Human Reproduction, Vol.29, No.5 pp. 880–903, 2014
Advanced Access publication on March 11, 2014 doi:10.1093/humrep/deu012

human reproduction

ESHRE PAGES ***Reproductive genetics***

ESHRE PGD Consortium data collection XII: cycles from January to December 2009 with pregnancy follow-up to October 2010†

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Submitted on November 18, 2013; resubmitted on November 18, 2013; accepted on December 10, 2013

STUDY QUESTION: How do data in the 12th annual data collection (Data XII) of the European Society of Human Reproduction and Embryology Preimplantation Genetic Diagnosis (PGD) Consortium compare with the cumulative data for collections I–XI?

SUMMARY ANSWER: Since the beginning of the data collections, there has been a steady increase in the number of cycles, pregnancies and babies reported annually.

WHAT IS KNOWN ALREADY: The PGD Consortium has collected, analysed and published 11 previous data sets since 1997.

STUDY DESIGN, SIZE, DURATION: Data were collected from each participating centre using a pre-designed FileMaker Pro database (versions 5–10). Separate FileMaker Pro files were used for the cycles, pregnancies and baby records. The study documented cycles performed during the calendar year 2009 and follow-up of the pregnancies and babies born which resulted from these cycles (until October 2010).

PARTICIPANTS/MATERIALS, SETTING, METHODS: Data were submitted by 60 centres (full PGD Consortium members), and the blank files were distributed to each PGD Consortium member centre at the end of 2008. The submitted data were thoroughly analysed to identify incomplete data entries and corrections were requested from the participating centres. Records remaining with incomplete data were excluded from the calculations. Corrections, tables and calculations were made by expert co-authors.

MAIN RESULTS AND THE ROLE OF CHANCE: For data collection XII, 60 centres reported data for 6160 cycles with oocyte retrieval (OR), along with details of the follow-up on 1607 pregnancies and 1238 babies born. A total of 870 OR were reported for chromosomal abnormalities, 113 OR for sexing for X-linked diseases, 1597 OR for monogenic diseases, 3551 OR for preimplantation genetic screening and 29 OR for social sexing.

LIMITATIONS, REASONS FOR CAUTION: These data cannot include every PGD cycle performed annually, and only indicate the trends in PGD worldwide.

WIDER IMPLICATION OF THE FINDINGS: The annual data collections provide an extremely valuable resource for data mining and for following trends in PGD practice.

STUDY FUNDING/COMPETING INTEREST(S): None.

Key words: PGD / preimplantation genetic screening / fluorescence *in situ* hybridization / PCR / ESHRE PGD consortium

†ESHRE pages content has not been externally peer reviewed. This manuscript has been approved by the Executive Committee of ESHRE.

Introduction

The European Society of Human Reproduction and Embryology (ESHRE) Preimplantation Genetic Diagnosis (PGD) Consortium, established in 1997, began collecting data on PGD cycles in 1999. To date, 11 data collections have been published, covering all applications of PGD, including autosomal and sex-linked monogenic diseases and chromosome abnormalities, preimplantation genetic screening (PGS) and social sex selection (ESHRE PGD Consortium Steering Committee, 1999, 2000, 2002; Sermon *et al.*, 2005, 2007; Harper *et al.*, 2006, 2008b, 2010b; Goossens *et al.*, 2008, 2012). An overview was also published after 10 years of data collection (Harper *et al.*, 2012). This report summarizes data XII collected for the calendar year 2009 and the subsequent pregnancies. Data XII also includes the delivery rate for each indication.

Materials and Methods

Data were submitted by the centres using a FileMaker Pro database (versions 5–10). Separate files were used for the cycles, pregnancies and baby records, and for this data collection, the blank files were distributed to each PGD Consortium member centre at the end of 2008. The submitted data were thoroughly analysed to identify omissions and any ambivalent data entries. Corrections were requested from the participating centres. Records with incomplete data, for example with no cycle, no patient identification, no clear indication or from an incorrect time period, were excluded from the calculations. Detailed corrections and tables were made by expert co-authors. Clinical pregnancies were defined as the presence of one or more fetal hearts at 6 weeks of gestation. The implantation rate was defined as the number of fetal hearts per 100 embryos transferred. The delivery rate was defined as the percentage of pregnancies with delivery per oocyte retrieval (OR) and per embryo transfer procedure.

Results

The number of centres that join the PGD Consortium increases each year. This report includes data from 60 centres, who, as they submit full data on PGD cycles have the status of full PGD Consortium membership. The results are represented in tables according to an established layout. Accompanying text is deliberately concise and seven tables are available in an electronic version only: Supplementary data, Table SIIc lists the abnormal karyotypes carried by the patients undergoing PGD, Supplementary data, Table SIIIc lists the X-linked diseases for which sexing was carried out, Supplementary data, Table SIVc lists the monogenic diseases for which PGD was carried out, Supplementary data, Table SVIIIa (data I–XI) and Supplementary data, Table SVIIIb (data XII) list the complications of pregnancy and Supplementary data, Table SXIIa (data I–XI) and Supplementary data, Table SXIIb (data XII) list the congenital malformations and the neonatal complications. An overview of all cycles collected previously in data collections I–XI can be found in Table Ia, while an overview of the current data collection can be found in Table Ib. For all PGD/PGS cycles, ICSI was the method most often used for fertilization and cleavage-stage aspiration was the most commonly used method of biopsy. Overall, zona pellucida drilling was more commonly performed using a laser (Table Ib).

PGD cycles for structural chromosomal abnormalities

Tables IIa and IIb summarize the 870 cycles with OR collected for data collection XII, a total number that is still increasing and 12% higher than for data XI (774). In 84 cycles, PGD for a structural chromosome abnormality was simultaneously performed for aneuploidy screening, a 5-fold increase when compared with data XI. In 11 cycles, PGD was simultaneously performed for an additional fluorescence *in situ* hybridization (FISH) indication.

As for all years, data XII showed that PGD for reciprocal translocations was performed more often than for any other type of structural chromosome abnormality (60%). For reciprocal translocations, the number of cycles performed for female carriers more or less equals that for male carriers, whereas for Robertsonian translocations (29% of total cycles), the majority (63%) is performed for male carriers.

Overall, 42% of cycles were performed for infertile patients. The rate of infertility ranged from 33% in the group with female carriers of a reciprocal translocation up to 58% as observed in the group with Robertsonian translocations carried by the male partner.

The mean female age was 36 years, nearly 3 years more than the mean female age in the cumulative data I–XI. The increase is primarily caused by the women's age in the group of male reciprocal translocation carriers. In 84% of all cycles, ICSI was used for fertilization compared with 79% in data XI. Nearly all (98%) cycles to OR reached the biopsy stage. The use of laser drilling for zona breaching is still increasing and covers three-quarter of all cycles in data XII. Aspiration of blastomeres from cleavage stage embryos remains the preferred biopsy method (90%).

For data XII, 11 130 oocytes were collected, a mean of 12.8 per cycle. Of these, 62% (6845/11 130) were fertilized (2 pronuclei) and 76% (5176/6 845) of the resulting embryos were biopsied. Of the embryos successfully biopsied, 94% (4798/5122) gave a diagnostic result, of which only 27% (1275/4798) were transferable. As expected, the lowest percentage of transferable embryos was found in the reciprocal translocation group (22% for male carriers and 20% for female carriers), whereas generally 40% of embryos were transferable in the male carrier of a Robertsonian translocation group, the deletion group and the inversion group. Of all transferable embryos, 70% were actually transferred and 14% were frozen.

From 870 cycles to OR, only 66% resulted in an embryo transfer procedure (ranging from ~80% for male Robertsonian translocation carriers and carriers of an inversion to 54% for carriers of a deletion). This is in agreement with previous data showing that a high level of chromosomally abnormal embryos is found in patients carrying chromosomal abnormalities.

A positive hCG was obtained in 239 cycles, with a positive heart beat in 187 cycles (21% per OR and 33% per embryo transfer). The clinical pregnancy rates per OR were higher for Robertsonian translocation carriers when compared with reciprocal translocation carriers, but this difference almost disappeared when comparing clinical pregnancy rate per embryo transfer. Overall, the implantation rate was 25% (218/891). Finally, the delivery rate was 17% per OR (150/870) and 26% per embryo transfer (150/572). Implantation and delivery rates have remained stable over the last years. There were 19 miscarriages

Table Ia Overall cycle data collection I–XI.

Indication	PGD	PGS	PGD-SS	Total
Cycles to OR	12 388[a]	20 207	676	33 271[a]
Number infertile	4518	16 929	104	21 551
Female age (years)	33	37	36	35
Cancelled before IVF/ICSI	52	2	0	20
ART method	0	0	0	0
IVF	1280	2256	168	3704
ICSI	10 865	17 495	484	28 844
IVF + ICSI	62	344	0	406
Frozen + ICSI + IVF + unknown	145[a]	60	24	229[a]
Unknown	20	50	0	70
Cancelled after IVF/ICSI	624	479	16	1119
Cycles to PGS/PGD	11 748	19 726	660	32 134
FISH	5851	19 723	478	26 052
PCR	5869	3	182	6054
FISH + PCR	28	0	0	28
Zona breaching				
AT drilling	4404	5343	26	9773
Laser drilling	6702	12 516	207	19 425
Mechanical	628	1802	427	2857
Unknown	14	65	0	79
Biopsy method				
PB biopsy	204[b]	3546[b]	0	3750[b]
Cleavage aspiration	10 885[b]	15 241[b]	158	26 284[b]
Cleavage extrusion	470	862	502	1834
Cleavage flow displacement	16	22	0	38
Blastocyst	101	4	0	105
PB and cleavage	67	0	0	67
Unknown	16	52	0	68
Embryology				
COCs	166 708	229 791	9376	405 875
Inseminated	140 685	190 179	7822	338 686
Fertilised	101 319	134 825	5471	241 615
Biopsied	75 624	107 663	4308	187 595
Successfully biopsied	74 624	106 520	4166	185 310
Diagnosed	67 674	98 814	3726	170 214
Transferable	25 218	34 469	1462	61 149
Transferred	16 044	25 567	998	42 609
Frozen	3844	4527	343	8714
Clinical outcome				
Cycles to ET	8931	14 482	494	23 907
hCG positive	3180	4975	197	8352
Positive heartbeat	2499	3925	143	6567
Clinical pregnancy rate (% per OR/% per ET)	20/28	19/27	21/29	20/27

PGD column includes PGD for chromosome abnormalities, sexing for X-linked disease and PGD for monogenic disorders. OR, oocyte retrieval; AT, acid Tyrode's; COC, cumulus–oocyte complex; SS, social sexing; PGS, preimplantation genetic screening; FISH, fluorescence *in situ* hybridization; ET, embryo transfer; ART assisted reproduction technology; PB, polar body.
[a]Includes two cycles with PGD on frozen embryos only. These cycles were not counted in the cycles with OR.
[b]Twelve cycles had PB biopsy and cleavage stage biopsy.

Table Ib Overall cycle data collection XII.

Indication	PGD	PGS	PGD-SS	Total
Cycles to OR	2580	3551	29	6160
Number infertile	733	2428	7	3168
Female age (years)	34.3	38.9	34.3	37.0
ART method				
IVF	188	316	1	505
ICSI	2352	3174	22	5548
IVF + ICSI	5	41	6	52
Frozen + ICSI, IVF	35	20	0	55
Cancelled after IVF/ICSI	56	1	1	58
Cycles to PGS/PGD	2524	3550	28	6102
FISH	946	3526	28	4500
PCR	1435	6	0	1441
FISH + PCR	43	0	0	43
PCR + WGA	97	0	0	97
FISH + PCR + WGA	2	0	0	2
Arrays	1	8	0	9
FISH + arrays	0	1	0	1
WGA + arrays	0	9	0	9
Zona breaching				
AT drilling	479	641	0	1120
laser drilling	1910	2635	28	4573
Mechanical	135	274	0	409
Biopsy method				
PB biopsy	66	931	0	997
Cleavage aspiration	2387	2508	23	4918
Cleavage extrusion	67	96	4	167
Blastocyst	2	3	1	6
PB and cleavage	2	12	0	14
Embryology				
COCs	33 696	38 815	383	72 894
Inseminated	27 960	32 088	324	60 372
Fertilized	21 703	23 337	242	45 282
Biopsied	16 086	18 991	217	35 294
Successfully biopsied	15 898	18 935	216	35 049
Diagnosed	14 576	17 905	201	32 682
Transferable	5481	6092	71	11 644
Transferred	3054	4527	37	7618
Frozen	1011	930	26	1967
Clinical outcome				
Cycles to ET	1872	2623	24	4519
hCG positive	731	1031	6	1768
Positive heartbeat	581	831	5	1417
Clinical pregnancy rate (% per OR/% per ET)	22/31	23/32	17/21	23/31
Number of fetal heartbeats	687	1025	6	1718
Implantation rate (fetal heartbeats/100 embryos transferred)	22	23	16	23
Deliveries	477	599	4	1080
Delivery rate (% per OR/% per ET)	18/25	17/23	14/17	17/24
Miscarriages	70	123	0	193
Miscarriage rate (% per clinical pregn − pregn lost to FU)[a]	13	17	0	15
Clinical pregnancies lost to FU	34	109	1	144

FU, follow-up; PGD column includes PGD for chromosome abnormalities, sexing for X-linked disease and PGD for monogenic disorders. WGA, whole genome amplification.
[a]% per number of clinical pregnancies minus the number of pregnancies that were lost to follow-up.

(10% per clinical pregnancy), half of them occurring in the female reciprocal translocation group. Eighteen clinical pregnancies were lost to follow-up.

PGD cycles for sexing for X-linked diseases

Tables IIIa and IIIb summarize the 1263 and 113 cycles to OR collected for data collections I–XI and XII, respectively. This year, again, FISH was the only method used for sexing cycles. For data XII, 1236 oocytes were collected, 66% (820/1236) fertilized, 72% (593/820) of the resulting embryos were biopsied, with a successful biopsy in 98% (583/593) of the cases. Of the embryos successfully biopsied, 94% (550/583) gave a diagnostic result, of which only 32% (179/550) were transferable (female). From 113 OR procedures, only 68% (77) resulted in an embryo transfer procedure. A positive hCG was obtained in 29 cycles, with a positive heart beat in 26 cycles (23% per OR and 34% per embryo transfer). This gave an implantation rate of 29% (30/102). Finally, the delivery rate was 20.4% per OR (23/113) and 30% per embryo transfer (23/77). There were three miscarriages (11% per clinical pregnancy) and no pregnancies were lost to follow-up.

PGD cycles for monogenic diseases

Tables IVa and IVb summarize the 6096 and 1597 cycles to OR collected for data collection I–XI and XII, respectively. The indications for the monogenic diseases of the current data collection are listed in Supplementary data, Table SIVc. For data XII the most common indications remained unchanged. With respect to PGD for autosomal recessive diseases, the most common indications were beta-thalassemia and/or sickle cell syndromes (175 cycles of which 8 cycles were combined with PGS and 1 with CF and another 52

Table IIa PGD for chromosomal abnormalities, data collection I–XI.

Indication	Robertsonian translocation, male carrier[a]	Robertsonian translocations, female carrier[b]	Reciprocal, male carrier[a,c]	Reciprocal, female carrier[e]	Sex chromosome aneuploidy[d]	Other	Total
Cycles to OR	905	535	1394	1477	370	346	5027
Number infertile	708	260	788	658	311	194	2919
Female age (years)	35	33	33	34	32	33	33
Cancelled before IVF/ICSI	0	0	4	2	7	2	15
ART method							
IVF	40	98	236	410	31	73	888
ICSI	848	420	1111	1021	327	263	3990
IVF + ICSI	4	8	10	15	4	4	45
Frozen + ICSI + IVF + unknown	12	9	32	29	1	4	87
Unknown	1	0	1	0	0	0	2
Cancelled after IVF/ICSI	50	25	89	95	24	19	302
Cycles to PGD	855	510	1301	1380	339	325	4710
Zona breaching							
AT drilling	345	251	652	720	119	135	2222
Laser drilling	486	244	604	608	182	156	2280
Mechanical	24	15	45	52	38	34	208
Biopsy method	0	0	0	0	0	0	0
PB biopsy	2	11	1	21	1	3	39
Cleavage aspiration	799	467	1222	1265	323	303	4379
Cleavage extrusion	50	31	65	80	12	18	256
Cleavage flow displacement	2	0	2	4	3	0	11
Blastocyst	2	1	11	10	0	1	25
Embryology							
COCs	12 605	7445	19 270	20 204	4560	4536	68 620
Inseminated	10 540	6349	16 389	17 568	3758	3922	58 526
Fertilised	7116	4628	11 643	12 844	2607	2821	41 659
Biopsied	5061	3517	8908	10 038	1840	2217	31 581
Successfully biopsied	5000	3480	8781	9900	1820	2191	31 172
Diagnosed	4548	3213	8153	9282	1681	2028	28 905
Transferable	1728	958	1635	1799	740	648	7508
Transferred	1153	682	1319	1443	506	434	5537
Frozen	246	107	103	112	77	79	724
Clinical outcome							
Cycles to ET	656	386	802	860	267	248	3219
hCG positive	256	138	260	286	88	68	1096
Positive heartbeat	218	108	196	224	68	56	870
Clinical pregnancy rate (% per OR/ % per ET)	24/33	20/28	14/24	15/26	18/25	16/23	17/27

[a]Five cycles included PGS, seven cycles were performed for an additional FISH indication.
[b]One cycle included PGS, two cycles included cystic fibrosis (CF) and one cycle sexing, four cycles were performed for an additional FISH indication.
[c]One cycle included social sexing, three cycles included PGS.
[d]Seven cycles included PGS.
[e]Five cycles included PGS, 10 included an additional FISH indication, 4 with an additional PCR indication.

Table IIb PGD for chromosomal abnormalities, data collection XII.

Indication	Robertsonian translocation, male carrier	Robertsonlan translocation, female carrier	Reciprocal translocation, male carrier	Reciprocal translocation, female carrier	Deletion	Inversion	Other	Total
Cycles to OR	160	95	244	277	14	44	36	870
Number infertile (%)	92 (58)	38 (40)	103 (42)	91 (33)	5 (36)	19 (43)	16 (44)	364 (42)
Female age (years)	33.92	34.53	41.17	34.38	33.99	34.78	36.69	36.33
Cancelled after OR before IVF/ICSI	0	0	0	0	0	0	0	0
ART method								
IVF	8	13	44	64	4	3	2	138
ICSI	148	79	196	211	9	40	33	716
IVF + ICSI	1	2	2	0	0	0	0	5
ICSI + frozen	3	1	2	2	1	1	1	11
Cancelled after IVF/ICSI	4	1	6	6	2	0	0	19
Cycles to PGD	156	94	238	271	12	44	36	851
Zona breaching								
AT drilling	36	22	54	60	1	8	6	187
Laser drilling	120	70	182	200	11	36	30	649
Mechanical	0	2	2	11	0	0	0	15
Biopsy method								
PB	1	5	1	18	0	1	0	26
Cleavage aspiration	155	81	219	225	11	43	36	770
Cleavage extrusion	0	8	18	28	1	0	0	55
Embryology								
COCs (mean/OR)	2227	1317	3075	3436	138	490	447	11 130
Inseminated	1825	1121	2638	2949	98	414	342	9387
Fertilized	1303	828	1925	2135	67	304	283	6845
Biopsied	926	641	1400	1727	53	233	196	5176
Successfully biopsied	913	630	1390	1708	53	232	196	5122
Diagnosed	865	592	1305	1585	49	212	190	4798
Transferable (%/diagnosed)	329 (38)	170 (29)	286 (22)	324 (20)	18 (37)	94 (44)	54 (28)	1275 (27)
Transferred	206	113	213	248	13	64	34	891
Frozen	50	29	38	39	1	15	4	176
Clinical outcome								
Cycles to ET (%/OR)	126 (79)	70 (74)	144 (59)	164 (59)	8 (54)	35 (80)	25 (69)	572 (66)
hCG positive	48	27	65	71	2	17	9	239
Positive heartbeat	38	25	46	58	2	12	6	187
Clinical pregnancy rate (% per OR/% per ET)	24/30	26/36	19/32	21/35	15/29	27/34	17/24	21/33
Number of fetal hearts	49	29	48	69	4	12	7	218
Implantation rate (fetal hearts/100 embryos transferred)	23.8	25.7	22.5	27.8	36.4	18.8	20.6	24.5
Deliveries	30	22	38	46	2	7	5	150
Delivery rate (% per OR/% per ET)	19/24	23/31	16/27	17/28	15/29	16/20	14/20	17/26
Miscarriages	2	2	4	9	0	2	0	19
Clinical pregnancies lost to FU	6	1	4	3	0	3	1	18

Table IIIa Sexing only for X-linked disease using PCR or FISH, data collection I–XI.

	FISH	PCR	Total
Cycles to OR	1197	66	1263
Number infertile	284	0	284
Female age (years)	33	31	32
Cancelled before IVF/ICSI	2	0	2
ART method			
IVF	336	10	346
ICSI	841	56	897
IVF + ICSI	14	0	14
ICSI + Frozen	3	0	3
IVF + Frozen	1	0	1
Cancelled after IVF/ICSI	59[a]	1[b]	60[a,b]
Cycles to PGD	1136	65	1201
Zona breaching			
AT drilling	556	52	608
Laser drilling	528	3	531
Mechanical	52	10	62
Biopsy method			
PB	2	0	2
Cleavage aspiration	1077	60	1137
Cleavage extrusion	50	5	55
Flow displacement	5	0	5
Blastocyst	2	0	2
Embryology			
COCs	15 721	912	16 633
Inseminated	13 812	701	14 513
Fertilised	9714	556	10 270
Biopsied	7441	458	7899
Successfully biopsied	7294	422	7716
Diagnosed	6748	329	7077
Transferable	2314	178	2492
Transferred	1575	139	1714
Frozen	398[c]	58[d]	456[c,d]
Clinical outcome			
Cycles to ET	900	55	955
hCG positive	286	24	310
Positive heartbeat	224	17	241
Clinical pregnancy rate (% per OR/ % per ET)	19/25[e]	26/31[e]	19/25[e]

[a]27 embryos from two cycles frozen before biopsy due to hyperstimulation.
[b]20 embryos frozen before biopsy.
[c]11 cycles with embryos frozen without biopsy or after failed diagnosis included.
[d]13 cycles with embryos frozen without biopsy or failed diagnosis included.
[e]11 embryos transferred removed from calculations due to lack of information regarding the number of fetal heartbeats in pregnancies resulting from the transfer of those embryos.

Table IIIb Sexing only for X-linked disease using PCR or FISH, data collection XII.

	FISH[a]	Total
Cycles to OR	113	113
Number infertile	29	29
Female age (years)	35.07	35.07
ART method		
IVF	47	47
ICSI	64	64
IVF + frozen	2	2
Cancelled after IVF/ICSI	5	5
Cycles to PGD	108	108
Zona breaching		
AT drilling	24	24
Laser drilling	76	76
Mechanical	8	8
Biopsy method		
Cleavage aspiration	96	96
Cleavage extrusion	12	12
Embryology		
COCs	1236	1236
Inseminated	1120	1120
Fertilized	820	820
Biopsied	593	593
Successfully biopsied	583	583
Diagnosed	550	550
Transferable	179	179
Transferred	102	102
Frozen	52	52
Clinical outcome		
Cycles to ET	77	77
hCG positive	29	29
Positive heartbeat	26	26
Clinical pregnancy rate (% per OR/% per ET)	23.4/33.7	23.4/33.7
Number fetal hearts	30	30
% Implantation rate (fetal heartbeats/ 100 embryos transferred)	29.4%	29.4%
Deliveries	23	23
Delivery rate (% per OR/% per ET)	20.4/29.9	20.4/29.9
Miscarriages	3	3
Miscarriage rate (% per clinical pregn − pregn lost to FU)	11.5	11.5
Clinical pregnancies lost to FU	0	0

[a]In two cycles, one cell was analysed with FISH, while a second cell was analysed with PCR for HLA compatibility.

Table IVa cycles performed for single gene disorders using PCR, data collection I–XI.

Indication	X-linked[a]		Autosomal recessive[b]		Autosomal dominant[c]		HLA				Other	Total	
							HLA only		HLA + monogenic disease				
		%		%		%		%		%			%
Cycles to OR	778		1876		1691		98		319		1334	6096	
Number infertile	155	20	613	33	294	17	2	2	14	4	237	1315	22
Female age (years)	33		34		32		36		34		31	33	
Cancelled before IVF/ICSI	0		0		3		0		0		1	4	
ART method													
IVF	15	1.9	19	1.0	1	0.1	0	0.0	0	0.0	12	47	0.77
ICSI	753	96.8	1830	97.5	1671	99.0	97	98.0	313	98.1	1309	5973	98.01
IVF + ICSI	2	0.3	0		1	0.1	0		0		0	3	0.05
IVF + frozen	0		0		1	0.1	0		0			1	0.02
ICSI + frozen	0		1	0.1	2	0.1	0		0			3	0.05
IVF + ICSI + Frozen	6	0.8	21	1.1	6	0.4	1	2.0	6	1.9	9[d]	49[d]	0.80
Unknown	2	0.3	5	0.3	6	0.4	0		0		5	18	0.30
Cancelled after IVF/ICSI	39	5	73	4	77	5	4	4	12	4	54	259	4
Cycles to PGD	739	95	1803	96	1611	95	94	95	307	96	1281	5835	96
Zona breaching													
AT drilling	160	21.7	612	34.0	458	28.4	4	4.3	33	9.9	312	1577	27.0
Laser drilling	513	69.4	1081	59.8	1063	65.9	90	95.7	271	89.1	866	3886	66.6
Mechanical	64	8.7	106	5.9	85	5.3	0		3	1.0	100	358	6.2
Unknown	2	0.3	4	0.2	5	0.3	0		0		3	14	0.2
Biopsy method													
PB biopsy	33[e]	4.5	30[e]	1.7	37[e]	2.3	0		0		63[e]	163[e]	2.8
Cleavage aspiration	667[e]	90.0	1662[e]	91.8	1521[e]	94.4	90	95.7	279	91.7	1147[e]	5366[e]	91.8
Cleavage extrusion	6	0.8	71	4.0	41	2.5	1	1.1	8	2.1	32	159	2.7
Blastocyst	6	0.8	33	1.9	1	0.1	3	3.2	21	6.2	11	75	1.3
PB + embryo	26	3.5	4	0.2	7	0.4	0		0		25	62	1.1
Unknown	3	0.4	7	0.4	5	0.3	0		0		6	21	0.4
Embryology													
COCs (mean/OR)	9368	(12.0)	25 467	(13.58)	22 207	(13.1)	1324	(13.5)	4572	(14.3)	18 511	81 449	(13.4)
Inseminated	7828		21 162		18 544		1072		3737		15 302	67 645	
Fertilized	5734		15 207		13 352		854		2976		11 265	49 388	
Biopsied (mean/OR)	4069	(5.2)	11 444	(6.10)	9446	(5.6)	615	(6.3)	2410	(7.6)	8159	36 143	(5.9)
Successfully biopsied	4003		11 299		9350		614		2400		8069	35 735	
Diagnosed (mean/OR)	3591	(4.6)	9847	(5.25)	8302	(4.9)	573	(5.8)	2200	(6.9)	7178	31 691	(5.2)
Transferable (mean/OR)	1870	(2.4)	5844	(3.12)	3575	(2.1)	119	(1.2)	334	(1.0)	3480	15 222	(2.5)
Transferred	1057		3286		2103		91		269		1987	8793	
Frozen	293		906		527		54		278		608	2666	
Clinical outcome													
Cycles to ET	570	77.1	1604	89.0	1289	80.0	60	63.8	178	58.0	1057	4758	81.5
hCG positive	201		635		434		24		79		401	1774	
Postive heartbeat	162		495		330		17		66		318	1388	
Clinical pregnancy rate (% per OR/% per ET	21/28		26/31		20/26		17/28		21/37		24/30	23/29	

[a]Included DMD, BMD, FRAXA and Haemophilia for data I–X. Other X-linked diseases are pooled in the 'other' category.
[b]Included CF,b-Thal, sickle cell anaemia and SMA for data I–X. Other autosomal recessive (AR) diseases are pooled in the 'other' category.
[c]Included DM1 and Huntington's disease (HD) for data I–X. Other autosomal dominant (AD) diseases are pooled in the 'other' category.
[d]Two cycles were on frozen–thawed embryos only so they were not counted as cycles with an OR, but were counted as cycles going to PGD.
[e]Eleven cycles had both PB biopsy and cleavage stage biopsy.

Table IVb Cycles performed for single gene disorders using PCR, data collection XII.

Indication	X-linked		Autosomal recessive		Autosomal dominant		HLA				Other		Total	
							HLA Only		HLA + Monogenic disease					
		%		%		%		%		%		%		%
Cycles to OR	269		525		683		40		78		2		1597	
Number infertile	52	19.3	157	29.9	127	18.6	0	0.0	4	5.2	0	0.0	340	21.3
Female age (years)	33		34		32		34		35		34		33	
Cancelled before IVF/ICSI	0		0		0		0		0		0		0	
ART method														
IVF	2	0.7	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	3	0.2
ICSI	263	97.8	514	97.9	679	99.4	40	100.0	74	94.8	2	100.0	1572	98.4
ICSI + frozen	4	1.5	11	2.1	3	0.4	0	0.0	4	5.2	0	0.0	22	1.4
Cancelled after IVF/ICSI	2	0.7	13	2.5	15	2.2	2	5.0	0	0.0	0	0.0	32	2.0
Cycles to PGD	267	99.3	512	97.5	668	97.8	38	95.0	78	100.0	2	100.0	1565	98.0
Zona breaching														
AT Drilling	48	18.0	99	19.3	114	17.1	0	0.0	4	5.2	2	100.0	267	17.1
Laser Drilling	189	70.8	382	74.6	508	76.0	38	100.0	68	87.0	0	0.0	1185	75.7
Mechanical	30	11.2	31	6.1	46	6.9	0	0.0	6	7.7	0	0.0	113	7.2
Biopsy method														
PB	8	3.0	11	2.1	21	3.1	0	0.0	0	0.0	0	0.0	40	2.5
Cleavage aspiration	258	96.6	498	97.3	646	96.7	38	100.0	78	100.0	2	100.0	1520	97.2
Blastocyst	0	0.0	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1
PB + embryo	1	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	3	0.2
Biopsy policy														
1 cell biopsy	85	31.8	316	61.7	247	36.9	32	84.2	60	76.9	0	0.0	740	47.3
2 cell biopsy	146	54.7	116	22.7	316	47.3	6	15.8	17	21.8	2	100.0	603	38.6
1 or 2 cell biopsy	31	11.6	70	13.7	97	14.5	0	0.0	1	1.3	0	0.0	199	12.7
>2 cells (including TE)	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	1	0.5
1 and 2 PB	5	1.9	6	1.2	5	0.7	0	0.0	0	0.0	0	0.0	16	1.0
Unknown	0	0.0	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1
1 PB	0	0.0	2	0.4	2	0.3	0	0.0	0	0.0	0	0.0	4	0.3
Amplification method														
FISH + PCR	9	3.4	21	4.1	8	1.2	3	7.9	0	0.0	0	0.0	41	2.6
PCR	232	86.9	444	86.7	637	95.3	35	92.1	77	98.7	2	100.0	1427	91.2
WGA + PCR	26	9.7	45	8.8	23	3.5	0	0.0	1	1.3	0	0.0	95	6.1
WGA + PCR + FISH	0	0.0	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1
Embryology (mean/OR)														
COCs	3240	12.1	7323	13.9	8987	13.1	567	14.9	1193	15.4	20	10.0	21 330	13.4
Inseminated	2741	10.3	5818	11.4	7392	10.8	467	12.3	1017	13.1	18	9.0	17 453	10.9
Fertilized	2228	8.3	4598	9.0	5907	8.6	394	10.4	900	11.6	11	5.5	14 038	8.8
Biopsied	1549	5.8	3567	7.0	4181	6.2	294	7.7	717	9.2	9	4.5	10 317	6.6
Successfully biopsied	1528	5.7	3512	6.9	4137	6.2	294	7.7	713	9.2	9	4.5	10 193	6.5
Diagnosed	1387	5.2	3168	6.2	3764	5.6	267	7.0	633	8.2	9	4.5	9228	5.9
Transferable	692	2.6	1589	3.1	1588	2.3	51	1.3	105	1.4	2	1.0	4027	2.5
Transferred	357	1.3	776	1.5	813	1.2	35	0.9	78	1.0	2	1.0	2061	1.3
Frozen	125	0.5	347	0.7	261	0.4	11	0.3	39	0.5	0	0.0	783	0.5

Continued

Table IVb *Continued*

Indication	X-linked		Autosomal recessive		Autosomal dominant		HLA				Other		Total	
							HLA Only		HLA + Monogenic disease					
		%		%		%		%		%		%		%
Clinical outcome														
Cycles to ET	213	79.8	419	81.8	517	77.4	24	63.2	48	61.5	0	0.0	1221	78.0
hCG Positive	71		171		196		5		20		0		463	
Positive heartbeat	57		136		153		3		19		0		368	
Clinical pregnancy rate (% per OR)		21.2		25.9		22.4		7.5		24.7		0.0		23.0
Clinical pregnancy rate (% per ET)		26.8		32.6		29.6		12.5		39.6		0.0		30.2
Number fetal heartbeats	69		162		183		3		22		0		439	
Implantation rate (fetal hearts/embryos transferred)		19.3		21.0		22.5		8.6		28.2		0.0		21.3
Deliveries	45		109		133		2		15		0		304	
Delivery rate (% per OR)		16.7		20.8		19.6		5.0		19.5		0.0		19.1
Delivery rate (% per ET)		21.1		26.1		25.9		8.3		31.3		0.0		25.0
Miscarriages	9		20		14		1		4		0		48	
Miscarriage rate (% per clinical pregn − pregn lost to FU)		16.7		15.5		9.1		33.3		21.1		0.0		13.6
Clinical pregnancies lost to FU	3		7		6		0		0		0		16	

TE, trophectoderm. XL: + 2 rec female; + 4 aneuploidy. AR: +3 XLR; +1Rob fem; +27 aneuploidy; +7 AR. AD: +1 rec female; +6 AD; +10 aneuploidy. HLA only: +5 aneuploid.

cycles in combination with HLA compatibility, see below), cystic fibrosis (CF) (140 cycles and 9 cycles for CF and a second indication) and spinal muscular atrophy (SMA) (52 cycles and another 6 for SMA and a second indication). Amongst the autosomal dominant diseases, most PGD cycles were performed for Huntington disease (136 cycles) and myotonic dystrophy type 1 (DM1) (119 cycles, plus 5 cycles for DM1 and a second indication), neurofibromatosis type 1 (43 cycles, plus 2 cycles for neurofibromatosis type 1 and a second indication) and familial adenomateous polyposis coli (30 cycles of which 3 cycles were combined with a second indication). For a specific diagnosis of X-linked diseases the most common indications were for fragile X syndrome (121 cycles and another 4 cycles combined with PGS), Duchenne and Becker muscular dystrophy (DMD/BMD) (51 cycles and 2 cycles for DMD and a second indication) and haemophilia A and B (17 cycles and 3 cycles, respectively). There were 40 cycles for HLA compatibility typing only (of which 5 were in combination with PGS) and 78 cycles for HLA typing along with a specific disorder. The most common indication here was beta-thalassemia/sickle cell anaemia (52 cycles). The total number of cycles with HLA typing which had decreased from 151 cycles in data X to 138 cycles in data XI has further decreased to 118 cycles in the current data collection.

For data XII, ICSI was used in the majority of cycles (98.4% of cycles to OR) and PCR was still the most widely used first-line method of DNA amplification (91.2% of cycles to OR). The percentage of cycles relying on whole genome amplification as method of DNA amplification (6.1% of cycles to OR) was not different from previous data collection (5.1%). In a small number of cycles (2.6%) both PCR and FISH methods were carried out.

The use of laser was the preferred method for biopsy (75.7% of cycles to PGD); acidic tyrode or mechanical action was applied in 17.1 and 7.2% of cycles to PGD, respectively. Day 3 cleavage-stage embryo biopsy was most frequently used (97.2% of cycles to PGD). Genetic testing was carried out on either 1 cell (47.3% of cycles to PGD) or 2 cells per embryo (38.6% of cycles to PGD). In 13.2% of cycles a mixture of 1 and 2 cells, 3 cells or trophectoderm biopsy was applied. A total number of 21 330 cumulus–oocyte complexes (COCs) were collected and 80.4% of the mature oocytes which were inseminated

Table Va Cycles performed for PGS, data collection I–XI.

Indication	AMA	AMA + miscarriage[a]	AMA + RIF1	Recurrent miscarriage	Recurrent IVF failure	Severe male factor[b]	Oocyte donation[c]	Prev abn preg[c]	No indication	Other[d]	Total
Cycles to OR	6740	736	1820	2491	4656	1766	256	75	529	1138	20 207
Number infertile	5496	517	1717	1458	4439	1574	199	29	505	995	16 929
Female age (years)	41	41	41	34	34	35	39	39	35	36	37
Cancelled before IVF/ICSI	0	0	0	0	1	0	0	0	0	1	2
ART method											
IVF	922	141	274	271	386	10	3	6	132	111	2256
ICSI	5703	573	1527	2157	4170	1715	250	69	346	986	17 496
IVF + ICSI	94	16	11	50	61	33	3	0	50	25	343
IVF + frozen	0	2	1	1	1	0	0	0	0	0	5
ICSI + Frozen	15	4	2	11	13	8	0	0	1	1	55[e]
Unknown	6	0	5	1	24	0	0	0	0	14	50
Cancelled after IVF/ICSI	186	26	10	44	127	34	0	0	27	24	478
Cycles to PGS	6554	710	1810	2447	4528	1732	256	75	502	1113	19 727
Zona breaching											
AT drilling	1492	182	427	850	1161	593	30	21	207	380	5343
Laser drilling	4794	431	995	1494	2743	921	144	54	258	683	12 517
Mechanical	255	97	388	102	587	218	82	0	37	36	1802
Unknown	13	0	0	1	37	0	0	0	0	14	65[e]
Biopsy method											
PB biopsy	957[f]	207	1068	127	790	29	0	0	103	265	3546[f]
Cleavage aspiration	5289[f]	470	671	2219	3480	1641	184	72	396	820	15 242[f]
Cleavage extrusion	289	33	71	96	213	61	72	1	3	23	862
Cleavage flow displacement	7	0	0	3	7	1	0	0	0	4	22
Blastocyst	0	0	0	1	0	0	0	2	0	1	4
Unknown	13	0	0	1	38	0	0	0	0	0	52[e]
Embryology											
COCs	65 322	7004	16 521	31 085	60 357	25 434	3214	835	5986	14 033	229 791
Inseminated	55 257	5722	12 927	25 771	49 540	20 564	2752	689	5135	11 822	190 179
Fertilized	38 566	4042	8959	18 945	35 611	14 283	2079	497	3531	8312	134 825
Biopsied	29 879	3625	9423	14 275	28 341	10 727	1581	367	2851	6594	107 663
Successfully biopsied	29 517	3610	9347	14 121	27 950	10 672	1575	361	2804	6533	106 490
Diagnosed	27 305	3401	8606	13 073[g]	26 177[g]	10 034	1550	344	2470[g]	5854[g]	98 814[g]
Transferable	7709	975	2972	4677[g]	9789[g]	3948	700	129	1164[g]	2406[g]	34 469[g]
Transferred[h]	6690	771	2425	3359[g]	6726[g]	2666	413	82	729[g]	1703[g]	25 564[g]
Frozen	804	104	293	688	1361	491	187	32	150	417	4527

Clinical outcome												
Cycles to ET	4050	472	1383	1883	3641	1445	225	53	418	912	14 482	
hCG positive	1194	117	302	769	1283	625	130	17	166	372	4975	
Positive heartbeat	910	84	253	606	997	528	111	17	139	290	3935	
Clinical pregnancy rate (% per OR/% per ET)	14/22	11/18	14/18	24/32	21/27	30/37	43/49	23/32	26/33	25/32	19/27	

AMA, advanced maternal age; RIF, repeated implantation failure; SMF, severe male factor.
[a]These data were not extracted from I to IV.
[b]These data were not extracted from I to III.
[c]These data were not extracted from data I to VIII.
[d]'Others' contains also cycles with multiple indications and previous abnormal pregnancies (data I–VIII).
[e]Several cycles had incomplete results.
[f]One cycle had cleavage stage biopsy and PB biopsy.
[g]Several cycles from one centre had no information on the number of embryos diagnosed as transferable, but patients did have embryos transferred. In these cases, undiagnosed/failed or abnormal embryos were transferred.
[h]Failed embryos were also transferred.

actually fertilized. A total of 73.5% of fertilized embryos were biopsied with a 98.8% success rate. Of the embryos successfully biopsied, 90.5% gave a diagnostic result, of which 43.6% were genetically transferable. From 1597 PGD procedures 76.5% (1221/1597) resulted in an embryo transfer. Per cycle on average 13.4 COCs were collected with 10.9 mature oocytes for insemination. This yielded on average 8.8 fertilized embryos of which 6.6 were suitable for biopsy. Diagnosis was achieved for 5.9 embryos, of which 2.5 embryos were shown to be genetically transferable. On average 1.3 embryos per OR could be transferred, while 0.5 embryos were used for cryopreservation. A positive hCG was obtained in 463 cycles, with a positive heart beat in 368 cycles (23.0% per OR and 30.2% per embryo transfer) and 439 fetal hearts, giving an overall implantation rate of 21.3% (439/2061). These data are all very similar to previous data collections (data X and XI). Finally, the delivery rate was 19.1% per OR and 25.0% per embryo transfer. There were 48/352 miscarriages (13.6% per clinical pregnancy) and 4.3% (16/368) clinical pregnancies were lost to follow-up. Overall, the number of PGD cycles performed for monogenic disorders between January and December 2009 further increased by 17% compared with data collection XI. Generally, there were no marked changes with respect to the progress and outcome of cycles, including the embryology, rates of diagnosis and clinical outcome, such as clinical pregnancy and embryo implantation rates (Goossens *et al.*, 2012).

Preimplantation genetic screening

The application of PGD to identify numerical chromosome errors (aneuploidies) in embryos, so-called PGS, was first reported by the PGD Consortium in data collections I–III for 787 cycles when it constituted 36% of all reported PGD (Harper *et al.*, 2012).

Overall, 3551 cycles of PGS are reported in data collection XII (Table Vb). The mean age of women undergoing PGS was 38.9 years. PGS was applied to cycles in women of advanced maternal age, those who had suffered from repeated implantation failure, repeated miscarriage, experience of a previous abnormal pregnancy, severe male factor and in some cases for more than one indication.

In the PGS group, a total number of 32 088 oocytes were inseminated, 23 337 (72.7%) were fertilized, 18 991 embryos were biopsied and 17 905 (94.6% of successfully biopsied) were diagnosed. Of these 6092 were transferrable, 4527 were transferred and 930 were frozen.

A total number of 2623 cycles with embryo transfer were performed with 1031 hCG-positive result. PGS represents 58% of all the PGD cycles to embryo transfer in the data collection XII. Positive heart beat was reported for 831 cycles, with a clinical pregnancy rate per embryo transfer of 31.7% (23.4% per OR) and an implantation rate (fetal hearts/100 embryos transferred) of 22.6%. The delivery rate per embryo transfer was 22.8% and the miscarriage rate per clinical pregnancy was 16.8%. A total number of 109 clinical pregnancies were lost to follow-up.

PGD cycles for social sexing

Tables VIa and VIb summarize the 676 and 29 cycles to OR collected for data collections I–XI and XII, respectively. For data XII, 383 oocytes

Table Vb Cycles performed for PGS, data collection XII.

Indication	AMA	AMA + misc	AMA + RIF	Rec.misc	RIF	SMF	Prev abn preg	RIF + SMF	AMA + SMF	Num abno	No indication	Ovum donation	Total
Cycles to OR	1231	212	470	446	509	343	45	70	51	31	95	48	3551
Number infertile	790	125	413	115	442	305	11	54	36	15	86	36	2428
Female age (years)	41.9	40.4	39.7	35.4	35.3	37.6	36.1	33.3	41.1	35.0	37.3	41.2	38.90
ART method													
IVF	140	48	64	27	18	1	5	0	0	3	9	1	316
ICSI	1080	161	399	401	485	333	40	70	49	28	81	47	3174
IVF + ICSI	5	1	4	14	4	7	0	0	1	0	5	0	41
ICSI + frozen	6	2	3	4	2	1	0	0	1	0	0	0	19
IVF + frozen	0	0	0	0	0	1	0	0	0	0	0	0	1
Cancelled post OR	0	0	0	0	1	0	0	0	0	0	0	0	1
Cycles to PGD	1231	212	470	446	508	343	45	70	51	31	/95	48	3550
Zona breaching													
AT drilling	141	18	101	56	120	128	9	1	13	0	48	6	641
Laser drilling	987	181	317	371	356	175	36	69	38	30	44	31	2635
Mechanical	103	13	52	19	32	40	0	0	0	1	3	11	274
Biopsy method													
PB	371	111	285	45	76	6	1	0	2	1	33	0	931
Cleavage aspiration	802	101	180	390	422	326	44	70	49	25	61	38	2508
Cleavage extrusion	51	0	2	11	7	10	0	0	0	5	0	10	96
Blastocyst	1	0	1	0	1	0	0	0	0	0	0	0	3
PB + embryo	6	0	2	0	2	1	0	0	0	0	1	0	12
Embryology													
COCs	11 446	1935	4515	5455	6039	4854	541	1250	667	371	1069	673	38 815
Inseminated	9738	1645	3599	4495	4822	3978	445	998	541	314	917	596	32 088
Fertilized	6996	1156	2514	3348	3585	2875	329	770	406	232	661	465	23 337
Biopsied	5560	1045	2466	2616	2859	2212	249	609	304	178	566	327	18 991

Successfully biopsied	5553	1044	2450	2613	2839	2209	246	609	303	176	566	327	18 935
Diagnosed	5255	942	2270	2502	2725	2106	227	569	282	174	544	309	17 905
Transferable	1452	276	648	953	1080	883	90	213	75	63	183	176	6092
Transferred	1206	268	602	644	769	527	62	140	53	42	128	86	4527
Frozen	/178	24	60	155	169	146	18	63	13	15	22	67	930
Clinical outcome													
Cycles to ET	768	157	348	360	425	295	37	63	34	23	70	43	2623
hCG positive	244	57	114	170	186	130	20	32	18	10	30	20	1031
Positive heartbeat	197	43	85	141	151	115	15	25	8	10	24	17	831
Clinical pregnancy rate (% per OR/% per ET)	16.0/25.7	20.3/27.4	18.0/24.4	31.6/39.2	29.7/35.5	33.5/39.0	33.3/40.5	35.7/39.7	15.7/23.5	32.2/43.5	25.2/34.3	35.4/39.5	23.4/31.7
Number of fetal hearts	231	48	104	182	184	151	19	30	11	15	30	20	1025
Implantation rate (fetal hearts/100 embryos transferred)	19.1	17.9	17.3	28.3	23.9	28.6	30.6	21.4	20.7	35.7	23.4	23.3	22.6
Deliveries	138	26	48	108	105	93	12	23	7	8	18	13	599
Delivery rate (% per OR/% per ET)	11.2/18.0	12.3/16.6	10.2/13.8	24.2/30.0	20.6/24.7	27.1/31.5	26.7/32.4	32.9/36.5	13.7/20.6	25.8/34.8	18.9/25.7	27.1/30.2	16.9/22.8
Miscarriages	36	12	16	19	15	14	2	2	1	1	3	2	123
Miscarriage rate (% per clinical pregn − pregn lost to FU)	20.7	31.6	25.0	14.3	13.0	13.1	14.3	8.0	12.5	10.0	12.5	13.3	16.8
Clinical pregnancies lost to FU	23	5	21	14	31	8	1	0	0	1	3	2	109

Table VIa PGD for social sexing, data collection I–XI.

Method for sexing	FISH (SS only)	FISH (SS + AS)[a]	PCR	Unknown	Total
Cycles to OR	360	122	189	5[b]	676[b]
Number infertile	60	27	16	1	104
Female age (years)	40	39	37	35	36
ART method					
IVF	136	19	10	3	168
ICSI	212	102	168	2	484
Frozen	3	0	2	0	5
Frozen + IVF + ICSI + unknown	9	1	9	0	19
Cancelled after IVF/ICSI	4	0	7	5	16
Cycles to PGD	356	122	182	0	660
Zona breaching					
AT drilling	16	0	10	0	26
Laser drilling	173	33	1	0	207
Mechanical	167	89	171	0	427
Biopsy method					
Cleavage aspiration	147	0	11	0	158
Cleavage extrusion	209	122	171	0	502
Embryology					
COCs	4788	1687	2878	23	9376
Inseminated	4145	1470	2188	19	7822
Fertilized	2982	1026	1452	11	5471
Biopsied	2389	776	1143	0	4308
Successfully biopsied	2275	775	1116	0	4166
Diagnosed	2019	658	1049	0	3726
Transferable	777	212	473	0	1462
Transferred	490	147	361	0	998
Frozen[c]	214	43	86	0[d]	343
Clinical outcome					
Cycles to ET	273	83	138	0	494
hCG positive	110	29	58	0	197
Positive heartbeat	84	20	39	0	143
Clinical pregnancy rate (% per OR/% per ET)	23/31	16/24	21/28	0/-	21/29

AS, aneuploidy screening.
[a]These data were not extracted from I to VII.
[b]One natural cycle included.
[c]Eleven cycles with embryos frozen without biopsy or failed diagnosis included.
[d]Three embryos frozen without biopsy were not included.

were collected, of which 324 were inseminated and 74.7% (242/324) fertilized. The percentage of embryos biopsied was 89.7% (217/242) of which all but 1 was successfully biopsied. Of the embryos successfully biopsied 93% (201/216) gave a diagnostic result, of which only 35.3% (71/201) were transferable (of the desired sex). In total, 37 embryos were transferred in 24/29 cycles initiated, with 6 cycles resulting in a hCG-positive test, and a fetal heartbeat was subsequently detected in 5 of these pregnancies, 1 of which was a twin pregnancy and the remaining 4 were singletons. Four pregnancies went to term and delivered four babies. The method of genetic analysis was FISH for all 29 cycles, of which 2 cycles were analysed also by PCR. The number of cycles for social sexing in data XII represents a relative increase from those reported in data XI (just 5 cycles) but it is lower than the number reported in data X (92 cycles). Overall, the number of cycles reported for social sexing may be biased according to the number of centres offering this service, which are relatively few anyway (only six full Consortium member-centres). Of additional note are the relatively low clinical pregnancy rates reported for the social sexing cycles compared with the other indications and compared with other years (17.2% per OR and 20.8% per embryo transfer).

Pregnancies and babies

Tables VIIa, IXa, IXb, Xa, Xb, XIa and XIb and in the Supplementary data, Table SXIIa summarize the pregnancy and baby data. Data XII is comparable to previous data collections. Data XII included 1607 clinical pregnancies (Table VIIb), with 1062 deliveries of 1287 babies. Of the 1296 cycles ending in a pregnancy with a positive heartbeat, follow-up data on 1217 pregnancies were reported. Neonatal data on 1238 babies were submitted. There were 67/1039 complications in

Table VIb PGD for social sexing, data collection XII.

	FISH[a]
Cycles to OR	29
Number infertile	7
Female age (years)	34.34
ART method	
IVF	1
ICSI	22
IVF + ICSI	6
Cancelled after IVF/ICSI	1
Cycles to PGD	28
Zona breaching	
Laser drilling	28
Mechanical	–
Biopsy method	
Cleavage aspiration	23
Cleavage extrusion	4
Blastocyst	1
Embryology	
COCs	383
Inseminated	324
Fertilized	242
Biopsied	217
Successfully biopsied	216
Diagnosed	201
Transferable	71
Transferred	37
Frozen	26
Clinical outcome	
Cycles to ET	24
hCG positive	6
Positive heartbeat	5
Clinical pregnancy rate (% per OR/% per ET)	17.2%/20.8%
Implantation rate (fetal hearts/ embryos transferred)	16.2%
Deliveries	4
Delivery rate (% per OR/% per ET)	13.7%/16.6%
Miscarriages	0
Miscarriage rate (% per clinical pregn − pregn lost to FU)	0
Clinical pregnancies lost to FU	1

[a]In two cycles also quantitative fluorescent-PCR was used.

Table VIIa Evolution of pregnancy, data I–XI.

	n pregnancies	*n* fetal sacs
Pregnancies	**7529**	
FISH cycles	5867	
PCR cycles	1630	
FISH + PCR	9	
WGA cycles only[a]	22	
WGA + PCR[a]	1	
Subclinical pregnancies[b]	1159	
Clinical pregnancies without fetal heartbeat[a]	66	
Clinical pregnancies with fetal heartbeat	**6304**	**7853**
Singletons	4657	4657
Twins	1382	2764
Triplets	129	387
Quadruplet	11	44
Unknown	125	1[c]
Lost to FU during first trimester	**70**	**80**
First trimester loss	739	911
Miscarriage	719[d]	784
TOP	13[e]	14
Extra-uterine pregnancy	53[f]	43
Vanishing twins/triplets or miscarriage multiplet		166
Reduction of multiple pregnancies		68
Quadruplet to twin		14
Triplet to twin		19
Triplet to singleton		16[g]
Twin to singleton		16[h]
Unknown		3
Ongoing pregnancies>12 weeks	**5391**	**6723**
Second trimester loss	115	188
Miscarriage	90[i]	124
Miscarriage twin to singleton		4
TOP	38[j]	40
Twin to twin transfusion	1	2
Reduction of multiple pregnancies		33
Quadruplet to twin		4
Triplet to twin		11
Triplet to singleton		14
Twin to singleton		4
Lost to FU during second trimester	1360[k]	216
Deliveries	**5090**	**6304**
Singletons	3919	3919

Continued

Table VIIa *Continued*

	n pregnancies	*n* fetal sacs
Twins	1128	2256
Triplets	43	129

[a]Data available since data collection XI.
[b]Subclinical pregnancy defined as pregnancy without any other clinical signs, but positive serum hCG.
[c]Number of fetal heartbeats not known for data I–VIII. Counted further as one fetal heart.
[d]One miscarriage after amniocentesis.
[e]TOP, termination of pregnancy. Two TOPs for ancephalocoele, one TOP for social reasons, one TOP of twin with misdiagnosis for Charcot-Marie-Tooth disease 1a, one TOP for 47,XY+13, one TOP for encephelocele and one TOP for 47,XY+21, two TOPs after ultrasound abnormalities, two TOPs for unknown reason and one because of divorce.
[f]One heterotrophic gestation continued as singleton after reduction of extrauterine gestation at 6 weeks.
[g]One triplet resulted in a singleton due to reduction of one fetus and vanishing of another fetus.
[h]One triplet: fetal reduction, followed by amniocentesis and loss of remaining twin at 16 weeks (1 fetal sac counted in reduction, 2 in miscarriage, 1 s trimester pregnancy loss after miscarriage counted).
[i]TOP after misdiagnosis: one misdiagnosis for sexing, FISH, female fetus, indication SS; one misdiagnosis for β-thalassemia, PCR; one misdiagnosis for DM1, PCR, one misdiagnosis after PGS, karyotype 45,X; one misdiagnosis for a reciprocal translocation 46,XY,der(15)t(13;15)(q25.1;q26.3). TOP after ultrasound (four): enlarged lateral ventricle, two singletons with cardiopathy, one singleton with tetralogy of Fallot. TOP after amniocentesis, not related to the PGD: trisomy 18, indication for PGD parent carrier of reciprocal translocation not involving chromosome 18; one polymalformation; one cystic hygroma, failed karyotype; one Turner mosaic, one spina bifida, 5 trisomy 21 pregnancies, one mosaic 46,XY/47,XY+18 (misdiagnosis), one hemivertebrae, hypoplastic cerebellum, hydrocephaly (46,XX), one abnormal chromosome 15, one polycystic kidney, one Finnish nefrosis twin (both affected), one confirmed cytomegalovirus infection, one elective termination (unknown cause) and one hydrocephaly termination of a 8-month pregnancy [started as quadruplet: two selective reductions, one miscarriage after chorionic villus sampling (CVS) and the last fetus TOP].
[j]One misdiagnosis for sexing, PCR, indication Duchenne, twin pregnancy, selective termination of male fetus. Cycle done in 1996, Y-specific amplification only, Two ultrasound abnormalities, one spina bifida and hydrocephaly and one cystic hygroma. TOP of two monozygotic fetus of a triplet because of misdiagnosis (AS repeated IVF failures), anamnios, 47,XY,+21, 47,XYY, microdeletion 18, two fetus with trisomy 13.
[k]One misdiagnosis (47,XXX after PGS for RIF) lost to FU.

Table VIIb Evolution of pregnancy, data XII.

	n pregnancies	*n* fetal hearts
Pregnancies	**1607**	
FISH only cycles	1151	
PCR only cycles	393	
WGA + array	6	
FISH + PCR	6	
WGA + PCR	51	
Subclinical pregnancies[a]	246	
Clinical pregnancies lost	**65**	
Clinical pregnancies, with fetal heartbeat	**1296**	**1591**
Singletons	1018	1018
Twins	261	522
Triplets	17	51
Quadruplets	0	0
Lost to FU during first trimester	26	34
First trimester loss	**126**	**172**
Miscarriage	123	134
TOP[b]	3	3
Vanishing/miscarriage multiplets	**0**	**30**
Twin to singleton		24
Triplet to twin		4
Triplet to singleton		2
Reduction of multiple pregnancies	**0**	**5**
Triplet to twin		4
Twin to singleton		1
Ongoing pregnancies (>12 weeks)	1144	1385
Second trimester loss	**29**	**34**
Miscarriage	22	26
TOP[c]	7	8
Vanishing/miscarriage multiplets	**0**	**2**
Twin to singleton		2
Lost to FU during second or third trimester	53	62
Deliveries	**1062**	**1287**
Singletons	844	844
Twins	211	422
Triplets	7	21

[a]Subclinical pregnancy defined as a pregnancy without any other clinical signs.
[b]One TOP for misdiagnosis of reciprocal translocation, one TOP for Down's syndrome following PGD for HLA compatibility, one TOP for complication in pregnancy following PGD for neurofibromatosis Type 1.
[c]One TOP for acrania following PGD for CF, one TOP for severe growth retardation following PGD for Fragile X, one TOP for agensis corpus callosum following PGS for maternal age, one TOP for limb body wall defect following PGS for AS male factor, one TOP for neural tube defect following PGS for male factor, twin TOP for Down's syndrome risk following PGS for male factor, one TOP due to malformation at 16 weeks in remaining twins where first twin miscarried at 8 weeks.

pregnancy reported. This reduction compared with previous data collections was partly due to premature birth no longer being included as a complication of pregnancy. The delivery rates per indication are reported in Tables IIb, IIIb, IVb, Vb and VIb. Caesarean section was performed for 52% of the deliveries (557/1062) (Table IXb). In 83 cases, the method of delivery was not known. Confirmation of the diagnosis was performed prenatally (197/548) and/or post-natally (351/548) (Table Xb). Table Xb and Supplementary data, Table SXIIb show the abnormalities found during pregnancy or post-natally. A malformation was described in 20 singletons and 2 twins out of 863 babies documented. Several abnormalities were found that were not related to PGD indication. This report again confirms that pregnancies and babies born after PGD are very similar to the pregnancies obtained and babies born after ICSI treatment (Bonduelle *et al.*, 2002). In our series, the number of multiple pregnancies remains high (275/1296, 22%), which indicates that 34% (432/1169) of all babies born are part of a multiplet at birth (Table VIIb).

Table IXa Method of delivery and gestational age, data collection I–XI.

	Total	Singletons	Twins	Triplets
No deliveries[a]	5031[a]	3873[a]	1116[a]	42
Method of delivery				
Vaginal	2119	1898	219	2
Caesarian	2408	1595	779	34
Vaginal and Caesarian	9	2	7	0
Unknown	495	378	111	6
Term at delivery				
Preterm	1361	594	737	30
Term	3323	3022	297	5
Post term	1	1	0	0
Unknown	345	256	81	7

[a]For one twin there was only partial information: pregnancy was reported as a twin, birth and baby as a singleton.

Table IXb Method of delivery and gestational age, data XII.

	Total	Singleton	Twin	Triplet
No. deliveries	1062	844	211	7
Method of delivery				
Vaginal	422	386	36	0
Caesarean	555	391	158	6
Vaginal and Caesarean	2	0	2	0
Unknown	83	67	15	1
Term at delivery				
Preterm	253	108	140	5
Term	761	697	63	1
Post term	3	3	0	0
Unknown	45	36	8	1

Misdiagnoses

Table XIIIa summarizes the misdiagnoses reported for data I–XI, with no misdiagnoses reported in data X and data XI. In data XII (Table XIIIb), three adverse misdiagnoses from FISH are reported which were identified by prenatal diagnosis. Two were following PGS for maternal age and recurrent miscarriages; of which one was a misdiagnosed sex of which the pregnancy was continued to delivery and one was a trisomy 21 which miscarried. The third case was after PGD for a reciprocal translocation where the fetus was found to have the karyotype 46,XY,der(17)t(5;17)(p13;p13)mat and termination of pregnancy (TOP) was performed. No misdiagnosis was reported for monogenic PGD cycles.

Success of individual centres

Figure 1 shows the pregnancy rate per centre for data XII. The pregnancy rate ranges from 0 to 100% with an average of 23.04%, compared with 21.27% for data XI and 21% for data X. As previously observed, pregnancy rates are not correlated with the number of cycles that each centre performs, and the findings indicate that some of the most active centres fall below the average 23.04% pregnancy rate and even have pregnancy rates lower than some of the centres performing only a few cycles.

Discussion

This 12th data report of the ESHRE PGD Consortium demonstrates an increase (9.2%) in the number of PGD cycles, and related pregnancies and babies. There were a couple of notable trends in data XII compared with previous years. The first was that the global pregnancy rate per OR improved compared with previous years (23 versus 21.7 and 21.0% for data XI and X, respectively), even though there was no change in the mean ages of the women undergoing PGD, the indications for PGD cycles, the number of oocytes retrieved and the number of biopsied embryos. The other trend was that for monogenic PGD cycles, 1-cell biopsy was more frequently applied than 2-cell biopsy in data XII cycles, in contrast to previous data collections. This could reflect the development of more robust multiplex PCR assays which support improved diagnostic accuracy.

The three cases with a misdiagnosis result reported in data XII were all for cases analysed with FISH; no cases were reported for PCR-based monogenic PCR. This is in contrast to data reported so far on misdiagnosis in PGD (Wilton *et al.*, 2009), whereby misdiagnosis for FISH-based PGD is reported to be much less common than that for PCR-based PGD (0.1 compared with 0.5%, respectively). This recent change may be explained by the general improvement of PCR-based tests in recent years, although it could also be a coincidental finding within data XII.

Of the misdiagnosis reported in data XII, two were from the same centre following PGS for maternal age and recurrent miscarriages. One was a misdiagnosed sex, constituting a benign misdiagnosis, and the pregnancy was continued to delivery. The other one was a trisomy 21 which miscarried. The third case, from another centre, was after PGD for a reciprocal translocation where the fetus was found to have the karyotype 46,XY,der(17)t(5;17)(p13;p13)mat during prenatal diagnosis, and TOP was performed.

To date, including all cycles up to data XII, misdiagnosis has been reported for only 12/7759 PCR-based cycles and 19/30 965 FISH-based PGD cycles. However, these numbers may not reflect the true misdiagnosis in PGD, as many embryo transfers have no follow-up (no pregnancy or birth), and only a minority of centres perform audit through re-analysis of untransferred supernumerary embryos. Due the importance of evaluating the diagnostic accuracy in PGD and PGS, and additionally identifying potential pitfalls in methods or the biological limits posed by the samples, the PGD Consortium set-up two multicentre studies to re-analyse embryos following either PCR-based PGD or FISH-based PGD. Both studies compared results at the time of PGD with the results of the embryo follow-up analysis in a large cohort of samples. The evaluation of the concordance of FISH-based analysis at PGD and follow-up was difficult and the results have not been finalized. However, the PCR-based PGD study in fact

Table Xa Confirmation of diagnosis per fetal sac, data collection I–XI.

Method	Result			
	n	Normal	Abnormal	Failed
Prenatal diagnosis				
FISH				
CVS	138	133[a]	5[b]	0
Amniocentesis	749[c]	728[a,c]	18[d]	3
Ultrasound	1447[c]	1432	14[c,e]	1
Unknown	3	3	0	0
Total	2334[f]	2296	37	4
PCR				
CVS	201	196	5[g]	0
Amniocentesis	272	257	14[h]	1
Ultrasound	41	37	4[i]	0
Unknown	2	2	0	0
Total	514[f]	491	22	1
Post-natal diagnosis				
FISH				
Karyo miscarriage	126	59	66[j]	1
Karyo post-natal	247	243	5[k]	0
FISH microdeletion	2	2	0	0
Physical examination	1610	1605	6[l]	0
Karyo post-natal + physical examination	27	27	0	0
Unknown	3[m]	3[m]	0	0
Total	2015	1939	77	1
PCR				
Karyotype miscarriage	13	8	4[n]	1
DNA test miscarriage	2	2	0	0
DNA test post-natal	159	157	2°	0
Sweat test	10	10	0	0
Physical examination	117	116	1	0
Karyotype	16	15	1[p]	0
Karyo + DNA	6	5	1[q]	0
Karyo + phys exam	31	31	0	0
Hearing test	3	3	0	0
Algo test	2	2	0	0
Unknown	21[r]	21	0	0
Total	380	370	9	1

XL, x-linked.

[a]Total three miscarriages after normal outcome amniocentesis (1 FISH, 2 PCR), one miscarriage after normal outcome CVS (FISH).

[b]XY,+21->TOP (AS maternal age, repeated IVF failure); two Trisomies 21, TOP (PGD for reciprocal translocation); TOP because of trisomy 13 (AS maternal age); TOP of two fetus of a triplet because of misdiagnosis (unspecified). These two fetus were monozygotic, the third fetus of the triplet was ongoing and resulted in the at-term birth of a healthy male (AS repeated IVF failures).

[c]Three fetal sacs with abnormalities on ultrasound (enlarged lateral ventricle, cardiopathy, hydrocephalus) with normal result on amniocentesis.

[d]9% mosaic XY/XXY (FISH AS), abnormal chromosome 15 and skeletal displasia ->TOP (AS maternal age); Mosaic : 46,XY/47, XY+18-> TOP (AS repeated IVF failures); 21 trisomy->TOP (AS maternal age, repeated IVF failures). One twin 46,XY, inv(1)(p13q14), ongoing pregnancy, resulting in healthy boy and girl (FISH for maternal inv(1)(p12q23)); Trisomy 21, TOP (AS maternal age and repeated IVF failures); Trisomy 21, TOP (PGD sexing for XL Alport syndrome); 47,XYY, ongoing pregnancy (PGD for reciprocal translocation); 46,XX,15p+, ongoing pregnancy, resulting in birth of baby girl, no abnormalities reported (AS); TOP because of 47,XYY (Robertsonian translocation).

[e]Encephalocele->TOP (AS repeated miscarriage); hemivertebrae, hypolastic cerebellum, hydrocephaly->TOP; cystic hygroma one twin miscarriage->ongoing singleton (reciprocal translocation FISH). Abnormality in bladder, CVS showed normal karyotype, pregnancy resulting in miscarriage (reciprocal translocation); one twin hydrops fetalis, TOP, other twin miscarriage but normal CVS result (AS); Tricuspid atresia on ultrasound, TOP (SS for male).

[f]Three fetal sacs had PCR and FISH at PGD.

[g]47,XY,+13->TOP (PCR: not affected of Zellweger); TOP because of trisomy 13 [CF/congenital bilateral absence of the vas deferens (CBAVD)].

[h]Monozygous twin affected with Finnish nefrosis, TOP (PGD for beta-thalassemia); TOP because of trisomy 21 (X-linked retinoschizis); TOP because of microdeletion 18 (CF/CBAVD).

[i]TOP because of ultrasound abnormalities, i.e. spina bifida and hydrocephalus (Charcot–Marie–Tooth type 1a).

[j]Mosaic 4n/2n (AS oocyte donation recurrent miscarriage); trisomy 20 (AS maternal age recurrent miscarriage); 92,XXXX (AS maternal age repeated IVF failures); 47,XX,+10 (AS recurrent miscarriages maternal age); 46,XY/45,X0 (AS oocyte donation); 45,X,t(2;4)(q11.2;q13) (FISH reciprocal translocation); 47,XY,t(11;22)(q23;q11.2),+16[11]/46,XY,t(11;22)[7] (FISH reciprocal translocation); trisomy 21, confirmation after TOP (AS maternal age and repeated IVF failures); 46XX, 16q+ (AS maternal age); trisomy 15 (AS maternal age); trisomy 17 (AS recurrent miscarriages); 45,XO (FISH Robertsonian translocation); trisomy 12 (AS maternal age); Embryo 46,XX, umbilical cord mosaic 47,XX,+14/48,XX,+14,+17 (AS maternal age); 45,XO (FISH reciprocal translocation); trisomy 8 (AS recurrent miscarriages); trisomy 21 (AS maternal age); 47,XX,+4 (AS SMF), two times trisomy 7 (twin pregnancy, AS recurrent miscarriages), trisomy 10 (AS maternal age), three times 47,XX,+14 (one twin pregnancy, AS maternal age and recurrent miscarriages), one twin pregnancy of which the karyotyping of the second fetus failed (AS maternal age and recurrent IVF failures), trisomy 16 (AS maternal age and repeated IVF failures), chromosomal abnormality 18 (AS recurrent miscarriages), 47,XY,+20 (AS maternal age), trisomy 21 (reciprocal translocation), 92,XXXX (AS repeated IVF failures), 92,XXYY (AS maternal age and repeated IVF failures).

[k]Weak gonosomales mosaicism (AS recurrent miscarriages).

[l]Misdiagnosis after gender selection for XL retinitis pigmentosa: male.

[m]Two children had unknown check and karyotype.

[n]Trisomy 9 (haemophilia B), trisomy 16 (CF/CBAVD).

[o]Expansion DMPK gene (DM1).

[p]Misdiagnosis PGD for tuberous sclerosis (TSC2): duodenal stenosis secondary to annular pancreas, possible giant cell astrocytoma at the foramen of Monroe, intracardial tuberomas, TSC2 in newborn confirmed.

[q]One girl of twin affected with congenital abnormalities due to 10% mosaic trisomy 9, other baby healthy (PCR SCA3).

[r]Sweat test (CF/CBAVD).

Table Xb Confirmation of diagnosis per fetal sac, data collection XII.

Method	*n*	Result		
		Normal	Abnormal	Failed
Prenatal diagnosis				
Array				
CVS	1	1	0	0
Total	1	1	0	0
FISH				
CVS	13	10	2[a]	1[b]
Amniocentesis	80	79	1[c]	0
Ultrasound	13	12	1[d]	0
Total	106	101	4	1
PCR				
CVS	21	20	1[e]	0
Amniocentesis	52	52	0	0
Ultrasound	17	16	1[f]	0
Total	90	88	2	0
Post-natal diagnosis				
Array				
Karyo post-natal	1	1	0	0
Karyo miscarriage	1	0	0	1
Total	2	1	0	1
FISH				
Karyo miscarriage	8	6	1[g]	1
Karyo post-natal	43	41	0	2
Physical examination	175	175	0	0
Karyo post-natal + physical examination	1	1	0	0
Karyo post-natal + DNA	1	1	0	0
Total	228	224	1	3
PCR				
Karyo miscarriage	3	2	0	1
Physical examination	33	33	0	0
DNA-test post-natal	48	48	0	0
Karyo post-natal	6	6	0	0
DNA-test + karyo	15	15	0	0
Other	2[h]	2	0	0
Unknown	14	14	0	0
Total	121	120	0	1

[a]Misdiagnosis of 46,XY,der(17)t(5;17)(p13;p13)mat after PGD for reciprocal translocation t(5;17)(p13;p13). Misdiagnosed sex after PGS for maternal age and recurrent miscarriages. Trisomy 21 after PGS for maternal age and recurrent miscarriages.
[b]Miscarried trisomy 21 after PGS for maternal age and recurrent miscarriages.
[c]47,XXX after PGD for reciprocal translocation t(9;10)(q32;p12.32).
[d]TOP of twins because of risk of Down's syndrome after PGS for SMF.
[e]TOP for trisomy 21 after PGD for HLA compatibility (HLA result confirmed).
[f]TOP for acrania following PGD for CF (CF result confirmed).
[g]47,XY+2 after PGD for reciprocal translocation (46,XY,t(8;9)(q21.2;p21).
[h]Enzymatic dosage (CF/CBAVD) and hearing test + physical examination (Leopard syndrome).

demonstrated the validity, robustness and high diagnostic value of PCR-based PGD protocols in current use by the PGD community (Dreesen *et al.*, 2013, accepted). Thus, it is likely that misdiagnosis is in fact minimal in PGD, indicating that overall PGD centres apply high standards in PGD practice, as outlined in the Best Practice Guidelines (Harton *et al*, 2011ab,c,d).

At the time of data collection there were two levels of membership of the PGD Consortium: full membership for centres who submit

Table XIa Data on live-born children, data collection I–XI.

Total children born		5063[a]
Sex		
Male		2784
Female		3014
Unknown		265
Mean birthweight (g)		
Singletons	3222	3385
Twins	2527	1878
Triplets	2040	82
Mean birth length (cm)		
Singletons	50	2235
Twins	46	1118
Triplets	45	23

[a]Numbers in the right column indicate the number of newborns for whom information is available.

Table XIb Data on children born, data collection XII.

Total children born		1238	
Sex			
Male		611	
Female		621	
Unknown		6	
Mean birthweight (g)			
Singletons		3223	(759/812)[a]
Twins		2317	(376/408)[a]
Triplets		1752	(18/18)[a]
Mean birth length (cm)			
Singletons		49.3	(545/812)[a]
Twins		47.6	(247/408)[a]
Triplets		46.1	(8/18)[a]
Mean head circumference (cm)			
Singletons		34.1	(177/812)[a]
Twins		32.0	(75/408)[a]
Triplets		32.8	(2/18)[a]
Apgar scores[b] after 1 min	Singletons	Twin	Triplet
Good[c]	231	90	2
Poor[c]	8	11	0
Apgar scores after 5 min			
Good[c]	229	93	2
Poor[c]	2	4	0
Apgar scores after 10 min			
Good[c]	96	41	0
Poor[c]	0	1	0

[a]Numbers within brackets indicate the number of newborns for whom information is available out of the total number of newborns.
[b]Exclusive stillborns, see Supplementary data, Table SXIIb
[c]Good is defined ≥7, poor is defined <7.

complete data on the PGD cycles and associate membership for centres who send in summary data. The latter are usually satellite PGD centres that collaborate with more than one IVF centre and often do not have access to information about the IVF cycles (associate members also included IVF laboratories performing transport PGD with a centre that is a full member, as well as new member centres). However, for data XII, very few associate centres (only four) sent in summary data and so these data were not included in this report. Due to the low response rate, the information requested for associated centres in the summary data they submit will be amended to include even fewer details. The Steering Committee (SC) considers that even only basic data such as the numbers and on minimal details on the genetic diagnosis in PGD cycles are important for the data collections.

Data collection is a very time consuming activity for all involved, including the centres that make the effort to submit data as well as the curators of the data. For this reason, the evaluation and publication of data collections is lagging. The SC acknowledges the effort of all contributing centres and aims to address the lag as soon as possible, although it is planned that by the end of 2014 there will be an on-line data submission platform ready for all consortium members to use. However, since the data collections do not represent real-time trends in PGD, the PGD Consortium SC has initiated a working group to monitor the introduction and application of new technologies in PGD. All PGD centres have been sent a questionnaire that they are invited to complete, which aims to evaluate the introduction of new technologies at all stages in PGD, including gamete fertilization, embryo biopsy practice and genetic testing strategies and technologies.

Overall, the data collection provides an extremely valuable resource for data mining and for following trends in PGD practice. Including all the cycles submitted from data I until data collections XIII and XIV (the latter including PGD cycles carried out between January and December 2010 or 2011 with babies delivered up to 2011 or 2012, respectively), the Consortium will have information on almost 52 000 cycles. So far a preliminary data mining effort has been initiated, including data collection IV through to XI (>29 000 cycles). This data set should highlight the trends in PGD practice over the earlier years. The aim is to be able to follow all trends in PGD practice more closely in order to facilitate selecting the most appropriate and optimized approach for each patient undergoing a clinical PGD cycle.

Supplementary data

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

Acknowledgements

Many thanks also to all of the centres who participated in data collection XII. *Argentina*: Fecunditas; *Australia*: Melbourne IVF; *Belgium*: Department of Embryology and Genetics of the VUB and Centre for Medical

Table XIIIa Summary of misdiagnosis from data I to XI (no misdiagnosis reported for data X and XI).

Indication	Method used	PND-Post-natal	Outcome	Reported in
Monogenics				
DM1	PCR	PND	TOP	I
β-Thalassemia	PCR	PND	TOP	II
β-Thalassemia	PCR	PND	TOP	VIII
Familial amyloid polyneuropathy	PCR	PND	Born	IV
CF	PCR	PND	Born	II
CF (one of twins)	PCR	Post	Born	IV
CMT1A	PCR	PND	born	Cycle reported in V but misdiagnosis in VII
SMA	PCR	Post	Born	Cycle reported in IV but misdiagnosis in VII
CMT1A (twins)	PCR	PND	TOP of both twins	VII
Fragile X	PCR	PND	Born	VIII
Sexing for X-linked disease				
46,XY in retinitis pigmentosa	PCR	PND	Born	IV
46,XY in DMD twin	PCR	PND	TOP of one twin	III
45,X, haemophilia A	FISH	PND	TOP	IV
46,XY, haemophilia A	FISH	Post	Born	VIII
Translocations				
Trisomy 13 after 45,XY,der(13;14)(q10;q10)	FISH	Miscarried	Miscarried	VI
47,XX,+der(22)t(11;22)(q23.3;q11.2)mat	FISH	PND	TOP	III
46,XY,der(15)t(13;15) (q25.1;q26.3)pat	FISH	PND	TOP	VII
PGS				
47,XXX	FISH	PND	Lost to follow-up	VII
45,X	FISH	PND	Miscarriage	VIII, reported in IX
Trisomy 16 after first PB biopsy only	FISH	Miscarried	Miscarried	VI
Trisomy 16 after first PB biopsy only	FISH	Miscarried	Miscarried	V
Trisomy 16	FISH	Miscarried	Miscarried	VI
Trisomy 16	FISH	Miscarried	Miscarried	VI
Trisomy 21	FISH	Post	Born	III
Trisomy 21	FISH	PND	TOP	IX
Trisomy 21	FISH	PND	TOP	IX
46,XY/47,XY+18	FISH	PND	TOP	IX
Social sexing				
Requested male but female fetus	FISH	PND	TOP	III

PND, prenatal diagnosis; DM1, myotonic dystrophy type 1; CMT1A, Charcot-Marie-Tooth; SMA, spinal muscular atrophy; DMD, Duchenne muscular dystrophy.
The numbers in the last column indicate the PGD Consortium report number.

Genetics of the Universitair Ziekenhuis Brussels; Hopital Erasme, ULB, Laboratoire FIV; Leuven Institute for Fertility and Embryology; Leuven University Fertility Centre; GIFT, ZOL Ziekenhuis; *Brazil*: Fertility-Assisted Reproductive Centre, Sao Paolo; *Czech Republic*: Sanatorium Repromeda; Institute Pronatal, Genetics; *Denmark*: Centre for Preimplantation Genetic Diagnosis, Aarhus University Hospital, Fertility Clinic; Fertility Clinic, University of Odense; Finland: Helsinki University Central Hospital, Department of Obstetrics & Gynaecology/IVF Unit; *France*: Hôpitaux Universitaires de Strasbourg, Unité de diagnostique préimplantatoire, Service de la Biologie de la Reproduction; Institut de biologie, Lab de Biochemie Génétique; *Germany*: University of Bonn, Department of Obstetrics & Gynaecology, Section of Reproductive Medicine; Centre for Gynecological Endocrinology, Reproductive Medicine and Human Genetics; University Clinic of Schleswig-Holstein, Campus Luebeck, Department of Obstetrics and Gynecology; Fertility Center Hamburg; Kinderwunschcentrum München; Gyn-Gen-Lehel München; Landes-Frauen und Kinderklinik, Humangenetische Untersuchungs- und Beratungsstelle & IVF-Kinderwunsch Abteilug; *Greece*: IVF & Genetics; University of Athens, St. Sophia's Children's Hosp, Laboratory of Medical Genetics; EMBRYOGENESIS, Centre for Subfertility Studies;

Table XIIIb Summary of misdiagnosis from data XII.

Indication	Method used	PND-post-natal	Outcome	Reported in
Translocations				
Reciprocal translocation	FISH	PND	TOP[a]	XII
PGS				
46,XY	FISH	PND	Born[b]	XII
Trisomy 21	FISH	PND	Miscarried[c]	XII

The numbers in the last column indicate the PGD Consortium report number.
[a]Karyotype 46,XY,der(17)t(5;17)(p13;p13)mat after PGD for reciprocal translocation t(5;17)(p13;p13).
[b]Misdiagnosed sex after PGS for maternal age and recurrent miscarriages.
[c]Trisomy 21 after PGS for maternal age and recurrent miscarriages.

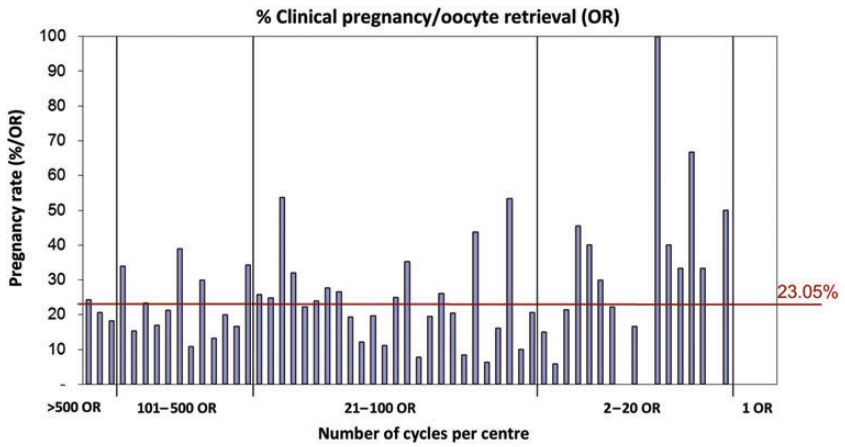

Figure 1 Pregnancy rate per centre for data XII.

IVF and Infertility Centre; Interbalkan European Medical Centre; Centre for Human Reproduction, Genesis Athens Clinic; *India*: Krishna IVF Clinic; *Israel*: Tel-Aviv Sourasky Center; Institute of Human Genetic, Sheba Medical Centre; Zohar PGD lab, Medical Genetics Unit; *Italy*: SISMER; Reproductive Medicine, European Hospital; EmbryorGen, Centre for Preimplantation Genetic Diagnosis; *Japan*: Kato Ladies Clinic Perinatal Genetics; St. Mother Hospital; Poland: INVICTA Fertility and Reproductive Centre; *Portugal*: Faculty of Medicine of Porto- Hospital S. Joao, Department of Medical Genetics; *Singapore*: Centre for Assisted Reproduction (CARE); *Spain*: Instituto Dexeus; Instituto Valenciano de Infertilidad; Institut Marquès, Servei de Diagnostic Genètic Preimplantacional; Sistemas Genomicos SL Valencia; Instituto de Reproduccion CEFER; Clinica GINEFIV; IVI Madrid, Embryology-PGD; *Sweden*: Department of Clinical Genetics, Karolinska Hospital; Sahlgrenska University Hospital, Department of Ob/Gyn; *Taiwan*: Lin-Kou Medical Centre, Chang Gung Memorial Hospital & Medical College, Department Of Ob/Gyn; *The Netherlands*: PGD working group Maastricht, The Centre for Reproductive Medicine, Department of Obstetrics and Gynaecology, Sub-departement Infertility, and Department of Clinical Genetics; University Medical Centre Utrecht; *Turkey*: Istanbul Memorial Hospital, reproductive endocrinology & ART centre; Acibadem Genetic Diagnosis and Cell Therapy Centre, Acibadem Genel Mudurluk; *UK*: University College – Medical School, UCL Centre for PGD – EGA Institute for Womens Health; St. Thomas' Hospital, Academic Department of Women's Health; Glasgow Royal Infirmary; Edingburgh Fertility and Reproductive Endocrine Centre, Simpson Centre for Reproductive Health, Edingburgh Royal Infirmary; *Ukraine*: Clinic of Reproductive Medicine 'Nadiya'; *USA*: Jones Inst. for Reproductive Medicine; Reproductive Biology associates.

Authors' roles

C.M.: cumulative tables and text merging; V.G.: analysis of the raw data and editing of the tables; E.C.: tables and text chromosomal abnormalities; M.d.R.: tables and text monogenic disorders; G.K.: tables sexing only; P.R.: tables and text pregnancies and babies; S.S.: tables and text pregnancies and babies; K.V.: tables and text PGS; J.T.-S.: tables and text social sexing, main text.

Funding

No external funding was either sought or obtained for this study.

Conflict of interest

None declared.

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