	13 611	NA	9277	7996	647	1005
Bulgaria	6312	5799	593	5206	NA	587	573	26	227
Croatia	NA	4547	1811	2736	NA	NA	131	0	0
Czech Republic	12 298	11 886	1739	10 147	NA	NA	5789	754	3875
Denmark	11 707	11 248	5970	5278	NA	3084	2566	134	209
Estonia	1806	1794	606	1188	NA	761	634	0	148
Finland	4785	4618	2475	2143	NA	NA	3319	18	702
France	NA	60 074	20 995	39 079	NA	23 841	21 296	658	954
Germany	NA	51 958	12 047	39 911	NA	19 293	18 466	0	0
Greece	NA	6672	1329	5343	NA	NA	1079	291	617
Hungary	NA	4422	920	3502	NA	401	398	7	44
Iceland	NA	405	199	206	NA	196	186	0	132
Ireland	2127	1826	904	922	NA	716	670	0	0
Italy	55 495	50 087	7397	42 690	NA	6513	5496	0	0
Kazakhstan	2263	2247	1188	1059	NA	465	436	57	358
Lithuania	NA	149	103	46	NA	NA	24	0	0
Moldova	1130	1096	429	667	NA	43	43	0	14
Montenegro	523	506	2	504	NA	17	14	0	0
Netherlands	16 748	15 261	7139	8122	NA	NA	8063	362	0
Norway	6320	6056	3131	2925	NA	2655	2208	0	0
Poland	10 714	10 467	450	10 017	NA	4969	4736	244	713
Portugal	5803	5223	1838	3385	NA	1135	1011	93	403
Romania	1574	1535	627	908	NA	338	333	0	44
Russia	47 718	46 206	21 144	25 062	NA	10 321	9880	760	3521
Serbia	2064	1896	510	1386	NA	NA	NA	0	0

(continued)

Table I Continued

Country	Non-donation cycles[2]								
	Fresh cycles[3]					FET cycles[3]			
	Initiated cycles	Aspiration cycles				Thaw cycles	Transfer cycles	PGT cycles[2]	Oocyte donation transfer cycles[2]
	Total	Total	IVF	ICSI	GIFT	Total	Total	Total	Total
Slovenia	3745	3509	1231	2278	NA	817	801	31	2
Spain	35 430	31 203	3277	27 926	NA	11 736	10 744	3161	16 710
Sweden	11 875	11 132	5437	5695	NA	5809	5244	191	405
Switzerland	5358	4836	710	4126	NA	4188	3697	0	0
Ukraine	8796	8499	3383	5116	NA	2258	2173	132	1081
UK	45 653	43 152	18 853	24 299	NA	11 069	10 253	844	2410
Argentina	6461	6019	504	5515	NA	2043	1971	91	3048
Bolivia	NA	210	148	62	NA	16	14	1	157
Brazil	16 030	15 007	1070	13 937	NA	4150	3895	972	1776
Chile	1563	1452	131	1321	NA	503	470	50	323
Colombia	977	915	293	622	NA	193	165	7	390
Dominican Republic	NA	77	42	35	NA	3	3	0	32
Ecuador	608	540	216	324	NA	123	121	0	233
Guatemala	NA	100	38	62	NA	7	7	0	20
Mexico	3345	3239	1222	2017	NA	786	757	64	1677
Nicaragua	NA	87	46	41	NA	NA	NA	0	10
Panama	245	199	7	192	NA	77	72	14	60
Peru	1264	1173	298	875	NA	236	231	469	864
Uruguay	293	253	20	233	NA	61	56	0	83
Venezuela	585	553	369	184	NA	128	118	10	345
Lebanon	NA	948	3	945	0	NA	17	33	195
Saudi Arabia	1850	1670	0	1670	NA	NA	68	364	0
Israel[1]	30 100	NA	NA	NA	NA	9506	9044	NA	NA
Canada	16 140	15 046	4552	10 494	0	7415	7028	198	1360
USA	88 775	78 642	20 233	58 397	12	34 732	34 197	5311	16 976

Region	Non-donation cycles[2]								
	Fresh cycles[3]					FET cycles[3]			
	Initiated cycles	Aspiration cycles				Thaw cycles	Transfer cycles	PGT cycles[1]	OD transfer cycles[1]
	Total	Total	IVF	ICSI	GIFT	Total	Total	Total	Total
Africa	>10 363	17 937	2074	15 863	NA	>2679	>3199	>50	>1392
Asia	>205 101	259 655	>88 869	>14 6877	>28	>118 373	131 850	>335	>7111
Australia and New Zealand	40 848	37 292	NA	NA	NA	22 952	21 753	2298	1690
Europe	>309 596	433 847	132 582	301 265	NA	>121 643	>129 360	8433	33 605
Latin America	>31 371	29 824	4404	25 420	NA	>8326	>7880	1678	9018
Middle East	>1850	2618	3	2615	NA	NA	85	397	195
Middle East (Israel)	30 100	NA	NA	NA	NA	9506	9044	NA	NA
North America	104 915	93 688	24 785	68 891	12	42 147	41 225	5509	18 336
Total	>734 144	>874 861	>252 717	>560 931	>40	>325 626	>344 396	>18 700	>71 347

[1]Countries that did not separate ICSI and IVF.
[2]Reported in the registers.
[3]Excluding preimplantation genetic testing (PGT) and oocyte donation (OD) cycles.
NA, not available; FET, frozen embryo transfer; GIFT, gamete intra-Fallopian transfer.

Table II Reported data and ICMART estimations for year 2012.

Country	Fresh						FET	Fresh + FET			
	IVF and ICSI										
	Aspirations[1]	PR/Asp[2] (%)	DR/Asp[3] (%)	DR/Asp[4] Cumul. (%)	Babies[5]/Asp Fresh (%)	Babies[5]/Asp Cumul. (%)	Babies[5]/ FET (%)	Estimated[6] or reported overall total number of cycles	Availability[7] Cycles/million	Total[8,9] babies reported from participating clinics	Total[9,10] babies estimated from all clinics
Benin	101	36.6	28.7	28.7	NA	NA	NA	117	12	**35**	**35**
Cameroon	406	19.5	15.5	15.5	10.3	NA	NA	430	21	**76**	**76**
Egypt	7848	35.0	17.9	20.2	28.0	33.5	23.2	**177 345**	**2119**	2626	**39 390**
Ghana	27	69.2	61.5	59.3	92.6	96.2	NA	**748**	**30**	42	**714**
Mali	154	53.9	53.2	48.7	NA	NA	NA	**177**	**11**	NA	NA
Morocco	559	29.2	**21.1**	**21.1**	NA	NA	NA	**10 710**	**331**	**142**	**2556**
Nigeria	1393	29.7	**21.6**	**22.0**	18.7	NA	50.0	**12 902**	**76**	138	**887**
South Africa	3417	28.0	**20.3**	**23.6**	NA	NA	NA	**7812**	147	**974**	**1498**
Togo	73	21.4	18.6	17.8	20.5	21.4	NA	170	24	23	23
Tunisia	3959	33.9	29.8	33.8	34.3	39.0	24.4	**16 710**	**1557**	1543	**5143**
India	23 881	35.2	29.7	36.7	38.5	47.1	41.0	**134 108**	**111**	14 457	**52 004**
Indonesia	3154	33.8	NA	NA	NA	NA	NA	**3922**	**16**	NA	NA
Japan	200 332	10.6	7.2	18.3	5.1	29.4	25.9	323 047	2536	40 419	40 419
South Korea	32 260	31.3	12.2	16.9	NA	NA	NA	**74 698**	1488	**6679**	**10 809**
Australia	34 418	25.4	19.3	31.2	19.3	35.8	24.3	62 779	2852	12 280	12 280
New Zealand	2874	35.5	28.6	40.4	28.2	45.7	26.5	5009	1138	1283	1283
Albania	204	41.7	33.8	41.2	36.8	46.6	51.3	**1698**	**565**	106	**636**
Austria	5839	31.9	**23.2**	**25.3**	35.6	35.6	NA	8179	995	2078	2078
Belarus	1888	42.2	29.8	30.6	37.8	39.2	25.2	**2797**	**290**	750	**1000**
Belgium	17 607	26.2	19.0	27.6	22.0	32.5	23.0	**29 683**	**2844**	6134	6134
Bulgaria	5799	22.0	15.8	18.4	19.5	23.1	36.3	**30 992**	**4404**	1437	**6227**
Croatia	4547	25.2	9.2	9.5	9.5	10.4	29.8	**3190**	**712**	471	471
Czech Republic	11 886	31.1	22.9	32.7	26.6	40.3	28.1	23 014	2192	6367	6367
Denmark	11 248	25.1	22.4	26.8	25.8	30.8	22.2	15 134	2730	3564	3564
Estonia	1794	28.4	23.2	27.5	26.5	31.0	12.9	2715	2130	598	598
Finland	4618	27.3	21.5	34.4	23.2	36.8	19.0	8995	1709	1701	1701
France	60 074	24.0	19.4	24.6	22.6	28.5	16.6	**89 441**	**1363**	17 401	17 401
Germany	51 958	26.7	18.0	22.7	22.0	28.7	18.9	**75 793**	**932**	14 903	**15 134**
Greece	6672	32.3	16.9	19.7	20.8	26.3	34.0	**34 770**	**3229**	2107	**8007**
Hungary	4422	32.3	**23.5**	**25.5**	NA	NA	NA	**5162**	**518**	**1359**	**1359**
Iceland	405	24.2	19.0	25.9	20.0	27.2	15.6	**527**	**1683**	145	145

(continued)

Table II Continued

Country	Fresh						FET	Fresh + FET			
	IVF and ICSI										
	Aspirations[1]	PR/Asp[2] (%)	DR/Asp[3] (%)	DR/Asp[4] Cumul. (%)	Babies[5]/Asp Fresh (%)	Babies[5]/Asp Cumul. (%)	Babies[5]/ FET (%)	Estimated[6] or reported overall total number of cycles	Availability[7] Cycles/million	Total[8,9] babies reported from participating clinics	Total[9,10] babies estimated from all clinics
Ireland	1826	33.2	24.5	30.1	28.1	36.0	21.3	**4975**	**1054**	657	**1150**
Italy	50 087	22.1	14.2	15.8	17.4	19.4	18.3	62 008	1012	9710	9710
Kazakhstan	2247	39.6	26.4	31.1	31.2	36.7	28.7	**15 715**	**897**	981	**4905**
Lithuania	149	38.9	28.9	32.2	40.9	44.3	20.8	**460**	**130**	66	**165**
Moldova	1096	37.8	34.7	35.4	44.3	45.2	20.9	1187	325	504	504
Montenegro	506	29.4	24.9	25.5	32.8	33.4	21.4	**720**	**1095**	169	**225**
Netherlands	15 261	29.1	20.6	29.0	22.2	30.9	16.5	25 588	1529	4759	4759
Norway	6056	28.7	23.4	30.1	26.2	33.5	20.1	8975	1907	2027	2027
Poland	10 467	34.5	26.2	35.0	30.3	41.9	25.5	**17 144**	**446**	4734	**4877**
Portugal	5223	30.5	23.4	26.5	28.4	32.1	19.2	7434	690	1879	1879
Romania	1535	35.0	28.0	30.6	34.5	38.8	19.8	**4781**	**219**	617	**1508**
Russia	46 206	31.9	22.6	26.6	27.7	33.4	26.3	**78 183**	**549**	16 831	**21 115**
Serbia	1896	34.8	28.2	28.2	39.6	39.6	NA	**3612**	**496**	750	**1313**
Slovenia	3509	27.7	22.2	26.8	25.2	30.4	22.7	4595	2301	1072	1072
Spain	31 203	31.2	18.3	24.4	23.9	33.6	28.2	**117 463**	**2497**	16 899	**29 611**
Sweden	11 132	30.7	24.8	35.6	26.2	37.4	23.8	18 280	2008	4307	4307
Switzerland	4836	23.1	17.1	30.1	20.6	35.9	20.1	**9913**	**1251**	1736	**1803**
Ukraine	8499	39.1	29.9	36.3	37.2	46.1	34.7	**14 567**	**325**	4373	**5193**
UK	43 152	31.4	27.5	33.1	32.7	39.3	27.8	59 976	942	18 179	18 179
Argentina	6019	25.9	19.1	24.8	21.5	31.1	24.2	**14 437**	**342**	3018	**3742**
Bolivia	210	36.5	26.4	28.1	36.7	38.9	28.6	**389**	**38**	83	83
Brazil	15 007	31.1	25.4	27.9	26.1	40.6	31.0	**48 269**	**242**	6110	**12 863**
Chile	1452	35.9	27.7	33.3	30.4	45.2	31.7	**3049**	**179**	708	**885**
Colombia	915	34.5	26.8	29.0	31.6	37.6	24.2	**2422**	**54**	532	**822**
Dominican Republic	77	15.8	13.2	13.0	19.5	19.7	0.0	**115**	11	26	26
Ecuador	540	34.9	28.3	33.3	35.2	45.6	36.4	964	63	340	340
Guatemala	100	28.6	19.4	20.0	25.0	26.5	14.3	**254**	**18**	37	**74**
Mexico	3239	35.9	28.9	32.4	35.2	44.1	27.6	**14 789**	**129**	2251	**5669**
Nicaragua	87	42.5	35.6	35.6	50.6	50.6	NA	**101**	**18**	52	52
Panama	199	40.4	29.1	31.7	23.6	51.8	36.1	**2376**	**677**	102	**612**
Peru	1173	24.4	19.2	24.3	19.1	35.2	52.4	**5666**	**192**	975	**1950**
Uruguay	253	32.9	28.1	32.0	33.6	39.0	21.4	437	132	133	133
Venezuela	553	37.9	29.6	33.3	32.2	45.1	38.1	**3051**	**109**	441	**1260**

(continued)

Table II Continued

Country	Fresh						FET	Fresh + FET			
	IVF and ICSI										
	Aspirations[1]	PR/Asp[2] (%)	DR/Asp[3] (%)	DR/Asp[4] Cumul. (%)	Babies[5]/Asp Fresh (%)	Babies[5]/Asp Cumul. (%)	Babies[5]/ FET (%)	Estimated[6] or reported overall total number of cycles	Availability[7] Cycles/million	Total[8,9] babies reported from participating clinics	Total[9,10] babies estimated from all clinics
Lebanon	948	43.9	38.3	32.8	41.2	48.3	0.0	NA	NA	481	NA
Saudi Arabia	1670	33.0	29.7	27.0	32.0	39.5	54.4	**14 853**	510	634	**4121**
Israel	**28 259**	**26.6**	**19.3**	**24.4**	NA	NA	NA	39 606	5218	**8310**	**8310**
Canada	15 046	35.1	26.3	36.0	29.4	45.5	29.7	**25 898**	**755**	7067	**7288**
USA	78 630	41.6	33.5	50.1	42.9	63.3	46.8	**153 872**	490	61 412	**64 815**

Region	Fresh						FET	Fresh + FET			
	IVF and ICSI										
	Aspirations[1]	PR/Asp[2] (%)	DR/Asp[3] (%)	DR/Asp[4] Cumul. (%)	Babies[5]/Asp Fresh (%)	Babies[5]/Asp Cumul. (%)	Babies[5]/ FET (%)	Estimated[6] or reported overall total number of cycles	Availability[7] Cycles/million	Total[8,10] babies reported from participating clinics	Total[9,10] babies estimated from all clinics
Africa	17 937	32.6	21.7	24.4	28.6	35.4	24.1	227 121	531	>5599	>50 322
Asia	259 627	17.3	10.8	26.2	12.1	32.0	26.6	535 775	329	>61 555	>103 232
Australia and New Zealand	37 292	26.2	20.0	34.1	21.3	36.5	24.4	67 788	2567	13 563	13 563
Europe	433 847	28.3	20.7	25.9	24.7	31.4	22.2	787 666	1062	149 371	185 124
Latin America	29 824	30.9	24.5	31.8	30.2	39.0	29.6	96 319	179	14 808	28 511
Middle East (Saudi Arabia)	2618	36.9	32.8	33.8	41.0	42.7	43.5	14 853	510	1115	>4121
Middle East (Israel)	28 259	26.6	19.3	24.4	NA	NA	NA	39 606	5218	8310	8310
North America	93 676	40.6	32.4	48.2	41.1	60.5	43.8	179 770	755	68 479	72 103
Total	903 080	27.1	19.8	28.9	24.2	35.7	27.0	>1 948 898	520	>322 800	>465 286

[1–10]Imputed/estimated data are printed in bold.

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

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

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

[4]Imputed by summing the deliveries issued from fresh and FET cycles and by dividing this total by the number of aspirations.

[5]In countries where the sum of singleton, twins and triplets were 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.

[6]Initiated cycles overall countries estimation. Step 1: Reported cycles for countries reporting them, or estimation by applying their cancellation rate to the aspiration 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.

[7]Total estimated number of cycles in the country divided by its population in 2012 (CIA World Fact Book).

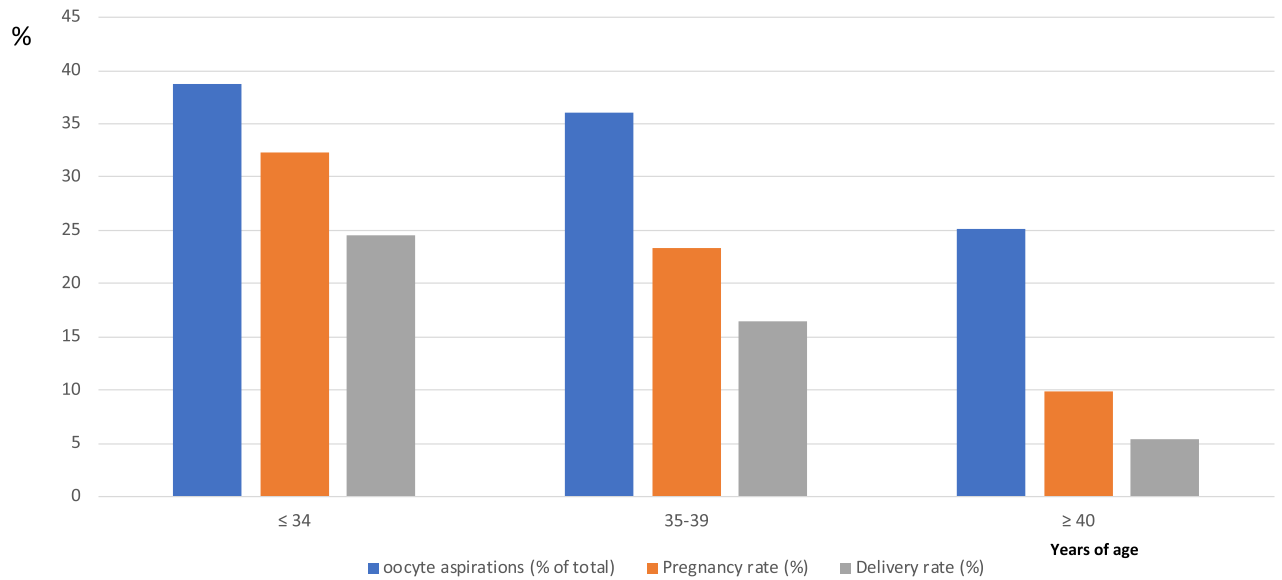
[8]Imputed by multiplying number of deliveries by the average number of babies per delivery category described in form 4.

[9]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.

[10]Total babies also include PGD and OD.

Asp, aspiration; PR, pregnancy rate; DR, delivery rate; Cumul, cumulative.

The total numbers and numbers by region were calculated only from the countries with complete data (e.g. both number of pregnancies and no. of oocyte aspirations).



	≤ 34	35-39	≥ 40
Oocyte aspirations (% of total)	38,8	36	25,2
Pregnancy rate (%)	32,3	23,3	9,9
Delivery rate (%)	24,5	16,4	5,4

Figure 1. Fresh non-donor IVF and ICSI: distribution of aspirations and outcomes by women's age for the year 2012.

For non-donor FET, the average number of embryos transferred decreased very slightly from 1.59 in 2011 to 1.54 in 2012 (Supplementary Table SIV). The rate of SET was 54.8% (51.6% in 2011), substantially higher than the SET rate in non-donor fresh ET cycles (33.7%). SET percentage was at more than 70% in only five countries (Japan, Australia, New Zealand, Finland and Sweden).

The 2012 PR and DR by number of transferred fresh and frozen embryos in non-donor IVF and ICSI cycles are reported in Supplementary Tables SIX and SX. The global DR for fresh non-donor SET was 21.2%, compared to 28.7% following double embryo transfer (DET). In non-donor FET cycles, the DR for SET was 23.4% compared to 24.0% following DET. The mean number of embryos transferred by country is shown in Supplementary Fig. S2 and varies from 1.24 to 3.19. The DR by country, ranked according to average number of transferred embryos, shows a significant increase in DR with increasing number transferred (Supplementary Fig. S3). Globally, the correlation between both is very significant ($r = 0.31$; $P < 0.01$) (Supplementary Fig. S4).

The triplet DR per delivery ranked by country in fresh non-donor IVF and ICSI cycles shows wide variations across countries (Supplementary Fig. S5). There is a clear relationship between the triplet DR and the mean number of transferred embryos by country (Supplementary Fig. S6), with a highly significant correlation (Supplementary Fig. S7) ($r = 0.62$; $P < 0.0001$). Highly significant correlations existed between the mean number of embryos transferred and the rate of multiple deliveries ($r = 0.86$; $P < 0.0001$), and the rate of prematurity ($r = 0.52$; $P < 0.01$) (Supplementary Fig. S8).

Globally, the multiple birth rate (MBR) following fresh non-donor ET was 18.0% for twins and 0.8% for triplets and higher (Supplementary Table SIII), lower than in 2011 (19.6% and 0.9%, respectively). Regional differences in rates of twin births ranged from 6.2% for Australia/New Zealand to 25.1% for North America. Regional rates of triplet and higher-order births ranged from 0.1% in Australia/New Zealand to 3.3% in Middle East (Supplementary Table SIII and Figs 5, 6 and 7). For FET non-donor cycles, twin and triplet and higher-order birth rates were 11.0% and 0.4%, respectively (Supplementary Table SIV), similar to rates in 2011.

The percentages of premature delivery and the perinatal mortality rates were lower for FET (17.8% and 15.9 per 1000, respectively) than for fresh embryo transfers (22.4% and 21.4 per 1000) (Supplementary Table SV), which is in great part, a reflection of the differences in the number of embryos transferred, and its impact on multiple births.

The frequency of severe ovarian hyperstimulation syndrome (associated with severe illness or hospitalization) in 2012 remained similar to 2011 (0.4% versus 0.5%, respectively, Supplementary Table SXI).

Special techniques (OD, PGT, IVM, surrogacy) and fetal reduction

Forty-nine countries provided data on OD (compared to 47 countries in 2011) (Supplementary Table SXII). Reporting clinics in 2012 performed 71 347 fresh and frozen transfers using donor oocytes—an increase of 14.0% from 2011. The USA recorded the highest number of

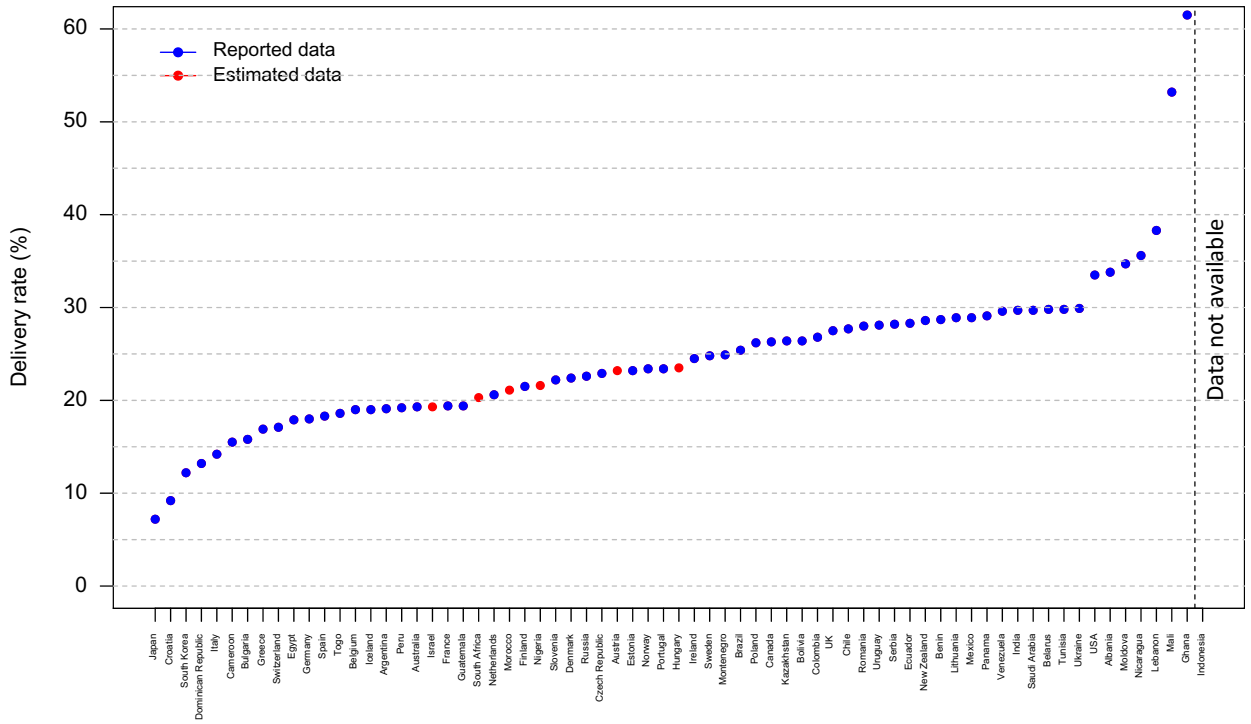


Figure 2. Fresh non-donor IVF and ICSI: reported and imputed delivery rate per aspiration by country for the year 2012.

OD transfer cycles (16 976), accounting for 23.8% of all OD transfer cycles globally. Transfers using donated oocytes constituted 6.5% of all embryo transfers, with wide variations: 13.4% in USA, 21.7% in Latin America and only 1.8% in Asia.

The average DR following OD including both fresh transfers and FET (63.3% and 36.7% of OD transfers, respectively) was 34.7% and resulted in a total of 31 319 babies born. The global multiple DR following oocyte recipient cycles was 27.6%—a slight decrease from 28.2% in 2011. Women aged ≥40 years old represented 65.9% of oocyte recipients (Supplementary Table SXII).

Only 37 of the 69 reporting countries (53.6%), provided information on PGT (Table I), a slight increase compared to 2011 (47.7%). The number of PGT cycles was 18 700 (+35.1%), resulting in 16 611 aspirations, 11 723 embryo transfers (Supplementary Table SXIII), 4827 clinical pregnancies and 3762 deliveries (41.2% and 22.7% per transfer, respectively).

Countries reporting IVM decreased from 24 in 2011 to 11 in 2012. Gestational carrier (surrogacy) was reported by six countries (same as in 2011) and 33 countries reported availability of fetal reduction compared to 27 in 2011 (Supplementary Table SXI).

Intrauterine insemination

Data on 207 837 IUI cycles with husband sperm (IUI-H, with or without ovarian stimulation) were provided by 33 countries (four fewer countries and 2.6% cycles more than in 2011), mostly from Europe (26 countries and 175 028 cycles). The global PR and DR per IUI-H cycle was 11.9% and 8.6%, respectively. The rate of multiple deliveries decreased from 10.6% (2011) to 9.6% (2012), with a wide range reported among countries (Supplementary Table SXIV). DR decreases with age to 4.1%/cycle for women aged 40 years or more.

Twenty-five countries reported 45 892 cycles of IUI with donor sperm (IUI-D), 10 fewer countries and 2.2% cycles more than in 2011. The resultant PR and DR per cycle were 16.6% and 12.0%, respectively, close to 2011 rates and higher than in IUI-H. The multiple DR was 7.7%, lower than that of IUI-H (Supplementary Table SXV).

Cross-border reproductive care

Cross-border reproductive care (CBRC) was reported by 19 countries (four more than in 2011: 12 from Europe, 2 from the Middle East, 4 from Africa, and 1 from the USA). The USA reported performing the largest number of the 12 447 non-donation and 2636 OD cycles (45.9% and 54.6%, respectively), followed by Spain. Among the 13 001 cycles for which the country of origin was reported, countries whose citizens crossed borders to obtain care came most often from Sweden (2854), followed by Norway (2085), Germany (1948), Italy (1426), Algeria (754), Canada (691), France (638), Japan (416), Mexico (369) and Russia (310) (Supplementary Table SXVI). The main reasons for CBRC were legal (36.5%), quality of care (35.5%) and ease of access (19.5%). Concerning OD, anonymous donation was reported in 2566 cycles and non-anonymous OD in 70 cycles.

Discussion

The ICMART World Collaborative Report on ART, 2012, is the 17th ICMART world report, all of them being the most comprehensive

global registry statistical reports on ART availability, practices and outcomes. Continual international monitoring of ART practice and outcomes is essential to quantify comparative utilization levels, monitor effectiveness of treatment and identify safety issues. In recognition of the right to universal access to reproductive health (Millennium Development Goal 5B, Sustainable Development Goal 3.7), the ICMART world reports are important documents at a global, regional and local level to inform policy development, clinical practice, education and advocacy. Besides journal publications, ICMART presents annually these data at major meetings globally and works with other professional organizations and as a non-state actor in official relations with the World Health Organization (WHO) to increase the impact of these data to improve access to treatment and quality of care of those with infertility.

This report summarizes global and regional results for treatments performed in 2012 and tabulates and graphically illustrates detailed outcomes in tables and figures. ICMART endeavors to standardize reporting that tracks trends over time.

After imputing missing clinic data, an estimated >1 948 898 cycles were initiated in 2012, an increase of 18.6% compared to 2011. This increase is not solely due to the new participating countries since, in countries reporting both in 2011 and 2012, 291 569 more cycles were reported in 2012 (+15.3%), this percentage decreasing to 7.0% after removing Egypt and Bulgaria where assumptions and approximations used for imputing estimates from actual reported data are doubtful. The increase is also partly explained by the increasing number of FET cycles (+16%). Treatments performed in 2012 resulted in the estimated births of >465 286 babies, an increase of 17.9% since 2011.

Utilization

Sixty-nine countries reported on utilization and outcomes of ART during 2012, representing more than 72% of ART clinics in these countries, with 30 countries having 100% participation, both percentages being similar to 2011. Three regions (Australia/New Zealand, North America and Europe) had high participation but participation was very low in the Middle East. Efforts of the African Network and Registry for Assisted Reproductive Technology (ANARA) are succeeding in increasing the uptake of data monitoring in Africa through a unifying regional registry (Dyer and Kruger, 2012).

Our results show substantial disparities in utilization not only between but also within regions; for example, in Europe, utilization rates vary from 130 to 4400 cycles per million. The overall global utilization was 520 cycles per million population, far from the demand estimation for ART treatment by ESHRE (ESHRE Capri Workshop Group, 2001), corrected by Collins in 2002 (Collins, 2002), of 3000 and 1500 cycles per million population, respectively: in the 2012 report, only 3 and 19 countries reached these levels, respectively, mostly in Israel, Europe, and Australia and New Zealand.

Access to ART treatment depends on socio-cultural and economic factors at the patient and country level with the cost of treatment borne by the patient playing a major role in who can afford treatment (Adamson, 2009; Dyer et al., 2013; Chambers et al., 2014). The disparities of utilization between countries are thus partly due to the level of public or third-party reimbursement, which may explain why the Nordic countries, Australia and Israel, which have high levels of support, have utilization rates three to four times higher than the USA and Canada. Low- and middle-income countries (LMIC) have substantially lower levels of utilization. Such inequity of access to reproductive health services across the globe does not adequately support the health and welfare of women and their families, and challenges the basic human right to create a family (Inhorn, 2009; Zegers-Hochschild et al., 2013). Finally, cultural determinants also play an important role for ART access (Praeg and Mills, 2017).

ART practice

The proportion of ICSI cycles appears to have stabilized at around two-thirds of aspiration cycles (Mansour et al., 2014) (Table I). The reasons for the large disparities observed across regions and countries are not fully understood, but are probably not related to significant differences in male infertility prevalence. Finally, the use of ICSI for non-male factor infertility has been questioned (Evers, 2016).

The proportion of FET cycles performed among non-donor cycles continued to increase, from 29.7% in 2010, to 31.2% in 2011 and 33.6% in 2012. This trend is probably related to the increasing practice of SET that leaves more good quality embryos/blastocysts to freeze and, also, to the increasing practice of vitrification for cryopreservation that is associated with a resultant better embryo survival and higher clinical pregnancy rate than that of the previously used slow-freezing method (AbdelHafez et al., 2010). An additional factor increasing FET is evidence that DR/transfer is at a similar level as that of fresh transfers, and neonatal outcomes are equivalent to fresh transfer, with some studies suggesting even better (Gu et al., 2019; Tannus et al., 2019). While further research is needed to confirm the optimal clinical roles of fresh and FET cycle transfers, FETs are likely to continue increasing.

The number of OD cycles continues to increase, representing 6.5% of all transfer cycles in this report (Table I). However, marked differences existed among regions and countries, mainly related to differences in national legislation and funding arrangements. For ethno-cultural reasons, OD is not available in Japan, most countries in the Middle East and several countries in Europe and North Africa. Moreover, in some countries, like France, the number of donors does not reach the level of the demand. Therefore, OD services often are provided as cross-border services. Other factors associated with CBRC include single-person treatment, non-traditional family treatment, PGT, gestational carrier (surrogacy), compensation for third-party reproduction, legal issues, financial issues and perceived quality of care (ESHRE Capri Workshop Group, 2013; Hughes and Adamson, 2015). ICMART continues to promote the importance of obtaining and reporting data on CBRC.

The increased number of PGT cycles reported compared to 2011 (+35.1%) likely reflects the uptake of PGT for aneuploidy (now renamed PGT-A) (Zegers et al., 2017). PGT-A is being increasingly used on the premise it can improve pregnancy and live birth rates, particularly in women of advanced maternal age and those with repeated implantation failure or miscarriage. Its optimal clinical roles, however, remain controversial, with few randomized controlled trials assessing cumulative live birth from intention to treat reported in a fertility clinic setting (Lee et al., 2015). However, some recent studies support its usefulness (Lee et al., 2019; Anderson et al., 2020). Continually advancing genetic diagnostic techniques for PGT-A, PGT-M (for monogenic/single gene defects) and PGT-SR (for chromosomal

structural rearrangements) will also likely result in increasing use of PGT (Lee *et al.*, 2015).

Effectiveness

Considerable variation in effectiveness of ART among countries must be noted. It likely reflects the great international heterogeneity in socioeconomics, demographics, strategies of health care, patients' selection criteria, clinical ART practice and other factors known and unknown. This variability exists between regions, between countries in the same region and between centers in the same country. For reasons related to the desire of getting quick information, results are often reported per aspiration (in fresh cycle) or per transfer (for FET and OD) cycle. However, with the increasing practice of SET and of freeze all and resulting increased proportion of FET cycles, it is clear that PR and DR per aspiration in fresh cycles do not give an overall accurate estimation of ART efficiency. It is time to use cumulative live birth rate (CLBR) per aspiration, combining the outcomes of FET cycles with the associated fresh cycle from which the embryos were obtained, and to obtain global consensus on this approach (Maheshwari *et al.*, 2015). It is currently not possible, though, to provide accurate cumulative data on a global basis since countries provide aggregated and not cycle-based data to ICMART. This is also the case for the European Register (De Geyter *et al.*, 2018), reporting on 35–40 national registries, many of them based on aggregated data. Among the regional registries, only Australia and New Zealand, based on two countries and Latin America, based on clinics' voluntary participation, are able to obtain cumulative data. The Society for Assisted Reproductive Technology in the USA is now also obtaining cumulative live birth data (www.sart.org). Despite this, cumulative data can be extrapolated, as described previously (Zegers *et al.*, 2017). Using this approach, the cumulative DR has been steadily increasing from 25.2% in 2006 (Mansour *et al.*, 2014;) to 28.9% in 2012. This has been paralleled by an increase in fresh and frozen SET (33.7% and 54.8% in 2012, respectively). The DR for fresh SET is now 21.2% and with FET SET it is 23.4%. Therefore, theoretically, if every patient had two good quality embryos the DR for fresh + frozen = 21.2% + (100 − 21.2) × 23.4% = 39.6%. Additional cryopreserved embryos could result in even higher CLBR. This compares exceptionally favorably with the DR of DET, which is 28.7%, but with a dramatically lower MBR. A variety of factors are likely responsible for this increasing cumulative DR, including the increased usage of SET and the introduction of vitrification as well as the empowerment of women and men on the risks and social difficulties that result from multiple births.

Difficulties resulting from lack of consensus regarding suitable numerators, denominators and time spans may be mitigated by implementation of definitions in the recently published International Glossary on Infertility and Fertility Care (Zegers *et al.*, 2017).

Safety

The proportion of women aged ≥ 40 years influences pregnancy, miscarriage and delivery rates and is increasing regularly every year, both for fresh and FET cycles. Women must be duly informed of the much lower PR and DR rates at this age to allow them to exercise an educated decision plus consent when deciding on the pros and cons of autologous reproduction at ≥40 years.

The most significant risk of ART treatment is multiple gestation with the associated risks to mother and babies, including preterm and extreme preterm birth (Practice Committee of the American Society for Reproductive Medicine, 2012; Sullivan *et al.*, 2012) (Supplementary Fig. S8). ART professionals increasingly consider this risk to be unacceptable. The average number of embryos transferred in fresh non-donor IVF and ICSI cycles has decreased every year with a concomitant rise in rates of SET (Dyer *et al.*, 2016). A similar trend was also observed for FET cycles. Given the high risk of twins following even DET, transferring more than one embryo should be reserved for poorer prognosis patients (Pandian *et al.*, 2013). The global MBR for fresh cycle transfer has decreased from 21.5% in 2010 to 20.5% in 2011 and 18.8% in 2012, and for FET cycles from 12.0% to 11.5% and 11.4%, respectively. However, there is considerable variation in the number of embryos transferred and, consequently, MBRs among countries and regions. In 2012, nine countries (Japan, Australia, New Zealand, Albania, Finland, Iceland, Netherlands, Sweden and Togo) reported fresh cycle MBRs of <10% (Supplementary Table SIII), and two countries more than in 2011.

The number of embryos transferred has been associated with out-of-pocket cost, less affordable treatment creating a financial incentive to transfer more embryos in the hope of getting pregnant with fewer cycles (Hamilton and McManus, 2012; Chambers *et al.*, 2014). Multiple pregnancy and births result in poorer outcomes and increased long-term costs for mothers and babies, commonly paid by society through government health plans in well-resourced countries (ESHRE Capri Workshop Group, 2013). In LMIC, affected patients and their households often bear the related financial burdens. Thus, supportive public or third-party insurance for ART treatment incentivizes SET and reduces societal costs associated with multiple pregnancies.

Limitations and strengths

The data presented depend on the quality and completeness of data submitted by individual countries either directly to ICMART or through regional registries. Although possible data errors and inconsistencies are queried with country/region representatives, further validation of the data is not possible since the ICMART registry is based on data summaries. The quality and completeness of the data in turn reflect local data collection practices, in particular: whether national data supply is mandatory or voluntary; and if national/regional registries are themselves based on summary or cycle-based data, with, or without, controls for validity. For example, among the 69 participating countries, the national register was compulsory only in 23 countries, mostly in Europe, and cycle-based in 33 countries, including 15 countries reporting to the Latin America register (Zegers-Hochschild *et al.*, 2019). Another limitation is the difficulty in reporting PR and DR per initiated cycle, which is the optimal denominator, yet was not reported by 21 countries. Among the 47 remaining countries, 16 countries had a cancellation rate of <5% and so likely under-reported. Furthermore, in several countries, including Africa, the follow up of ART pregnancies is low resulting in uncertainty regarding the ultimate effectiveness and safety of ART in these countries. Thus, data quality varies by country and region and needs continuous efforts to be improved. Finally, an important limitation of our report is low participation in some regions, including the Middle East, and the absence of data from China, which

represents a significant proportion of the missing data. Efforts are being made to develop contacts with China in order to solve this problem.

Nevertheless, this report covers approximately two-thirds of world ART activity. ICMART, as a non-state actor in official relations with the WHO, works at global, regional and national levels to facilitate data collection: to assist countries and regions to establish national and regional ART registries, such as in Africa (ANARA); to facilitate data collection through standard, consensus data definitions provided by the International Glossary on Infertility and Fertility Care (Zegers *et al.*, 2017); by providing a data collection 'tool kit', and now an electronic data collection platform (Dyer and Kruger, 2012).

Conclusion

For over a quarter century, the ICMART world reports have provided the most comprehensive global statistical census and review of ART utilization, effectiveness and safety. Increases in ART cycles started and the CLBR have continued, with wide disparities in access to treatment among regions and countries. Changes in ART technology and practices make analysis and interpretation of the data challenging. The continued trend to SET is to be encouraged. The MBR in most countries remains unacceptably high and should be the focus of continued policy and practice improvement. The growing body of evidence that affordable ART treatment reduces disparities in access to treatment while incentivizing safe embryo transfer practices calls for policies that support public or third-party funding. ICMART continues to support countries and regions in data collection and is making significant progress in improving the comprehensiveness, analysis and reporting of worldwide ART data.

Supplementary data

Supplementary data are available at *Human Reproduction* online.

Acknowledgements

The authors gratefully acknowledge all individuals as well as national and regional organizations and registries, including the African Network and Registry for Assisted Reproductive Technology (ANARA), American Society for Reproductive Medicine (ASRM), Australian and New Zealand Assisted Reproduction Database (ANZARD), European Society for Human Reproduction and Embryology (ESHRE), European IVF Monitoring Consortium (EIM), Fertility Society of Australia (FSA), Japan Society of Obstetrics and Gynecology (JSOG), Japan Society for Reproductive Medicine (JSRM), Latin American Network for Reproductive Medicine (REDLARA), Middle East Fertility Society (MEFS) and Society for Assisted Reproductive Technology (SART) for the submission of data to ICMART. We wish to thank N. Hadziosmanovic at Uppsala University for his statistical support.

Authors' roles

All authors contributed to study design, collection and interpretation of the data and the overall conduct of the study. J.d.M. prepared the manuscript and all authors were involved in the revision. The final manuscript and order of authorship has been approved by all authors.

Funding

ICMART received financial support from the following organizations: American Society for Reproductive Medicine; Asia Pacific Initiative on Reproduction (ASPIRE); European Society for Human Reproduction and Embryology (ESHRE); Fertility Society of Australia (FSA); Japan Society for Reproductive Medicine (JSRM); Japan Society of Fertilization and Implantation (JSFI); Red Latinoamericana de Reproduccion Asistida (REDLARA); Society for Assisted Reproductive Technology (SART); and Ferring Pharmaceuticals and Abbott (unrestricted grant support from each company).

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.

References

AbdelHafez FF, Desai N, Abou-Setta AM, Falcone T, Goldfarb J. Slow freezing, vitrification and ultra-rapid freezing of human embryos: a systematic review and meta-analysis. *Reprod Biomed Online* 2010;**2**:209–222.

Adamson GD. Global cultural and socioeconomic factors that influence access to assisted reproductive technologies. *Womens Health* 2009;**5**:351–358.

Adamson GD, de Mouzon J, Chambers GM, Zegers-Hochschild F, Mansour R, Ishihara O, Banker M, Dyer S. International committee for monitoring assisted reproductive technology: world report on assisted reproductive technology, 2011. *Fertil Steril* 2018;**110**:1067–1080.

Anderson RE, Whitney JB, Schiewe MC. Clinical benefits of preimplantation genetic testing for aneuploidy (PGT-A) for all in vitro fertilization treatment cycles. *Eur J Med Genet* 2020;**63**:103731.

Chambers GM, Hoang VP, Sullivan EA, Chapman MG, Ishihara O, Zegers-Hochschild F, Nygren KG, Adamson GD. The impact of consumer affordability on access to assisted reproductive technologies and embryo transfer practices: an international analysis. *Fertil Steril* 2014;**101**:191–198.e194.

Collins J. An international survey of the health economics of IVF and ICSI. *Hum Reprod Update* 2002;**8**:265–277.

De Geyter C, Calhaz-Jorge C, Kupka MS, Wyns C, Mocanu E, Motrenko T, Scaravelli G, Smeenk J, Vidakovic S, Goossens V; European IVF-monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE). ART in Europe, 2014: results generated from European registries by ESHRE: The European IVF-monitoring Consortium (EIM) for the European Society of Human Reproduction and Embryology (ESHRE). *Hum Reprod* 2018;**33**:1586–1601.

Dyer SJ, Chambers GM, de Mouzon J, Nygren KG, Zegers-Hochschild F, Mansour R, Ishihara O, Banker M, Adamson GD. International Committee for Monitoring Assisted Reproductive

Technologies world report: assisted reproductive technology 2008, 2009 and 2010. *Hum Reprod* 2016;**31**:1588–1609.

Dyer SJ, Kruger TF. Assisted reproductive technology in South Africa: first results generated from the South African Register of Assisted Reproductive Techniques. *South Afr Med J* 2012;**102**: 167–170.

Dyer SJ, Sherwood K, McIntyre D, Ataguba JE. Catastrophic payment for assisted reproduction techniques with conventional ovarian stimulation in the public health sector of South Africa: frequency and coping strategies. *Hum Reprod* 2013;**28**:2755–2764.

ESHRE Capri Workshop Group. Social determinants of human reproduction. *Hum Reprod* 2001;**16**:1518–1526.

ESHRE Capri Workshop Group. Failures (with some successes) of assisted reproduction and gamete donation programs. *Hum Reprod Update* 2013;**19**:354–365.

Evers JLH. Santa Claus in the fertility clinic. *Hum Reprod* 2016;**31**: 1381–1382.

Gu F, Li S, Zheng L, Gu J, Li T, Du H, Gao C, Ding C, Quan S, Zhou C et al. Perinatal outcomes of singletons following vitrification versus slow-freezing of embryos: a multicenter cohort study using propensity score analysis. *Hum Reprod* 2019;**34**:1788–1798.

Hamilton BH, McManus B. The effects of insurance mandates on choices and outcomes in infertility treatment markets. *Health Econ* 2012;**21**:994–1016.

Hughes E, Adamson GD. Cross-border reproductive care in North America: a pilot study testing a prospective data collection program for IVF clinics in Canada and the United States. *Fertil Steril* 2016;**105**:786–790.

Inhorn MC. Right to assisted reproductive technology: overcoming infertility in low-resource countries. *Int J Gynaecol Obstet* 2009; **106**:172–174.

Lancaster PA. Registers of in-vitro fertilization and assisted conception. *Hum Reprod* 1996;**11(Suppl 4)**:89–104.

Lee E, Costello MF, Botha WC, Illingworth P, Chambers GM. A cost-effectiveness analysis of preimplantation genetic testing for aneuploidy (PGT-A) for up to three complete assisted reproductive technology cycles in women of advanced maternal age. *Aust N Z J Obstet Gynaecol* 2019;**59**:573–579.

Lee E, Illingworth P, Wilton L, Chambers GM. The clinical effectiveness of preimplantation genetic diagnosis for aneuploidy in all 24 chromosomes (PGD-A): systematic review. *Hum Reprod* 2015;**30**: 473–483.

Maheshwari A, McLernon D, Bhattacharya S. Cumulative live birth rate: time for a consensus? *Hum Reprod* 2015;**30**:2703–2707.

Mansour R, Ishihara O, Adamson GD, Dyer S, de Mouzon J, Nygren KG, *et al*. International Committee for Monitoring Assisted Reproductive Technologies world report: assisted reproductive technology 2006. *Hum Reprod* 2014;**29**:1536–1551.

Pandian Z, Marjoribanks J, Ozturk O, Serour G, Bhattacharya S. Number of embryos for transfer following in vitro fertilisation or intra-cytoplasmic sperm injection. *Cochrane Database Syst Rev* 2013;**7**:CD003416.

Practice Committee of the American Society for Reproductive Medicine. Multiple gestation associated with infertility therapy. *Fertil Steril* 2012;**97**:825–834.

Praeg P, Mills MC. Cultural determinants influence assisted reproduction usage in Europe more than economic and demographic factors. *Hum Reprod* 2017;**32**:2305–2314.

Sullivan EA, Wang YA, Hayward I, Chambers GM, Illingworth P, McBain J, *et al*. Single embryo transfer reduces the risk of perinatal mortality, a population study. *Hum Reprod* 2012;**27**:3609–3615.

Tannus S, Cohen Y, Henderson S, Al Ma'mari N, Shavit T, Son WY, Dahan MH. Fresh transfer of Day 5 slow-growing embryos versus deferred transfer of vitrified, fully expanded Day 6 blastocysts: which is the optimal approach? *Hum Reprod* 2019;**34**:44–51.

Wahlberg A. The birth and routinization of IVF in China. *Reprod Biomed Soc Online* 2016;**2**:97–107

Zegers FZ, Adamson GD, Dyer S, Racowsky C, de Mouzon J, Sokol R, Rienzi L, Sunde A, Schmidt L, Cooke ID *et al*.. The international glossary on infertility and fertility care. *Published simultaneously in Hum Reprod* 2017;**32**:1786–1801 and *Fertil Steril* 2017;**108**: 393–406.

Zegers-Hochschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, Nygren K, Sullivan E, van der Poel S; on behalf of ICMART and WHO. The International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary on ART terminology, 2009. *Hum Reprod* 2009;**24**:2683–2687.

Zegers-Hochschild F, Dickens BM, Dughman-Manzur S. Human rights to in vitro fertilization. *Int J Gynaecol Obstet* 2013;**123**:86–89.

Zegers-Hochschild F, Mansour R, Ishihara O, Adamson GD, de Mouzon J, Nygren KG, Sullivan EA. International Committee for Monitoring Assisted Reproductive Technology: world report on assisted reproductive technology, 2005. *Fertil Steril* 2014;**101**: 366–378.

Zegers-Hochschild F, Schwarze JE, Crosby JA, Musri C, Urbina MT. Assisted reproductive techniques in Latin America: The Latin American Registry, 2016. *Reprod Biomed Online* 2019;**39**:452–460.