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ESHRE PAGES

ESHRE PGD Consortium data collection XIII: cycles from January to December 2010 with pregnancy follow-up to October 2011†

M. De Rycke[1,*], F. Belva[1], V. Goossens[2], C. Moutou[3], S.B. SenGupta[4], J. Traeger-Synodinos[5], and E. Coonen[6]

[1]Centre for Medical Genetics, UZ Brussel, Laarbeeklaan 101, 1090 Brussels, Belgium [2]ESHRE Central Office, Meerstraat 60, 1852 Grimbergen, Belgium [3]Université de Strasbourg, Hôpitaux Universitaires de Strasbourg, Service de la Biologie de la Reproduction, CMCO, 19, Rue Louis Pasteur, BP120, 67303 Schiltigheim, France [4]UCL Centre for PG & D, Institute for Women's Health, University College London, London, UK [5]Laboratory of Medical Genetics, University of Athens, St. Sophia's Children's Hospital, 11527 Athens, Greece [6]PGD Working Group Maastricht, Department of Clinical Genetics, Maastricht University Medical Centre, PO Box 5800, 6202 AZ Maastricht, The Netherlands

*Correspondence address. E-mail: martine.derycke@uzbrussel.be

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STUDY QUESTION: How do data in the 13th annual data collection (Data XIII) of the European Society of Human Reproduction and Embryology (ESHRE) PGD Consortium compare with the cumulative data for collections I–XII?

SUMMARY ANSWER: The 13th retrospective collection represents valuable data on PGD/PGS cycles, pregnancies and children: the main trend observed is the decrease in the routine implementation of PGS.

WHAT IS KNOWN ALREADY: Since 1999, the PGD Consortium has collected, analysed and published 12 data sets and an overview of the first 10 years of data collections.

STUDY DESIGN, SIZE, DURATION: Data were collected from each participating centre using a FileMaker Pro database (versions 5–11). Separate predesigned FileMaker Pro files were used for the cycles, pregnancies and baby records. The study documented cycles performed during the calendar year 2010 and follow-up of the pregnancies and babies born which resulted from these cycles (until October 2011).

PARTICIPANTS/MATERIALS, SETTING, METHODS: Data were submitted by 62 centres (full PGD Consortium members). The submitted data were thoroughly analysed to identify incomplete data entries and corrections were requested from the participating centres. Records remaining with incomplete or inconsistent data were excluded from the calculations. Corrections, calculations and tables were made by expert co-authors.

MAIN RESULTS AND THE ROLE OF CHANCE: For data collection XIII, 62 centres reported data for 5780 cycles with oocyte retrieval (OR), along with details of the follow-up on 1503 pregnancies and 1152 babies born. A total of 1071 OR were reported for chromosomal abnormalities, 108 OR for sexing for X-linked diseases, 1574 OR for monogenic diseases, 2979 OR for preimplantation genetic screening and 48 OR for social sexing.

LIMITATIONS, REASONS FOR CAUTION: The findings apply to the 62 participating centres and may not represent worldwide trends in PGD.

WIDER IMPLICATIONS OF THE FINDINGS: The annual data collections provide an important 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

Introduction

The European Society of Human Reproduction and Embryology (ESHRE) PGD Consortium was established in 1997. Its major objectives are to establish guidelines, to promote best practice and to collect data on PGD cycles, pregnancies, deliveries and children. Four guidelines on different aspects of PGD (organization of a PGD centre, fluorescence

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Table Ia Overall cycle data collection I–XII.

Indication	PGD	PGS	PGD-SS	Total
Cycles to OR	14 968[a]	23 758	705	39 431
Number infertile	5251	19 357	111	24 719
Female age (years)	33	37	36	35
Cancelled before IVF/ICSI	52	2	0	54
ART method				
IVF	1468	2572	169	4209
ICSI	13 217	20 669	506	34 392
IVF + ICSI	67	385	6	458
Frozen + ICSI + IVF + unknown	180	80	24	284
Unknown	20	50	0	70
Cancelled after IVF/ICSI	680	480	17	1177
Cycles to PGS/PGD	14 272	23 276	688	38 236
FISH	6797	23 249	506	30 552
PCR	7304	9	182	7495
FISH + PCR	71	0	0	71
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	4883	5984	26	10 893
laser drilling	8612	15 151	235	23 998
Mechanical	763	2076	427	3266
Unknown	14	65	0	79
Biopsy method				
PB biopsy	270[b]	4477[b]	0	4747[b]
Cleavage aspiration	13 272[b]	17 749[b]	181	31 202[b]
Cleavage extrusion	537	958	506	2001
Cleavage flow displacement	16	22	0	38
Blastocyst	103	7	1	111
PB and cleavage	69	12	0	81
Unknown	16	52	0	68
Embryology				
COC's	200 404	268 606	9759	478 769
Inseminated	168 645	222 267	8146	399 058
Fertilized	123 022	158 162	5713	286 897
Biopsied	91 710	126 654	4525	222 889
Successfully biopsied	90 522	125 455	4382	220 359
Diagnosed	82 250	116 719	3927	202 896
Transferable	30 699	40 561	1533	72 793
Transferred	19 098	30 094	1035	50 227
Frozen	4855	5457	369	10 681
Clinical outcome				
Cycles to ET	10 803	17 105	518	28 426
hCG positive	3911	6006	203	10 120
Positive heart beat	3080	4756	148	7984
Clinical pregnancy rate (% per OR/% per ET)	21/29	20/28	21/29	20/28

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 complexes; SS, social sexing; PGS, preimplantation genetic screening; FISH, fluorescence *in situ* hybridization; ET, embryo transfer; ART, assisted reproductive technology; PB, polar body; WGA, whole genome amplification.
[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 XIII.

Indication	PGD	PGS	Total
Cycles to OR	2753	2979	*5732
Number infertile	851	2063	2914
Female age (years)	33	39	36
Cancelled before IVF/ICSI	1	1	2
ART method			
IVF	204	271	475
ICSI	2513	2679	5192
IVF + ICSI	22	19	41
Frozen + ICSI + IVF	9	9	18
Unknown	4	1	5
Cancelled after IVF/ICSI	79	1	80
Cycles to PGS/PGD	2673	2978	5651
FISH	1043	2844	3887
PCR	1408	1	1409
FISH + PCR	22	0	22
PCR + WGA	99	0	99
Arrays	62	119	181
PCR + arrays	37	5	42
PCR + WGA + arrays	2	6	8
FISH + arrays		3	3
Zona breaching			
AT drilling	449	509	958
laser drilling	2031	2219	4250
Mechanical	193	250	443
Biopsy method			
PB biopsy	59	762	821
Cleavage aspiration	2454	2072	4526
Cleavage extrusion	108	83	191
Blastocyst	39	47	86
PB and embryo	13	14	27
Embryology			
COC's	34 446	31 588	66 034
Inseminated	28 627	26 166	54 793
Fertilized	21 329	19 084	40 413
Biopsied	16 768	15 163	31 931
Successfully biopsied	16 458	15 068	31 526
Diagnosed	15 247	14 548	29 795
Transferable	5408	4529	9937
Transferred	3023	3241	6264
Frozen	1336	633	1969
Clinical outcome			
Cycles to ET	1982	2012	3994
hCG positive	831	762	1593
Positive heart beat	675	594	1269
Clinical pregnancy rate (% per OR/% per ET)	25/34	20/30	22/32
Number fetal heartbeats	795	720	1515
Implantation rate (fetal hearts/embryos transferred)	26	22	24

Continued

Table Ib *Continued*

Indication	PGD	PGS	Total
Deliveries	567	430	997
Delivery rate (% per OR/per ET)	21/29	14/21	17/25
Miscarriages	54	99	153
Miscarriage rate (% per clinical pregn − pregn lost to FU)	9	18	13
Clinical pregnancies lost to FU	54	39	93

PGD column includes PGD for chromosome abnormalities, sexing for X linked disease and PGD for monogenic disorders; *48 cycles for social sexing have not been included in this table. FU, follow-up.

in situ hybridization (FISH)-based testing, amplification-based testing and biopsy) have been written (Harton *et al*., 2011a,b,c,d). To date, 12 extensive data collections have been published, covering all applications of PGD, including monogenic diseases, HLA typing and chromosome abnormalities, preimplantation genetic screening (PGS) and social sex selection (Geraedts *et al*., 1999, 2000; ESHRE PGD Consortium Steering Committee, 2002; Sermon *et al*., 2005, 2007; Harper *et al*., 2006, 2008, 2010b; Goossens *et al*., 2008, 2009, 2012; Moutou *et al*., 2014). An overview has been presented after 10 years of data collection (Harper *et al*., 2012). This 13th report summarizes data collected for the calendar year 2010 and follow-up of pregnancies and babies born until October 2011.

Materials and Methods

Participating centres anonymously reported data on PGD cycles, pregnancies and babies in separate files using a FileMaker Pro database (versions 5–11). The blank FileMaker Pro files were distributed to each PGD Consortium member centre at the end of 2009. Submitted data were 'cleaned' by the science manager of ESHRE. This preliminary analysis allowed the identification of omissions and any ambivalent data entries. Records with incomplete data were excluded from the calculations whereas data inconsistencies were clarified following contact with the relevant participating centre. The different files were then assigned to expert co-authors for an in-depth analysis, followed by calculations and presentation of results in tables.

Clinical pregnancies were defined as the presence of one or more fetal hearts at 6 weeks of gestation. Implantation rate was defined as the number of fetal hearts per 100 embryos transferred. Delivery rate was defined as the percentage of pregnancies with delivery per oocyte retrieval procedure (OR) and per embryo transfer procedure.

Results

Only data from centres with a full PGD Consortium membership were taken into account, as only these members can provide full information on all aspects of PGD. This report includes data from 62 centres. The results are represented in tables according to an established lay out. Accompanying text is deliberately concise and seven tables are available in an electronic version only: Supplementary Table SIIc lists the abnormal karyotypes carried by the patients undergoing PGD, Supplementary Table SIIIc lists the X-linked diseases for which sexing was carried out, Supplementary Table SIVc lists the monogenic diseases for which PGD was carried out, Supplementary Tables SVIIIa (data I–XII) and SVIIIb (data XIII) list the complications of pregnancy and Supplementary Tables SXIIa (data I–XII) and SXIIb (data XIII) list the congenital malformations and the neonatal complications. An overview of all cycles collected previously in data collections I–XII can be found in Table Ia, while an overview of the current data collection can be found in Table Ib. The data for social sexing (48 cycles) have not been included in this last table, see below. For all PGD/PGS cycles (5780 cycles to OR), ICSI was the method most often used for fertilization (5192/5780, 90%). For all cycles to biopsy (5651), zona pellucida drilling was more commonly performed using a laser (4250/5651, 75%) and cleavage-stage aspiration was the preferential stage/method for biopsy (4526/5651, 80%) (Table Ib).

PGD cycles for structural chromosomal abnormalities

Table IIb summarizes the 1071 cycles with OR for data collection XIII, a total number that has increased by 23% compared with data XII (870). In 64 cycles, PGD for a structural chromosome abnormality was performed simultaneously with aneuploidy screening, a slight decrease as compared with data XII. In 15 cycles, PGD was performed simultaneously for an additional FISH (13 cycles) or monogenic indication (2 cycles). Two PGD cycles were performed for a complex chromosomal rearrangement.

As for all years (cumulative data shown in Table IIa), data XIII 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 equalled that for male carriers, whereas for Robertsonian translocations (28% of total cycles), the number of cycles performed for male carriers was about 2-fold that of female carriers. The Robertsonian translocation male carrier group was dominated by the 45,XY,der(13;14) karyotype (61%), an indication that is known to coincide with male infertility (70% of couples in this group).

Overall, 47% of cycles were performed for infertile patients. The rate of infertility ranged from 35% for female carriers up to 70% for male carriers, both in the group with Robertsonian translocations.

Mean female age was 33 years, a figure that shows little variation over the years. In 82% of all cycles to OR, ICSI was used for fertilization, similar to data XII. Nearly all cycles to OR (96%) reached the biopsy stage. The use of laser drilling for zona breaching covered 77% of all cycles in data XIII. Aspiration of blastomeres from cleavage-stage embryos remained the preferred biopsy method (89%). The majority of cycles has been

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

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	1065	630	1638	1754	370	440	5897
Number infertile	800	298	891	749	311	234	3283
Female age (years)	35	33	34	34	32	35	33
Cancelled before IVF/ICSI	0	0	4	2	7	2	15
ART method							
IVF	48	111	280	474	31	82	1026
ICSI	996	499	1307	1232	327	345	4706
IVF + ICSI	5	10	12	15	4	4	50
Frozen + ICSI + IVF + unknown	15	10	34	31	1	7	98
Unknown	1	0	1	0	0	0	2
Cancelled after IVF/ICSI	54	26	95	101	24	21	321
Cycles to PGD	1011	604	1539	1651	339	417	5561
Zona breaching							
AT drilling	381	273	706	780	119	150	2409
Laser drilling	606	314	786	808	182	233	2929
Mechanical	24	17	47	63	38	34	223
Biopsy method							
PB biopsy	3	16	2	39	1	4	65
Cleavage aspiration	954	548	1441	1490	323	393	5149
Cleavage extrusion	50	39	83	108	12	19	311
Cleavage flow displacement	2	0	2	4	3	0	11
Blastocyst	2	1	11	10	0	1	25
Embryology							
COC's	14 832	8762	22 345	23 640	4560	5611	79 750
Inseminated	12 365	7470	19 027	20 517	3758	4776	67 913
Fertilized	8419	5456	13 568	14 979	2607	3475	48 504
Biopsied	5987	4158	10 308	11 765	1840	2699	36 757
Successfully biopsied	5913	4110	10 171	11 608	1820	2672	36 294
Diagnosed	5413	3805	9458	10 867	1681	2479	33 703
Transferable	2057	1128	1921	2123	740	814	8783
Transferred	1359	795	1532	1691	506	545	6428
Frozen	296	136	141	151	77	99	900

Continued

Table IIa *Continued*

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
Clinical outcome							
Cycles to ET	782	456	946	1024	267	316	3791
hCG positive	304	165	325	357	88	96	1335
Positive heart beat	256	133	242	282	68	76	1057
Clinical pregnancy rate (% per OR/% per ET)	24/33	21/29	15/26	16/28	18/25	17/24	18/28

[a]Five cycles included PGS, seven cycles were performed for an additional FISH indication.
[b]One cycle included PGS, two cycles included 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, ten included an additional FISH indication, four with an additional PCR indication.

analysed by FISH (93%), while array technology or PCR were applied in a minority of cycles (6 and 1% respectively).

For data XIII, 13 211 oocytes were collected, a mean of 12.3 per cycle. Of these, 61% (8042/13 211) were fertilized (2 pronuclei) and 77% (6209/8042) of the resulting embryos were biopsied. Of the embryos successfully biopsied, 94% (5810/6149) gave a diagnostic result, of which only 24% (1403/5810) were transferable. This was in line with previous years (data I–XII) where a mean of 13.5 oocytes per cycle were collected and 26% of diagnosed embryos were genetically transferable. As expected, the lowest percentage of transferable embryos was found in the reciprocal translocation group (19% for male carriers and 16% for female carriers). Of all transferable embryos, 68% were actually transferred and 18% were frozen.

From 1071 cycles to OR, only 62% resulted in an embryo transfer procedure (ranging from about 49% for female reciprocal translocation carriers to 80% for carriers of a deletion). This is in agreement with previous data (embryo transfer in 64% of cycles to OR; data I–XII 3791/5897) showing that a high level of chromosomally abnormal embryos is found in patients carrying chromosomal abnormalities.

A positive hCG was obtained in 261 cycles, with a positive heart beat in 206 cycles (19% per OR and 31% per embryo transfer). The poorest outcome, 12% positive heart beat per OR, in the group of female reciprocal translocation carriers is a consequence of the lowest percentage of transferable embryos available for this group. Overall, the implantation rate was 26% (246/951), ranging from 22% in the male carrier of a Robertsonian translocation group to 33% in the female carrier of a reciprocal translocation group. Finally, the delivery rate was 15% per OR (165/1071) and 25% per embryo transfer procedure (165/659). There were 10 reported miscarriages and 31 clinical pregnancies were lost to follow-up. Implantation and delivery rates have remained stable over the last years: the delivery rate for data I–XII is 18% per OR and 28% per embryo transfer procedure.

PGD cycles for sexing for X-linked diseases

Tables IIIa and IIIb summarize the 1376 and 108 cycles to OR collected for data collections I–XII and XIII, respectively. As holds true for the PGD cycles for a chromosomal abnormality, the majority of cycles for X-linked diseases in data XIII (Table IIIB) was performed with ICSI (78%; 77/99), laser drilling (80%; 79/99) and biopsy by cleavage-stage aspiration (96%; 95/99). FISH was no longer the only method used for sexing cycles: PCR was applied in 12% of cycles.

For data XIII, 1294 oocytes were collected (a mean of 12.0 per OR), 73% (821/1132) of inseminated oocytes were fertilized and 74% (608/821) of the resulting embryos were biopsied. Of the embryos successfully biopsied, 95% (564/594) gave a diagnostic result, of which only 32% (178/564) were transferable. From 178 transferable embryos, 118 were actually transferred in 80 cycles (74% of cycles to OR). A positive hCG was obtained in 33 cycles, with a positive heart beat in 23 cycles (21% per OR and 29% per embryo transfer). This gave an implantation rate of 23% (27/118). Finally, the delivery rate was 19% per OR (20/108) and 25% per embryo transfer (20/80). There were two reported miscarriages and one pregnancy was lost to follow-up.

PGD cycles for monogenic diseases

Tables IVa and IVb summarize the 7693 and 1574 cycles to OR collected for data collection I–XII and XIII, respectively. Overall, the number of

Table IIb PGD for chromosomal abnormalities, data collection XIII.

Indication	Robertsonian translocation, male carrier	Robertsonian translocation, female carrier	Reciprocal translocation, male carrier	Reciprocal translocation, female carrier	Deletion	Inversion	Other	Total
Cycles to OR	197	101	301	347	15	51	59	1071
Number infertile (%)	138 (70)	35 (35)	142 (47)	130 (38)	7 (47)	25 (49)	31 (53)	508
Female age (years)	35	34	34	29	33	36	34	33
Cancelled after OR before IVF/ICSI	0	0	1	0	0	0	0	1
ART method								
IVF	6	15	52	89	1	7	2	172
ICSI	189	84	242	252	14	44	57	882
IVF + ICSI	1	2	5	5	0	0	0	13
ICSI + frozen	1	0	1	1	0	0	0	3
Cancelled after IVF/ICSI	7	2	7	16	0	2	5	39
Cycles to PGD	190	99	293	331	15	49	54	1031
Zona breaching								
AT drilling	34	19	58	62	1	17	14	205
Laser drilling	150	75	221	256	14	32	40	788
Mechanical	6	5	14	13				38
Biopsy method								
PB		7		17		2	1	27
Cleavage aspiration	176	79	269	296	14	46	41	921
Cleavage extrusion	10	13	21	17	1	1	11	74
Blastocyst	3		3				1	7
PB + embryo	1			1				2
Analysis method								
FISH	172	90	273	308	14	46	52	955
Array	16	5	16	20	0	3	2	62
PCR	2	4	4	3	1	0	0	14
Embryology								
COCs (mean/OR)	2496 (12.7)	1338 (13.3)	3675 (12.3)	4306 (12.4)	171 (11.4)	549 (10.8)	676 (11.5)	13 211 (12.3)
Inseminated	2059	1125	3156	3669	121	467	578	11 175
Fertilized	1396	806	2288	2684	84	352	432	8042
Biopsied	1018	622	1818	2051	69	301	330	6209
Successfully biopsied	1009	613	1801	2032	68	300	326	6149
Diagnosed	954	571	1714	1921	67	278	305	5810
Transferable (%/diagnosed)	383 (40)	161 (28)	333(19)	304 (16)	26 (39)	76 (27)	120 (39)	1403 (24)

Continued

Table IIb *Continued*

Indication	Robertsonian translocation, male carrier	Robertsonian translocation, female carrier	Reciprocal translocation, male carrier	Reciprocal translocation, female carrier	Deletion	Inversion	Other	Total
Transferred	225	107	247	229	16	53	74	951
Frozen	67	22	78	43	3	14	30	257
Clinical outcome								
Cycles to ET (%/OR)	144 (73)	67 (66)	187 (62)	170 (49)	12 (80)	36 (71)	43 (73)	659 (62)
hCG positive	59	24	87	55	4	13	19	261
Positive heart beat	49	18	68	41	4	12	14	206
Clinical pregnancy rate (% per OR/% per ET)	25/34	18/27	23/37	12/25	27/33	24/33	24/33	19/31
Number of fetal hearts	57	24	82	46	5	14	18	246
Implantation rate (fetal hearts/100 embryos transferred)	25.3	22.4	33.2	20.1	31.3	26.4	24.3	25.9
Deliveries	38	16	55	35	2	9	10	165
Delivery rate (% per OR/% per ET)	19.3/26.4	15.8/23.9	18.3/29.4	10.1/20.6	13.3/16.7	17.6/25.0	16.9/23.3	15.4/25.0
Miscarriages	2	0	4	1	1	0	2	10
Clinical pregnancies lost to FU	9	2	9	5	1	3	2	31

PGD cycles performed for monogenic disorders between January and December 2010 slightly decreased compared with data collection XII (1597). The indications for the monogenic diseases of the current data collection are listed in Supplementary Table SIVc. For data XIII the most common indications remained unchanged.

For data XIII, ICSI was used in the majority of cycles (99% of cycles to OR) and PCR was still the most widely used first-line method of DNA amplification (90% of cycles to PGD). The percentage of cycles relying on whole genome amplification as method of DNA amplification (6% of cycles to PGD) was the same as the previous data collection (6%). Genome-wide array technologies for monogenic disorders have now been introduced in nearly 3% of cycles.

The use of laser was the preferred method for biopsy (75% of cycles to PGD); acidic tyrode or mechanical action was applied in 15 and 10% of cycles to PGD, respectively. These results were very similar to data collection XII. Day 3 cleavage-stage embryo biopsy was most frequently used (93% of cycles to PGD) while the use of blastocyst biopsy remained low (2%). This was in line with previous data collections: 93 and 1% for cleavage-stage and blastocyst biopsy respectively. Genetic testing was carried out on either one blastomere (43% of cycles to PGD) or two blastomeres per embryo (37% of cycles to PGD). In 14% of cycles a mixture of one and two blastomeres was applied. Polar bodies or trophectoderm (TE) cells were used in the remaining 6% of cycles. A total number of 19 941 cumulus-oocyte complexes (COC) were collected and 76% of mature oocytes that were inseminated actually fertilized. A total of 80% of fertilized embryos were biopsied with a 98% success rate. Of the embryos successfully biopsied, 91% gave a diagnostic result, of which 43% were genetically transferable. From 1543 PGD procedures, 81% resulted in an embryo transfer. Per cycle to OR on average 12.7 COCs were collected with 10.4 mature oocytes for insemination. This yielded on average 7.9 fertilized embryos. Per PGD cycle on average 6.4 embryos were suitable for biopsy. Diagnosis was achieved for 5.8 embryos, of which 2.5 embryos were shown to be genetically transferable. On average 1.3 embryos could be transferred while 0.7 embryos were used for cryopreservation, which was very similar to data XII. A positive hCG was obtained in 537 cycles, with a positive heart beat in 446 cycles (28.0% per OR and 36% per embryo transfer) and 522 fetal hearts, giving an overall implantation rate of 27% (522/1954). Finally, the delivery rate was 24% per OR and 31% per embryo transfer; this corresponded with the results from the cumulative data I–XII (23% per OR and 29% per embryo transfer). There were 10% miscarriages and 22 clinical pregnancies were lost to follow-up.

Preimplantation genetic screening

Overall, 2979 PGS cycles were reported in data collection XIII (Table Vb). This represents a 6% reduction compared with Data XII (3551). The mean age of women undergoing PGS was 39 years. The most common indications for PGS were for women with advanced maternal age (36%), couples who had experienced repeated implantation failure (15%) or recurrent miscarriage (14%) and males with a variety of phenotypes grouped as severe male factor (9%). Other indications were previous abnormal pregnancies, individuals with abnormal karyotypes, including mosaicism for numerical chromosomal abnormalities and couples with more than one indication. A small number of couples underwent PGS following oocyte donation or without a reported medical indication.

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

	FISH[f]	PCR	Total
Cycles to OR	1310	66	1376
Number infertile	313	0	313
Female age (years)	33	31	32
Cancelled before IVF/ICSI	2	0	2
ART method			
IVF	383	10	393
ICSI	905	56	961
IVF + ICSI	14	0	14
ICSI + Frozen	5	0	5
IVF + Frozen	1	0	1
Cancelled after IVF/ICSI	64[a]	1[b]	65[a,b]
Cycles to PGD	1244	65	1309
Zona breaching			
AT drilling	580	52	632
Laser drilling	604	3	607
Mechanical	60	10	70
Biopsy method			
PB	2	0	2
Cleavage aspiration	1173	60	1233
Cleavage extrusion	62	5	67
Flow displacement	5	0	5
Blastocyst	2	0	2
Embryology			
COC's	16 957	912	17 869
Inseminated	14 932	701	15 633
Fertilized	10 534	556	11 090
Biopsied	8034	458	8492
Successfully biopsied	7877	422	8299
Diagnosed	7298	329	7627
Transferable	2493	178	2671
Transferred	1677	139	1816
Frozen	450[c]	58[d]	508[c,d]
Clinical outcome			
Cycles to ET	977	55	1032
hCG positive	315	24	339
Positive heartbeat	250	17	267
Clinical pregnancy rate (% per OR/% per ET)	19/26[e]	26/31[e]	19/26[e]

[a]27 embryos from 2 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 dues to lack of information regarding the number of fetal heart beats (FHB) in pregnancies resulting from the transfer of those embryos.
[f]In two cycles, one cell was analysed with FISH while a second cell was analysed with PCR for HLA compatibility.

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

Cycles to OR	108
Number infertile	23
Female age (years, mean)	34
ART method	
IVF	30
ICSI	77
IVF + frozen	1
Cancelled after IVF/ICSI	9
Cycles to PGD	99
Zona breaching	
AT drilling	12
Laser drilling	79
Mechanical	8
Biopsy method	
Cleavage aspiration	95
Cleavage extrusion	2
Blastocyst	2
Analysis method	
FISH	87
PCR	12
Embryology	
COCs (mean/OR)	1294 (12.0)
Inseminated	1132
Fertilized	821
Biopsied	608
Successfully biopsied	594
Diagnosed	564
Transferable	178
Transferred	118
Frozen	37
Clinical outcome	
Cycles to ET (%/OR)	80 (74)
hCG positive	33
Positive heart beat	23
Clinical pregnancy rate (%per OR/% per ET)	21/29
Number fetal hearts	27
% Implantation rate (FHB/100 embryos transferred)	23
Deliveries	20
Delivery rate (% per OR/% per ET)	19/25
Miscarriages	2
Miscarriage rate (% per clinical pregn – pregn lost to FU)	10
Clinical pregnancies lost to FU	1

The majority of biopsies (2072/2978, 70%) were at cleavage stage. Laser biopsy was the preferred method (2219/2978, 75%); acidic tyrode's or mechanical zona breaching was applied in 17 and 8% of cycles to PGS, respectively. Only 4% of cycles involved the use of arrays and FISH was used in almost all of the remaining cycles. From a total of 26 166 oocytes that were inseminated, 19 084 (73%) were fertilized. Of 15 068 embryos that were successfully biopsied, 14 548 resulted in a diagnosis (56% of all oocytes inseminated and 96% of all

Table IVa Cycles performed for single gene disorders using PCR, data collection I–XII.

Indication	X-linked[a]	Autosomal recessive[b]	Autosomal dominant[c]	HLA		Other	Total
				HLA only	HLA + monogenic disease		
Cycles to OR	1047	2401	2374	138	397	1336	7693
Number infertile	207	770	421	2	18	237	1655
Female age (years)	33	34	32	35	34	31	33
Cancelled before IVF/ICSI	0	0	3	0	0	1	4
Art method							
IVF	17	19	2	0	0	12	50
ICSI	1016	2344	2350	137	387	1311	7545
IVF + ICSI	2	0	1	0	0	0	3
IVF + frozen	0	0	1	0	0	0	1
ICSI + frozen	4	12	5	0	4	0	25
IVF + ICSI + Frozen	6	21	6	1	6	9[d]	49[d]
Unknown	2	5	6	0	0	5	18
Cancelled after IVF/ICSI	41	86	92	6	12	54	291
Cycles to PGD	1006	2315	2279	132	385	1283	7400
Zona breaching							
AT drilling	208	711	572	4	37	314	1846
Laser drilling	702	1463	1571	128	339	866	5069
Mechanical	94	137	131	0	9	100	471
Unknown	2	4	5	0	0	3	14
Biopsy method							
PB biopsy	41[e]	41[e]	58[e]	0	0	63[f]	203[f]
Cleavage aspiration	925[e]	2160[e]	2167[e]	128	357	1149[f]	6886[f]
Cleavage extrusion	6	71	41	1	8	32	159
Blastocyst	6	35	1	3	21	11	77
PB + embryo	27	5	8	0	0	25	65
Unknown	3	7	5	0	0	6	21
Embryology							
COCs (mean/OR)	12 608	32 790	31 194	1891	5765	18 531	102 779
Inseminated	10 569	26 980	25 936	1539	4754	15 320	85 098
Fertilized	7962	19 805	19 259	1248	3876	11 276	63 426
Biopsied (mean/OR)	5618	15 011	13 627	909	3127	8168	46 460
Successfully biopsied	5531	14 811	13 487	908	3113	8078	45 928
Diagnosed (mean/OR)	4978	13 015	12 066	840	2833	7187	40 919
Transferable (mean/OR)	2562	7433	5163	170	439	3482	19 249
Transferred	1414	4062	2916	126	347	1989	10 854
Frozen	418	1253	788	65	317	608	3449
Clinical outcome							
Cycles to ET	783	2023	1806	84	226	1057	5979
hCG positive	272	806	630	29	99	401	2237
Positive heart beat	219	631	483	20	85	318	1756
Clinical pregnancy rate (% per OR/% per ET)	21/28	26/31	20/27	14/24	21/38	23/30	23/29

X-linked (XL): +2 rec female; +4 aneuploidy.
Autosomal recessive (AR): +3 XLR; +1Rob fem; +27 aneuploidy; +7 AR.
Autosomal dominant (AD): +1 rec female; +6 AD; +10 aneuploidy.
HLA only: +5 aneuploidy.
[a]Included: DMD (Duchenne muscular dystrophy), BMD (Becker muscular dystrophy), FRAXA (fragile X syndrome) and Haemophilia for data I to X. Other X-linked (XL) diseases are pooled in the 'other' category.
[b]Included : CF (cystic fibrosis), b-Thal (b-thalassaemia), sickle cell anaemia and SMA (spinal muscular atrophy) for data I to X. Other AR diseases are pooled in the 'other' category.
[c]Included : DM1 (myotonic dystrophy type 1) and HD (Huntington's disease) for data I to X. Other 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 XIII.

Indication	X-linked		Autosomal recessive		Autosomal dominant		HLA				Other		Total	
		%		%		%	Only		+ monogenic disease			%		%
Cycles to OR	283		437		740		36		72		6		1574	
Number infertile	51		131		133		0		3		2		320	20
Female age (years)	30		34		34		33		35		33		33	
Cancelled before IVF/ICSI	0		0		0		0		0		0		0	
ART method														
IVF			2										2	
ICSI	282	99	429		734		32		71		6		1554	99
IVF + ICSI	1		2		3		2		1				9	
ICSI + frozen			2		3								5	
Unknown			2				2						4	
Cancelled after IVF/ICSI	6		11		14		0		0		0		31	
Cycles to PGD	277		426		726		36		72		6		1543	
Zona breaching														
AT Drilling	58	21	62	15	107	15			1	1	4	66.7	232	15
Laser Drilling	186	67	307	72	571	79	33	92	65	90	2	33.3	1164	75
Mechanical	33	12	57	13	48	7	3	8	6	8			147	10
Biopsy method														
PB	10		9		13								32	
Cleavage aspiration	260	94	392	92	699	96	17	47	64	89	6	100.0	1438	93
Cleavage extrusion	3		16		4		9						32	
Blastocyst	1	0.4	4	1	7	1	10	28	8	11			30	2
PB + embryo	3		5		3								11	
Biopsy policy														
1 cell biopsy	96	35	266	62	229	32	24	67	44	61			659	43
2 cell biopsy	124	45	94	22	334	46	2	6	18	25	6	100.0	578	37
1 or 2 cell biopsy	38	14	47	11	133	18			2	3			220	14
>2 cells (including TE)	6	2	5	1	14	2	10	28	8	11			43	3
1 and 2 PB	5	2	7	1	4	0.6							16	1
1 and 2 PB and cell	3	1	5	1	3	0.4							11	0.7
1 PB	5	2	2	0.5	9	1							16	1
Amplification method														
FISH	1												1	0.1
FISH + PCR	8		5		4		1		4				22	1
PCR	245	88	362	85.0	675	93.0	26	72	68	94	6	100.0	1382	90

Continued

Table IVb *Continued*

Indication	X-linked		Autosomal recessive		Autosomal dominant		HLA				Other		Total	
		%		%		%	Only		+ monogenic disease			%		%
PCR + WGA	19		38		42								99	6
PCR + array	4		19		5		9						37	2
PCR + WGA + array			2										2	0.1
*Embryology**														
COCs	3104	*11.0*	5792	*13.3*	9509	*12.9*	532	*14.8*	932	*12.9*	72	*12.0*	19 941	*12.7*
Inseminated	2573	*9.1*	4736	*10.8*	7815	*10.6*	401	*11.1*	733	*10.2*	62	*10.3*	16 320	*10.4*
Fertilized	1962	*6.9*	3605	*8.3*	5942	*8.0*	323	*9.0*	595	*8.3*	39	*6.5*	12 466	*7.9*
Biopsied	1502	5.4	2949	6.9	4686	6.4	291	8.1	488	6.8	35	5.8	9951	6.4
Successfully biopsied	1466	5.3	2863	6.7	4586	6.3	288	8.0	477	6.6	35	5.8	9715	6.3
Diagnosed	1334	4.8	2581	6.1	4220	5.8	259	7.2	449	6.2	30	5.0	8873	5.8
Transferable	598	2.2	1399	3.3	1713	2.4	43	1.2	69	1.0	5	0.8	3827	2.5
Transferred	351	1.3	633	1.5	891	1.2	29	0.8	49	0.7	1	0.2	1954	1.3
Frozen	127		432		402		19		61		1		1042	0.7
Clinical outcome														
Cycles to ET	219		373		596		21		33		1		1243	81
hCG Positive	92		171		248		10		16		0		537	
Positive heartbeat	75		145		201		10		15		0		446	
Clinical pregnancy rate (% per OR)	27		33		27		28		21		0		28	
Clinical pregnancy rate (% per ET)	34		39		34		48		45		0		36	
Number FHB	87		174		232		10		19		0		522	
Implantation rate (fetal hearts/embryos transferred)	25		27		26		34		39		0		27	
Deliveries	61		123		176		8		14		0		382	
Delivery rate (% per OR)	22		28		24		22		19		0		24	
Delivery rate (% per ET)	28		33		30		38		42				31	
Miscarriages	12		13		15		1		1		0		42	
Miscarriage rate (% per clinical pregn − pregn lost to FU)	16		10		8		11		7		0		10	
Clinical pregnancies lost to FU	2		9		10		1		0		0		22	

*Results expressed as % indicated in Italic are per OR, others are per biopsy.

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

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	7971	948	2290	2937	5165	2109	304	120	624	1290	23 758
Number infertile	6286	642	2130	1573	4881	1879	235	40	591	1100	19 357
Female age (years)	41	41	41	34	34	35	39	38	35	36	37
Cancelled before IVF/ICSI	0	0	0	0	1	0	0	0	0	1	2
ART method											
IVF	1062	189	338	298	404	11	4	11	141	114	2572
ICSI	6783	734	1926	2558	4655	2048	297	109	427	1133	20 670
IVF + ICSI	99	17	15	64	65	40	3	0	55	26	384
IVF + frozen	0	2	1	1	1	1	0	0	0	0	6
ICSI + Frozen	21	6	5	15	15	9	0	0	1	2	74[d]
Unknown	6	0	5	1	24	0	0	0	0	14	50
Cancelled after IVF/ICSI	186	26	10	44	128	34	0	0	27	24	479
Cycles to PGS	7785	922	2280	2893	5036	2075	304	120	597	1265	23 277
Zona breaching											
AT drilling	1633	200	528	906	1281	721	36	30	255	394	5984
Laser drilling	5781	612	1312	1865	3099	1096	175	90	302	820	15 152
Mechanical	358	110	440	121	619	258	93	0	40	37	2076
Unknown	13	0	0	1	37	0	0	0	0	14	65[e]
Biopsy method											
PB	1328[f]	318	1353	172	866	35	0	1	136	268	4477[f]
Cleavage aspiration	6091[f]	571	851	2609	3902	1967	222	116	457	964	17 750[f]
Cleavage extrusion	340	33	73	107	220	71	82	1	3	28	958
Cleavage flow displacement	7	0	0	3	7	1	0	0	0	4	22
Blastocyst	1	0	1	1	1	0	0	2	0	1	7
PB + embryo	6	0	2	0	2	1	0	0	1	0	12
Unknown	13	0	0	1	38	0	0	0	0	0	52[e]
Embryology											
COC's	76 768	8939	21 036	36 540	66 396	30 288	3887	1376	7055	16 321	268 606
Inseminated	64 995	7367	16 526	30 266	54 362	24 542	3348	1134	6052	13 675	22 2267
Fertilized	45 562	5198	11 473	22 293	39 196	17 158	2544	826	4192	9720	15 8162
Biopsied	35 439	4670	11 889	16 891	31 200	12 939	1908	616	3417	7685	126 654
Successfully biopsied	35 070	4654	11 797	16 734	30 789	12 881	1902	607	3370	7621	125 425
Diagnosed	32 560	4343	10 876	15 575[g]	28 902[g]	12 140	1859	571	3014[g]	6879[g]	11 6719[g]
Transferable	9161	1251	3620	5630[g]	10 869[g]	4831	876	219	1347[g]	2757[g]	40 561[g]

Continued

Table Va *Continued*

Indication	AMA	AMA + miscarriage[a]	AMA + RIF	Recurrent miscarriage	Recurrent IVF failure	Severe male factor[b]	Oocyte donation[c]	Prev abn preg[c]	No indication	Other[d]	Total
Transferred[h]	7896	1039	3027	4003[g]	7495[g]	3193	499	144	857[g]	1938[g]	30 091[g]
Frozen	982	128	353	843	1530	637	254	50	172	508	5457
Clinical outcome											
Cycles to ET	4818	629	1731	2243	4066	1740	268	90	488	1032	17 105
HCG positive	1438	174	416	939	1469	755	150	37	196	432	6006
Positive heart beat	1107	127	338	747	1148	643	128	32	163	333	4766
Clinical pregnancy rate (% per OR/% per ET)	14/23	13/20	15/19	25/33	22/28	30/37	42/48	27/36	26/33	26/32	20/28

AMA, advanced maternal age; RIF, repeated implantation failure; SMF, severe male factor.
[a]These data were not extracted from I–IV.
[b]These data were not extracted from I–III.
[c]These data were not extracted form data I–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.

embryos biopsied). Of these 31% were genetically transferrable, 72% were actually transferred and 14% were frozen. This was in accordance with the cumulative data of previous years (Table Va) where 35% of diagnosed embryos were transferable and 74% were used for transfer while 13% were cryopreserved.

A positive hCG was obtained in 762 cycles, with a positive heart beat in 594 cycles, yielding a clinical pregnancy rate of 20% per OR or 30% per embryo transfer procedure. This was comparable with the overall clinical pregnancy rates from data I–XII (20% per OR and 28% per embryo transfer). There were 430 reported deliveries, although 39 clinical pregnancies were lost to follow-up. Overall, of 2979 cycles that reached OR, 2012 (68%) had an embryo transfer giving an overall delivery rate of 14% per cycle to OR and 21% per cycle to embryo transfer. The miscarriage rate per clinical pregnancy was 18%, which is not different from the 17% reported in data XII.

PGD cycles for social sexing

The number of reported cycles for social sexing in data XIII was similar to previous data collections, accounting for <1% (48/5780) of all cycles submitted. There have been 705 cycles for social sexing reported so far (data I–XII) (Table VIa). Because social sexing as an indication for PGD is debatable, only the cycle numbers will be included in this and future consortium reports; cycle details will no longer be presented.

Pregnancies and babies

Tables VIIa, VIIb, IXa, IXb, Xa, Xb, XIa, XIb and the Supplementary Tables SVIIIa, SVIIIb, SXIIa and SXIIb summarize the pregnancy and baby data. Data XIII included 1503 pregnancies (Table VIIb) with 982 deliveries of 22 stillborns and 1152 live borns. Of the 1210 cycles ending in a pregnancy with a positive heartbeat, follow-up data on 1131 pregnancies were reported. There were 121/1131 complications in pregnancy reported (Supplementary Table SVIIIb). The delivery rates per indication were reported in Tables IIb, IIIb, IVb and Vb. Caesarean section was performed for 39% of the deliveries (380/982) (Table IXb). In 150 cases, the method of delivery was not known. Confirmation of the diagnosis was performed prenatally (251/639) and/or post-natally (388/639) (Table Xb). Table Xb and Supplementary Table SXIIb describe the data on congenital malformations, neonatal complications and perinatal deaths as were collected from 601 out of 1152 (52%) babies. It was clear that the organization of adequate children follow-up is more difficult than the follow-up of the pregnancies (only 79/1210 clinical pregnancies were lost to follow-up). Moreover, data indicate that major and minor malformations as well as neonatal complications have been classified differently among centres. A major malformation was reported in 8 singletons and 4 twins out of 601 babies documented; minor malformations were identified in 3 singletons and 3 twins. Several abnormalities were found that were not related to the PGD indication. The number of multiple pregnancies remained high (243/1210, 20%) (Table VIIb); this is not different from data XII (22%). Overall, for pregnancies and babies, data XIII was comparable to previous data collections. It should be noted that for data collection X, XI and XII, the total number of children born, as shown in the cumulative Table XIa was not correct. In data XII, the total number should have been 6063 instead of 5063; similarly, in data X and XI, 1000 children were missing in the total number. This error has been corrected in data collection XIII, meaning

Table Vb Cycles performed for PGS, data collection XIII.

Indication	AMA	AMA + misc	AMA + RIF	Rec.misc	RIF	SMF	Prev abn preg	AMA + Rec mis Pre abn Preg	Num Abnor	AMA + Num abno	No indication	Ovum donation	AMA + Ovum donation	Total
Cycles to OR	1083	265	312	415	456	278	44	2	33	1	51	37	2	2979
Number infertile	688	162	297	145	405	245	14	0	25	1	43	36	2	2063
Female age (years)	39	37	40	36	32	37	36	42	36	41	37	43	44	39
ART method														
IVF	113	46	52	25	22	1	3	2	0	0	7	0	0	271
ICSI	965	219	258	378	429	274	41	0	33	1	42	37	2	2679
IVF + ICSI	3	0	2	9	2	1	0	0	0	0	2	0	0	19
ICSI + frozen	1	0	0	3	3	2	0	0	0	0	0	0	0	9
IVF + frozen	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Unknown	1	0	0	0	0	0	0	0	0	0	0	0	0	1
Cancelled post OR	0	0	0	0	0	1	0	0	0	0	0	0	0	1
Cycles to PGD	1083	265	312	415	456	277	44	2	33	1	51	37	2	2978
Zona breaching														
AT drilling	113	17	105	47	85	106	6	0	3	0	23	2	2	509
Laser drilling	909	229	178	349	319	131	38	2	28	1	19	16	0	2219
Mechanical	61	19	29	19	52	40	0	0	2	0	9	19	0	250
Biopsy method														
PB	288	152	163	64	76	4	0	0	0	0	15	0	0	762
Cleavage aspiration	763	103	143	322	351	260	38	2	32	1	31	25	2	2072
Cleavage extrusion	27	1	4	7	19	9	2	0	2	0	0	12	0	83
Blastocyst	2	6	1	21	9	3	4	0	0	0	1	0	0	47
PB + embryo	3	3	1	1	1	1	0	0	0	0	4	0	0	14
Embryology														
COCs	10 142	2439	2742	5173	5471	3752	470	12	390	2	515	459	21	31 588
Inseminated	8531	2042	2241	4262	4370	3079	417	12	326	2	454	410	20	26 166
Fertilized	6124	1493	1545	3201	3180	2287	334	8	249	1	341	305	16	19 084
Biopsied	4685	1333	1417	2452	2623	1698	251	7	172	1	274	236	14	15 163
Successfully biopsied	4655	1314	1409	2440	2607	1694	251	7	171	1	270	235	14	15 068
Diagnosed	4504	1258	1351	2353	2540	1636	240	7	165	1	255	225	13	14 548
Transferable	1047	268	310	902	908	698	104	1	78	0	88	116	9	4529
Transferred	881	244	289	547	625	410	61	1	46	0	73	60	4	3241
Frozen	107	19	44	165	116	99	37	0	19	0	8	15	4	633

Continued

Table Vb *Continued*

Indication	AMA	AMA + misc	AMA + RIF	Rec.misc	RIF	SMF	Prev abn preg	AMA + Rec mis Pre abn Preg	Num Abnor	AMA + Num abno	No indication	Ovum donation	AMA + Ovum donation	Total
Clinical outcome														
Cycles to ET	598	163	185	324	365	237	36	1	28	0	39	34	2	2012
hCG positive	187	55	43	153	148	104	21	0	14	0	20	16	1	762
Positive heart beat	143	50	28	121	114	81	18	0	11	0	17	10	1	594
Clinical pregnancy rate (% per OR/% per ET)	13/24	19/31	9/15	29/37	25/31	29/34	41/50		33/39		33/44	27/29	50/50	20/30
Number of fetal hearts	161	59	34	157	136	102	25	0	17	0	18	10	1	720
Implantation rate (fetal hearts/100 embryos transferred)	18	24	12	29	22	25	41	0	37	0	25	17	25	22
Deliveries	104	40	15	90	74	61	15	0	9	0	15	6	1	430
Delivery rate (% per OR/% per ET)	10/17	15/25	5/8	22/28	16/20	22/26	34/42	0	27/32	0	29/38	16/18	50/50	14/21
Miscarriages	33	6	7	18	19	9	1	0	1	0	2	3	0	99
Miscarriage rate (% per clinical pregn – pregn lost to FU)	23	13	30	16	19	12	6	0	9	0	11	33	0	18
Clinical pregnancies lost to FU	2	3	5	5	14	8	1	0	0	0	0	1	0	39

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

Method for sexing	FISH (SS only)[e]	FISH (SS + AS)[a]	PCR	Unknown	Total
Cycles to OR	389	122	189	5[b]	705[b]
Number infertile	67	27	16	1	111
Female age (years)	40	39	37	35	36
ART method					
IVF	137	19	10	3	169
ICSI	234	102	168	2	506
Frozen	9	0	2	0	11
Frozen + IVF + ICSI + unknown	9	1	9	0	19
Cancelled after IVF/ICSI	5	0	7	5	17
Cycles to PGD	384	122	182	0	688
Zona breaching					
AT drilling	16	0	10	0	26
Laser drilling	201	33	1	0	235
Mechanical	167	89	171	0	427
Biopsy method					
Cleavage aspiration	170	0	11	0	181
Cleavage extrusion	213	122	171	0	506
Blastocyst	1	0	0	0	1
Embryology					
COC's	5171	1687	2878	23	9759
Inseminated	4469	1470	2188	19	8146
Fertilized	3224	1026	1452	11	5713
Biopsied	2606	776	1143	0	4525
Successfully biopsied	2491	775	1116	0	4382
Diagnosed	2220	658	1049	0	3927
Transferable	848	212	473	0	1533
Transferred	527	147	361	0	1035
Frozen[c]	240	43	86	0[d]	369
Clinical outcome					
Cycles to ET	297	83	138	0	518
hCG positive	116	29	58	0	203
Positive heart beat	89	20	39	0	148
Clinical pregnancy rate (% per OR/% per ET)	23/30	16/24	21/28	0/–	21/29

AS, aneuploidy screening.
[a]These data were not extracted from I–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.
[e]In two cycles also Quantitative Fluorescent-PCR was used.

that the total number of children born after data collection I–XII is 7301, as indicated in Table XIa.

Misdiagnoses

Table XIIIa summarizes the misdiagnoses reported for data I–XII, with no misdiagnoses reported in data X and data XI. In data XIII, three adverse misdiagnoses were reported (Table XIIIb). One case from a PGD for Fragile X syndrome was identified by prenatal diagnosis. This involved a cycle in which three of the five transferrable embryos had been chosen for transfer. When the patient underwent amniocentesis it was found that the fetus was a female carrier and the pregnancy was terminated. Re-analysis of the first PCR products corresponding to the transferred embryos confirmed the diagnosis obtained in the PGD (one healthy female and two healthy males). Closer examination of other parameters indicated that the embryo transfer in this cycle had been carried out exceptionally by only one embryologist, and it was assumed that a mistake was made during the transfer and a contiguous embryo was picked instead of a correct one. Subsequently, the centre has been very strict about double checks and embryo transfer is

always carried out under the control of two embryologists. A second case occurred following PGS for maternal age and recurrent miscarriages using FISH of nine chromosomes; only one cell had been removed on Day 3. No aneuploidy was found and the embryo was transferred. A trisomy 21 was found at prenatal diagnosis and a termination of pregnancy was performed. The third case was after PGS for recurrent miscarriages where a child was born with trisomy 21. The pregnancy ensued from a cycle with FISH for chromosomes X, 13, 15, 16, 17, 18, 21 and 22 on first and second polar bodies. Two embryos had been transferred; one with all information available for the chromosomes under study, showing a normal euploid embryo, and another embryo for which the first polar body showed normal results, but information on chromosome 13, 18, 21 and 22 was missing in the second polar body.

Success of individual centres

Figure 1 shows the clinical pregnancy rate (per OR) per centre for data XIII. The clinical pregnancy showed an average of 22%, compared with

Table VIIa Evolution of pregnancy, data I–XII.

	No. of pregnancies	No. of fetal sacs
Pregnancies	**1607**	
FISH cycles	1151	
PCR cycles	393	
FISH + PCR	6	
WGA cycles only[a]	6	
WGA + PCR[a]	51	
Subclinical pregnancies[b]	1405	
Clinical pregnancies without FHB[a]	131	
Clinical pregnancies with FHB	**7600**	**9444**
Singletons	5675	5675
Twins	1643	3286
Triplets	146	438
Quadruplet	11	44
Unknown	125	1[c]
Lost to FU during first trimester	**96**	**114**
First trimester loss	865	1083
Miscarriage	842[d]	918
TOP	16[e]	17
Extra-uterine pregnancy	53[f]	43
Vanishing twins/triplets or miscarriage multiplet	0	196
Reduction of multiple pregnancies	0	73
Quadruplet to twin	0	14
Triplet to twin	0	23
Triplet to singleton	0	17[g]
Twin to singleton	1144	1401[h]
Unknown	29	37
Ongoing pregnancies > 12 weeks	**5391**	**6723**
Second trimester loss	115	188
Miscarriage	112[i]	150
Miscarriage twin to singleton	0	4
TOP	45[j]	48
Twin to twin transfusion	1	2
Reduction of multiple pregnancies	0	35
Quadruplet to twin	0	4
Triplet to twin	0	11
Triplet to singleton	0	14
Twin to singleton	0	6

Continued

Table VIIa *Continued*

	No. of pregnancies	No. of fetal sacs
Lost to FU during second trimester	1413[k]	278
Deliveries	**6152**	**7591**
Singletons	4763	4763
Twins	1339	2678
Triplets	50	150

[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 FHBs not known for data I–VIII. Counted further as 1 fetal heart.
[d]One miscarriage after amniocentesis.
[e]TOP, termination of pregnancy. One TOP for misdiagnosis of reciprocal translocation, one TOP for Down syndrome following PGD for HLA compatibility, one TOP for complication in pregnancy following PGD for NF1 (NF1, neurofibromatosis type I), two TOPs for ancephalocoele, one TOP for social reasons, one TOP of twin with misdiagnosis for CMT (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 extra-uterine 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 second trimester pregnancy loss after miscarriage counted).
[i]TOP after misdiagnosis : One misdiagnosis for sexing, FISH, female fetus, indication social sexing; one misdiagnosis for □-Thal, PCR; one misdiagnosis for myotonic dystrophy, PCR, one misdiagnosis after PGS, karyotype 45,X; one misdiagnosis for a reciprocal translocation 46,XY,der(15)t(3;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 confirms cytomegalovirus infection, one elective termination (unknown cause) and one Hydrocephaly termination of a 8 months pregnancy (started as quadruplet: 2 selective reductions, one miscarriage after chorionic villous sampling (CVS) and the last fetus TOP).
[j]One TOPs for acrania following PGD for CF, one TOP for severe growth retardation following PGD for Fragile X, one TOP for agenesis 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 syndrome risk following PGS for male factor, one TOP due to malformation at 16 weeks in remaining twin where first twin miscarried at 8 weeks, 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 2 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.

23% for data XII and 21% for data XI. As previously observed, pregnancy rates did not correlate with the number of cycles that each centre performs.

Discussion

This 13th data report of the ESHRE PGD Consortium demonstrates a slight decrease (6%) in the number of PGD cycles, and related pregnancies and babies. This is mainly because of the decline in PGS cycles, which decreased from 3401/5641 (60%) in data XI and 3551/6160 (58%) in data XII to 2979/5780 (52%) in data XIII. In preceding years, the number of PGS cycles had increased annually but by 2010, a number of RCTs had clearly demonstrated that routine PGS using FISH at cleavage stage was not beneficial and a consensus was published by the ESHRE PGD Consortium stating that future studies with alternative biopsy timing and genetic testing were necessary to evaluate the clinical benefit of PGS (Harper *et al.*, 2010a).

For the three cases with a misdiagnosis result reported in data XIII, transfer of the wrong embryo was proposed as most likely cause for one of them. The centre involved strengthened their internal quality control steps as a measure to help preventing further adverse outcomes. Such double control steps are an important factor within a quality management system. Laboratories can implement a quality management system without having an external evaluation but an assessment against international standards by an independent accreditation body has been recommended and even been required in many countries. In 2008, only 33% of 53 European PGD centres had achieved or were preparing for accreditation (Corveleyn *et al.*, 2008). Results from a survey in 2014 showed an improvement on this, with 56% of 46 IVF units and 50% of 46 diagnostic units in the field of PGD having obtained accreditation according to national standards or international standards (the general quality management standard ISO9001 and ISO15189 which is specific for medical laboratories) (unpublished data).

The other two misdiagnoses reported in data XIII included a trisomy 21 following PGS. In the first case, the pregnancy had ensued from a cycle with FISH on first and second polar bodies, although the information was incomplete for the second polar body. In fact, this is the third case reported to the PGD consortium data collections in which a lack of results from the second polar body leads to a misdiagnosis (Table XIIIa). For the second trisomy 21 misdiagnosis case, the single cell shown to be euploid after FISH, may have been derived from a chromosomally mosaic euploid/aneuploid embryo. Alternatively, the embryo was truly trisomic, but the single cell analysed was interpreted as euploid because of a technical error that occurred during the FISH procedure.

To date, including all cycles up to data XIII, misdiagnosis has been reported for only 13/9317 PCR-based cycles and 21/34 855 FISH-based PGD cycles. 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, the numbers reported in the data collections may not reflect the true misdiagnosis in PGD. However, a recent multicentre retrospective study,

Table VIIb Evolution of pregnancy, data XIII.

	No. of pregnancies	No. of fetal hearts	
Pregnancies	**1503**		
FISH only cycles	922		
PCR only cycles	467		
Array	43		
PCR + WGA	50		
PCR + Array	16		
FISH + Array	2		
FISH + PCR	3		
Subclinical pregnancies[1]	293		
Clinical pregnancies, with FHB	**1210**	**1468**	
Singletons	967	967	
Twins	228	456	
Triplets	15	45	
Lost to follow-up during first trimester	35	47	
First trimester loss			
Miscarriage	131	142	
TOP[2]	2	2	
Vanishing/miscarriage multiplets	0	19	
Twin to singleton		16	
Triplet to twin		1	
Triplet to singleton		2	
Reduction of multiple pregnancies	0	**7**	
Triplet to twin		1	
Twin to singleton		2	
Triplet to singleton		4	
Ongoing pregnancies (>12 weeks)	**1042**	**1251**	
Second trimester loss			
Miscarriage	11	12	
TOP[3]	5	6	
Vanishing/miscarriage/reduction multiplets	0	4	
Lost to follow-up during second or third trimester	44	55	
Deliveries	**982**	**1174**[4]	**1152**[5]
Singletons	797	797	787
Twins	178	356	345
Triplets	7	21	20

[1]Subclinical pregnancy (i.e. biochemical and blighted ovum) defined as a pregnancy without any other clinical signs.
[2]TOP: one TOP for Trisomy 21 following PGS for AS maternal age; one TOP for Trisomy 21 following PGD for spinal muscular atrophy.
[3]TOP: one TOP for personal matters (twin); one TOP for Trisomy 21 following PGD for Stargardt disease; one TOP for misdiagnosis following PGD for Fragile X: the embryo was diagnosed as female carrier; one TOP for pronounced microcephaly diagnosed at 32 weeks of gestation following PGD for Familial adenomatous polyposis coli one TOP for fetal malformations following PGS.
[4]Live borns and stillborns.
[5]Live borns.

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

	Total	Singletons	Twins	Triplets
No deliveries[1]	6093	4717	1327	49
Method of delivery				
Vaginal	2541	2284	255	2
Caesarian	2963	1986	937	40
Vaginal and Caesarian	11	2	9	0
Unknown	578	445	126	7
Term at delivery				
Preterm	1614	702	877	35
Term	4084	3719	360	6
Post term	4	4	0	0
Unknown	390	292	89	8

[1]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 XIII.

	Total	Singleton	Twin	Triplet
No. of deliveries	982	797	178	7
Method of delivery				
Vaginal	452	410	42	0
Caesarean	380	257	116	7
Unknown	150	130	20	0
Term at delivery				
Preterm (<37 weeks)	172	75	91	6
Term	674	614	60	0
Post term (>42 weeks)	3	3	0	0
Unknown	133	105	27	1

which assessed the validity of PCR-based PGD through reanalysis of untransferred embryos from monogenic-PGD cycles, reassuringly demonstrated the high diagnostic value of PCR-based PGD. Based on re-analysis of almost 1000 embryos from 6 different PGD centres the sensitivity of PCR-based PGD for monogenic diseases was demonstrated to be 99.2% (Dreesen *et al.*, 2014).

The number of cycles has increased annually since the start of the data collection, except for data XIII, where for the first time, a decrease in the total cycle number was reported. Nevertheless, the number of participating centres (62) was still slightly higher than for the previous data collection XII (60). Data submitting is a time consuming activity and the steering committee acknowledges the effort of all contributing centres. Curating the data is time consuming as well, explaining the growing lag in evaluation and publication of data collections. An on-line data

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

Method	Result			
	N	Normal	Abnormal	Failed
Prenatal diagnosis				
Array				
CVS	1	1	0	0
Total	1	1	0	0
FISH				
CVS	151	143[a]	7[b]	1[s]
Amniocentesis	829[c]	807[a,c]	19[d]	3
Ultrasound	1460[c]	1444	15[c,e]	1
Unknown	3	3	0	0
Total	2440[f]	2398	42	4
PCR				
CVS	222	216	6[g]	0
Amniocentesis	324	309	14[h]	1
Ultrasound	58	53	5[i]	0
Unknown	2	2	0	0
Total	604[f]	579	24	1
Post-natal diagnosis				
Array	0	0	0	0
Karyo miscarriage	1	0	0	1
Karyo post-natal	1	1	0	0
Total	2	1	0	1
FISH				
Karyo miscarriage	134	65	67[j]	2
Karyo post-natal	290	284	5[k]	2
FISH microdeletion	2	2	0	0
Physical examination	1785	1780	6[l]	0
Karyo post-natal + physical examination	28	28	0	0
Karyo post-natal + DNA	1	1	0	0
Unknown	3[m]	3[m]	0	0
Total	2243	2163	78	4
PCR				
Karyotype miscarriage	16	10	4[n]	2
DNA test miscarriage	2	2	0	0

Continued

Table Xa *Continued*

Method	Result			
	N	Normal	Abnormal	Failed
DNA test post-natal	207	205	2[o]	0
Sweat test	10	10	0	0
Physical examination	150	149	1	0
Karyotype	22	21	1[p]	0
Karyo + DNA	21	20	1[q]	0
Karyo + phys exam	31	31	0	0
Hearing test	3	3	0	0
Algo test	2	2	0	0
Other	2[t]	2	0	0
Unknown	35[r]	35	0	0
Total	501	490	9	2

[a]Total 3 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). 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.
[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) ; 47,XXX after PGD for reciprocal translocation t(9;10)(q32;p12.32).
[e]Encephalocele ->TOP (AS repeated miscarriage); hemivertebrae, hypoplastic cerebellum, hydrocephaly->TOP; cystic hygroma 1 twin miscarriage->ongoing singleton (rec. 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 (social sexing for male); TOP of twins because of risk of Down syndrome after PGS for SMF.
[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/CBAVD) (Congenital bilateral absence of the vas deferens); TOP for trisomy 21 after PGD for HLA compatibility (HLA result confirmed).
[h]Monozygous twin affected with Finnish Nefrosis, TOP (PGD for beta-thalassemia); TOP because of trisomy 21 (X-linked retinoschisis); TOP because of microdeletion 18 (CF/CBAVD).
[i]TOP because of ultrasound abnormalities, i.e. spina bifida and hydrocephalus (Charcot Marie Tooth type 1a); TOP for acrania following PGD for CF (CF result confirmed).
[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); 47,XY+2 after PGD for reciprocal translocation (46,XY,t(8;9)(q21.2;p21).
[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 (Myotonic dystrophy type 1).
[p]Misdiagnosis PGD for 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).
[s]Miscarried trisomy 21 after PGS for maternal age and recurrent miscarriages.
[t]Enzymatic dosage (CF/CBAVD) and hearing test+ physical examination (Leopard syndrome).

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

Method	*N*	Result		
		Normal	Abnormal	Failed
Prenatal diagnosis				
Array				
CVS	2	2		
Amniocentesis	1	1		
Ultrasound	2	2		
FISH				
CVS	7	7		
Amniocentesis	96	91	5[1]	
Ultrasound	48	48		
PCR				
CVS	35	32	3[2]	
Amniocentesis	52	45	6[3]	1[4]
Ultrasound	6	6		
PCR+WGA				
CVS	1	1		
Amniocentesis	1	1		
Total	**251**			
Post-natal diagnosis				
Array				
Karyo + physical examination	4	4		
FISH				
Karyo	31	31		
Physical examination	166	165	1[5]	
Karyo + physical examination	56	56		
PCR				
Physical examination	29	29		
DNA-test	19	19		
Karyo post-natal	3	3		
Other	9	9[6]		
Karyo + DNA-test	36	36		
Karyo + physical examination	6	6		
FISH + Array				
Physical examination	1	1		
PCR + WGA				
DNA-test	26	26		
PCR + Array				
Karyo + DNA-test	1	1		
Other	1	1[7]		
Total	**388**			

[1]46XX,(1;8;2)(p42;p21;p11,5) after PGD for reciprocal translocation (ongoing pregnancy), 45XY,der(14;21)(q10;q10)/46XXYder(14;21)(15/5) after PGD for Robertsonian translocation (ongoing pregnancy), 46XY,t(5;18)(p14.1∼15;Q21.2∼23) after PGD for reciprocal translocation (ongoing pregnancy), 47XXX after PGD for reciprocal translocation (ongoing pregnancy), Trisomy 21 after PGS for maternal age and recurrent miscarriage (misdiagnosis/TOP).
[2]Heterozygous carrier after social sexing-selection female and aneuploidy#21 (ongoing pregnancy), carrier after PGD for beta-thalassaemia (ongoing pregnancy), Trisomy 21 after PGD for spinal muscular atrophy (TOP).
[3]Carrier F508del after PGD for CF (ongoing pregnancy), carrier after PGD for beta-thalassaemia (stillborn), carrier after PGD for non-immune hydrops fetalis (ongoing pregnancy, twin), Trisomy 21 after PGD for Stargardt disease (TOP), carrier after PGD for Fragile X (misdiagnosis/TOP).
[4]PGD for Hunter syndrome (stillborn).
[5]Trisomy 21 after PGD for recurrent miscarriages (misdiagnosis/live birth).
[6]Immunoreactive Trypsinogen Test.
[7]Mini-sequencing in cord blood.

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

Total children born		7301[1]
Sex		
Male		3395
Female		3635
Unknown		271
Mean birthweight (g)		
Singletons	6445	4144
Twins	4844	2254
Triplets	3792	100
Mean birth length (cm)		
Singletons	50	2780
Twins	46	1365
Triplets	45	31

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

submission platform is planned for launch in the summer of 2015. It will have built-in data checks and should substantially improve the process of data collection. The new platform will take into account that many PGD cycles are no longer carried out within the timeframe of a single procedure, from OR through to fresh embryo transfer. Alternative strategies have emerged where several hormonal stimulation cycles are planned for oocyte/embryo accumulation and the improved survival rate following (biopsied) embryo vitrification has allowed PGD centres to perform embryo biopsy, testing and embryo transfer in completely separate time frames if necessary. Thus data registration has become more complex, but the new on-line data platform will offer a clear overview of all segments and can be potentially used by all consortium members.

Supplementary data

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

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Table XIb Data on live born children, data collection XIII.

Total live born children	1152		
Sex			
Male	534		
Female	531		
Unknown	87		
Mean birthweight (g)			
Singletons	3240	(709/787)[1]	
Twins	2460	(302/345)[1]	
Triplets	1688	(15/20)[1]	
Mean birth length (cm)			
Singletons	49.8	(493/787)[1]	
Twins	45.5	(184/345)[1]	
Triplets	43.9	(6/20)[1]	
Mean head circumference (cm)			
Singletons	36.0	(185/787)[1]	
Twins	32.5	(59/345)[1]	
Triplets	30.0	(3/20)[1]	
Apgar scores after 1 min	Singletons	Twin	Triplet
Good[2]	252	99	3
Poor[2]	9	3	0
Apgar scores after 5 min			
Good[2]	254	98	3
Poor[2]	3	1	0
Apgar scores after 10 min			
Good[2]	142	46	0
Poor[2]	0	0	0

[1]Numbers between brackets indicate the number of newborns for whom information is available out of the total number of newborns.
[2]Good is defined ≥ 7, poor is defined < 7.

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

Indication	Method used	PND-Post-natal	Outcome	Reported in
Monogenics				
DM I	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 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(3;15)(q25.1;q26.3)pat	FISH	PND	TOP	VII
46,XY,der(17)t(5;17)(p13;p13)mat	FISH	PND	TOP[1]	XII
PGS				
47,XXX	FISH	PND	Lost to follow-up	VII
45,X	FISH	PND	Miscarriage	VIII, reported in IX
Trisomy 16 after 1st PB biopsy only	FISH	Miscarried	Miscarried	VI
Trisomy 16 after 1st 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
46,XY	FISH	PND	Born[2]	XII
Trisomy 21	FISH	PND	Miscarried[3]	XII
Social sexing				
Requested male but female fetus	FISH	PND	TOP	III

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

of Embryology and Genetics of the VUB and Centre for Medical Genetics of the Universitair Ziekenhuis Brussels; Hopital Erasme, ULB, Laboratoire FIV; Leuven Institute for Fertility and Embryology; Leuven University Fertility Centre; Brazil: Fertility-Assisted Reproductive Centre, Sao Paolo; Czech Republic: Sanatorium Repromeda; Institute Pronatal, Genetics; Denmark: Fertility clinic, Skejby Sygehus, Obs & Gyn; 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; Women's Hospital University Kiel, Reproductive Medicine; Zentrum Für Humangenetik, Humangenetisches Labor; University Clinic of

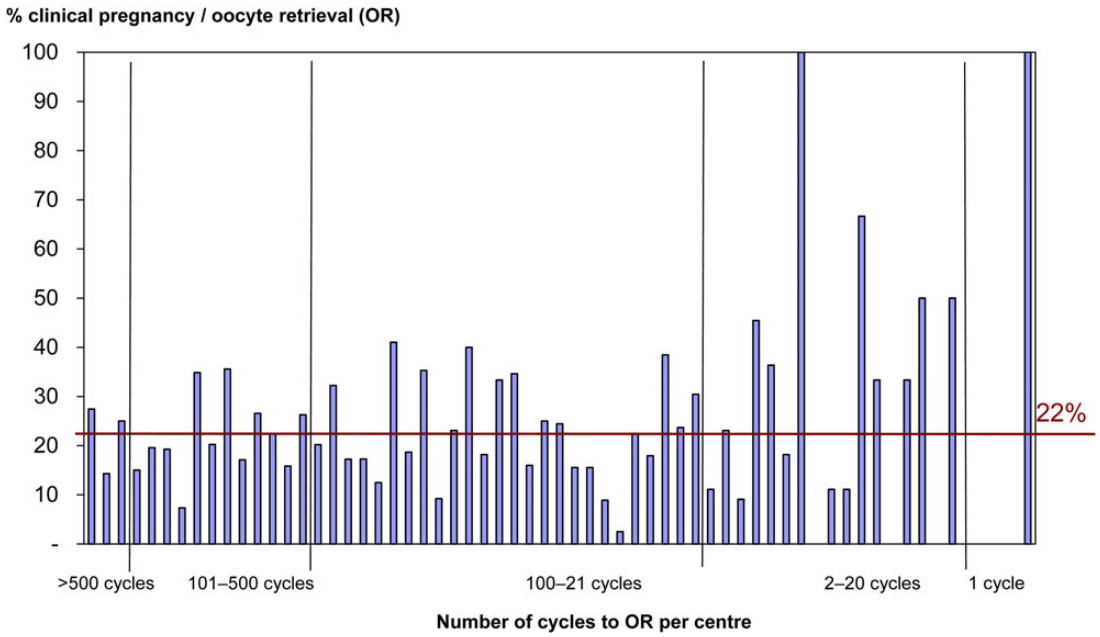

Figure 1 Clinical pregnancy rates per centre. OR: oocyte retrieval.

Table XIIIb Summary of misdiagnosis from data XIII.

Indication	Method used	PND-Post-natal	Result	Outcome
PGD for Fragile X	PCR	PND	Female carrier	TOP
PGS for maternal age and recurrent miscarriages	FISH	PND	Trisomy 21	TOP
PGS for recurrent miscarriages	FISH	Post-natal	Trisomy 21	live born

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; Kinderwunschzentrum an der Gedächtniskirche; Greece: IVF & Genetics; University of Athens, St. Sophia's Children's Hosp, Laboratory of Medical Genetics; EMBRYOGENESIS, Centre for Subfertility Studies; Centre for Human Reproduction, Genesis Athens Clinic; India: Krishna IVF Clinic; Israel: Lis Maternity Hospital, dept. of IVF; 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; St. Luke Clinic; 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; Fundacion Puigvert, Seminologia i Reproduccion; Sweden: Department of Clinical Genetics, Karolinska Hospital; Sahlgrenska University Hospital, Department of Ob/ Gyn; Taiwan: 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, Subdepartement Infertility, and Department of Clinical Genetics; University Medical Centre Utrecht; Turkey: Istanbul Memorial Hospital, reproductive endocrinology & ART centre; UK: University College – Medical School, UCL Centre for PGD – EGA Institute for Womens Health; St. Thomas' Hospital, Academic Department of Women's Health; Hammersmith Hospital, Institute of Ob/Gyn – RPMS; 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

V.G. was responsible for raw data analysis and editing of the tables; S.B.S. was responsible for preparing the tables and text of the PGS section; E.C. prepared the tables and text of the section about

chromosomal abnormalities; F.B. prepared the tables and text of the section about pregnancies and babies; J.T.-S. revised the manuscript; C.M. made the cumulative tables; M.D.R. prepared the tables and text for the monogenic disorders and was responsible for final editing of the main text and tables.

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None declared

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