

# ESHRE PGD consortium data collection X: cycles from January to December 2007 with pregnancy follow-up to October 2008<sup>†</sup>

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**ABSTRACT:** The 10th report of the European Society of Human Reproduction and Embryology (ESHRE) PGD Consortium is presented, documenting cycles collected for the calendar year 2007 and follow-up of the pregnancies and babies born until October 2008 which resulted from these cycles. Since the beginning of the data collections there has been a steady increase in the number of cycles, pregnancies and babies reported annually. For data collection X, 57 centres participated, reporting on 5887 cycles to oocyte retrieval (OR), along with details of the follow-up on 1516 pregnancies and 1206 babies born. A total of 729 OR were reported for chromosomal abnormalities, 110 OR for sexing for X-linked diseases, 1203 OR for monogenic diseases, 3753 OR for preimplantation genetic screening and 92 OR for social sexing. Data X is compared with the cumulative data for data collections I–IX.

**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. Since 1999, nine data collections of PGD for autosomal and sex-linked monogenic diseases and chromosome abnormalities, preimplantation genetic screening (PGS) and social sex selection have been published (ESHRE PGD Consortium Steering Committee, 1999, 2000, 2002; Sermon *et al.*, 2005; Harper *et al.*, 2006; 2008a,b; Sermon *et al.*, 2007; Goossens *et al.* 2008, 2009). This report summarizes data X collected for the calendar year 2007 and the subsequent pregnancies. As it was reported for the first time in data VIII, data X also includes the delivery rate for each indication.

## Materials and Methods

Data were collected using a FileMaker Pro 5, 6 or 8 database, consisting of files for cycle, pregnancy and baby records. The submitted data were

thoroughly analyzed to identify omissions and any ambivalent data. Corrections were requested from the participating centres. Records with insufficient data, e.g. with no cycle or patient identification, no clear indication or from the wrong time period were excluded from the calculations. In-depth 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 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 (OR) and per embryo transfer procedure.

## Results

The number of centres that become members of the PGD Consortium increases annually. Data from 57 centres were included in this report. The results are represented in tables according to an established lay-out. The accompanying text is deliberately concise and seven tables are available in an electronic version only: Supplementary

<sup>†</sup>This manuscript has not been externally peer-reviewed.

**Table 1a Overall cycle data collection I–IX.**

Indication	PGD	PGS	PGD–SS	Total
Cycles to OR	8 111 <sup>1</sup>	13 053	579	21 743 <sup>1</sup>
Number infertile	3078	11 304	47	14 429
Female age (years)	33	37	37	35
Cancelled before IVF/ICSI	18	2	0	20
ART method				
IVF	876	1495	146	2517
ICSI	7054	11 241	416	18 711
IVF + ICSI	39	225	0	264
Frozen + ICSI + IVF + unknown	106 <sup>1</sup>	40	17	163 <sup>1</sup>
Unknown	20	50	0	70
Cancelled after IVF/ICSI	472	442	16	930
Cycles to PGS/PGD	7623	12 609	563	20 795
FISH	4211	12 606	381	17 198
PCR	3405	3	182	3590
FISH + PCR	7	0	0	7
Zona breaching				
AT drilling	3423	3970	19	7412
Laser drilling	3769	7404	131	11 304
Mechanical	417	1170	413	2000
Unknown	14	65	0	79
Biopsy method				
PB biopsy	121 <sup>2</sup>	1816 <sup>2</sup>	0	1937 <sup>2</sup>
Cleavage aspiration	7067 <sup>2</sup>	10 093 <sup>2</sup>	141	17 301 <sup>2</sup>
Cleavage extrusion	323	625	422	1370
Cleavage flow displacement	16	22	0	38
Blastocyst	71	2	0	73
PB and cleavage	20	0	0	20
Unknown	16	52	0	68
Embryology				
COC's	110 851	152 595	7952	271 398
Inseminated	94 019	126 398	6604	22 7021
Fertilized	67 592	89 479	4573	161 644
Biopsied	50 165	71 440	3582	125 187
Successfully biopsied	49 448	70 623	3455	123 526
Diagnosed	44 545	65 181	3141	112 867
Transferable	16 544	23 380	1241	41 165
Transferred	10 926	16 975	860	28 761
Frozen	2309	3165	290	5764
Clinical outcome				
Cycles to ET	5850	9433	419	15 702
hCG positive	1970	3145	161	5276
Positive heartbeat	1542	2429	120	4091
Clinical pregnancy rate (% per OR/% per ET)	19/26	19/26	21/29	19/26

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 reproduction technology; PB, polar body.

PGD column includes PGD for chromosome abnormalities, sexing for X-linked disease and PGD for monogenic disorders.

<sup>1</sup>Includes two cycles with PGD on frozen embryos only. These cycles were not counted in the cycles with OR.

<sup>2</sup>Twelve cycles had PB biopsy and cleavage stage biopsy.

**Table 1b Overall cycle data collection X.**

Indication	PGD	PGS	PGD-SS	Total
Cycles to OR	2042	3753	92	5887
Number infertile	688	2726	57	3471
Female age (years)	34	38	35	36
ART method				
IVF	203	373	20	596
ICSI	1793	3261	65	5119
IVF + ICSI	13	99	0	112
Frozen + ICSI, IVF	33	20	7	60
Cancelled after IVF/ICSI	53	20	0	73
Cycles to PGS/PGD	1989	3733	92	5814
FISH	806	3733	92	4631
PCR	1173	0	0	1173
FISH + PCR	10	0	0	10
Zona breaching				
AT drilling	487	718	7	1212
Laser drilling	1413	2679	71	4163
Mechanical	89	336	14	439
Biopsy method				
PB biopsy	41	892	0	933
Cleavage aspiration	1808	2712	15	4535
Cleavage extrusion	91	129	77	297
Blastocyst	20	0	0	20
PB and cleavage	29	0	0	29
Embryology				
COCs	26 535	40 656	1377	68 568
Inseminated	22 021	33 129	1175	56 325
Fertilized	16 134	23 713	866	40 713
Biopsied	12 200	18 964	703	31 867
Successfully biopsied	12 078	18 750	692	31 520
Diagnosed	11 015	17 415	568	28 998
Transferable	3973	5898	213	10 084
Transferred	2482	4568	133	7183
Frozen	614	719	53	1386
Clinical outcome				
Cycles to ET	1488	2638	73	4199
hCG positive	583	940	36	1559
Positive heartbeat	472	781	23	1276
Clinical pregnancy rate (% per OR/% per ET)	23/32	21/30	25/31	22/30
Number of FHB	569	971	31	1571
Implantation rate (FHB/100 embryos transferred)	23	21	23	22
Deliveries	391	586	18	995
Delivery rate (% per OR/% per ET)	19/26	16/22	20/25	17/24
Miscarriages	56	93	4	153
Miscarriage rate (% per clinical pregnancy – pregnancy lost to FU)*	12	14	18	13
Clinical pregnancies lost to FU	25	102	1	128

FHB, fetal heartbeats; FU, follow-up.

PGD column includes PGD for chromosome abnormalities, sexing for X-linked disease and PGD for monogenic disorders.

\*% per number of clinical pregnancies minus the number of pregnancies that were lost to FU.

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

Indication	Robertsonian translocation, male carrier <sup>1</sup>	Robertsonian translocations, female carrier <sup>2</sup>	Reciprocal, male carrier <sup>3</sup>	Reciprocal, female carrier <sup>5</sup>	Sex chromosome aneuploidy <sup>4</sup>	Others	Total
Cycles to OR	611	398	945	1028	292	250	3524
Number infertile	499	191	557	462	255	137	2101
Female age (years)	34	33	33	33	32	33	33
Cancelled before IVF/ICSI	0	0	3	0	7	2	12
ART method							
IVF	26	64	130	261	24	54	559
ICSI	572	322	781	731	258	188	2852
IVF + ICSI	3	6	5	10	2	2	28
Frozen + ICSI + IVF + unknown	9	6	25	26	1	4	71
Unknown	1	0	1	0	0	0	2
Cancelled after IVF/ICSI	37	22	69	76	19	15	238
Cycles to PGD	574	376	873	952	266	233	3274
Zona breaching							
AT drilling	273	207	491	568	108	117	1764
Laser drilling	283	159	348	345	121	86	1342
Mechanical	18	10	34	39	37	30	168
Biopsy method							
PB biopsy	2	7	0	12	1	1	23
Cleavage aspiration	538	346	825	876	258	219	3062
Cleavage extrusion	32	23	37	50	4	13	159
Cleavage flow displacement	2	0	2	4	3	0	11
Blastocyst	0	0	9	10	0	0	19
Embryology							
COC's	8836	5625	13 649	14 703	3714	3245	49 772
Inseminated	7385	4742	11 584	12 847	3036	2822	42 416
Fertilized	5022	3504	8270	9540	2133	2065	30 534
Biopsied	3502	2675	6364	7437	1489	1654	23 121
Successfully biopsied	3451	2646	6277	7339	1471	1634	22 818
Diagnosed	3113	2442	5836	6854	1355	1521	21 121
Transferable	1180	712	1150	1328	607	470	5447
Transferred	798	531	935	1087	414	329	4094
Frozen	144	65	53	73	61	49	445
Clinical outcome							
Cycles to ET	447	288	542	609	214	181	2281
hCG positive	156	97	167	182	69	47	718

Positive heartbeat	135	78	123	141	51	39	567
Clinical pregnancy rate (% per OR/% per ET)	22/30	20/27	13/23	14/23	17/24	16/22	16/25

<sup>1</sup>Five cycles included PGS.  
<sup>2</sup>One cycle included PGS, two cycles included centric fusion and one cycle sexing.  
<sup>3</sup>One cycle included SS, three cycles included PGS.  
<sup>4</sup>Seven cycles included PGS.  
<sup>5</sup>Five cycles included PGS three cycles include the male partner with a reciprocal translocation, and one cycle with the male partner with a supernumerary chromosome derived from chromosome 15.

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–IX) and SVIIIb (data X) list the complications of pregnancy and Supplementary Tables SXIIa (data I–IX) and SXIIb (data X) list the congenital malformations and the neonatal complications.

An overview of all cycles collected previously in data collections I–IX can be found in Table Ia, while an overview of the current data collection can be found in Table Ib.

For all indications for PGD/PGS (data I–IX and X), ICSI was the most often used method of fertilization and cleavage stage aspiration was the most commonly used method of biopsy. Overall zona pellicula drilling was more commonly performed using a laser.

### PGD cycles for chromosomal abnormalities

Tables IIa and IIb summarize the 3524 and 729 cycles to OR collected for data collection I–IX and X, respectively. As for previous years, data X showed that PGD for reciprocal translocations was performed more often than for Robertsonian translocations or other types of chromosome abnormalities. For data X 9045 oocytes were collected, 69% (5325/7727) fertilized, 74% (3947/5325) embryos were biopsied and 99% (3902/3947) embryos were successfully biopsied. Of the embryos successfully biopsied 94% (3652/3902) gave a diagnostic result, of which only 26% (938/3652) were transferable. From 729 OR procedures only 62% (450/729) resulted in an embryo transfer procedure. This is in agreement with previous data showing that a high level of chromosomally abnormal embryos is found in these patients. A positive hCG was obtained in 184 cycles, with a positive heart beat in 152 cycles [21% per OR (152/729) and 34% per embryo transfer (152/450)]. This gave an implantation rate of 26% (176/681). Finally, the delivery rate was 16% per OR (120/729) and 27% per embryo transfer (120/450). There were 18/138 miscarriages (13% per clinical pregnancy) and 9% (14/152) pregnancies were lost to follow-up.

### PGD cycles for sexing for X-linked diseases

Tables IIIa and IIIb summarize the 1057 and 110 cycles to OR collected for data collection I–IX and X, respectively. This year, again, fluorescence *in situ* hybridization (FISH) was the only method used for sexing cycles. For data X, 1485 oocytes were collected, 70% (866/1238) fertilized, 79% (685/866) embryos were biopsied and 99% (681/685) were successfully biopsied. Of the embryos successfully biopsied, 94% (638/681) gave a diagnostic result, of which only 37% (236/638) were transferable (female). From 110 OR procedures only 78% (86/110) resulted in an embryo transfer procedure. A positive hCG was obtained in 25 cycles, with a positive heart beat in 22 cycles [20% per OR (22/110) and 26% per embryo transfer (22/86)]. This gave an implantation rate of 19% (27/141). Finally, the delivery rate was 16% per OR (18/110) and 21% per embryo transfer (18/86). There were 2/20 miscarriages (10% per clinical pregnancy) and 9% (2/22) pregnancies were lost to follow-up.

**Table IIB PGD for chromosomal abnormalities, data collection X.**

Indication	Robertsonian translocation, male carrier	Robertsonian translocation, female carrier	Reciprocal translocation, male carrier	Reciprocal translocation, female carrier	Sex chromosome aneuploidy	Others	Total
Cycles to OR	131	73	211	229	45	40	729
Number infertile	91	44	100	113	32	24	404
Female age (years)	36	35	34	34	33	33	34
ART method							
IVF	7	20	53	74	4	12	170
ICSI	120	49	148	150	40	27	534
IVF + ICSI	1	1	3	2	1	1	9
IVF + Frozen	1	2	5	3	0	0	11
ICSI + Frozen	2	1	2	0	0	0	5
Cancelled after IVF/ICSI	5	3	10	8	3	2	31
Cycles to PGD	126	70	201	221	42	38	698
Zona breaching							
AT drilling	32	23	77	78	8	9	227
Laser drilling	91	43	117	135	33	28	447
Mechanical	3	4	7	8	1	1	24
Biopsy method							
PB	0	3	1	6	0	0	10
Cleavage aspiration	118	63	188	198	41	36	644
Cleavage extrusion	8	4	12	17	1	2	44
Embryology							
COCs	1625	948	2634	2798	511	529	9045
Inseminated	1325	839	2275	2369	445	474	7727
Fertilized	888	574	1593	1668	284	318	5325
Biopsied	634	426	1172	1282	199	234	3947
Successfully biopsied	630	421	1151	1269	199	232	3902
Diagnosed	576	389	1076	1208	188	215	3652
Transferable	222	116	223	230	74	73	938
Transferred	151	75	178	179	52	46	681
Frozen	34	13	24	14	8	14	107
Clinical outcome							
Cycles to ET	91	49	123	128	29	30	450
hCG positive	48	20	40	53	14	9	184
Positive heartbeat	39	16	34	43	13	7	152
Clinical pregnancy rate (% per OR/% per ET)	30/43	22/33	16/28	19/34	29/45	18/23	21/34
Number of fetal hearts	49	18	36	49	14	10	176
Implantation rate (fetal hearts/100 embryos transferred)	33	24	20	27	27	22	26
Deliveries	31	14	27	33	10	5	120
Delivery rate (% per OR/% per ET)	24/34	19/29	13/22	14/26	22/34	13/17	16/27
Miscarriages	2	0	4	9	3	0	18
(% per clinical pregnancy – pregnancy lost to FU)	6	0	13	21	23	0	13
Clinical pregnancies lost to FU	6	2	3	1	0	2	14

**Table IIIa Sexing only for X-linked disease, data collection I–IX.**

	FISH	PCR	Total
Cycles to OR	991	66	1057
Number infertile	220	0	220
Female age (years)	33	31	32
Cancelled before IVF/ICSI	2	0	2
ART method			
IVF	264	10	274
ICSI	714	56	770
IVF + ICSI	8	0	8
ICSI + Frozen	2	0	2
IVF + Frozen	1	0	1
Cancelled after IVF/ICSI	57 <sup>1</sup>	1 <sup>2</sup>	58 <sup>1,2</sup>
Cycles to PGD	932	65	997
Zona breaching			
AT drilling	489	52	541
Laser drilling	398	3	401
Mechanical	45	10	55
Biopsy method			
Cleavage aspiration	885	60	945
Cleavage extrusion	40	5	45
Flow displacement	5	0	5
Blastocyst	2	0	2
Embryology			
COC's	13 047	912	13 959
Inseminated	11 532	701	12 233
Fertilized	8138	556	8694
Biopsied	6174	458	6632
Successfully biopsied	6038	422	6460
Diagnosed	5573	329	5902
Transferable	1918	178	2096
Transferred	1318	139	1457
Frozen	350 <sup>3</sup>	58 <sup>4</sup>	408 <sup>3,4</sup>
Clinical outcome			
Cycles to ET	739	55	794
hCG positive	242	24	266
Positive heartbeat	189	17	206
Clinical pregnancy rate (% per OR/% per ET)	19/26 <sup>5</sup>	26/31 <sup>5</sup>	19/26 <sup>5</sup>

<sup>1</sup>Twenty-seven embryos from two cycles frozen before biopsy owing to hyperstimulation.

<sup>2</sup>Twenty embryos frozen before biopsy.

<sup>3</sup>Eleven cycles with embryos frozen without biopsy or after failed diagnosis included.

<sup>4</sup>Thirteen cycles with embryos frozen without biopsy or failed diagnosis included.

<sup>5</sup>Eleven embryos transferred removed from calculations owing to lack of information regarding the number of FHB in pregnancies resulting from the transfer of those embryos.

**Table IIIb Sexing only for X-linked disease, data collection X.**

	FISH	Total
Cycles to OR	110	110
Number infertile	40	40
Female age (years)	34	34
ART method		
IVF	32	32
ICSI	74	74
IVF + ICSI	4	4
Cancelled after IVF/ICSI	1	1
Cycles to PGD	109	109
Zona breaching		
AT drilling	38	38
Laser drilling	65	65
Mechanical	6	6
Biopsy method		
PB	2	2
Cleavage aspiration	100	100
Cleavage extrusion	7	7
Embryology		
COCs	1485	1485
Inseminated	1238	1238
Fertilized	866	866
Biopsied	685	685
Successfully biopsied	681	681
Diagnosed	638	638
Transferable	236	236
Transferred	141	141
Frozen	36	36
Clinical outcome		
Cycles to ET	86	86
hCG positive	25	25
Positive heartbeat	22	22
Clinical pregnancy rate (% per OR/% per ET)	20/26	20/26
Number fetal hearts	27	27
Implantation rate (% FHB/100 embryos transferred)	19	19
Deliveries	18	18
Delivery rate (% per OR/% per ET)	16/21	16/21
Miscarriages	2	2
Miscarriage rate (% per clinical pregnancy – pregnancy lost to FU)	10	10
Clinical pregnancies lost to FU	2	2

common indications for PGD for autosomal recessive diseases were  $\beta$ -thalassaemia and/or sickle cell syndromes (135 cycles), plus 115 cycles for  $\beta$ -thalassaemia/sickle cell with HLA typing, cystic fibrosis (CF) (107 cycles, including 4 cycles for CF and a second indication) and spinal muscular atrophy (SMA) (51 cycles, of which 1 was for SMA and a second indication). Amongst the autosomal dominant

## PGD for monogenic diseases

Tables IVa and IVb summarize the 3530 and 1203 cycles to OR collected for data collection I–IX and X, respectively. The most

**Table IVa** Cycles performed for single gene disorders, data collection I–IX.

Indication	Autosomal recessive				Autosomal dominant		Specific X-linked			Others <sup>8</sup>	Total
	CF <sup>1</sup>	β-Thal/SC <sup>2</sup> and β-Thal/ SC + HLA	SMA and SMA + Retinitis Pigmentosa <sup>3</sup>	HLA compatibility HLA + specific disease	DMI <sup>4</sup>	HD and HD exclusion	DMD and BMD <sup>5</sup>	FRAXA <sup>6</sup>	Haem <sup>7</sup>		
Cycles to OR	536	450	234	47	491	424	131	234	60	923	3530
Number infertile	190	168	23	0	81	63	15	61	9	147	757
Female age (years)	34	34	33	35	32	31	34	33	32	31	32
Cancelled before IVF/ICSI	0	0	0	0	3	0	0	0	0	1	4
Art method											
IVF	16	0	2	0	1	0	3	4	6	11	43
ICSI	512	444	225	47	481	419	122	228	52	902	3432
IVF + ICSI	0	0	0	0	1	0	1	0	1	0	3
IVF + ICSI + Frozen	3	6	7	0	2	2	5	0	1	6 <sup>9</sup>	32 <sup>9</sup>
Unknown	5	0	0	0	3	3	0	2	0	5	18
Cancelled after IVF/ICSI	22	24	11	6	29	13	9	14	2	46	176
Cycles to PGD	514	426	223	41	459	411	122	220	58	878 <sup>8</sup>	3352 <sup>8</sup>
Zona breaching											
AT drilling	231	178	81	7	138	142	45	43	24	229	1118
Laser drilling	253	240	123	34	298	247	74	156	32	569	2026
Mechanical	26	8	19	0	21	19	3	19	2	77	194
Unknown	4	0	0	0	2	3	0	2	0	3	14
Biopsy method											
PB biopsy	15 <sup>10</sup>	2	2	0	13 <sup>10</sup>	5	1	10 <sup>10</sup>	2 <sup>10</sup>	48 <sup>10</sup>	98 <sup>10</sup>
Cleavage aspiration	469 <sup>10</sup>	383	195	36	432 <sup>10</sup>	378	119	199 <sup>10</sup>	56 <sup>10</sup>	793 <sup>10</sup>	3060 <sup>10</sup>
Cleavage extrusion	27	12	26	1	10	24	0	2	1	16	119
Blastocyst	1	29	0	3	0	1	2	4	0	10	50
PB + embryo	0	0	0	0	3	0	0	3	0	9	15
Unknown	7	0	0	0	2	3	0	3	0	6	21
Embryology											
COCs	6965	6405	3294	621	5968	5872	1759	2622	759	12 855	47 120
Inseminated	5991	5337	2581	507	5116	4894	1442	2176	668	10 658	39 370
Fertilized	4194	3808	1840	354	3715	3453	1089	1582	484	7845	28 364
Biopsied	3167	2812	1364	227	2535	2496	791	1060	339	5621	20 412
Successfully biopsied	3138	2753	1356	227	2517	2468	770	1048	338	5555	20 170
Diagnosed	2712	2334	1158	213	2153	2157	708	911	280	4896	17 522
Transferable	1648	1213	724	48	931	960	458	426	160	2433	9001
Transferred	902	825	413	35	634	554	246	263	100	1403	5375



Frozen	306	179	85	19	94	168	93	46	23	443	1456
Clinical outcome											
Cycles to ET	446	363	202	23	366	332	105	152	51	735	2775
hCG positive	155	153	65	8	111	113	36	51	17	277	986
Positive heartbeat	124	114	55	2	85	87	31	41	11	219	769
Clinical pregnancy rate (% per OR/% per ET)	23/28	25/31	54/27	4/9	17/23	21/26	24/30	18/27	18/22	24/30	22/28

CF, cystic fibrosis (various mutations);  $\beta$ -thal,  $\beta$ -thalassaemia; SMA, spinal muscular atrophy; SC, sickle cell anaemia; DMI, myotonic dystrophy type I; HD, Huntington's disease; FRAXA, fragile X syndrome; DMD, Duchenne muscular dystrophy (specific); BMD, Becker muscular dystrophy; Haem, haemophilia.

<sup>1</sup>Five cycles for two indications: CF and FRAXA; CF and SS, CF + PGS for diabetes insipidus, CF + diabetes insipidus (sexing) and CF + PGS.

<sup>2</sup>Includes two cycles performed also with FISH for a Robertsonian translocation.

<sup>3</sup>Includes three cycles for SMA and PGS, and 5 cycles performed also for retinitis pigmentosa.

<sup>4</sup>Includes one cycle also for DMD.

<sup>5</sup>Includes one cycle for BMD and PGS.

<sup>6</sup>Includes three cycles for FRAX A testing and PGS.

<sup>7</sup>Includes one cycle for Haem A and PGS.

<sup>8</sup>Includes one cycle for Tuberous Sclerosis and PGS + 3 cycles using FISH for a microdeletion.

<sup>9</sup>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.

<sup>10</sup>Eleven cycles had both PB biopsy and cleavage stage biopsy.

**Table IVb** Cycles performed for single gene disorders, data collection X.

Indication	$\beta$ -Thal and/or SC (+HLA) <sup>1</sup>	Autosomal recessive			Autosomal dominant				Specific sex-linked			Others	Total
		CF <sup>2</sup>	SMA <sup>3</sup>	HLA <sup>4</sup> (HLA + specific disease)	HD <sup>5</sup>	DMI	NFI	CMT <sup>6</sup>	DMD	Haem	FRAXA <sup>7</sup>		
Cycles to OR	135 (115)	107	51	36 (29)	106	95	25	17	26	15	77	369	1203
Number infertile	39 (4)	46	8	1 (2)	14	21	7	2	3	1	15	81	244
Female age (years)	34	34	34	36	32	33	34	27	31	34	33	33	33
ART method													
IVF	0	0	0	0	0	0	0	0	0	0	0	1	1
ICSI	131 (111)	106	51	35 (27)	104	95	25	17	26	15	77	365	1185
IVF + Frozen	0	0	0	1 (0)	0	0	0	0	0	0	0	1	2
ICSI + Frozen	4 (4)	1	0	0 (2)	2	0	0	0	0	0	0	2	15
Cancelled after IVF/ICSI	2 (2)	3	1	0	1	2	1	0	1	0	1	7	21
Cycles to PGD	133 (113)	104	50	36 (29)	105	93	24	17	25	15	76	362	1182
Zona breaching													
AT Drilling	7 (0)	28	11	0 (6)	57	16	1	0	3	0	11	82	222

Continued

Table IVb Continued

Indication	$\beta$ -Thal and/or SC (+HLA) <sup>1</sup>	Autosomal recessive			Autosomal dominant				Specific sex-linked			Others	Total
		CF <sup>2</sup>	SMA <sup>3</sup>	HLA <sup>4</sup> (HLA + specific disease)	HD <sup>5</sup>	DMI	NFI	CMT <sup>6</sup>	DMD	Haem	FRAXA <sup>7</sup>		
Laser Drilling	124 (109)	72	37	36 (23)	45	69	22	17	19	15	55	258	901
Mechanical	2 (4)	4	2	0	3	8	1	0	3	0	10	22	59
Biopsy method													
PB	0	4	0	0	0	5	4	0	3	0	2	11	29
Cleavage Aspiration	128 (102)	94	48	35 (21)	99	85	17	17	18	15	65	320	1064
Cleavage Extrusion	2 (0)	4	2	0 (5)	6	1	0	0	1	0	2	17	40
Cyst	3 (11)	1	0	1 (3)	0	0	0	0	0	0	0	1	20
PB + embryo	0	1	0	0	0	2	3	0	3	0	7	13	29
Embryology													
COCs	1743 (1671)	1454	678	444 (421)	1369	1214	281	246	295	216	844	5129	16 005
Inseminated	1428 (1334)	1152	537	335 (363)	1134	980	241	196	250	174	725	4207	13 056
Fertilized	1081 (1190)	825	403	292 (287)	830	727	195	161	189	144	555	3064	9943
Biopsied	829 (1037)	647	292	225 (232)	607	522	164	131	143	97	399	2243	7568
Successfully biopsied	814 (1034)	642	292	225 (229)	605	512	164	129	138	97	393	2221	7495
Diagnosed	680 (945)	576	262	205 (190)	542	469	155	125	127	91	356	2002	6725
Transferable	325 (135)	342	160	41 (44)	225	206	54	55	61	47	166	938	2799
Transferred	211 (124)	166	88	30 (28)	141	122	33	19	41	22	103	532	1660
Frozen	48 (60)	42	28	11 (17)	24	37	11	17	7	13	19	137	471
Clinical outcome													
Cycles to ET	112 (79)	95	46	21 (18)	89	79	18	14	18	13	60	290	952
hCG Positive	50 (31)	38	18	10 (8)	30	30	7	9	3	6	26	108	374
Positive heartbeat	45 (24)	25	17	8 (8)	24	21	6	7	2	6	19	86	298
Clinical pregnancy rate (% per OR/% per ET)	33/40 (22/30)	23/26	33/37	22/38 (28/44)	23/27	22/27	24/33	41/50	8/11	40/46	25/32	23/30	25/31
Number FHB	59 (29)	29	20	8 (9)	33	24	6	7	2	9	23	108	366
Implantation rate (% fetal hearts/embryos transferred)	28 (24)	17	23	27 (32)	23	20	18	37	5	41	22	20	22
Deliveries	35 (21)	20	16	8 (5)	21	18	6	6	2	6	17	72	253
Delivery rate (% per OR/% per ET)	26/31 (19/27)	19/21	32/35	22/38 (17/28)	20/24	19/23	24/33	35/43	8/11	40/46	22/28	20/25	21/27
Miscarriages	8 (3)	5	1	0	3	2	0	1	0	0	2	12	37

Miscarriage rate (% miscarriages/ per clinical pregnancy – pregnancy lost to FU)	19 (12)	20	6	0	0	10	10	0	14	0	0	0	10	14	12
Clinical pregnancies lost to FU	2 (0)	0	0	0	1 (2)	0	1	0	0	0	0	0	0	2	8

CMT, Charcot-Marie-Tooth; NF1, neurofibromatosis type I.  
<sup>1</sup>FISH was carried out in addition to PCR in one cycle for a reciprocal translocation.  
<sup>2</sup>In four cycles there was a second indication: in one CF was combined with HD, in two CF was combined with Haem (once via PCR and one via sexing), in a fourth CF was combined with PGS.  
<sup>3</sup>One cycle was also carried out for Marfan.  
<sup>4</sup>In three cycles HLA typing was combined with PGS.  
<sup>5</sup>There were five cycles with a double indication: one cycle for PGS, two cycles for Marfan and two cycles for Antley-Bixler.  
<sup>6</sup>2/17 cycles were performed for an X-linked form of CMT.  
<sup>7</sup>In one cycle PCR for FRAXA was combined with FISH for X-linked mental retardation (sexing).

diseases, the most PGD cycles were performed for Huntington disease (HD) (106 cycles, including 5 cycles for HD and a second indication) and myotonic dystrophy type I (DM1) (95 cycles), neurofibromatosis (25 cycles) and Charcot Marie-Tooth (17 cycles). For a specific diagnosis of X-linked diseases the most common indications were for fragile X syndrome (FRAXA) (77 cycles, of which 1 was for FRAXA and a second indication), Duchenne and Becker muscular dystrophy (DMD/BMD) (24 cycles and 2 cycles, respectively) and haemophilia A and B (15 cycles). PGD cycles for an additional 115 monogenic diseases were initiated in 369 cycles (included under 'others' in Table IVb) and they are listed in Supplementary Table SIVc. Besides the 115 cycles for  $\beta$ -thalassemia and/or sickle cell syndromes with HLA typing, there were 36 cycles for HLA compatibility typing plus a further 29 cycles for HLA typing along with a specific disorder. The most common indications here were Fanconi anaemia, Gaucher disease, adrenoleukodystrophy and osteopetrosis.

For data X, 16 005 oocytes were collected and 76% (9943/13 056) fertilized. ICSI was used in 1185 cycles (of which 15 were subsequently frozen) and IVF in 3 cycles. A total of 76% (7568/9943) of the embryos were biopsied and 99% (7495/7568) were successfully biopsied. Of the embryos successfully biopsied, 90% (6725/7495) gave a diagnostic result, of which 42% (2799/6725) were transferable. From 1203 OR procedures 79% (952/1203) resulted in an embryo transfer procedure. A positive hCG was obtained in 374 cycles, with a positive heart beat in 298 cycles [25% per OR (298/1203) and 31% per embryo transfer (298/952)] and 366 fetal hearts, giving an overall implantation rate of 22% (366/1660). These pregnancy rates were notably higher than in the previous data collections. Finally, the delivery rate was 21% per OR (253/1203) and 27% per embryo transfer (253/952). There were 37/290 miscarriages (13% per clinical pregnancy) and 3% (8/298) clinical pregnancies were lost to follow-up.

Overall, the number of PGD cycles performed for monogenic disorders between January and December 2007 further increased compared with data collection IX. This increase is primarily a result of a marked increase in the cycles for  $\beta$ -thalassemia and/or sickle cell syndromes (with HLA typing) (245 cycles in data X versus 110 cycles in data IX) and an increase in cycles for less frequent monogenic disorders (column 'others' in Table IVb). Overall, 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.*, 2009).

## Preimplantation genetic screening

Tables Va and Vb summarize the 13 053 and 3753 cycles to OR reported for data collection I–IX and X, respectively. For data X, 40 656 oocytes were collected, 72% (23 713/33 129) fertilized, 80% (18 964/23 713) embryos were biopsied and 99% (18 750/18 964) were successfully biopsied. Of the embryos successfully biopsied, 93% (17 415/18 750) gave a diagnostic result, of which only 34% (5898/17 415) were transferable. From 3753 OR procedures only 70% (2638/3753) resulted in an embryo transfer procedure. A positive hCG was obtained in 940 cycles, with a positive heart beat in 781

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

Indication	AMA	AMA + miscarriage <sup>1</sup>	AMA + RIFI	Recurrent miscarriage	Recurrent IVF failure	SMF <sup>2</sup>	Oocyte donation <sup>3</sup>	Prev abn preg <sup>3</sup>	No indication	Others <sup>4</sup>	Total
Cycles to OR	4150	399	1063	1696	3380	1164	67	25	357	752	13 053
Number infertile	3485	288	996	1165	3275	1043	47	13	347	645	11 304
Female age (years)	41	41	41	34	34	35	41	35	35	35	37
Cancelled before IVF/ICSI	0	0	0	0	1	0	0	0	0	1	2
ART method											
IVF	626	63	128	187	284	3	1	1	116	86	1495
ICSI	3443	325	922	1464	3024	1124	66	24	206	643	11 241
IVF + ICSI	66	7	7	36	36	32	0	0	34	7	225
IVF + Frozen	0	2	0	1	1	0	0	0	0	0	4
ICSI + Frozen	9	2	1	7	10	5	0	0	1	1	36
Unknown	6	0	5	1	24	0	0	0	0	14	50 <sup>5</sup>
Cancelled after IVF/ICSI	180	25	8	40	114	26	0	0	26	23	442
Cycles to PGS	3970	374	1055	1656	3265	1138	67	25	331	728	12 609
Zona breaching											
AT drilling	1161	119	270	707	952	417	0	2	101	241	3970
Laser drilling	2644	187	521	880	1856	609	45	23	197	442	7404
Mechanical	152	68	264	68	420	112	22	0	33	31	1170
Unknown	13	0	0	1	37	0			0	14	65 <sup>5</sup>
Biopsy method											
PB biopsy	332 <sup>6</sup>	101	611	50	494	11	0	0	72	145	1816 <sup>6</sup>
Cleavage aspiration	3395 <sup>6</sup>	249	402	1527	2562	1074	45	25	256	558	10 093 <sup>6</sup>
Cleavage extrusion	224	24	42	74	164	52	22	0	3	20	625
Cleavage flow displacement	7	0	0	3	7	1	0	0	0	4	22
Blastocyst	0	0	0	1	0	0	0	0	0	1	2
Unknown	13	0	0	1	38	0	0	0	0	0	52 <sup>5</sup>
Embryology											
COC's	40 898	3807	9764	21 558	44 663	17 110	940	319	4054	9482	15 2595
Inseminated	34 640	3063	7561	17 811	36 878	13 912	799	262	3498	7974	12 6398
Fertilized	24 192	2138	5225	13 055	26 561	9536	584	199	2383	5606	89 479

Biopsied	18 910	1984	5776	9884	20 818	7141	436	136	1950	4405	71 440
Successfully biopsied	18 640	1981	5725	9760	20 575	7105	435	133	1906	4363	70 623
Diagnosed	17 042	1851	5371	8935 <sup>7</sup>	19 259 <sup>7</sup>	6637	433	129	1637 <sup>7</sup>	3887 <sup>7</sup>	65 181 <sup>7</sup>
Transferable	5050	550	1870	3249 <sup>7</sup>	7267 <sup>7</sup>	2675	204	51	811 <sup>7</sup>	1653 <sup>7</sup>	23 380 <sup>7</sup>
Transferred	4394	408	1397	2340 <sup>7</sup>	4873 <sup>7</sup>	1824	106	26	490 <sup>7</sup>	1117 <sup>7</sup>	16 975 <sup>7</sup>
Frozen	553	63	171	468	1026	342	73	11	100	358	3165
Clinical outcome											
Cycles to ET	2577	248	814	1282	2614	953	61	16	277	591	9433
hCG positive	749	56	172	495	887	401	37	5	109	234	3145
Positive heartbeat	557	38	140	384	685	328	30	5	93	173	2433
Clinical pregnancy rate (% per OR/% per ET)	13/22	10/15	13/17	23/30	20/26	28/34	45/49	20/31	26/34	23/29	19/26

AMA, advanced maternal age; RIF, repeated implantation failure; SMF, severe male factor.

<sup>1</sup>These data were not extracted from I to IV.

<sup>2</sup>These data were not extracted from I to III.

<sup>3</sup>These data were not extracted from data I–VIII.

<sup>4</sup>'Others' contains also cycles with multiple indications and previous abnormal (prev abn) pregnancies (data I–VIII).

<sup>5</sup>Several cycles had incomplete results.

<sup>6</sup>One cycle had cleavage stage biopsy and PB biopsy.

<sup>7</sup>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.

**Table Vb Cycles performed for PGS, data collection X.**

Indication	AMA	RIF	Recurrent miscarriage	AMA + RIF	AMA + miscarriage	SMF	AMA + SMF	RIF + SMF	Miscarriage + SMF	Oocyte donation	Prev abn preg	No indication	Others	Total
Cycles to OR	1250	713	404	410	147	334	39	40	5	88	23	105	195	3753
Number infertile	763	658	154	381	70	296	37	38	5	56	9	95	164	2726
Female age (years)	41	32	36	40	41	34	40	33	36	41	37	36	36	38
ART method														
IVF	129	57	38	84	24	1	1	2	0	1	1	14	21	373
ICSI	1091	637	349	322	112	330	37	37	5	86	22	75	158	3261
IVF + ICSI	24	16	13	2	9	0	1	1	0	1	0	16	16	99
IVF + Frozen embryos	0	0	0	1	0	0	0	0	0	0	0	0	0	1
ICSI + Frozen embryos	6	3	4	1	2	3	0	0	0	0	0	0	0	19
Cancelled post OR	3	7	4	1	1	4	0	0	0	0	0	0	0	20
Cycles to PGD	1247	706	400	409	146	330	39	40	5	88	23	105	195	3733
Zona breaching														
AT drilling	189	119	75	77	27	89	3	1	1	5	9	56	67	718
Laser drilling	1004	494	309	256	104	191	35	39	4	57	14	47	125	2679
Mechanical	54	93	16	76	15	50	1	0	0	26	0	2	3	336
Biopsy method														

Continued

Table Vb Continued

Indication	AMA	RIF	Recurrent miscarriage	AMA + RIF	AMA + miscarriage	SMF	AMA + SMF	RIF + SMF	Miscarriage + SMF	Oocyte donation	Prev abn preg	No indication	Others	Total
PB	240	169	35	265	37	18	26	23	0	0	0	25	54	892
Cleavage aspiration	975	505	356	129	102	308	12	17	5	62	22	80	139	2712
Cleavage extrusion	32	32	9	15	7	4	1	0	0	26	1	0	2	129
Embryology														
COCs	11 516	8676	4893	3587	1446	4719	393	514	59	1115	248	1224	2266	40 656
Inseminated	9576	6963	4019	2766	1164	3739	322	445	47	941	192	1025	1930	33 129
Fertilized	6725	5082	2957	1975	833	2637	204	312	37	713	139	714	1385	23 713
Biopsied	5072	4245	2223	1998	745	1923	173	270	29	536	110	556	1084	18 964
Successfully biopsied	5036	4150	2206	1975	738	1911	173	267	29	532	108	554	1071	18 750
Diagnosed	4742	3832	2073	1734	705	1807	152	238	29	519	101	508	975	17 415
Transferable	1267	1393	711	655	192	673	47	98	9	231	35	201	386	5898
Transferred <sup>1</sup>	1068	1047	507	594	162	461	46	76	8	138	28	140	293	4568
Frozen	122	170	108	68	17	69	1	18	1	66	9	35	35	719
Clinical outcome														
Cycles to ET	683	572	297	317	91	271	29	37	5	76	17	84	159	2638
hCG positive	199	224	132	71	20	110	6	21	3	46	6	33	69	940
Positive heartbeat	160	175	110	65	15	98	6	21	4	36	6	27	58	781
Clinical pregnancy rate (% per OR/% per ET)	13/23	24/31	27/37	16/20	10/16	29/36	15/21	52/57	80/80	41/47	26/35	26/32	30/36	21/30
Number of fetal hearts	190	213	142	79	19	129	6	30	3	49	10	31	70	971
Implantation rate (fetal hearts/100 embryos transferred)	18	20	28	13	12	28	13	40	37	35	36	22	24	21
Deliveries	118	134	90	37	7	80	4	13	2	31	6	17	44	586
Delivery rate (% per OR/% per ET)	9/17	19/23	22/30	9/12	7/11	24/30	10/14	32/35	40/40	35/41	26/35	16/20	23/28	16/22
Miscarriages	29	10	8	9	4	13	2	4	2	2	0	4	6	93
Miscarriage rate (% per clinical pregnancy – pregnancy lost to FU)	20	7	8	20	29	14	33	23	50	6	0	19	12	14
Clinical pregnancies lost to FU	13	31	12	19	1	5	0	4	0	3	0	6	8	102

<sup>1</sup>'Others' contains also cycles with multiple indications.

<sup>1</sup>Failed embryos were also transferred.

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

Method for sexing	FISH (SS only)	FISH (SS + AS) <sup>1</sup>	PCR	Unknown	Total
Cycles to OR	296	89	189	5 <sup>2</sup>	579 <sup>2</sup>
Number infertile	25	5	16	1	47
Female age (years)	35	39	37	35	36
ART method					
IVF	123	10	10	3	146
ICSI	168	78	168	2	416
Frozen	3	0	2	0	5
Frozen + IVF + ICSI + unknown	2	1	9	0	12
Cancelled after IVF/ICSI	4	0	7	5	16
Cycles to PGD	292	89	182	0	563
Zona breaching					
AT drilling	9	0	10	0	19
Laser drilling	126	4	1	0	131
Mechanical	157	85	171	0	413
Biopsy method					
Cleavage aspiration	130	0	11	0	141
Cleavage extrusion	162	89	171	0	422
Embryology					
COC's	3824	1227	2878	23	7952
Inseminated	3341	1056	2188	19	6604
Fertilized	2362	748	1452	11	4573
Biopsied	1891	548	1143	0	3582
Successfully biopsied	1791	548	1116	0	3455
Diagnosed	1624	468	1049	0	3141
Transferable	617	151	473	0	1241
Transferred	397	102	361	0	860
Frozen <sup>3</sup>	170	34	86	0 <sup>4</sup>	290
Clinical outcome					
Cycles to ET	221	60	138	0	419
hCG positive	83	20	58	0	161
Positive heartbeat	68	13	39	0	120
Clinical pregnancy rate (% per OR/% per ET)	23/31	15/22	21/28	0	21/29

AS, aneuploidy screening.

<sup>1</sup>These data were not extracted from I to VII.<sup>2</sup>One natural cycle included.<sup>3</sup>Eleven cycles with embryos frozen without biopsy or failed diagnosis included.<sup>4</sup>Three embryos frozen without biopsy were not included.

**Table V1b PGD for social sexing, data collection X.**

	FISH (SS only)	FISH (SS + AS)	Total
Cycles to OR	59	33	92
Number infertile	35	22	57
Female age (years)	33	38	36
ART method			
IVF	11	9	20
ICSI	41	24	65
ICSI + frozen embryos	7	0	7
Cancelled after IVF/ICSI	0	0	0
Cycles to PGD	59	33	92
Zona breaching			
AT	7	0	7
Laser drilling	42	29	71
Mechanical	10	4	14
Biopsy method			
Cleavage aspiration	15	0	15
Cleavage extrusion	44	33	77
Embryology			
COCs	917	460	1377
Inseminated	761	414	1175
Fertilized	588	278	866
Biopsied	475	228	703
Successfully biopsied	465	227	692
Diagnosed	378	190	568
Transferable	152	61	213
Transferred	88	45	133
Frozen	44	9	53
Clinical outcome			
Cycles to ET	50	23	73
hCG positive	27	9	36
Positive heartbeat	16	7	23
Clinical pregnancy rate (% per OR/% per ET)	27/32	21/30	25/32
Number FHB	23	8	31
Implantation rate (fetal hearts/embryos transferred)	26	18	23
Deliveries	11	7	18
Delivery rate (% per OR/% per ET)	19/22	21/30	20/25
Miscarriages	4	0	4
Miscarriage rate (% per clinical pregnancy – pregnancy lost to FU)	27	0	18
Clinical pregnancies lost to FU	1	0	1

cycles [21% per OR (781/3753) and 30% per embryo transfer (781/2638)]. This gave an implantation rate of 21% (971/4568). These pregnancy rates were similar to the previous data collections. Finally,

the delivery rate was 16% per OR (586/3753) and 22% per embryo transfer (586/2638). There were 93/679 miscarriages (14% per clinical pregnancy) and 13% (102/781) clinical pregnancies lost to follow-up.

The main indications were advanced maternal age (AMA) (1250 OR) and repeated implantation failure (RIF) (713 OR). There were still a number of cycles reported where no indication was given (105 OR). All indications involving AMA showed a somewhat lower pregnancy rate (between 10 and 16% per OR) in comparison with the other indications, although the pregnancy rates were higher than in previous data collections. Patients with severe male factor (SMF) showed a relatively high pregnancy rate [29% per OR (98/334)] as did patients where oocyte donation was performed [41% per OR (36/88)]. Patients with no indication had a pregnancy rate of 26% per OR (27/105).

From 3753 cycles, 387 involved the biopsy of only one embryo and 555 involved the biopsy of two embryos. As stated in data VII (Harper et al., 2008a,b), in the majority of cases these embryos should be replaced without biopsy.

There was only one cycle where PCR and FISH was used, in all other 3752 cycles to OR FISH was used.

In Table Vb, the column 'others' contains various indications such as mosaic embryos and single or double embryo transfer, as well as cycles with multiple indications.

The PGD Consortium recently published a position statement on the use of PGS (Harper et al., 2010a). All RCTs for PGS using FISH and mainly cleavage-stage biopsy show no improvements in success rates. The Consortium recommendation was that the use of arrays on either polar bodies or trophoctoderm biopsies should be validated and appropriate RCTs performed. The ESHRE PGS Task Force has conducted a pilot into the feasibility of using arrays for polar body biopsy (Geraedts et al., 2010) and is in the process of setting up an RCT.

## PGD cycles for social sexing

Tables VIa and VIb summarize the 579 and 92 cycles to OR collected for data collection I–IX and X, respectively. For data X, 1377 oocytes were collected, 74% (866/1175) fertilized, 81% (703/866) embryos were biopsied and 98% (692/703) were successfully biopsied. Of the embryos successfully biopsied 82% (568/692) gave a diagnostic result, of which only 38% (213/568) were transferable (of the desired sex). From 92 OR procedures only 79% (73/92) resulted in an embryo transfer procedure. A positive hCG was obtained in 36 cycles, with a positive heart beat in 23 cycles [25% per OR (23/92 and 32% per embryo transfer (23/73)]. This gave an implantation rate of 23% (31/133). These pregnancy rates were similar to the previous data collections. Finally, the delivery rate was 20% per OR (18/92) and 25% per embryo transfer (18/73). There were 4/22 miscarriages (18% per clinical pregnancy) and 4% (1/23) was lost to follow-up.

## Pregnancies and babies

Tables VIIa, VIIb, IXa–XIb, and Supplementary Tables SVIIIa, SVIIIb, SXIIa, SXIIb summarize the pregnancy and baby data. Data X was comparable to previous data collections. Data X included 1516 clinical pregnancies which resulted in 1609 fetal sacs (Table VIIb). There were 977 deliveries of 1206 babies. Of the 1291 cycles ending in a



**Table VIIa** Evolution of pregnancy, data I–IX.

	<b>n pregnancies</b>	<b>n fetal sacs</b>
Pregnancies	4595	4874
FISH cycles	3688	
PCR cycles	902	
FISH + PCR	5	
Subclinical pregnancies <sup>1</sup>	699	
Clinical pregnancies	3896	4874
Singletons	2822	2822
Twins	877	1754
Triplets	91	273
Quadruplet	6	24
Unknown	100	1 <sup>2</sup>
Lost to FU during first trimester	42	43
First trimester loss	528	653
Miscarriage	417 <sup>3</sup>	461
TOP	8 <sup>4</sup>	9
Extra-uterine pregnancy	45 <sup>5</sup>	35
Vanishing twins/triplets or miscarriage multiplet		110
Reduction of multiple pregnancies		35
Quadruplet to twin		8
Triplet to twin		12
Triplet to singleton		8
Twin to singleton		7 <sup>8</sup>
Unknown	58	3
Ongoing pregnancies > 12 weeks	3326	4178
Second trimester loss	78	141
Miscarriage	57 <sup>6</sup>	83
Miscarriage twin to singleton		3
TOP	20 <sup>7</sup>	20
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	85 <sup>9</sup>	108
Deliveries	3163	3929
Singletons	2424	2424
Twins	712	1424
Triplets	27	81

<sup>1</sup>Subclinical pregnancy defined as pregnancy without any other clinical signs, but positive serum hCG.

<sup>2</sup>Number of FHBs not known for data I–VIII. Counted further as one fetal heart.

<sup>3</sup>One miscarriage after amniocentesis.

<sup>4</sup>TOP, termination of pregnancy. Two TOPs for anencephalocele, one TOP for social reasons, one TOP of twin with misdiagnosis for CMT disease 1a, one TOP for 47,XY+13, one TOP for encephalocele and one TOP for 47,XY+21.

<sup>5</sup>One heterotrophic gestation continued as singleton after reduction of extra-uterine gestation at 6 weeks.

<sup>6</sup>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).

<sup>7</sup>TOP after misdiagnosis: one misdiagnosis for sexing, FISH, female fetus, indication SS; one misdiagnosis for  $\beta$ -Thal, PCR; one misdiagnosis for MD, 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, one trisomy 21, one mosaic 46,XY/47,XY+18 (misdiagnosis), one Hemivertebrae, hypoplastic cerebellum, hydrocephaly (46,XX), one abnormal chromosome 15, one polycystic kidney.

<sup>8</sup>One misdiagnosis for sexing, PCR, indication Duchenne, twin pregnancy, selective termination of male fetus. Cycle done in 1996, Y-specific amplification only.

<sup>9</sup>One misdiagnosis (47,XXX after PGS for RIF) lost to FU.

**Table VIIb Evolution of pregnancy, data X.**

	n pregnancies	n fetal sacs
Pregnancies	1516	1609
FISH only cycles	1151	
PCR only cycles	362	
FISH + PCR	3	
Subclinical pregnancies <sup>1</sup>	225	
Clinical pregnancies	1291	1609
Singletons	973	973
Twins	270	540
Triplets	21	63
Quadruplet	2	8
Unknown	25	25
Lost to FU during first trimester	20	25
First trimester loss	211	258
Miscarriage	198	206
TOP	5 <sup>2</sup>	5
Extra-uterine pregnancy	8	8
Vanishing/miscarriage multiples		
Twin to singleton	33	33
Triplet to twin or singleton	3	4
Quadruplet to twin	1	2
Reduction of multiple pregnancies	9	12
Quadruplet to twin	1	2
Triplet to twin	3	3
Triplet to singleton	2	4
Twin to singleton	3	3
Ongoing pregnancies (> 12 weeks)	1060	1314
Second trimester loss	37	47
Miscarriage	29	37
TOP	8 <sup>3</sup>	9
Miscarriage twin to singleton	1	1
Lost to FU during second trimester	46	61
Deliveries	977	1206
Singletons	758	758
Twins	209	418
Triplets	10	30

<sup>1</sup>Subclinical pregnancy defined as pregnancy without any other clinical signs, but positive serum hCG.

<sup>2</sup>Two ultrasound abnormalities, two unknown reason, one divorce.

<sup>3</sup>Finnish nefrosis twins, both affected, confirmed cytomegalovirus infection, elective termination unknown cause, Hydrocephaly termination 8 month pregnancy [pregnancy started as quadruplet: two selective reduction, one miscarriage after chorionic villous sampling (CVS), last fetus TOP], four pregnancies affected with trisomy 21.

pregnancy with a positive heartbeat, follow-up data on 1271 pregnancies were reported. Of the 977 pregnancies reported to have ended with a delivery (total number of babies: 1206), neonatal data on 1206 babies were submitted. The delivery rates per indication are reported in Tables IIb, IIIb, IVb, Vb and VIb. Fifty per cent of the deliveries were by Caesarean section (489/977) (Table IXb). In 132 cases the method of delivery was not known.

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

	Total	Singletons	Twins	Triplets
No deliveries	3163 <sup>1</sup>	2424 <sup>1</sup>	712 <sup>1</sup>	27
Method of delivery				
Vaginal	1315	1169	145	1
Caesarian	1490	988	482	20
Vaginal and Caesarian	7	2	5	0
Unknown	351	265	80	6
Term at delivery				
Preterm	898	402	476	20
Term	1985	1807	176	2
Unknown	279	215	59	5

<sup>1</sup>For one twin there was only partial information: pregnancy was reported as a twin, the birth and baby as a singleton.

**Table IXb Method of delivery and gestational age, data X.**

	Total	Singleton	Twin	Triplet
No deliveries	977	758	209	10
Method of delivery				
Vaginal	356	328	27	1
Caesarean	489	327	153	9
Unknown	132	103	29	0
Term at delivery				
Preterm	206	89	112	5
Term	705	628	75	3
Unknown	66	41	22	2

Confirmation of the diagnosis was performed prenatally (441/1609) and/or postnatally (401/1609) (Table Xb). Supplementary Table SXIIb shows the abnormalities found during or after the pregnancy. Several abnormalities were found that were not related to the PGD.

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 (293/1291, 23%). This means 37% (448/1206) of the babies born are part of a multiplet at birth.

## Misdiagnoses

Table XIIIa summarizes the misdiagnoses reported for data I–IX. For data X, no misdiagnoses have been reported. The Consortium has published a paper on the possible causes of misdiagnosis in PGD (Wilton et al., 2009).

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

Method	Result			
	n	Normal	Abnormal	Failed
Prenatal diagnosis				
FISH				
CVS	106	105 <sup>1</sup>	1 <sup>2</sup>	0
Amniocentesis	593 <sup>3</sup>	578 <sup>1,3</sup>	12 <sup>4</sup>	3
Ultrasound	973 <sup>3</sup>	961	11 <sup>3,5</sup>	1
Unknown	3	3	0	0
Total	1672 <sup>6</sup>	1647	24	4
PCR				
CVS	145	141	4 <sup>7</sup>	0
Amniocentesis	170	159	10	1
Ultrasound	34	31	3	0
Unknown	2	2	0	0
Total	349 <sup>6</sup>	332	16	1
Post-natal diagnosis				
FISH				
Karyotype miscarriage	89	46	43 <sup>8</sup>	0
Karyotype post-natal	180	177	4	0
FISH microdeletion	2	2	0	0
Physical examination	1142	1137	6 <sup>9</sup>	0
Karyo post-natal + physical examination	15	15	0	0
Unknown	2 <sup>10</sup>	2 <sup>10</sup>	0	0
Total	1430	1379	53	0
PCR				
Karyotype miscarriage	6	4	2	0
DNA test miscarriage	2	2	0	0
DNA test post-natal	84	83	1	0
Sweat test	8	8	0	0
Physical examination	83	82	1	0
Karyotype	15	15	0	0
Karyotype + DNA	3	3	0	0
Karyotype + phys exam	1	1	0	0
Hearing test	3	3	0	0
Algo test	2	2	0	0
Unknown	11	11	0	0
Total	218	214	4	0

<sup>1</sup>Total 3 miscarriages after normal outcome amniocentesis (1 FISH, 2 PCR), one miscarriage after normal outcome (CVS) (FISH).

<sup>2</sup>XY, + 21 → TOP (AS maternal age, repeated IVF failure).

<sup>3</sup>Three fetal sacs with abnormalities on ultrasound (enlarged lateral ventricle, cardiopathy, hydrocephalus) with normal result on amniocentesis.

<sup>4</sup>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).

<sup>5</sup>Encephalocele → TOP (AS repeated miscarriage); hemivertebrae, hypoplastic cerebellum, hydrocephaly → TOP; cystic hygroma | twin miscarriage → ongoing singleton (rec. translocation FISH).

<sup>6</sup>Three fetal sacs had PCR and FISH at PGD.

<sup>7</sup>47,XY, + 13 → TOP (PCR: not affected of Zellweger).

<sup>8</sup>Mosaic 4n/2n (AS oocyte donation recurrent miscarriage); trisomy 20 (AS maternal age recurrent miscarriage); 92,XXXXX (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).

<sup>9</sup>Misdiagnosis after gender selection for XL retinitis pigmentosa: male.

<sup>10</sup>Two children had unknown check and karyotype.

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

Method	Result			
	n	Normal	Abnormal	Failed
Prenatal diagnosis				
FISH				
CVS	12	10	2 <sup>1</sup>	0
Amniocentesis	80	75	5 <sup>2</sup>	0
Ultrasound	250	247	3 <sup>3</sup>	0
Total	342	332	10	0
PCR				
CVS	26	26	0	0
Amniocentesis	70	68	2 <sup>4</sup>	0
Ultrasound	3	3	0	0
Total	99	97	2	0
Post-natal diagnosis				
FISH				
Karyotype miscarriage	18	8	10 <sup>5</sup>	0
Karyotype post-natal	55	55	0	0
Physical examination	221	221	0	0
Karyo post-natal + physical examination	3	3	0	0
Total	297	287	10	0
PCR				
Karyotype miscarriage	2	2	0	0
Physical examination	21	21	0	0
DNA test post-natal	38	38	0	0
Karyotype post-natal	1	0	1 <sup>6</sup>	0
Karyo post-natal + physical examination	30	30	0	0
DNA test + karyotype	2	1	1 <sup>7</sup>	0
Unknown	10	10	0	0
Total	104	102	2	0

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

Total children born		2841 <sup>1</sup>
Sex		
Male		1723
Female		1964
Unknown		154
Mean birthweight (g)		
Singletons	3217	2131
Twins	2389	1208
Triplets	1883	54
Mean birth length (cm)		
Singletons	50	1399
Twins	46	685
Triplets	44	15

<sup>1</sup>Numbers in the right column indicate the number of newborns for whom information is available.

## Success of individual centres

Figure 1 shows the pregnancy rate for each centre for data X. The average pregnancy rate is 21.73%. Success rate tends to be higher and more homogenous in the most active centres (performing more than 100 OR per year). Centres carrying out lower numbers of cycles may have lower rates owing to less experience. The findings, however, indicate that some of the most active centres fall below the average 22% pregnancy rate and even have pregnancy rates lower than some of the centres performing few cycles. A more detailed statistical analysis comparing success rates according to various factors (indication, women age at OR, etc.) should be performed to confirm these differences.

## Discussion

This 10th report of the ESHRE PGD Consortium demonstrates, as in previous years, the continuing increase in the number of PGD cycles, with subsequent pregnancies and babies.

The number of centres participating in the data collection of 2007 was equal to 2006. There are still two levels of membership of the

**Table X1b Data on children born, data collection X.**

Total children born	1206		
Sex			
Male	551		
Female	555		
Unknown	100		
Mean birthweight (g)		1024/1206 <sup>1</sup>	
Singletons	3224	648/758 <sup>1</sup>	
Twins	2374	357/418 <sup>1</sup>	
Triplets	1922	19/30 <sup>1</sup>	
Mean birth length (cm)		679/1206 <sup>1</sup>	
Singletons	49.9	428/758 <sup>1</sup>	
Twins	45.8	244/418 <sup>1</sup>	
Triplets	46.3	7/30 <sup>1</sup>	
Mean head circumference (cm)		235/1206 <sup>1</sup>	
Singletons	34.3	157/758 <sup>1</sup>	
Twins	32.8	74/418 <sup>1</sup>	
Triplets	33.9	4/30 <sup>1</sup>	
Apgar scores after 1 min	Singleton	Twin	Triplet
Good <sup>2</sup>	213	86	6
Poor <sup>2</sup>	7	8	1
Apgar scores after 5 min			
Good <sup>2</sup>	215	88	7
Poor <sup>2</sup>	4	4	0
Apgar scores after 10 min			
Good <sup>2</sup>	119	54	6
Poor <sup>2</sup>	2	1	1

<sup>1</sup>Indicates the number of newborns for whom information is available out of the total number of newborns.

<sup>2</sup>Good is defined  $\geq 7$ , poor is defined  $< 7$ .

Consortium; full membership for centres who submit annual data and associate membership for centres who cannot submit data (including new clinics, IVF units who work with a diagnostic laboratory that is a member of the Consortium). Associate centres performing PGD must send in summary data. For data X, only six associate centres sent in summary data and so these data were not included in this report. Most associate centres are satellite PGD centres that work with many IVF centres and they have reported that they cannot obtain information about the IVF cycles. Therefore, we have amended the information we will collect from associate centres to just include data on the diagnosis.

As always, the centres who submit data have access to the raw data while the associate centres are allowed to participate in the annual Consortium meetings and they are sent the quarterly Consortium newsletter.

Besides data collection, the Consortium is involved with a number of activities through the working groups. Currently there are five working groups: accreditation, misdiagnosis auditing and monitoring, guidelines, database and molecular methods. The accreditation working group has organized two quality management meetings and

has two more scheduled: 2011 (Athens) and 2012 (Istanbul) in collaboration with EuroGentest. The group has also written a paper on the accreditation process specifically relating to PGD and ISO15189 (Harper *et al.*, 2010b). This group annually collects data on the number of centres accredited. In many countries it is now becoming mandatory for all diagnostic laboratories to be accredited and the Consortium supports this as accreditation ensures quality of treatment. The FISH and PCR external quality assessment schemes (EQA) continue to operate annually and it is hoped that an array EQA will be set up in the near future. The misdiagnosis auditing and monitoring group are conducting two studies to examine the follow-up of embryos after PGD; one for PCR and one for FISH diagnoses. It is key that all centres utilize their untransferred embryos to validate and audit the methods that they are using and to calculate the efficacy of their techniques. The misdiagnosis working group wrote a paper on the causes of misdiagnosis (Wilton *et al.*, 2009). The guidelines working group has almost finished its task. Four new specific guidelines have been written: organization of a PGD/PGS Centre, Amplification-based PGD, FISH-based PGD and Embryo Biopsy and Embryology. Three of the four documents are available on the ESHRE website for discussion and suggestion, whereas the Embryo Biopsy Guideline is in the final stages of preparation and will be available online soon. All four guideline documents should be published before the end of 2010. The database working group has been refining the data collection and developing a database for the frozen embryo data. This will become more important as centres move to arrays and vitrification for their diagnoses (Harper and Harton, 2010). The molecular methods working group has set up a database of primers which is only open to full Consortium members. It is essential that all primer sets are validated in individual laboratories before clinical use.

From the ten data collections, the Consortium now has detailed data on 27 630 cycles and 4047 babies born after PGD/PGS.

The large amount of detailed information the Consortium has collected is unique and studies are underway to analyse many aspects of the data in more depth.

## Supplementary data

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

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**Table XIIIa** Summary of misdiagnosis from data I–IX.

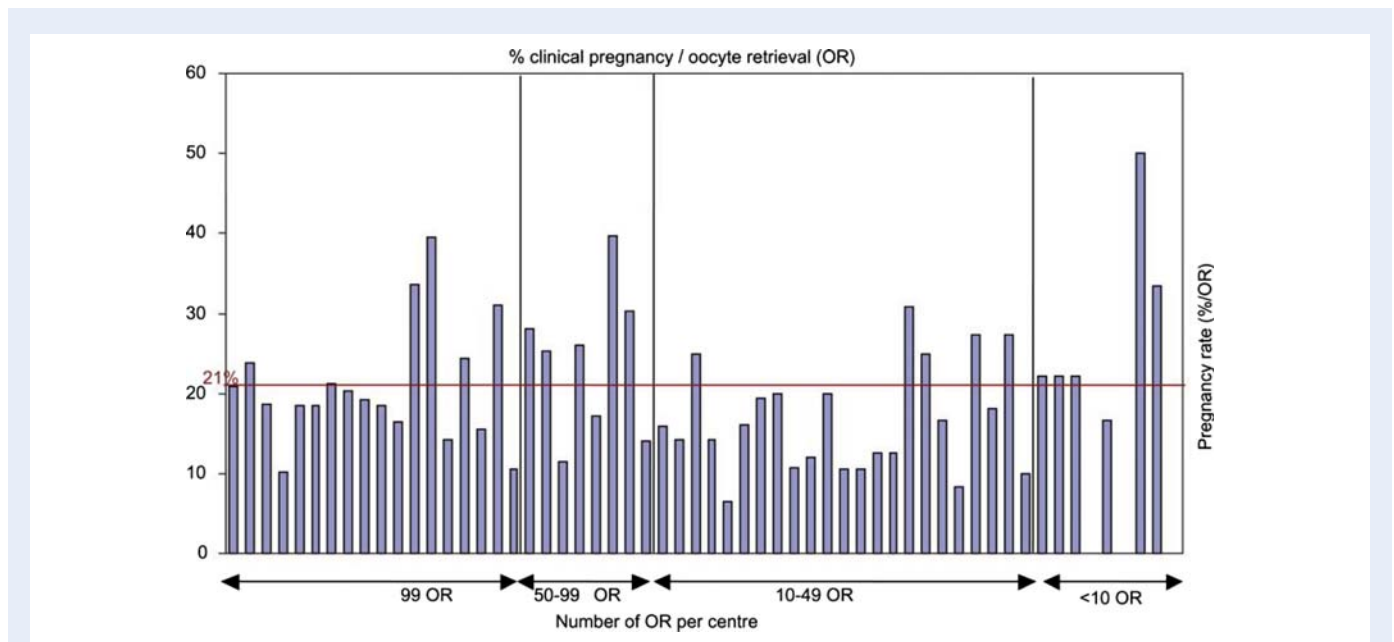
Indication	Method used	PND-post-natal	Outcome	Reported in
Monogenics				
DM I	PCR	PND	TOP	I
β-Thal	PCR	PND	TOP	II
β-Thal	PCR	PND	TOP	VIII
Familial amyloid polyneuropathy	PCR	PND	Born	IV
CF	PCR	PND	Born	II
CF (one of twins)	PCR	Post	Born	IV
CMT IA	PCR	PND	born	Cycle reported in V but misdiagnosis in VII
SMA	PCR	Post	Born	Cycle reported IV but misdiagnosis in VII
CMT IA (twins)	PCR	PND	TOP of both twins	VII
FRAXA	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, Haem A	FISH	PND	TOP	IV
46,XY, Haem 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 FU	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
SS				
Requested male but female fetus	FISH	PND	TOP	III

PND, prenatal diagnosis.

The numbers in the last column indicate the PGD Consortium report number.

diagnostique pré-implantatoire, Service de la Biologie de la Reproduction; Institut de biologie, Lab de Biochimie Génétique; Germany: University of Bonn, Department of Obstetrics & Gynaecology, Section of Reproductive Medicine; University Women's Hospital, Kiel; Centre for Gynecological Endocrinology, Reproductive Medicine and Human Genetics; University Clinic of Schleswig-Holstein, Campus Luebeck, Department of Obstetrics and Gynecology; IVF-SAAR; Fertility Center Hamburg; Kinderwunschzentrum München; 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: Tel-Aviv Sourasky Center; Institute of Human Genetic, Sheba Medical Centre; Zohar PGD lab, Medical

Genetics Unit; Italy: SISMER; EmbryoGen, Centre for Preimplantation Genetic Diagnosis; Japan: St Mother Hospital; Poland: INVICTA Fertility and Reproductive Centre; Portugal: Faculty of Medicine of Porto-Hospital S. Joao, Department of Medical Genetics; Spain: Instituto Dexeus; Instituto Valenciano de Infertilidad; Institut Marqués, Servei de Diagnòstic Genètic Preimplantacional; Sistemas Genomicos SL Valencia; Clinica GINEFIV; Sweden: Department of Clinical Genetics, Karolinska Hospital; Sahlgrenska University Hospital, Department of Ob/Gyn; Taiwan: Lin-Kou Medical Centre, Chang Gung Memorial Hospital & Medical Collega, Department of Ob/Gyn; The Netherlands: PGD Working Group Maastricht, The Centre for Reproductive Medicine; Departement of Obstetrics and Gynaecology, Subdepartement Infertility, and Departement of Clinical Genetics;



**Figure 1** Clinical pregnancy rates per centre.

University Medical Centre Utrecht; Turkey: Istanbul Memorial Hospital, Reproductive Endocrinology & ART Centre; Acibadem Genetic Diagnosis and Cell Therapy Centre, Acibadem Genel Mudurluk; UK: UCL Centre for PGD, Department of Cytogenetics and Centre for Preimplantation Genetic Diagnosis; Centre for PGD, Assisted Conception Unit, Guy's Hospital; Institute of Ob/Gyn-RPMS, Hammer-smith Hospital; Ukraine: Clinic of Reproductive Medicine 'Nadiya'; USA: Jones Inst. for Reproductive Med; Genetics and IVF Institute; Reproductive Biology Associates Atlanta.

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