

# ESHRE PGD Consortium data collection VIII: cycles from January to December 2005 with pregnancy follow-up to October 2006

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The eighth report of the European Society of Human Reproduction and Embryology PGD Consortium is presented documenting cycles collected for the calendar year 2005 and follow-up of the pregnancies and babies born until October 2006 which resulted from these cycles. For the first time, the delivery rates for each indication are presented and also the pregnancy rates for each centre are reported anonymously. Since the first data collections, there has been a steady increase in the number of cycles, pregnancies and babies reported annually. For data collection VIII, 39 centres have participated, reporting on 3488 cycles to oocyte retrieval (OR), along with details of the follow-up on 845 pregnancies and 670 babies born. Five hundred and twenty OR were reported for chromosomal abnormalities, 108 OR for sexing for X-linked diseases, 500 OR for monogenic diseases, 2275 OR for preimplantation genetic screening and 85 OR for social sexing. Data VIII is compared with the cumulative data for data collections I–VII.

**Keywords:** 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. Seven 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, 2007; Harper *et al.*, 2006, 2008b). This report summarizes data VIII collected for the calendar year 2005 and the subsequent pregnancies. For the first time, data VIII includes the delivery rate for each indication and a graph of the pregnancy rates for each centre is also included (Fig. 1).

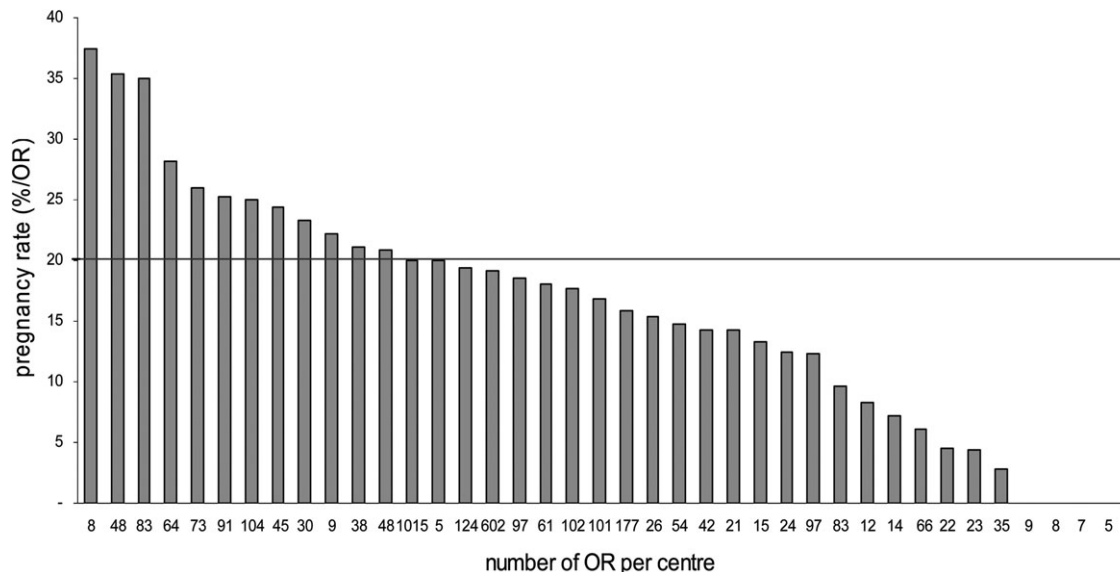
## Materials and Methods

Data were collected using a FileMaker Pro 5, 6 or 8 database and consisted of files for cycle, pregnancy and baby records. The first round of data analysis was a general evaluation to identify omissions and any ambivalent data. Corrections were requested from participating

centres. This was followed by a more in-depth correction and analysis by expert co-authors. Records with insufficient data, e.g. with no cycle or patient identification or no clear indication, from the wrong time period, or reported after the closure of the collection period, were excluded from the calculations. 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

Data from 39 centres were included in this report. The results are represented in tables according to an established lay-out. Accompanying text is deliberately concise and seven tables are only available in an electronic version: Supplementary Table IIc is listing the abnormal karyotypes carried by the patients undergoing PGD, Supplementary Table IIIc listing the X-linked diseases for which sexing was carried out, Supplementary Table IVc listing the monogenic diseases for which PGD was carried out, Supplementary Tables VIIa



**Figure 1:** Pregnancy rate for each centre (% per oocyte retrieval). The numbers on x-axis and the numbers of oocyte retrievals performed in each centre.

(data I–VII) and VIIIb (data VIII) listing the complications of pregnancy and Supplementary Tables XIIa (data I–VII) and XIIb (data VIII) with the congenital malformations and the neonatal complications. An overview of all cycles collected previously in data collections I–VII can be found in Table Ia, whereas an overview of the current data collection can be found in Table Ib.

For all indications for PGD/PGS, ICSI was the most often used method of fertilization, and cleavage stage aspiration was the most commonly used method of biopsy. Overall, zona pellucida drilling was more commonly performed using a laser. The mechanical method was used more often, most notably for social sexing, since the centre that reported the largest proportion of the cycles for social sexing often uses the mechanical method.

#### **PGD cycles for chromosomal abnormalities**

Tables IIa and IIb summarize the 2192 and 520 cycles to OR collected for data collection I–VII and VIII, respectively. As for previous years, data VIII showed that PGD for reciprocal translocations was performed more often than for Robertsonian translocations or other types of chromosome abnormalities. For data VIII, 7060 oocytes were collected, 71% (4251/6008) fertilized, 79% (3342/4251) embryos biopsied and 99% (3299/3342) embryos successfully biopsied. Of the embryos successfully biopsied, 95% (3130/3299) gave a diagnostic result, of which only 24% (761/3130) were transferable. From 520 OR procedures, only 63% (328/520) resulted in an embryo transfer procedure. This is in agreement with previous data showing that a high level of chromosomally abnormal embryos are found in these patients. A positive hCG was obtained in 121 cycles, with a positive heartbeat in 94 cycles [18% per OR (94/520) and 29% per embryo transfer (94/328)]. This gave an implantation rate of 23% (122/540). These pregnancy rates were slightly higher than in the previous data collections. Finally, the delivery rate was 16% per OR (81/520) and 25%

per embryo transfer (81/328). There were 12/93 spontaneous abortions (13% per clinical pregnancy) and 1/94 pregnancy was lost to follow-up.

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

Tables IIIa and IIIb summarize the 816 and 108 cycles to OR collected for data collection I–VII and VIII, respectively. This year, fluorescence *in situ* hybridization (FISH) was the only method used for sexing cycles. For data VIII, 1355 oocytes were collected, 71% (830/1164) fertilized, 80% (668/830) embryos biopsied and 99% (658/668) successfully biopsied. Of the embryos successfully biopsied, 96% (630/658) gave a diagnostic result, of which only 31% (205/658) were transferable (female). From 108 OR procedures, only 77% (83/108) resulted in an embryo transfer procedure. A positive hCG was obtained in 34 cycles, with a positive heartbeat in 24 cycles [22% per OR (24/108) and 29% per embryo transfer (24/83)]. This gave an implantation rate of 22% (29/130). These pregnancy rates were slightly higher than in the previous data collections. Finally, the delivery rate was 17% per OR (18/108) and 22% per embryo transfer (18/83). There were 5/23 spontaneous abortions (22% per clinical pregnancy), and 1/24 clinical pregnancy was lost to follow-up.

#### **PGD for monogenic diseases**

Tables IVa and IVb summarize the 2099 and 500 cycles to OR collected for data collection I–VII and VIII, respectively. The most common indications for PGD for autosomal recessive diseases were cystic fibrosis (CF) (54 cycles, plus one cycle for CF and PGS),  $\beta$ -thalassemia (46 cycles, plus one cycle for  $\beta$ -thalassemia with HLA typing), spinal muscular atrophy (SMA) (26 cycles, plus one cycle for SMA and PGS) and sickle cell anaemia (SC) (seven cycles, plus seven cycles for SC with HLA typing). There were 18 cycles for HLA typing only. The most common indications in the group of autosomal dominant diseases were myotonic dystrophy type I (76 cycles),

**Table Ia.** Overall cycle data collection I–VII.

Indication	PGD	PGS	PGD-SS	Total
Cycles to OR	5107 <sup>1</sup>	6878	412	12 397 <sup>1</sup>
Number infertile	1985	6330	42	8357
Female age (years)	33	36	37	35
Cancelled before IVF/ICSI	15	0	0	15
<i>ART method</i>				
IVF	566	785	123	1474
ICSI	4412	5937	273	10 622
IVF+ICSI	25	79	0	104
Frozen+ICSI+IVF+unknown	71 <sup>1</sup>	27	16	114 <sup>1</sup>
Unknown	20	50	0	70
Cancelled after IVF/ICSI	328	249	16	593
Cycles to PGS/PGD	4766	6629	396	11 791
FISH	2722	6629	214	9565
PCR	2044	0	182	2226
<i>Zona breaching</i>				
AT drilling	2560	2938	19	5517
laser drilling	1980	3141	114	5235
Mechanical	212	485	263	960
Unknown	14	65	0	79
<i>Biopsy method</i>				
PB biopsy	48 <sup>2</sup>	707 <sup>2</sup>	0	755 <sup>2</sup>
Cleavage aspiration	4481 <sup>2</sup>	5477 <sup>2</sup>	132	10 090 <sup>2</sup>
Cleavage extrusion	201	378	264	843
Cleavage flow displacement	2	16	0	18
Blastocyst	29	0	0	29
Unknown	16	52	0	68
<i>Embryology</i>				
COCs	70 160	83 256	5731	159 147
Inseminated	59 756	69 023	4670	133 449
Fertilized	42 713	48 849	3179	94 741
Biopsied	32 029	38 796	2545	73 370
Successfully biopsied	31 518	38 250	2427	72 195
Diagnosed	28 053	34 769	2257	65 079
Transferable	10 579	12 548	878	24 005
Transferred	7221	9378	633	17 232
Frozen	1366	1656	194	3216
<i>Clinical outcome</i>				
Cycles to ET	3719	4971	288	8978
hCG positive	1162	1612	118	2892
Positive heart beat	912	1217	89	2218
Clinical pregnancy rate (% per OR/% per ET)	18/25	18/24	22/31	18/25

ART, assisted reproduction technology; PGS, preimplantation genetic screening; ET, embryo transfer; FISH, fluorescence *in situ* hybridization; OR, oocyte retrieval; AT, acid tyrode's; COC, cumulus oocyte complexes. 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 polar body (PB) biopsy and cleavage stage biopsy.

Huntington disease (44 cycles, plus 12 cycles for Huntington exclusion testing), tuberous sclerosis (TSC) (14 cycles, plus one cycle for TSC and PGS) and Marfan syndrome (13 cycles). The most common indications where a specific diagnosis of X-linked diseases was carried out were for fragile X syndrome (FRAXA) (50 cycles, plus one cycle for FRAXA and PGS), Duchenne and Becker muscular dystrophy (7 cycles) and haemophilia A and B (11 cycles). PGD cycles for an additional 46 monogenic diseases were initiated in 110 cycles (included under 'other' in Table IVb), and they are listed in Supplementary Table IVc. Besides the 8 cycles for  $\beta$ -thalassaemia or SC with HLA typing and the 18 cycles for HLA typing only, HLA typing was carried out with PGD for Fanconi anaemia in 4 cycles.

For the first time, the monogenic data includes two cycles that were performed using FISH for a microdeletion. Previously, all diagnoses for monogenic disorders have used PCR.

For data VIII, 6716 oocytes were collected, 71% (3979/5588) fertilized, 72% (2871/3979) embryos biopsied and 98% (2808/2871) successfully biopsied. ICSI was used in 496 cycles and IVF in 4 cycles. IVF is not recommended when PCR is used because sperm embedded in the zona can enter the PCR tube and contaminate the blastomere (Thornhill *et al.*, 2005). In the majority of cycles, biopsy was carried out using cleavage stage aspiration but in 13/494 cycles (2.6%) trophectoderm biopsy in blastocysts was used and in 31/494 cycles (6.0%) polar body biopsy was used, five of which also had embryo biopsy. Of the embryos successfully biopsied, 88% (2481/2808) gave a diagnostic result, of which 49% (1224/2481) were transferable. From 500 OR procedures, 81% (405/500) resulted in an embryo transfer procedure. A positive hCG was obtained in 156 cycles, with a positive heart-beat in 109 cycles [22% per OR (109/500) and 27% per embryo transfer (109/405)]. This gave an implantation rate

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

Indication	PGD	PGS	PGD-SS	Total
Cycles to OR	1128	2275	85	3488
Number infertile	432	1839	4	2275
Female age (years)	34	38	37	37
Cancelled after OR but before IVF/ICSI	3	2	0	5
<i>ART method</i>				
IVF	126	135	15	276
ICSI	989	2072	69	3130
IVF+ICSI	1	65	0	66
Frozen+ICSI, IVF	9	1	1	11
Cancelled after IVF/ICSI	36	80	0	116
Cycles to PGS/PGD	1089	2193	85	3367
FISH	595	2193	85	2873
PCR	494	0	0	494
<i>Zona breaching</i>				
AT drilling	334	434	0	768
Laser drilling	657	1407	5	2069
Mechanical	98	352	80	530
<i>Biopsy method</i>				
PB biopsy	34	300	0	334
Cleavage aspiration	950	1791	5	2746
Cleavage extrusion	60	94	80	234
Cleavage flow displacement	14	6	0	20
Blastocyst	26	2	0	28
PB and cleavage	5	0	0	5
<i>Embryology</i>				
COCs	15 131	26 576	1071	42 778
Inseminated	12 760	21 478	946	35 184
Fertilized	9060	15 237	673	24 970
Biopsied	6881	12 463	469	19 813
Successfully biopsied	6765	12 372	463	19 600
Diagnosed	6241	11 820	390	18 451
Transferable	2190	4236	154	6580
Transferred	1385	2753	108	4246
Frozen	312	647	21	980
<i>Clinical outcome</i>				
Cycles to ET	816	1626	66	2508
hCG positive	311	553	23	887
Positive heart beat	227	418	18	663
Clinical pregnancy rate (% per OR/% per ET)	20/28	18/26	21/27	19/26
Number of fetal heartbeats	296	540	21	857
Implantation rate (fetal heartbeats/100 embryos transferred)	21	20	19	20
Deliveries	194	351	13	558
Delivery rate (% per OR/% per ET)	17/24	15/21	15/20	16/22
Miscarriages	26	37	5	68
Miscarriage rate (% per clinical pregn–pregn lost to FU)*	12	10	28	11
Clinical pregnancies lost to FU	7	30	0	37

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.

of 20% (145/715). These pregnancy rates were slightly higher than in the previous data collections. Finally, the delivery rate was 19% per OR (95/500) and 23% per embryo transfer (95/405). There were 9/104 spontaneous abortions (9% per clinical pregnancy), and 5/109 clinical pregnancies were lost to follow-up.

Overall, the number of PGD cycles performed for monogenic disorders between January and December 2005 represents a slight decrease compared with the previous year (data collection VII). One cycle each for CF, SMA, TSC and FRAXA was combined with PGS by the FISH analysis. However, the number of cycles involving HLA typing increased from 20 (data VII) to 30, including 18 cycles for HLA-compatibility typing alone and 12 cycles for HLA typing along with diagnosis for a monogenic disease.

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, there are no marked changes compared with previous data collections.

#### **Preimplantation genetic screening**

Tables Va and Vb summarize the 6878 and 2275 cycles to OR reported for data collection I–VII and VIII, respectively. For data VIII, 26 576 oocytes were collected, 71% (15 237/21 478) fertilized, 82% (12 463/15 237) embryos biopsied and 99% (12 372/12 463) successfully biopsied. Of the embryos successfully biopsied, 96% (11 820/12 372) gave a diagnostic result, of which only 36% (4236/11 820) were transferable. From 2275 OR procedures, only 71%

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

Indication	Robertsonian translocation, male carrier	Robertsonian translocations, female carrier	Reciprocal, male carrier	Reciprocal, female carrier	Sex chromosome aneuploidy	Other	Total
Cycles to OR	365	270	591	601	205	160	2192
Number infertile	316	139	366	301	188	84	1394
Female age (years)	34	33	33	33	32	33	33
Cancelled before IVF/ICSI	0	0	3	0	5	2	10
<i>ART method</i>							
IVF	16	38	66	150	19	38	327
ICSI	341	225	502	426	180	117	1791
IVF+ICSI	2	2	2	7	0	2	15
Frozen+ICSI+IVF+unknown	5	5	17	18	1	1	47
Unknown	1	0	1	0	0	0	2
Cancelled after IVF/ICSI	23	15	48	54	14	6	160
Cycles to PGD	342	255	540	547	186	152	2022
<i>Zona breaching</i>							
AT drilling	198	159	349	389	94	94	1283
Laser drilling	140	91	168	141	63	46	649
Mechanical	4	5	23	17	29	12	90
<i>Biopsy method</i>							
PB biopsy	1	5	0	5	0	0	11
Cleavage aspiration	332	236	509	511	183	142	1913
Cleavage extrusion	9	14	26	27	3	10	89
Cleavage flow displacement	0	0	1	1	0	0	2
Blastocyst	0	0	4	3	0	0	7
<i>Embryology</i>							
COCs	5394	3790	8593	8822	2603	2099	31 301
Inseminated	4534	3151	7290	7665	2137	1837	26 614
Fertilized	3118	2314	5196	5754	1527	1318	19 227
Biopsied	2136	1852	4062	4570	1052	1045	14 717
Successfully biopsied	2097	1828	4005	4510	1038	1026	14 504
Diagnosed	1855	1663	3688	4183	934	943	13 266
Transferable	720	494	758	839	447	302	3560
Transferred	488	381	634	703	304	223	2733
Frozen	81	35	28	39	36	20	239
<i>Clinical outcome</i>							
Cycles to ET	264	203	349	376	150	118	1460
hCG positive	88	67	97	101	42	28	423
Positive heart beat	76	52	73	77	29	25	332
Clinical pregnancy rate (% per OR/% per ET)	21/29	19/26	12/21	13/20	14/19	16/21	15/23

(1626/2275) resulted in an embryo transfer procedure. A positive hCG was obtained in 553 cycles, with a positive heartbeat in 418 cycles [18% per OR (418/2275) and 26% per embryo transfer (418/1626)]. This gave an implantation rate of 20% (540/2753). These pregnancy rates were similar to the previous data collections. Finally, the delivery rate was 15% per OR (351/2275) and 22% per embryo transfer (351/1626). There were 37/523 spontaneous abortions (7% per clinical pregnancy) and 30/553 clinical pregnancies lost to follow-up.

The main indications were advanced maternal age (AMA) (688 OR) and repeated implantation failure (RIF) (596 OR). There were still a large number of cycles reported where no indication was given (45 OR). All indications involving AMA showed pregnancy rates per OR below 13%. Patients with two indications involving AMA [AMA plus spontaneous abortion, AMA plus RIF and AMA plus severe male factor (SMF)] all did poorly with a pregnancy rate per OR of <11%. SMF showed a relatively high pregnancy rate [26% per OR (65/252)] as did patients with previous abnormal pregnancies [29% per OR (7/24)]. Patients with no indication had a pregnancy rate of 24% per OR (11/45).

From 2275 cycles, 142 involved the biopsy of only one embryo and 233 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.

The column ‘others’ contains various indications such as oocyte donation, mosaic embryos, abnormal FISH on sperm and single embryo transfer, as well as cycles with multiple indications.

The Consortium has set up a PGS Working Group (see Discussion), and ESHRE has a PGS Task Force to set up a multicentre randomized controlled study for PGS. There are ongoing discussions about the efficacy of PGS, and the PGD Consortium has recently published a comment (Harper *et al.*, 2008a).

#### *PGD cycles for social sexing*

Tables VIa and VIb summarize the 412 and 85 cycles to OR collected for data collection I–VII and VIII, respectively. For data VIII, 1071 oocytes were collected, 71% (673/946) fertilized, 70% (469/673) embryos biopsied, and 99% (463/469) successfully biopsied. Of the embryos successfully biopsied, 84% (390/463) gave a diagnostic result, of which only 39% (154/390) were transferable (of the desired sex). From 85 OR procedures, only 78% (66/85) resulted in an embryo transfer procedure. A positive hCG was obtained in 23 cycles, with a

**Table IIIb.** PGD for chromosomal abnormalities, data collection VIII.

Indication	Robertsonian translocation, male carrier	Robertsonian translocations, female carrier <sup>1</sup>	Reciprocal, male carrier <sup>2</sup>	Reciprocal, female carrier <sup>1</sup>	Sex chromosome aneuploidy <sup>3</sup>	Other	Total
Cycles to OR	85	45	146	167	34	43	520
Number infertile	71	16	79	69	26	29	290
Female age (years)	32	34	33	34	35	35	33
Cancelled after OR before IVF/ICSI	0	0	0	0	2	0	2
<i>ART method</i>							
IVF	1	12	26	47	3	7	96
ICSI	83	32	115	118	28	36	412
IVF+ICSI	0	0	0	0	1	0	1
ICSI+Frozen	1	1	5	2	0	0	9
Cancelled after IVF/ICSI	5	0	8	9	1	3	26
Cycles to PGD	80	45	138	158	31	40	492
<i>Zona breaching</i>							
AT drilling	20	22	54	66	8	10	180
Laser drilling	52	23	78	77	22	19	271
Mechanical	8	0	6	15	1	11	41
<i>Biopsy method</i>							
PB	0	1	0	6	1	0	8
Cleavage aspiration	69	42	125	130	27	37	430
Cleavage extrusion	9	2	7	12	0	3	33
Cleavage flow	2	0	1	3	3	0	9
Blastocyst	0	0	5	7	0	0	12
<i>Embryology</i>							
COCs	1195	576	2080	2167	423	619	7060
Inseminated	952	511	1779	1902	330	534	6008
Fertilized	621	373	1228	1385	241	403	4251
Biopsied	481	274	959	1146	169	313	3342
Successfully biopsied	476	273	942	1127	169	312	3299
Diagnosed	433	266	893	1079	163	296	3130
Transferable	168	75	159	218	54	87	761
Transferred	104	56	128	156	40	56	540
Frozen	27	11	6	21	10	11	86
<i>Clinical outcome</i>							
Cycles to ET	67	31	81	94	23	32	328
hCG positive	21	15	28	35	11	11	121
Positive heart beat	19	14	21	25	7	8	94
Clinical pregnancy rate (% per OR/ET)	22/28	31/45	14/26	15/27	21/301	19/25	18/29
Number of fetal hearts	26	19	23	37	8	9	122
Implantation rate (fetal hearts/100 embryos transferred)	25	34	18	24	20	16	23
Deliveries	16	12	19	20	7	7	81
Delivery rate (% per OR/% per ET)	19/24	27/39	13/23	12/21	21/30	16/22	16/25
Miscarriages	2	2	2	5	0	1	12
Miscarriage rate (% per clinical pregn–pregn lost to FU)	11	14	10	20	0	13	13
Clinical pregnancies lost to FU	1	0	0	0	0	0	1

<sup>1</sup>One cycle included PGS.<sup>2</sup>One cycle included social sexing (SS).<sup>3</sup>Four cycles included PGS.

positive heartbeat in 18 cycles [21% per OR (18/85) and 27% per embryo transfer (18/66)]. This gave an implantation rate of 19% (21/108). These pregnancy rates were similar to the previous data collections. Finally, the delivery rate was 15% per OR (13/85) and 20% per embryo transfer (13/66). There were 5/18 spontaneous abortions (28% per clinical pregnancy) and no clinical pregnancies lost to follow-up.

Almost two-thirds of the cycles were for couples who requested a male embryo (55 cycles) rather than a female embryo (30 cycles) which is similar to the last data collection (Harper *et al.*, 2008a,b). There are more males requested than females as a large number of cases are done in the USA where MicroSort<sup>®</sup> sperm separation is used and is more efficient at selecting X-bearing sperm.

### **Pregnancies and babies**

Supplementary Tables VIII and XII and Tables VIIa, VIIb, IX–XIb summarize the pregnancy and baby data. Data VIII was comparable to previous data collections. Data VIII included 845 pregnancies which resulted in 837 fetal sacs (Table VIIIb). There were 550 deliveries of 696 babies. Of the 663 cycles ending in a pregnancy with a positive heartbeat, follow-up data on 650 pregnancies were reported. Of the 550 pregnancies reported to have ended with a delivery (total number of babies: 696), neonatal data on 670 babies born from 529 deliveries were submitted. Five hundred and twenty-five of the 529 reported deliveries, ended in the birth of at least one live born baby (Tables IXb and XIb). The delivery rates per indication are reported in Tables IIb, IIIb, IVb, Vb and VIb. Almost half of

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

	FISH	PCR	Total
Cycles to OR	750	66	816
Number infertile	132	0	132
Female age (years)	33	31	33
Cancelled before IVF/ICSI	1	0	1
<i>ART method</i>			
IVF	195	10	205
ICSI	546	56	602
IVF+ICSI	7	0	7
Frozen+ICSI	1	0	1
Cancelled after IVF/ICSI	49 <sup>1</sup>	1 <sup>2</sup>	50 <sup>1,2</sup>
Cycles to PGD	700	65	765
<i>Zona breaching</i>			
AT drilling	402	52	454
Laser drilling	264	3	267
Mechanical	34	10	44
<i>Biopsy method</i>			
Cleavage aspiration	673	60	733
Cleavage extrusion	26	5	31
Blastocyst	1	0	1
<i>Embryology</i>			
COCs	9945	912	10 857
Inseminated	8794	701	9495
Fertilized	6167	556	6723
Biopsied	4655	458	5113
Successfully biopsied	4536	422	4958
Diagnosed	4143	329	4472
Transferable	1438	178	1616
Transferred	1025	139	1164
Frozen	257 <sup>3</sup>	58 <sup>4</sup>	315 <sup>3,4</sup>
<i>Clinical outcome</i>			
Cycles to ET	558	55	613
hCG positive	176	24	200
Positive heartbeat	140	17	157
Clinical pregnancy rate (%per OR/% per ET)	19/25 <sup>5</sup>	26/31 <sup>5</sup>	19/26 <sup>5</sup>

<sup>1</sup>27 embryos from two cycles frozen before biopsy due 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 due to lack of information regarding the number of fetal heartbeats in pregnancies resulting from the transfer of those embryos.

the deliveries were by Caesarean section (263/550) (Table IXb). In 63 cases, the method of delivery was not known.

Confirmation of the diagnosis was performed prenatally (374/837) and/or post-natally (337/837) (Table Xb). Supplementary Table XIIb 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 (175/650, 27%). This means 41% (286/696) of the babies born are part of a multiplet at birth.

### Misdiagnoses

Tables XIIIa and XIIIb summarize the misdiagnoses reported for data collected I–VII and VIII, respectively. For data VIII, three misdiagnoses have been reported, two after PCR and

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

	FISH	Total
Cycles to OR	108	108 <sup>1</sup>
Number infertile	36	36
Female age (years)	34	34
Cycles cancelled before ART	1	1
<i>ART method</i>		
IVF	26	26
ICSI	81	81
IVF+ICSI	0	0
Cancelled after IVF/ICSI	4	4
Cycles to PGD	103	103
<i>Zona breaching</i>		
AT drilling	41	41
Laser drilling	55	55
Mechanical	7	7
<i>Biopsy method</i>		
Cleavage aspiration	89	89
Cleavage extrusion	8	8
Flow Displacement	5	5
Blastocyst	1	1
<i>Embryology</i>		
COCs	1355	1355
Inseminated	1164	1164
Fertilized	830	830
Biopsied	668	668
Successfully biopsied	658	658
Diagnosed	630	630
Transferable	205	205
Transferred	130	130
Frozen	29	29
<i>Clinical outcome</i>		
Cycles to ET	83	83
hCG positive	34	34
Positive heart beat	24	24
Clinical pregnancy rate (%per OR/% per ET)	22/29	22/29
Number fetal hearts	29	29
Implantation rate (fetal heart beats/100 embryos transferred)	22	22
Deliveries	18	18
Delivery rate (%per OR/% per ET)	17/ 22	17/22
Miscarriages	5	5
Miscarriage rate (% per clinical pregn–pregn lost to FU)	22	22
Clinical pregnancies lost to FU	1	1

<sup>1</sup>In six cycles also PGS was performed.

one after FISH. The Consortium is preparing a paper on misdiagnosis (see Discussion).

### Success of individual centres

Figure 1 shows the pregnancy rate for each centre for data VIII. The pregnancy rate ranges from 0% to 37% with the average being 19%. The number of cycles each centre performs ranged from 3 to 1015. Although it could be expected that centres carrying out lower numbers of cycles may have lower rates owing to less experience, the findings indicate that some of the most active centres fall below the average (19%) pregnancy rate and even have pregnancy rates lower than that in some of the centres performing few cycles.

### Discussion

This eighth 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. For the first time,

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

Indication	CF <sup>1</sup>	β-Thal and β-Thal+HLA	SMA and SMA+Retinitis Pigmentosa <sup>2</sup>	SC and SC+β-Thal and SC+HLA	DM1	HD and HD exclus.	DMD and BMD <sup>2</sup>	FRAXA <sup>4</sup>	Haem	Other	Total
Cycles to OR	403	225	151	54	317	270	79	108	38	454	2099
Number infertile	136	108	16	11	38	48	10	20	8	64	459
Female age (years)	33	34	34	35	33	32	32	34	31	33	33
Cancelled before IVF/ICSI	0	0	0	0	3	0	0	0	0	1	4
<i>Art method</i>											
IVF	16	0	2	0	1	0	3	2	6	4	34
ICSI	379	224	143	54	307	266	72	104	30	440	2019
IVF+ICSI	0	0	0	0	1	0	1	0	1	0	3
Frozen+IVF+ICSI	3	1	6	0	2	1	3	0	1	6 <sup>5</sup>	23 <sup>5</sup>
Unknown	5	0	0	0	3	3	0	2	0	5	18
Cancelled after IVF/ICSI	18	16	8	2	23	9	5	7	1	29	118
Cycles to PGD	385	209	143	52	291	261	74	101	37	426 <sup>5</sup>	1979 <sup>5</sup>
<i>Zona breaching</i>											
AT drilling	199	137	58	23	105	86	30	25	22	138	823
Laser drilling	167	72	70	26	180	157	44	72	13	263	1064
Mechanical	15	0	15	3	4	15	0	2	2	22	78
Unknown	4	0	0	0	2	3	0	2	0	3	14
<i>Biopsy method</i>											
PB biopsy	6 <sup>3</sup>	0	0	2	4 <sup>3</sup>	5	0	2 <sup>3</sup>	2 <sup>3</sup>	16 <sup>3</sup>	37 <sup>3</sup>
Cleavage aspiration	355 <sup>3</sup>	200	121	47	283 <sup>3</sup>	233	72	94 <sup>3</sup>	35 <sup>3</sup>	398 <sup>3</sup>	1835 <sup>3</sup>
Cleavage extrusion	23	5	22	3	3	19	0	0	1	5	81
Blastocyst	0	4	0	0	0	1	2	4	0	10	21
Unknown	6	0	0	0	2	3	0	2	0	3	16
<i>Embryology</i>											
COCs	5211	3332	2020	738	3935	3827	1098	1149	504	6188	28 002
Inseminated	4542	2798	1591	603	3395	3219	910	975	443	5171	23 647
Fertilized	3181	1926	1104	426	2440	2215	673	692	307	3799	16 763
Biopsied	2448	1373	863	304	1613	1588	529	465	213	2803	12 199
Successfully biopsied	2428	1347	860	302	1600	1564	511	463	212	2769	12 056
Diagnosed	2093	1133	734	251	1362	1335	462	403	166	2376	10 315
Transferable	1267	598	466	149	594	591	314	171	93	1160	5403
Transferred	687	440	285	98	413	358	159	104	69	711	3324
Frozen	251	70	31	38	50	86	70	21	10	185	812
<i>Clinical outcome</i>											
Cycles to ET	333	187	131	45	231	208	61	65	32	353	1646
hCG positive	110	79	38	12	66	61	23	21	11	118	539
Positive heart beat	87	59	31	9	53	46	20	17	9	92	423
Clinical pregnancy rate	22/26	26/32	21/24	17/20	17/23	17/22	25/33	16/26	24/28	20/26	20/26
% per OR/% per ET											

CF, cystic fibrosis (various mutations); β-thal, β-thalassaemia; SMA, spinal muscular atrophy; SC, sickle-cell anaemia; DM1, myotonic dystrophy type 1; HD, Huntington's Disease; HDexcl, Huntington's disease by exclusion; FRAXA, fragile-X syndrome; DMD, Duchenne muscular dystrophy (specific); BMD, becker muscular dystrophy; Haem, haemophilia.

<sup>1</sup>Two cycles for two indications: CF and FRAXA; CF and social sexing.

<sup>2</sup>Includes each time 1 cycle for specific disease and PGS.

<sup>3</sup>Eleven cycles had both PB biopsy and cleavage stage biopsy.

<sup>4</sup>Includes 3 cycles for FRAXA testing and PGS.

<sup>5</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.

we are able to report the delivery rate for every indication and show the pregnancy rate for each centre. It should be emphasized that the follow-up of pregnancies, resulting from PGD cycle, and preferably also babies born, is, as part of good practice, essential to complete the evaluation of the overall procedure and is strongly recommended for all centres involved in PGD.

The number of centres participating in the data collection of 2005 was slightly lower compared with 2004 (39 versus 45). There are now two levels of membership of the 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 lab who is a member of the consortium or full members who cannot submit data). As always the centres who submit data have access to the raw data whereas the associate centres

will be allowed to participate in the annual consortium meetings and they are sent the quarterly Consortium newsletter.

The work of the four consortium working groups is ongoing. The PGS working group (along with some other contributors) wrote a comment on PGS (Harper *et al.*, 2008a) and is preparing a detailed regression analysis of the 9153 cycles of PGS. This working group forms part of the ESHRE PGS Task Force. The database working group is developing an XML database which will replace the FP database and will be more user friendly as well as less time consuming for analysis. The accreditation working group is preparing a paper on a beginners guide to accrediting a PGD lab and a workshop. The misdiagnosis working group is preparing a detailed analysis of causes of misdiagnosis in PGD/PGS and has launched a study of confirmation of diagnosis in untransferred embryos.

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

Indication	Autosomal recessive				Autosomal dominant				Specific sex-linked			Others	Total
	CF (+PGS for sexing diabetes insipidus) <sup>1</sup>	β-thal and/ or sickle (+HLA)	SMA (+ PGS) <sup>1</sup>	HLA Compatibility	HD (HDexcl)	DM1	Tuberous Sclerosis (+PGS) <sup>1</sup>	MS	DMD (BMD)	Haem A (Haem B)	FRAX A (+PGS) <sup>1</sup>		
Cycles to OR	54 (1)	53(8)	26 (1)	18	44 (12)	76	14 (1)	13	5 (2)	9 (2)	50 (1)	110	500
Number infertile	26 (0)	16 (0)	1 (0)	0	4 (0)	15	0	0	1 (0)	1 (0)	26 (1)	15	106
Female age	35	34	33	35	31	32	32	29	37	33	33	33	33
<i>ART method</i>													
IVF	0	0	0	0	0	0	0	0	0	0	2 (0)	2	4
ICSI	54 (1)	53 (8)	26 (1)	18	44 (12)	76	14 (1)	13	5 (2)	9 (2)	48 (1)	108	496
ICSI+Frozen	0	0	0	0	0	0	0	0	0	0	0	0	0
Cancelled after IVF/ICSI	0	0	0	1	1 (0)	2	0	0	0	1 (0)	0	1	6
Cycles to PGD	54 (1)	53 (8)	26 (1)	17	43 (12)	74	14 (1)	13	5 (2)	8 (2)	50 (1)	109	494
PCR	54 (1)	53 (8)	26 (1)	17	43 (12)	74	14 (1)	13	5 (2)	8 (2)	50 (1)	107	492
FISH <sup>2</sup>	0	0	0	0	0	0	0	0	0	0	0	2	2
<i>Zona breaching</i>													
AT Drilling	14	8 (0)	10 (0)	1	12 (1)	21	0	0	2 (0)	0	11 (0)	33	113
Laser Drilling	32 (1)	43 (8)	14 (1)	16	30 (11)	47	13 (1)	13	2 (2)	8 (2)	29 (1)	57	331
Mechanical	8	2 (0)	2 (0)	0	1 (0)	6	1 (0)	0	1 (0)	0	10	19	50
<i>Biopsy method</i>													
PB biopsy	5	0	2 (0)	0	0	4	0	0	1 (0)	0	6 (0)	8	26
Cleavage Aspiration	47 (1)	38 (8)	22 (1)	16	42(12)	66	14 (1)	13	4 (2)	8 (2)	41 (1)	92	431
Cleavage Extrusion	1	2 (0)	2 (0)	1	1 (0)	4	0	0	0	0	2 (0)	6	19
Blastocyst	0	13 (0)	0	0	0	0	0	0	0	0	0	0	13
PB+embryo	1	0	0	0	0	0	0	0	0	0	1 (0)	3	5
<i>Embryology</i>													
COCs	742 (17)	735 (97)	409 (5)	229	621 (155)	862	207 (15)	163	36 (14)	97 (26)	528 (7)	1751	6716
Inseminated	627 (15)	634 (76)	324 (5)	208	512 (124)	736	155 (13)	128	28 (10)	88 (21)	426 (7)	1451	5588
Fertilized	413 (8)	508 (51)	225 (4)	144	369 (91)	549	94 (5)	103	16 (8)	71 (14)	296 (2)	1008	3979
Biopsied	287 (8)	388 (26)	150 (4)	97	272 (64)	408	59 (5)	80	17 (6)	51 (14)	198 (2)	735	2871
Successfully biopsied	279 (8)	372 (26)	147 (4)	97	272 (64)	404	59 (5)	80	15 (6)	51 (14)	189 (2)	714	2808
Diagnosed	257 (7)	304 (24)	133 (4)	94	249 (58)	349	49 (5)	78	13 (6)	48 (14)	153 (2)	634	2481
Transferable	154 (2)	171 (4)	81 (2)	20	117 (26)	155	19 (2)	37	9 (3)	31 (7)	76 (0)	308	1224
Transferred	89 (1)	113 (3)	45 (2)	16	65 (11)	100	11 (2)	15	8 (3)	14 (4)	52 (0)	161	715

Continued

**Table IVb.** *Continued*

Indication	Autosomal recessive				Autosomal dominant				Specific sex-linked			Others	Total
	CF (+PGS for sexing diabetes insipidus) <sup>1</sup>	β-thal and/or sickle (+HLA)	SMA (+ PGS) <sup>1</sup>	HLA Compatibility	HD (HDexcl)	DM1	Tuberous Sclerosis (+PGS) <sup>1</sup>	MS	DMD (BMD)	Haem A (Haem B)	FRAX A (+PGS) <sup>1</sup>		
Frozen	28 (0)	10 (3)	17 (0)	2	18 (7)	16	0	8	0	4 (0)	3 (0)	81	197
<i>Clinical outcome</i>													
Cycles to ET	47 (1)	48 (2)	24 (1)	11	35 (9)	63	7 (1)	11	4 (2)	8 (2)	35 (0)	94	405
hCG Positive	17 (0)	25 (1)	11 (1)	5	18(0)	15	3 (1)	4	0 (1)	3 (0)	9 (0)	42	156
Positive heartbeat	15 (0)	18 (0)	9 (1)	1	12 (0)	10	1 (1)	3	0 (1)	1 (0)	6 (0)	30	109
Clinical pregnancy rate (%per OR/% per ET)	28/32 (0/0)	34/38 (0/0)	35/38 (100/100)	6/9	27/34 (0/0)	13/16	7/14 (100/100)	23/27	0/0 (50/50)	11/13 (0/0)	12/17 (0)	27/32	22/27
Number fetal heartbeats	19 (0)	25 (0)	13 (1)	1	16 (0)	11	2 (1)	4	0 (1)	1 (0)	7 (0)	43	145
Implantation rate (fetal hearts/100 embryos transferred)	21 (0)	22 (0)	29 (50.0)	6	25 (0)	11	18 (50)	27	0 (33)	7 (0)	13 (0)	27	20
Deliveries	13 (0)	12 (0)	9 (1)	1	12 (0)	10	1 (1)	3	0 (1)	1 (0)	5 (0)	25	95
Delivery rate (% per OR/% per ET)	24/28 (0/0)	23/25 (0/0)	35/37 (100/100)	5/9	27/34 (0/0)	13/16	7/14 (100/100)	23/27	0 (50/50)	11/12 (0/0)	10/14 (0)	23/27	19/23
Miscarriages	1	3	0	0	0	0	0	0	0	0	0	5	9
Miscarriage rate (% per clinical pregn–pregn lost to FU)	7	20	0	0	0	0	0	0	0	0	0	17	9
Clinical pregnancies lost to FU	1	3	0	0	0	0	0	0	0	0	1	0	5

MS, Marfan's syndrome. Numbers between brackets are not included in the numbers before the parentheses.

<sup>1</sup>Includes each time 1 cycle for the specific disease and PGS.

<sup>2</sup>Two cycles were performed using FISH for a microdeletion.

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

Indication	AMA	AMA+miscarriage <sup>1</sup>	AMA+RIF <sup>1</sup>	Recurrent miscarriage	Recurrent IVF failure	Severe male factor <sup>2</sup>	No indication	Other	Total
Cycles to OR	2059	190	514	990	2036	547	183	359	6878
Number infertile	1848	166	469	863	2012	503	177	292	6330
Female age (years)	40.5	41	40.5	36	35	33.5	33.5	35	36.5
<i>ART method</i>									
IVF	265	28	44	106	190	2	78	72	785
ICSI	1763	156	459	858	1799	534	99	269	5937
IVF+ICSI	20	4	5	22	14	6	5	3	79
Frozen+ICSI	5	2	1	3	9	5	1	1	27
Unknown	6	0	5	1	24	0	0	14	50 <sup>4</sup>
Cancelled after IVF/ICSI	89	15	3	19	84	21	8	10	249
Cycles to PGS	1970	175	511	971	1952	526	175	349	6629
<i>Zona breaching</i>									
AT drilling	869	75	208	561	791	181	53	200	2938
Laser drilling	1001	79	216	385	917	324	101	118	3141
Mechanical	87	21	87	24	207	21	21	17	485
Unknown	13	0	0	1	37	0	0	14	65 <sup>4</sup>
<i>Biopsy method</i>									
PB biopsy	161 <sup>3</sup>	51	227	28	213	0	19	8	707 <sup>3</sup>
Cleavage aspiration	1621 <sup>3</sup>	116	282	890	1598	482	154	334	5477 <sup>3</sup>
Cleavage extrusion	169	8	2	51	97	43	2	6	378
Cleavage flow displacement	7	0	0	1	6	1	0	1	16
Unknown	13	0	0	1	38	0	0	0	52 <sup>4</sup>
<i>Embryology</i>									
COCs	20 910	1728	4877	13 378	27 540	7858	2187	4778	83 256
Inseminated	17 669	1411	3788	11 062	22 856	6347	1898	3992	69 023
Fertilized	12 425	963	2619	7974	16 357	4287	1357	2867	48 849
Biopsied	9988	932	2839	6045	12 520	3183	1072	2217	38 796
Successfully biopsied	9862	929	2802	5937	12 343	3161	1034	2182	38 250
Diagnosed	8812	887	2666	5274 <sup>5</sup>	11 504 <sup>5</sup>	2856	860 <sup>5</sup>	1910 <sup>5</sup>	34 769 <sup>5</sup>
Transferable	2453	260	882	1972 <sup>5</sup>	4380 <sup>5</sup>	1261	506 <sup>5</sup>	834 <sup>5</sup>	12 548 <sup>5</sup>
Transferred	2342	194	652	1450 <sup>5</sup>	2964 <sup>5</sup>	894	273 <sup>5</sup>	609 <sup>5</sup>	9378 <sup>5</sup>
Frozen	278	30	86	274	609	148	72	159	1656
<i>Clinical outcome</i>									
Cycles to ET	1296	118	391	754	1543	452	148	269	4971
hCG positive	375	25	79	288	481	202	54	108	1612
Positive heart beat	281	17	59	226	357	160	45	76	1221
Clinical pregnancy rate (% per OR/% per ET)	14/22	9/14	11/15	23/30	18/23	29/35	25/30	21/28	18/25

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

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

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

<sup>3</sup>One cycle had cleavage stage biopsy and PB biopsy.

<sup>4</sup>Several cycles had incomplete results.

<sup>5</sup>Several cycles from one centre had no information on the number of embryos diagnosed, number embryos diagnosed as transferable, but patients did have embryos transferred. In these cases, undiagnosed or abnormal embryos were transferred; other, includes data with two indications.

Finally, other activities of the Consortium include: (i) the paediatric follow-up of PGD babies, which has been launched and for which the first results are being analysed; (ii) the creation of external quality assurance schemes which are being developed for single-cell PCR and FISH and (iii) the updating of the PGD guidelines (Thornhill *et al.*, 2005).

From the first eight data collections, the consortium now has detailed data on 15 885 cycles and 2658 babies born after PGD/PGS. Data IX (cycles performed in 2006) has been collected and is currently being analysed by the steering committee. It is hoped that in the report of data IX we will be able to report an overview on what percentage of the centres performing PGD conform to the ESHRE PGD guidelines.

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

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

Indication	AMA	AMA+miscarriage	AMA+RIF	Recurrent miscarriage	RIF	SMF	Prev abn preg	AMA+SMF	No indication	Other	Total
Cycles to OR	688	77	181	298	596	252	24	15	45	99	2275
Number infertile	517	45	170	149	576	232	5	13	41	91	1839
Female age (years)	41	41	41	36	35	38	36	39	34	35	38
Cycles cancelled before ART	0	0	0	0	1	0	0	0	0	1	2
<i>ART method</i>											
IVF	39	12	9	39	33	0	1	0	2	0	135
ICSI	625	62	170	252	555	242	23	12	34	97	2072
IVF+ICSI	24	3	2	6	7	10	0	3	9	1	65
IVF+frozen embryos	0	0	0	0	0	0	0	0	0	0	0
ICSI+frozen embryos	0	0	0	1	0	0	0	0	0	0	1
Cancelled post OR	36	6	4	10	16	3	2	0	0	3	80
Cycles to PGD	652	71	177	288	579	249	22	15	45	95	2193
<i>Zona breaching</i>											
AT drilling	129	14	22	58	86	87	2	13	16	7	434
Laser drilling	490	38	56	203	384	117	20	0	20	79	1407
Mechanical	33	19	99	27	109	45	0	2	9	9	352
<i>Biopsy method</i>											
PB biopsy	58	15	112	11	95	0	0	0	9	0	300
Cleavage aspiration	578	49	46	263	457	245	20	13	36	84	1791
Cleavage extrusion	16	7	19	11	26	4	0	2	0	9	94
Cleavage flow displ.	0	0	0	2	1	0	1	0	0	2	6
Blastocyst	0	0	0	1	0	0	1	0	0	0	2
<i>Embryology</i>											
COCs	6872	766	1612	3524	7582	3763	310	221	549	1377	26 576
Inseminated	5704	601	1112	2826	6149	3049	258	180	431	1168	21 478
Fertilized	3926	404	783	2116	4435	2136	186	106	283	862	15 237
Biopsied	3008	354	1035	1624	3669	1667	143	89	258	616	12 463
Successfully biopsied	2985	354	1023	1616	3636	1655	143	89	257	614	12 372
Diagnosed	2869	333	983	1552	3442	1596	141	82	236	586	11 820
Transferable	817	106	383	557	1250	630	55	37	112	289	4236
Transferred	606	75	227	387	816	401	34	27	59	121	2753
Frozen	68	11	47	93	185	83	11	5	24	120	647
<i>Clinical outcome</i>											
Cycles to ET	390	49	132	232	470	206	19	13	32	83	1626
hCG positive	121	12	26	82	166	80	9	1	14	42	553
Positive heart beat	86	5	20	65	127	65	7	1	11	31	418
Clinical pregnancy rate (% per OR/% per ET)	13/22	6/10	11/15	22/28	21/27	26/32	29/37	7/8	24/34	31/37	18/26
Number of fetal hearts	100	6	22	83	170	92	9	1	14	43	540
Implantation rate (fetal hearts/100 embryos transferred)	17	8	10	21	21	23	26	4	24	36	20
Deliveries	74	4	11	56	109	57	7	0	9	24	351
Delivery rate (% per OR/% per ET)	11/19	5/8	6/8	19/24	18/23	23/28	29/37		20/28	24/29	15/21
Miscarriages	11	0	2	5	10	6	0	1	1	1	37
Miscarriage rate (% per clinical pregn–pregn lost to FU)	13	0	15	8	8	10	0	100	10	4	10
Clinical pregnancies lost to FU	1	1	7	4	8	2	0	0	1	6	30

'Others' contains cycles with multiple indications.

subfertility studies; ISRAEL: The Danek Gertner Institute of Human Genetic, Sheba Medical Centre; Zohar PGD Lab, Medical Genetics Unit, Shaare Zedek Medical Centre; ITALY: SISMER; KOREA: Kwadong University College of Medicine, Cheil General Hospital, Department of Obstetrics and Gynaecology, Division of Reproductive Endocrinology and Infertility; POLAND: INVICTA Fertility and Reproductive Center; PORTUGAL: Faculty of Medicine of Porto-Hospital S. Joao, Department of Medical Genetics; SPAIN: Instituto Dexeus; Instituto Valenciano de Infertilidad; Institut Marquès, Servei de Diagnòstic Genètic Preimplantacional; Instituto de Reproduccion CEFER; Sistemas Genomicos SL Valencia; Centro de Medicina Embrionaria; SWEDEN: Department of Clinical Genetics, Karolinska Hospital; Sahlgrenska University Hospital, Department of Obstetrics and Gynaecology; TAIWAN:

Lin-Kou Medical Centre, Chang Gung Memorial Hospital and Medical Collega, Department of Obstetrics and Gynaecology; THE NETHERLANDS: PGD Working Group Maastricht, The Centre for Reproductive Medicine; UK: UCL Centre for PGD, Department of Cytogenetics and Centre for Preimplantation Genetic Diagnosis; Thomas Guy House, Guy's Hospital, Assisted Conception Unit; USA: Jones Institute for Reproductive Medicine; Genetics and IVF Institute.

### Supplementary data

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

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

Method for sexing	FISH	PCR	Unknown	Total
Cycles to OR	218	189	5 <sup>1</sup>	412 <sup>1</sup>
Number infertile	25	16	1	42
Female age (years)	36	37	35	37
<i>ART method</i>				
IVF	110	10	3	123
ICSI	103	168	2	273
Frozen	3	2	0	5
Frozen+IVF+ICSI+unknown	2	9	0	11
Unknown	0	0	0	0
Cancelled after IVF/ICSI	4	7	5	16
Cycles to PGD	214	182	0	396
<i>Zona breaching</i>				
AT drilling	9	10	0	19
Laser drilling	113	1	0	114
Mechanical	92	171	0	263
<i>Biopsy method</i>				
Cleavage aspiration	121	11	0	132
Cleavage extrusion	93	171	0	264
<i>Embryology</i>				
COCs	2830	2878	23	5731
Inseminated	2463	2188	19	4670
Fertilized	1716	1452	11	3179
Biopsied	1402	1143	0	2545
Successfully biopsied	1311	1116	0	2427
Diagnosed	1208	1049	0	2257
Transferable	405	473	0	878
Transferred	272	361	0	633
Frozen <sup>2</sup>	108	86	0 <sup>3</sup>	194
<i>Clinical outcome</i>				
Cycles to ET	150	138	0	288
hCG positive	60	58	0	118
Positive heart beat	50	39	0	89
Clinical pregnancy rate (% per OR/% per ET)	23/33	21/28	–	22/31

<sup>1</sup>One natural cycle included.<sup>2</sup>11 cycles with embryos frozen without biopsy or failed diagnosis included.<sup>3</sup>Three embryos frozen without biopsy were not included.**Table VIb.** PGD for social sexing, data collection VIII.

	FISH (SS only)	FISH (SS+AS)	Total
Cycles to OR	38	47	85
Number infertile	0	4	4
Female age	34	38	37
<i>ART method</i>			
IVF	7	8	15
ICSI	31	38	69
ICSI+Frozen embryos	0	1	1
Cancelled after IVF/ICSI	0	0	0
Cycles to PGD	38	47	85
<i>Zona breaching</i>			
Laser drilling	5	0	5
Mechanical	33	47	80
<i>Biopsy method</i>			
Cleavage aspiration	5	0	5
Cleavage extrusion	33	47	80
<i>Embryology</i>			
COCs	462	609	1071
Inseminated	413	533	946
Fertilized	309	364	673
Biopsied	225	244	469
Successfully biopsied	219	244	463
Diagnosed	190	200	390
Transferable	92	62	154
Transferred	58	50	108
Frozen	15	6	21
<i>Clinical outcome</i>			
Cycles to ET	34	32	66
hCG positive	12	11	23
Positive heart beat	11	7	18
Number of fetal hearts	13	8	21
Clinical pregnancy rate (% per OR/% per ET)	29/32	15/22	21/27
Implantation rate (fetal hearts/100 embryos transferred)	22	16	19
Delivered	8	5	13
Delivery rate (% per OR/% per ET)	21/23	11/16	15/20
Miscarriages	3	2	5
Miscarriage rate (% per clinical pregn–pregn lost to FU)	27	29	28
Clinical pregnancies lost to FU	0	0	0

AS, aneuploidy screening; 30 cycles were performed for sexing female and 55 cycles for sexing male.

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

	<i>N</i> pregnancies	<i>N</i> fetal sacs
Pregnancies	2313	2521
FISH only cycles	1839	
PCR only cycles	473	
FISH+PCR	2	
Subclinical pregnancies <sup>1</sup>	359	
Clinical pregnancies	1954	2521
Singletons	1437	1437
Twins	443	886
Triplets	56	168
Quadruplet	4	16
Unknown	14	14 <sup>2</sup>
Lost to FU during first trimester	22	26
First trimester loss	190	292
Miscarriage	167 <sup>3</sup>	184
TOP	4 <sup>4</sup>	5
Extra-uterine pregnancy	19 <sup>5</sup>	21
Vanishing twins/triplets		82
Reduction of multiple pregnancies <sup>(10)</sup>	(6)	8
Quadruplet to twin	(2)	4
Triplet to twin	(2)	2
Twin to singleton	(2)	2
Ongoing pregnancies (>12 weeks)	1742	2221
Second trimester loss	42	57
Miscarriage	28 <sup>6</sup>	43
TOP <sup>6</sup>	14 <sup>7</sup>	14
Reduction of multiple pregnancies <sup>(10)</sup>	(23)	32
Quadruplet to twin	(2)	4
Triplet to twin	(11)	11
Triplet to singleton	(7)	14
Twin to singleton	(3)	3 <sup>8</sup>
Lost to FU during second trimester	67 <sup>9</sup>	79
Deliveries	1633	2027
Singletons	1254	1254
Twins	364	728
Triplets	15	45

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

<sup>2</sup>Number of fetal heart beats not known. Counted further as 1 fetal heart beat.

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

<sup>4</sup>Two TOPs for anencephalocele, one TOP for social reasons, one TOP of twin with misdiagnosis for Charcot-Marie-Tooth disease 1a.

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

<sup>6</sup>One triplet: fetal reduction, followed by amniocentesis and loss of remaining twin at 16 weeks (one fetal sac counted in reduction, two in miscarriage, one second trimester pregnancy loss after miscarriage counted).

<sup>7</sup>TOP, termination of pregnancy. TOP after misdiagnosis (five): one misdiagnosis for sexing, FISH, female fetus, indication social sexing; one misdiagnosis for  $\beta$ -thal, PCR; one misdiagnosis for myotonic dystrophy, PCR, one misdiagnosis after PGS, karyotype 45,X; and one misdiagnosis for a reciprocal translocation 46,XY,der(15)t(13;15)(q25.1;q26.3). TOP after ultrasound (four): enlarged lateral ventricle on ultrasound, two singletons with cardiopathy on ultrasound, one singleton with tetralogy of Fallot TOP for abnormalities found after amniocentesis, not related to the PGD (five): 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.

<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.

<sup>10</sup>Numbers between parentheses are there for your information only, these pregnancies were not lost, only the number of fetal sacs reduced.

**Table VIIIb.** Evolution of pregnancy, data VIII.

	<i>N</i> pregnancies	<i>N</i> fetal sacs
Pregnancies	845	837
FISH only cycles	697	696
PCR only cycles	148	141
FISH+PCR	0	0
Subclinical pregnancies <sup>1</sup>	195	
Clinical pregnancies	650	837
Singletons	466	466
Twins	154	308
Triplets	21	63
Quadruplet	0	0
Unknown	9	
Lost to FU during first trimester	7	7
First trimester loss	76	106
Miscarriage	59	66
TOP	1 <sup>2</sup>	1
Extra-uterine pregnancy	13	5
Vanishing twins/triplets	0	13
Unknown	3	3
Reduction of multiple pregnancies		18
Quadruplet to twin		9
Triplet to twin		3
Twin to singleton		6
Ongoing pregnancies (>12 weeks)	567	724
Second trimester loss	7	12
Miscarriage	6	10
TOP	1 <sup>3</sup>	1
Miscarriage twin to singleton		1
Lost to FU during second trimester	10	16
Deliveries	550	696
Singletons	410	410
Twins	134	268
Triplets	6	18

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

<sup>2</sup>Singleton with misdiagnosis for  $\beta$ -thal.

<sup>3</sup>Amnio failed, suspicion of 18q deletion.

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

	Total	Singletons	Twins	Triplets
No deliveries	1633 <sup>1</sup>	1254 <sup>1</sup>	364 <sup>1</sup>	15
Method of delivery				
Vaginal	696	625	70	1
Caesarian	796	531	253	12
Vaginal and Caesarian	4	2	2	0
Unknown	137	96	39	2
Term at delivery				
Preterm	434	196	227	11
Term	1010	916	92	2
Unknown	188	142	44	2

<sup>1</sup>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 VIII.

	Total	Singleton	Twin	Triplet
No deliveries	550	410	134	6
Method of delivery				
Vaginal	224	198	26	0
Caesarean	263	162	97	4
Vaginal and Caesarean	0	0	0	0
Unknown	63	50	11	2
Term at delivery				
Preterm	175	73	98	4
Term	335	308	27	0
Unknown	40	29	9	2

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

Method	N	Result		
		Normal	Abnormal	Unknown
<b>Prenatal diagnosis</b>				
FISH				
CVS	68	68	0	0
Amnio	387 <sup>2</sup>	377 <sup>2</sup>	8	2
Ultrasound	424 <sup>2</sup>	416	8 <sup>2</sup>	0
Unknown	3	3	0	0
Total	879 <sup>1</sup>	864	16	2
PCR				
CVS	97	96	1	0
Amnio	99	89	10	0
Ultrasound	26	23	3	0
Unknown	2	2	0	0
Total	222 <sup>1</sup>	209	13	0
<b>Post-natal diagnosis</b>				
FISH				
Karyo miscarriage	56	27	29	0
Karyo post-natal	100 <sup>3</sup>	97 <sup>3</sup>	3	0
Physical examination	660 <sup>3</sup>	656 <sup>3</sup>	4	0
Unknown	2 <sup>3</sup>	2 <sup>3</sup>	0	0
Total	814	778	36	0
PCR				
Karyotype miscarriage	5	4	1	0
DNA test miscarriage	2	2	0	0
DNA test post-natal	39	38	1	0
Sweat test	6	6	0	0
Physical examination	25	24	1	0
Karyotype	8	8	0	0
Karyo+DNA	2	2	0	0
Algo test	2	2	0	0
Unknown	6	6	0	0
Total	95	92	3	0

<sup>1</sup>Three fetal sacs had PCR and FISH at PGD.

<sup>2</sup>Three fetal sacs with abnormalities on US (enlarged lateral ventricle, cardiopathy, hydrocephalus) with normal result on amniocentesis.

<sup>3</sup>Two children had physical examination and karyotype, two children had unknown check and karyotype.

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

Method	N	Result		
		Normal	Abnormal	Failed
<b>Prenatal diagnosis</b>				
FISH				
CVS	14	14	0	0
Amniocentesis	93	92	0	1 <sup>1</sup>
Ultrasound	220	219	0	1 <sup>2</sup>
Total	327	325	0	2
PCR				
CVS	25	23	2 <sup>3</sup>	0
Amniocentesis	20	19	0	1 <sup>4</sup>
Ultrasound	2	2	0	0
Total	47	44	2	1
<b>Post-natal diagnosis</b>				
FISH				
Karyo miscarriage	14	7	7 <sup>5</sup>	0
Karyo post-natal	10	9	1 <sup>6</sup>	0
Physical examination <sup>7</sup>	252	251	1 <sup>7</sup>	0
Karyo post-natal+physical examination	13	13	0	0
Total	289	280	9	0
PCR				
Karyo miscarriage	1	0	1 <sup>8</sup>	0
Physical examination <sup>9</sup>	28	28 <sup>9</sup>	0	0
DNA test post-natal	11	11	0	0
Karyotype	1	1	0	0
Physical examination+karyo	1	1	0	0
DNA test+karyo	1	1	0	0
Unknown	5	5	0	0
Total	48	47	1	0

<sup>1</sup>TOP because of suspicion 18q deletion after PGS for RIF.

<sup>2</sup>Inconclusive for gender after PGD for Haem A.

<sup>3</sup>Misdiagnosis for B-thal, Misdiagnosis for FRAXA.

<sup>4</sup>Failed in one twin.

<sup>5</sup>Trisomy 15 after PGS for RIF; 47,XX,+16 after PGD for robertsonian translocation der(13;14); 47,XX,t(3;5)(q21;p14),+15 after PGD for reciprocal translocation t(3;5); 48,XY,+7,+mar after PGS for maternal age and recurrent miscarriages; 47,XX,+7,inv(12)(p13;q11) after a PGD for inv(12); 92,XXXX,t(1;10)(q21.3;q24.3)x2 after PGD for reciprocal translocation t(1;10); 47,XY,+20 after PGS for maternal age.

<sup>6</sup>Syndrome of Rubinstein–Taybi after PGS for RIF.

<sup>7</sup>Includes one test for factor VIII in blood, misdiagnosis after PGD for Haem A.

<sup>8</sup>47,XY,+16 after PGD for Facioscapulohumeral dystrophy.

<sup>9</sup>Includes one sweat test after a PGD for CF.

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

Total children born	1988 <sup>1</sup>
Sex	
Male	857
Female	1048
Unknown	83
Mean birthweight (g)	
Singletons	3220
Twins	2385
Triplets	1835
Mean birth length (cm)	
Singletons	50
Twins	46
Triplets	44

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

**Table XIb.** Data on children born, data collection VIII.

Total children born	670	
Sex		
Male	304	
Female	357	
Unknown	9	
Mean birthweight (g)		
Singletons	3218	( <i>n</i> = 361/394) <sup>1</sup>
Twins	2348	( <i>n</i> = 236/258) <sup>1</sup>
Triplets	1751	( <i>n</i> = 9/18) <sup>1</sup>
Mean birth length (cm)		
Singletons	49.8	( <i>n</i> = 234/394) <sup>1</sup>
Twins	45.6	( <i>n</i> = 142/258) <sup>1</sup>
Triplets	—	( <i>n</i> = 0/18) <sup>1</sup>
Mean head circumference (cm)		
Singletons	34.5	( <i>n</i> = 134/394) <sup>1</sup>
Twins	32.2	( <i>n</i> = 70/258) <sup>1</sup>
Triplets	—	( <i>n</i> = 0/18) <sup>1</sup>
Apgar scores after 1 min		( <i>n</i> = 223/670) <sup>1</sup>
Good <sup>2</sup>	220	
Poor <sup>2</sup>	3	
Apgar scores after 5 min		( <i>n</i> = 222/670) <sup>1</sup>
Good <sup>2</sup>	220	
Poor <sup>2</sup>	2	
Apgar scores after 10 min		( <i>n</i> = 107/670) <sup>1</sup>
Good <sup>2</sup>	106	
Poor <sup>2</sup>	1	

<sup>1</sup>Numbers between brackets indicate 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  $< 7$ .

**Table XIIIb.** Summary of misdiagnosis from data VIII.

Indication	Method used	PND-Post-natal	Outcome	Reported in
<b>Monogenics</b>				
β-Thal	PCR	PND	TOP	VIII
FRAXA	PCR	PND	Born	VIII
<b>Sexing for X-linked disease</b>				
46,XY, Haem A	FISH	Post-natal	Born	VIII

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

Indication	Method used	PND-post-natal	Outcome	Reported in
<b>Monogenics</b>				
DM1	PCR	PND	TOP	I
β-thal	PCR	PND	TOP	II
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
<b>Sexing for X-linked disease</b>				
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
<b>Translocations</b>				
T13 after 45,XY,der(13;14)(q10;q10)	FISH	Miscarried	Miscarried	VI
47,XX,+der(22)t(11;22)(q23.3;q11.2)	FISH	PND	TOP	III
46,XY,der(15)t(13;15)(q25.1;q26.3)pat	FISH	PND	TOP	VII
<b>PGS</b>				
T16 after 1st PB biopsy only	FISH	Miscarried	Miscarried	VI
T16 after 1st PB biopsy only	FISH	Miscarried	Miscarried	V
47,XX,+16	FISH	Miscarried	Miscarried	VI
47,??,+16	FISH	Miscarried	Miscarried	VI
47,XX,+21	FISH	Post	Born	III
47,XXX	FISH	PND	Lost to follow-up	VII
<b>Social Sexing</b>				
Requested male but female fetus	FISH	PND	TOP	III

PND, prenatal diagnosis. The numbers in the last column indicate the PGD Consortium report number.

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