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Introductory letter to "Preimplantation Genetic Diagnosis and Related Activites in Canada"

A survey of the extent of preimplantation genetic diagnosis (PGD) and related genetic counselling activities in Canada was carried out in 2008 to establish the volume of service, likely changes in demand in the near future, the degree of cross-border service and the overall human resources dimensions and implications. This report presents the information gathered from that survey, and gives a general overview of professional experiences with PGD in Canada.

The survey was designed by Dr. Jeff Nisker and Dr. Kathy Nixon Speechley (University of Western Ontario) and approved by Steering Committee members from the Canadian College of Medical Geneticists (CCMG), the Canadian Association of Genetic Counsellors (CAGC), Health Canada (HC), the Society of Obstetricians and Gynaecologists Canada (SOGC) and the Canadian Fertility and Andrology Society (CFAS). Medical Directors of all Canadian fertility clinics and Directors of clinical genetics units in Canada were invited to complete the survey online.

This report was commissioned by Assisted Human Reproduction Canada (AHRC). The views are the authors' and do not necessarily reflect official views of AHRC or the participating professional societies.

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Preimplantation Genetic Diagnosis and Related Activities in Canada

Report Prepared for Assisted Human Reproduction Canada

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BACKGROUND

In the late 1980s preimplantation genetic diagnosis (PGD) was developed (Handyside et al., 1989) to permit genetic assessment of embryos created through *in vitro* fertilization (IVF) (Handyside, Kontogianni, Hardy, & Winston, 1990). PGD was embraced as a potential compassionate alternative to testing fetuses (Nisker & Gore-Langton, 1995) through amniocentesis (Serr, Sachs, & Danon, 1955) at approximately 16 weeks gestational age or chorionic villus sampling (CVS) (Neilson & Alfirevic, 2006) a few weeks earlier, in that genetic abortion could be avoided (Nisker & Gore-Langton, 1995).

In PGD, a single cell can be withdrawn from embryos at the 8-cell stage (Handyside et al., 1989; Nisker & Gore-Langton, 1995) or from trophectoderm at the blastocyst stage for genetic analysis (Muggleton-Harris, Glazier, & Pickering, 1993; Kokkali et al., 2007; McArthur et al., 2008). Desired embryos are then transferred to the woman's uterus or frozen for subsequent use (Verlinsky, 1999). Many IVF clinics in some countries are increasingly utilizing routine 'screening' of IVF embryos or polar bodies for chromosomal anomalies in order to avoid both miscarriages and children 'affected' by irregular chromosome patterns (Verlinsky et al., 2004).

Although PGD may provide an alternative to the emotional and physical stress of second trimester genetic abortion, PGD requires the woman to accept the risks of harm from IVF drugs (Abramov, Elchalal, & Schenker, 1999), surgery (Alsalili et al., 1995), and a decreased possibility of becoming pregnant (Nisker & Gore-Langton, 1995; Mastenbroek et al., 2007). Worldwide, there is approximately one successful pregnancy in every four PGD cycles, and of these only half lead to a live birth (ESHRE Preimplantation Genetic Diagnosis Consortium, 2002).

Assessment of blastomeres (Handyside et al., 1989; Handyside et al., 1990), trophectoderm (Muggleton-Harris et al., 1993) and polar bodies (Verlinsky et al., 1990) is performed molecularly through polymerase chain reaction (PCR) (Mullis & Faloona, 1987) and cytogenetically through fluorescent in situ hybridization (FISH) (Delhanty et al., 1993; Mykitiuk & Nisker, 2008). Genetic determinations of an embryo through PGD may be used not only to implant embryos to avoid a specific genetic disorder, but to implant embryos with particular characteristics (Mykitiuk & Nisker, 2009), for example embryos of a specific histocompatibility in a saviour sibling scenario (Pennings, Schots, & Liebaers, 2002; Mykitiuk & Nisker, 2009; Sheldon & Wilkinson, 2009), or embryos that will result in a child who is deaf (Levy, 2002) or who has dwarfism (Nunes, 2006; Mykitiuk & Nisker, 2008).The possible uses of PGD are regulated in several countries, and include: a) selecting embryos that do not carry genetic markers, b) detecting chromosomal anomalies, c) determining the sex of the embryo and/or, d) determining the histocompatibility of an embryo with an existing person (e.g. HFEA (HFEA, 1990), French regulatory body (Van Wager, Mykitiuk, & Nisker, 2008). In Canada, although the *Assisted Human Reproduction Act (AHR)* (2004) governs all uses of embryos, there is no legislation nor professional policy guidelines that regulate PGD (Mykitiuk & Nisker, 2008), except for section 5 of the *AHR Act* that prohibits sex selection (2004)**.**

In Europe (Corveleyn et al., 2008) and the United States (Verlinsky et al., 1990; Verlinsky, 1999), PGD appears to be utilized much more frequently, with many units performing embryo biopsy as well as chromosomal and molecular analysis. Although no data has been accrued in Canada, it is believed that PGD is offered in some IVF units. The number and methods of embryo biopsy procedures, cytogenetic and molecular analyses that are performed in those units, or the number and destination of genetic materials that are referred for cytogenic and

molecular analysis is unknown. It is hypothesized that when PGD is offered to a woman/couple in Canada, it is generally with the understanding that their embryos will be transported to laboratories in the United States or other laboratories in Canada for biopsy and genetic analysis.

The purpose of this study was to provide a "scan" of PGD in Canada to learn the extent of the offering of PGD, the methods and centres in which PGD is performed, the indications for PGD, and the extent and description of the genetic counselling performed. In addition, we wish to determine the referral patterns for biopsy, analysis and counselling, and what are the desires of clinicians and scientists involved in assisted reproduction and genetics for the future practice of PGD in Canada.

DESIGN AND METHODS

Two groups of Canadian clinicians, directors of IVF clinics and directors of genetics clinics, were invited to participate and include, in formulating their responses, other members of the clinical and laboratory teams in order to report information relating to their respective units. The two full populations of directors of such units were targeted for invitation, rather than drawing a sample from each, given the relatively small size of their communities in Canada. The names and contact information of the two groups of directors who would be invited and the strategy for approaching them regarding the study were provided by the members of the Assisted Human Reproduction Canada (AHRC) committee convened to advise on the creation of the survey. These include representatives of the Canadian Fertility and Andrology Society (CFAS), Canadian College of Medical Geneticists (CCMG), and Canadian Association of Genetic Counsellors (CAGC), Health Canada, and AHRC. The disciplines and positions of the advisors included a reproductive endocrinologist who was a medical director of an IVF clinic, an IVF laboratory director, a medical geneticist, a molecular geneticist, a cytogeneticist, a genetic counsellor, and health policy personnel with knowledge of genetics and assisted reproduction. Through this committee, two lists of names and email addresses were established: medical directors of all IVF clinics in Canada (n=28), and all directors of genetic departments/divisions units in Canada (n=18).

This committee also assisted in the development of the questionnaire. This was accomplished through a series of teleconferences in which committee members provided feedback on the content and organization of the questionnaire. Several iterations of the questionnaire ensued before a questionnaire was approved by the committee to be used in this study. The questionnaire was intended to collect comprehensive information regarding the

current practice of PGD and related genetic counselling activities in Canada as well as the planned and desired future practice of PGD in Canada.

The survey was administered electronically following Dillman's tailored design method (Dillman, 2007). Directors of IVF and Genetics units received an email from a leader of their respective organization (CFAS or CCMG) endorsing the survey and urging participation. This was followed by an emailed letter of information (see Appendix I) from Dr. Elinor Wilson, President, AHRC, describing the study, requesting that they complete the survey with members of their team. The letter included a link to access a webpage containing the survey and a Personal Identification Number (PIN) to enter. Participants submitted their responses to the survey via email identified only by their PIN. They each received an automated message indicating successful submission and thanking them. A copy of the survey is provided in Appendix II. To ensure confidentiality, the list of names and PIN numbers was kept in a locked cabinet in a locked research office with access limited only to KNS and the Study Coordinator, and to be destroyed upon study conclusion. Three weeks after the initial letter of information was sent, a reminder letter was sent to non-responders. A final reminder letter was sent to non-responders two weeks later including the option to mail back a paper copy of the completed questionnaire if that was more convenient.

Completed surveys were imported and analyzed in SPSS version 16.0. Frequencies and percentages are presented for categorical variables. The numbers of patients reported by individual participating clinics were summed to calculate the total number of patients served by all participating clinics.

RESULTS

A) IVF Clinics

Directors of 17 of the 28 IVF clinics in Canada (as identified by representatives of CFAS) responded to the survey for a response rate of 61%.

The distribution of activities performed by IVF clinics is presented in Table 1. Of the 17 IVF clinics responding, 14 provided the number of patients receiving IVF in their unit in the past five years, and 16 clinics provided the number of patients in 2008 and estimated for 2009. A combined total of 22,769 patients received IVF over the past five years in 14 clinics. A combined total of 6,584 patients received IVF in 16 clinics in 2008, and 6,688 patients were estimated for 2009.

Table 1 (Q1): Activities Performed by IVF Clinics

Activity				# of Patients (range)		
	n	%		Past 5 Years	2008	2009
IVF	17	100		350-3969 n=14	120-1004 n=16	18-1050 n=16
IVF & perform embryo biopsy	6	35		10-150 n=5	3-40 n=6	5-45 n=5
IVF with no PGD/PGS offered	12	71		350-2490 n=6	120-497 n=6	160-545 n=5
IVF & refer to other unit in Canada for embryo biopsy	7	41		1-10 n=6	0-5 n=6	1-3 n=4
IVF & refer to unit in USA for embryo biopsy	3	18		2, 150 n=2	1, 60 n=2	60 n=1
Perform cytogenetic (e.g., familial chromosome enumeration & translocation/inversion) analysis	4	24		50-200 n=3	10-3200 n=3	10-2100 n=3
Perform molecular (familial gene disorder) analysis	4	24		10-50 n=3	3-10 n=3	3-10 n=3
Refer for cytogenetic analysis to another unit in Canada	4	24	In prov.	0-500 n=3	0-100 n=3	0-100 n=3
			Out of prov.	0-25 n=3	0-5 n=3	0-5 n=3
Refer for cytogenetic analysis to a unit in USA	4	24		14 n=1	2-40 n=3	10, 40 n=2
Refer for molecular analysis to another unit in Canada	3	18	In prov.	0-15 n=3	0, 15 n=2	0, 20 n=2
			Out of prov.	2 n=1	1 n=2	1 n=1
Refer for molecular analysis to a unit in USA	6	35		10-30 n=4	2-20 n=5	5-20 n=5
Accept embryos for cytogenetic analysis	1	6			0 n=1	
Accept embryos for molecular analysis	1	6			0 n=1	
Accept blastomeres for cytogenetic analysis	1	6			0 n=1	
Accept blastomeres for molecular analysis	0	0				
Accept cells from blastocysts for cytogenetic analysis	1	6			0 n=1	
Accept cells from blastocysts for molecular analysis	0	0			0 n=1	

Embryo biopsies are performed in 6 IVF clinics (Figure 1). The combined total for the number of patients whose embryos were biopsied in their units was 239 for the past five years among the 5 IVF clinics that provided patient numbers, 99 in 2008 among 6 IVF clinics reporting patient numbers, and 96 predicted for 2009 among 5 IVF clinics providing such an estimate (Figure 2). The number of patients whose embryos were biopsied in one of these clinics over the past five years ranged from 10 to 150, in 2008 from 3 to 40, and estimated in 2009 to be from 5 to 45 (Table 1)**.** The types of embryo biopsy performed by the responding IVF clinics is shown in Table 2.

Figure 1: Canadian IVF units and embryo biopsy

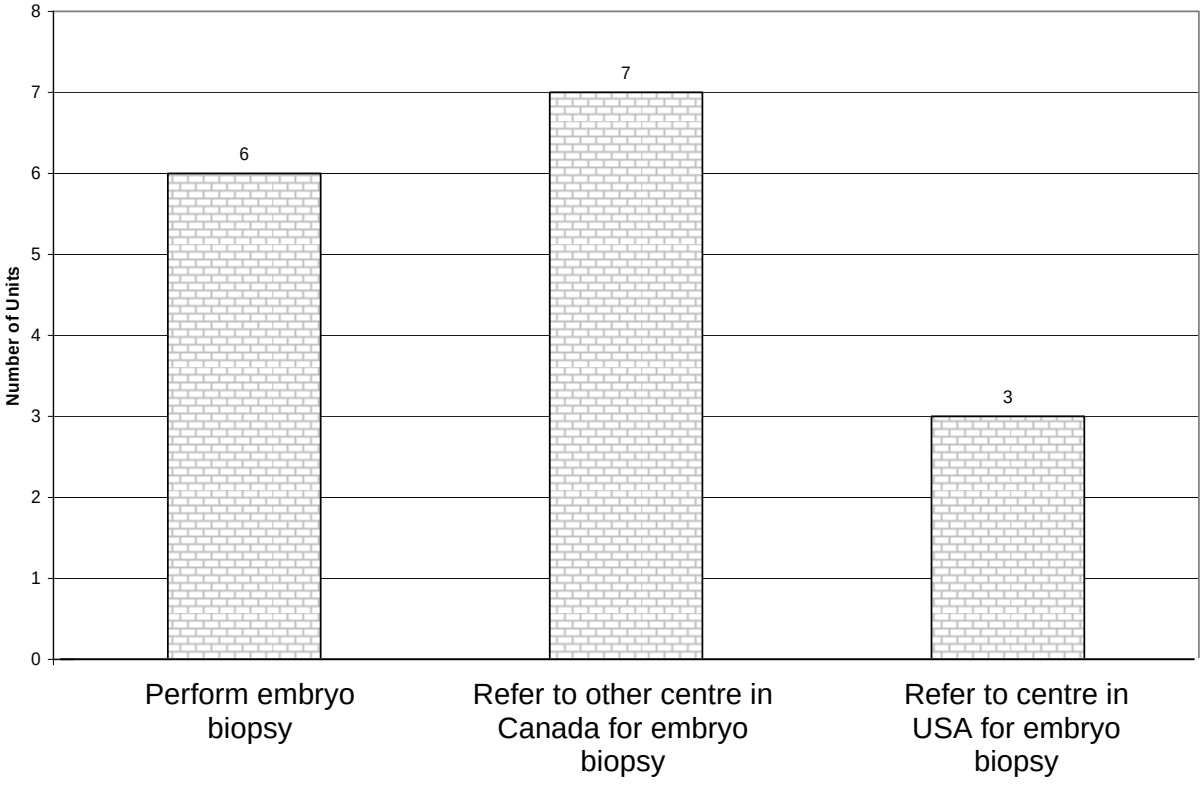


Figure 2: Number of patients whose embryos underwent biopsy

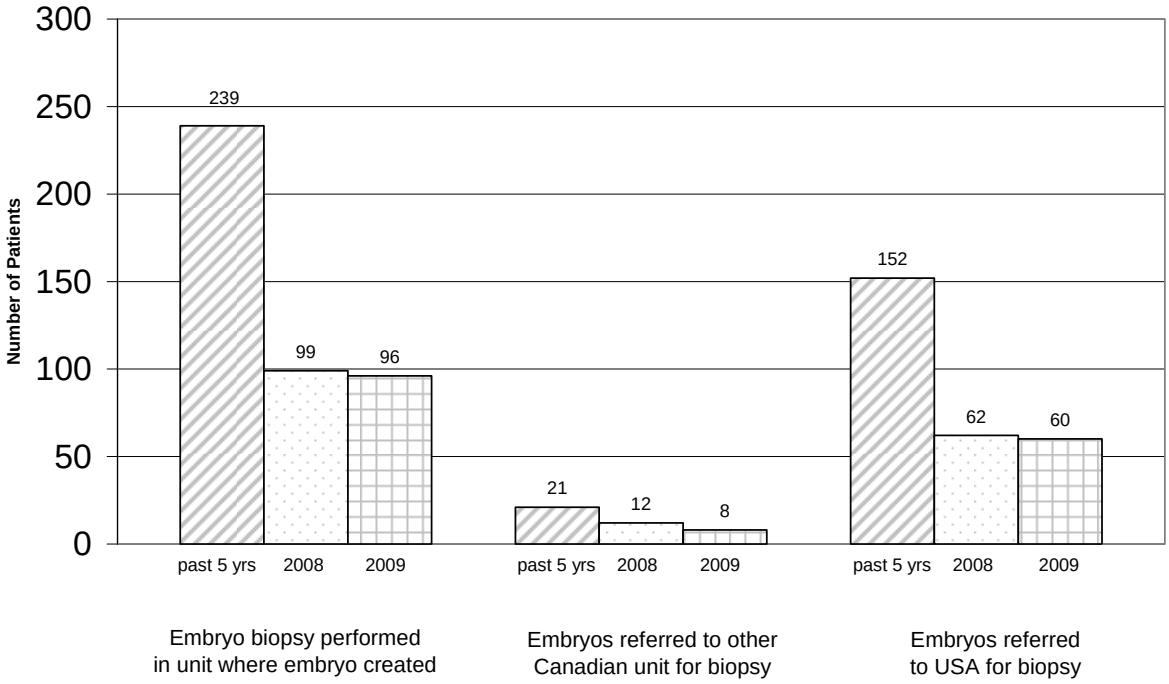


Table 2 (Q2): Types of embryo biopsy performed by IVF Clinics

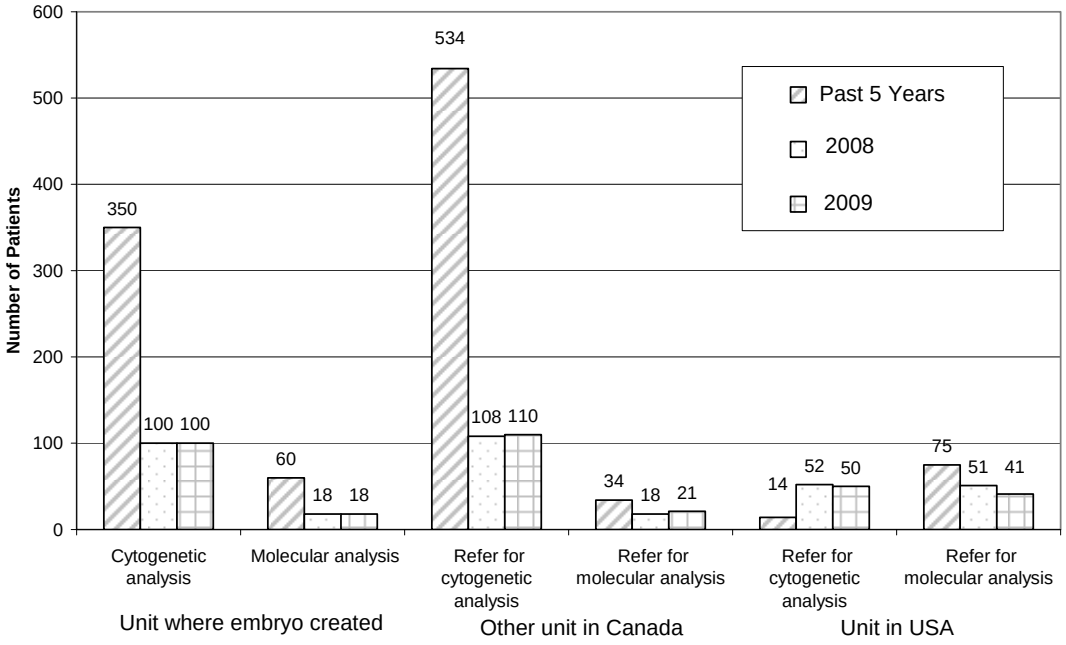
	n	%
Single blastomeres	6	35
Two blastomeres	0	0
Blastocyst, trophectoderm biopsy	3	18

The number of clinics that referred embryos created in the units to other units for embryo biopsy was 10, with 7 referring to other units in Canada and 3 to units in the United States. Six of these clinics reported referring a total number of 21 patients' embryos for biopsy to other units in Canada over the past five years and a total of 12 in 2008. Five of these clinics estimated a combined total of 8 such referrals in 2009 (Figure 2). Two of these clinics reported referring a combined total of 152 patients' embryos to an assisted reproduction unit in the United States

over the past five years and 62 in 2008. The one clinic that provided a prediction for this number in 2009 estimated 60 patients (Figure 2).

Figure 3 illustrates where the cytogenetic and molecular analysis of the embryo biopsy material was performed for patients whose embryos were created in responding Canadian IVF units. Of the four IVF clinics reported performing cytogenetic analysis in their own unit, three of these units reported patient numbers for a combined total of 350 patients in the past five years, 100 in 2008, and 100 expected in 2009. Of the four clinics reporting that they perform molecular analysis in their unit, three reported a combined total of 60 patients in the past five years, 18 in 2008 and 18 predicted for 2009. Of the four IVF clinics that reported referring their patients' embryos for cytogenetic analysis to another unit in Canada, three reported a combined total of 534 such referrals over the past five years (501 within province and 33 out of province), 108 in 2008 (101 within province and 7 out of province), and an estimated 110 for 2009 (103 within province and 7 out of province). The three IVF clinics that refer patients' embryos for molecular analysis to another unit in Canada, reported a combined total of 34 referrals over the past five years (32 within province and 2 out of province), 18 in 2008 (16 within province and 2 out of province), and an estimated 21 for 2009 (20 within province and 1 out of province). Of the 4 IVF clinics that reported referring patients' embryos for cytogenetic analysis in the USA, one clinic reported 14 referrals in the past five years, 3 clinics reported a combined total of 52 referrals in 2008 and 2 reported a combined total of 50 estimated for 2009. Six of the responding Canadian IVF clinics reported referring their patients' embryos for molecular analysis to an American clinic, with 4 of them reporting a combined total of 75 referrals over the past five years. The combined total of such referrals to the USA of 6 clinics providing the information was 51 in 2008, and of 5 clinics providing information, a total of 41 referrals estimated for 2009.

Figure 3: Unit where embryos underwent cytogenetic and molecular analysis



The reasons why some IVF clinics do not perform PGD are illustrated in Figure 4. Of the clinics that do not perform PGD, 7 (41%) indicated that they would like to offer PGD but did not have the resources/staff/money/expertise to make it available (Table 3). The second most common reason, indicated by 18% of clinics, was that no patient had requested it (no market demand). The lack of current capacity of IVF clinics to perform PGD testing of embryos for translocations, gene disorders and HLA matching is presented in Table 4. Table 5 provides results indicating that one to three clinics plan to perform such testing in the future. Table 6 provides IVF clinics responses regarding how likely they believe it is that their unit will offer PGD in the future.

Figure 4: Reasons why units do not perform PGD

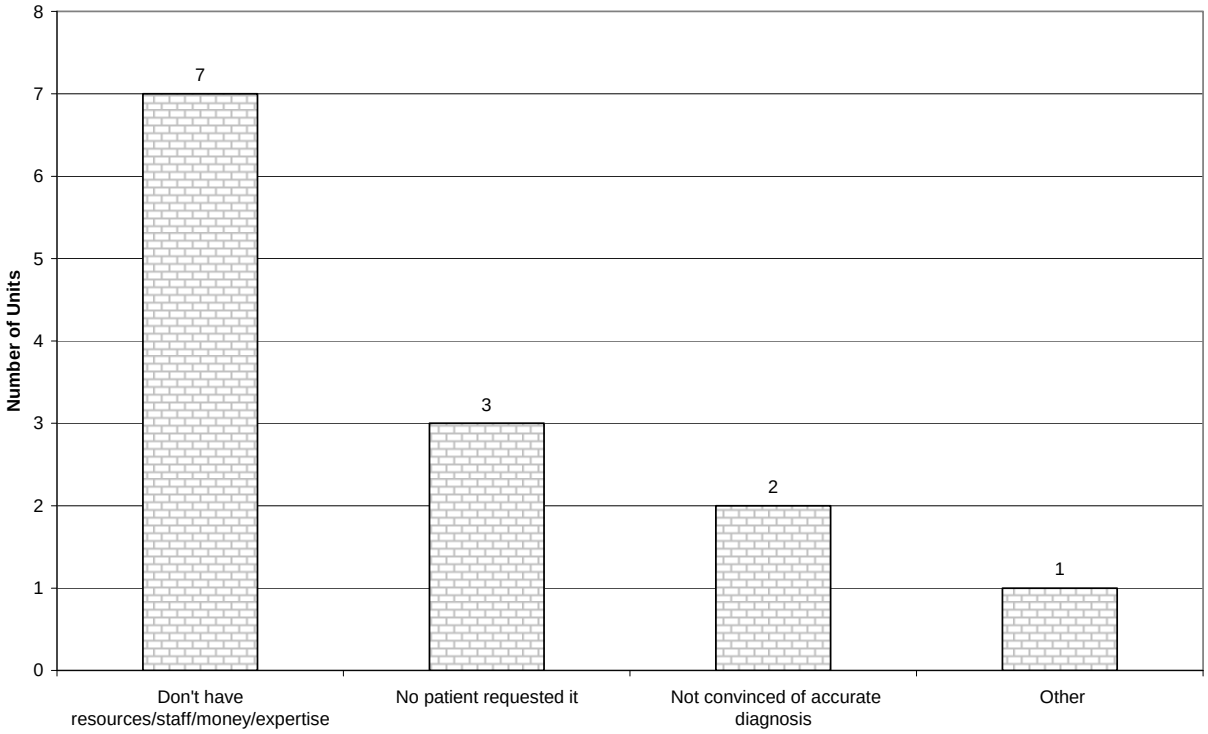


Table 3 (Q5): Reasons why units do not perform PGD

	n	%
Unfamiliar with it PGD is considered experimental	0	0
No patient has requested it (no market demand)	3	18
We would like to offer it but do not have the resources/staff/money/expertise to make it available	7	41
PGD is considered experimental	--	--
Not convinced it does not harm the embryo	--	--
Not convinced it yields accurate diagnosis	2	12
Ethical/moral concerns about its use	--	--
Concerned about liability	--	--
Other	1	6

Table 4 (Q6): Does your unit <u>currently</u> have the capacity to perform PGD testing for embryos for:

	n	%
Translocations		
Yes	0	0
No	17	100
Blank	0	0
Gender testing for X linked & other conditions		
Yes	1*	6
No	16	94
Blank	0	0
Gene Disorders		
Yes	0	0
No	17	77
Blank	0	0
HLA matching		
Yes	0	0
No	17	77
Blank	0	0

* FISH

Table 5(Q7): Does your unit plan to perform PGD testing <u>in the future</u> for:

	n	%
Translocations		
Yes	3*	18
No	14	82
Blank	0	0
Gender testing for X linked & other conditions		
Yes	3**	18
No	14	85
Blank	0	0
Gene Disorders		
Yes	1	6
No	16	94
Blank	0	0
HLA matching		
Yes	2	12
No	15	88
Blank	0	0

* 2 for FISH, 1 for Array CGH

** 1 for FISH, other 2 not recorded

Table 6 (Q8): What is the likelihood your unit will offer PGD in the future?

	n	%
Certain we will offer-Process underway	0	0
Very likely	2	12
Fairly likely	5	29
Unlikely	7	41
Certain we will not offer	0	0
Blank	3	18

When the medical directors of IVF clinics were asked which PGD and related services they would like to see in Canada, at least 94% indicated that they would like to see embryo biopsy, one cell chromosomal enumeration and translocation/inversion testing, gene disorder testing on blastomeres, and genetic counselling with expertise in PGD (Table 7).

Table 7 (Q9): What services would you like to see provided in Canada?

	n	%
Embryo biopsy	16	94
One cell Chromosomal enumeration and translocation/inversion testing (FISH)	17	100
Gene disorder testing on blastomeres	17	100
Genetic counselling with expertise in PGD	17	100

Regarding on-site genetic counselling, four of the five clinics providing genetic counselling on site reported that genetic counselling is recommended to all patients considering PGD (Table 8). Of the five clinics responding that they provide genetic counselling within their walls, certified genetic counsellors provided the counselling in 3 units, REI physicians in 2 units, and nurses in 1 unit (Figure 5). This would indicate that one clinic has more than one discipline providing the genetic counselling. Five IVF clinics responded that they provide on site genetic counselling other than for PGD (Table 9). Regarding the referral of patients for genetic

counselling off site, 10 indicated that they refer to a certified genetic counsellor, 7 to an MD geneticist, and one each to an REI physician and counsellor not certified in genetics (Table 10).

Figure 5: Discipline of provider of genetic counselling in IVF Units

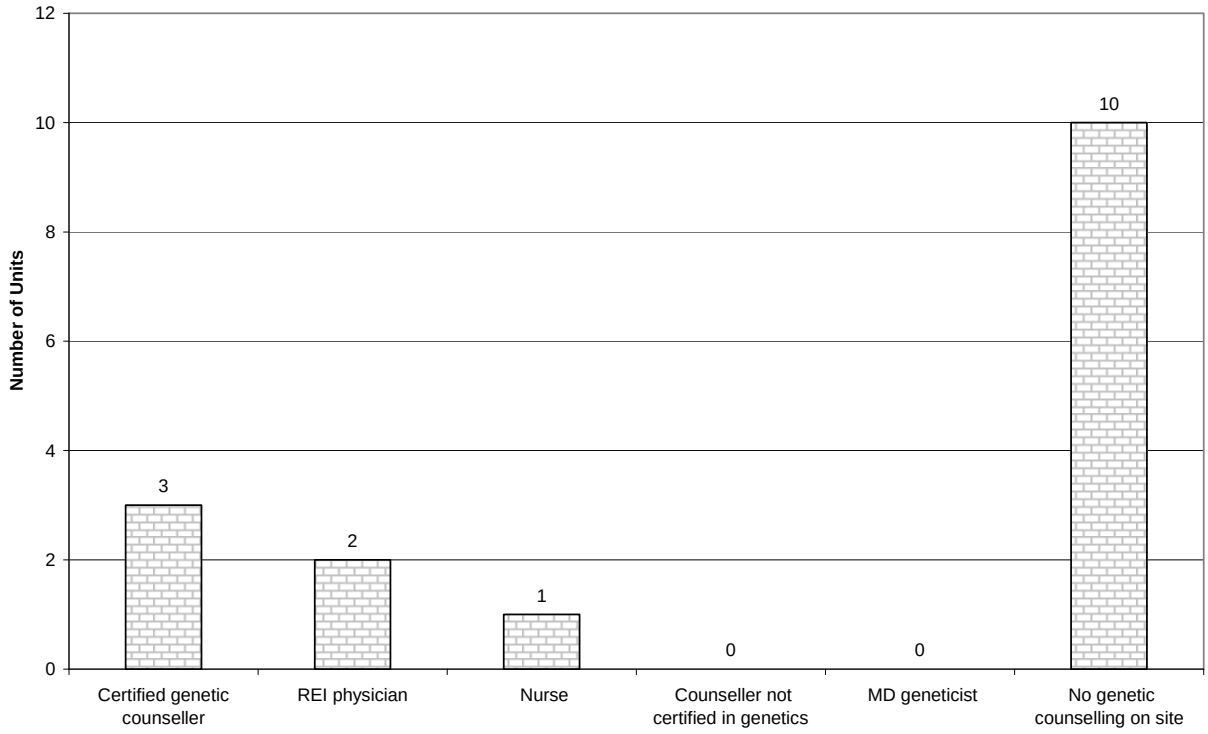


Table 8 (Q10a): For 5 IVF units providing genetic counselling on site, type of provider and number of patients

Provider	n	%	# of patients (range)		
			Past 5 years	2008	2009 (anticipated)
Reproductive endocrinology and infertility (REI) physician	2	12	75 n=1	6, 15 n=2	20 n=1
Nurse	1	6	--	6 n=1	--
Counsellor	0	0	--	--	--
Certified genetic counsellor	3	18	10-1500 n=3	3-500 n=3	5-500 n=3
MD geneticist	0	0	0	0	0

Note: 4 (80%) IVF units providing genetic counselling on site reported that counselling is recommended to all patients considering PGD.

Table 9 (Q10b): Provision of on site genetic counselling other than PGD by IVF Clinics

			# of patients (range)		
	n	%	Past 5 years	2008	2009 (anticipated)
Yes	5	29			
No	10	59	20-1500	4-500	7-500
Blank	2	12	n=4	n=5	n=4

Table 10 (Q10c): IVF Clinics' Provision of genetic counselling off site by type of provider and number of patients

	n	%	# of patients (range)		
			Past 5 years	2008	2009 (anticipated)
Reproductive endocrinology and infertility (REI) physician					
yes	1	6	5	1	1
no	10	59			
blank	6	35			
Nurse					
yes	0	0			
no	9	53	--	--	--
blank	8	47			
Counsellor					
yes	1	6	--	--	--
no	10	59			
blank	6	35			
Certified genetic counsellor					
yes	10	59	14-300	4-50	4-50
no	5	29	n=6	n=6	n=6
blank	2	12			
MD geneticist					
yes	7	41	15-50	7-50	4-20
no	6	35	n=4	n=5	n=4
blank	4	24			

Information regarding the number of IVF clinics that perform PGS for aneuploidy and/or plan to in the future in provided in Table 11. Tables 12 and 13 provide information regarding the number of clinics that freeze post PGD embryos for clinical and/or research purposes and Table 14 describes units' practice regarding the confirmation of PGD findings by amniocentesis or CVS. Tables 15 presents estimates given by IVF clinics for the percentage of patients inquiring about PGD or PGS who actually pursue it, and Table 16 describes the main reasons given for why patients interested in PGD or PGS do not pursue it. Table 17 reports when patients are offered genetic counselling.

Table 11 (Q11): For IVF Clinics, does your unit perform PGS for aneuploidy and/or plan to in future?

	Currently		In the future	
	n	%*	n	%*
Of polar bodies				
no	15	88	10	59
On request	0	0	3	18
routinely	0	0	0	0
blank	2	12	4	24
Of embryos				
no	11	65	8	47
On request	3	18	6	35
routinely	0	0	0	0
blank	3	18	3	18
For women with recurrent pregnancy loss				
no	11	65	8	47
On request	2	12	4	24
routinely	1	6	2	12
blank	3	18	3	18
For women >35 years of age				
no	13	77	9	53
On request	1	6	4	24
routinely	0	0	0	0
blank	3	18	4	24
For all women				
No	14	82	11	65
On request	0	0	2	12
routinely	0	0	0	0
blank	3	18	4	24

*Percentages that do not add to 100% are due to rounding.

Table 12 (Q12): Does your unit freeze post PGD embryos that are not at risk of the condition?

	n	%
Yes	6*	35
No	8	47
Blank	3	18

* Of the 6 IVF Clinics, all 6 freeze embryos for clinical purposes and 1 for research purposes also

Table 13 (Q13): Does your unit freeze post PGD embryos that ARE at risk of the condition?

	n	%**
Yes	3*	18
No	11	65
Blank	3	18

* Of the 3 IVF Clinics, 2 freeze embryos for clinical purposes and 3 for research purposes
** Percentages that do not add to 100% are due to rounding.

Table 14 (Q14): Does your unit confirm PGD finding by amniocentesis/CVS?

	n	%
Recommended	8	47
Suggested	3	18
Varies according to situation	2	12
Not mentioned	0	0
Blank	4	24

Table 15 (Q17): In your opinion, what percentage of patients who inquire actually pursue PGD or PGS?

	PGD		PGS	
	n	%	n	%*
Less than 25%	11	65	12	71
26-50%	2	12	3	18
51-75%	2	12	1	6
More than 75%	2	12		
Blank			1	6

* Percentages that do not add to 100% are due to rounding.

Table 16 (Q18): In your opinion what are the main reasons patients who are interested in PGD or PGS do NOT pursue it?

	PGD		PGS	
	n*	%	n*	%
Not available locally	7	41	5	29
Too expensive	16	94	11	65
Low chance of successful pregnancy outcome	3	18	6	36
Other, please specify	--	--	1	6

* Multiple responses allowed

Table 17 (Q19): When are patients offered genetic counselling?*

	n	%
Before PGD/PGS	14	82
After PGD/PGS	2	12
Never	--	--

*Multiple responses allowed

The final four tables, Tables 18-21, present information regarding types of inherited condition or other scenarios e.g. HLA testing for saviour siblings for which the IVF clinics offer PGD or plan to in the future.

Table 18 (Q21a-c): Please indicate which of the following YOUR UNIT has done or plans to do in the future?

		Has Done		Plans to in the Future	
		n	%*	n	%*
Translocations					
	Yes	4	24	6	35
	No	12	71	8	47
	Blank	1	6	3	18
Gender testing for X linked					
	Yes	4	24	7	41
	No	12	71	7	41
	Blank	1	6	3	18
Gender testing for other conditions					
	Yes	2	12	5	29
	No	14	82	9	53
	Blank	1	6	3	18

* Percentages that do not add to 100% are due to rounding.

Table 19 (Q21d): Please indicate which of the following YOUR UNIT has done or plans to do in the future?

	Has Done		Plans to in the Future	
	n	%	n	%
Recessive monogenic conditions				
Yes	4	24	5	29
No	12	71	8	47
Blank	1	6	4	24
If Yes…				
Cystic Fibrosis	3	18	3	18
B-thalassemia	3	18	14	82
Sickle cell disease	3	18	15	88
Spinal Muscular Atrophy	2	12	15	88
Steinert Myotonic Dystrophy	2	12	15	88
Charcot-Marie-Tooth disease	2	12	2	12
Fragile X syndrome	2	12	2	12
Haemophilia A/B genes	1	6	3	18
Duchenne/Becker Muscular Dystrophy	3	18	2	18
Other	3	18	0	0

Table 20 (Q21e): Please indicate which of the following YOUR UNIT has done or plans to do in the future?

	Has Done		Plans to in the Future	
	n	%*	n	%*
Adult-onset conditions				
Yes	2	12	2	12
No	13	77	10	59
Blank	2	12	5	29
If Yes…				
Huntington's	3	18	2	12
BRCA 1 or 2	0	0	1	6
Alzheimer's	0	0	0	0
Other	0	0	0	0

* Percentages that do not add to 100% are due to rounding.

Table 21 (Q21f): Please indicate which of the following YOUR UNIT has done or plans to do in the future?

	Has Done		Plans to in the Future	
	n	%	n	%
HLA Matching				
Yes	2	12	3	18
No	14	82	9	53
Blank	1	6	5	29
If Yes…				
In combination with genetic testing	1	6	2	12
In absence of heritable mutation	1	6	2	12

B) Genetics Clinics

Seven of the 18 genetics clinics responded to the survey (Response Rate = 39%). Due to this low response rate, the data cannot necessarily be considered representative of the population of genetics clinics, making it impossible to perform any meaningful analysis or draw any conclusions from them. As such, this report presents the information obtained from the seven responding genetics clinics in relation to each item on the questionnaire in Appendix III in Tables III-1 to III-22.

None of the genetic clinics that responded to our questionnaire indicated that they accepted embryos, blastomeres, or cells from blastocysts/trophectoderm for cytogenetic or molecular analysis, suggesting that these clinics did not participate in PGD in any way. Further, none of the responding genetics clinics indicated that they have plans to participate in PGD in the future.

DISCUSSION

This report provides a "scan" of PGD activities in Canada, including the number of women receiving assistance in Canadian IVF units whose embryos underwent PGD; and the number of Canadian IVF units that perform embryo biopsy or refer embryos to be biopsied in Canadian units, or units in the United States. In addition, the report provides data regarding the location (on-site, other Canadian unit, American unit) where the cytogenetic and molecular analysis of embryos, blastomeres, and blastocyst/trophectoderm tissue resulting from Canadian IVF patients are analyzed. The report provides reasons why some Canadian IVF units do not perform PGD and others do, and also describes the state of genetic counselling in the units that offer PGD. Further, the report provides information on what the medical directors of Canadian IVF units, in association with members of their teams, envision for the future practice of PGD in Canada.

Although the response rate for directors of IVF clinics of 61% is comparable to the rates reported in the literature for surveys of physicians in general (Cummings, Savitz, & Konrad, 2001), it is a noteworthy response rate given the amount of time required for members of the team to accumulate the data required to complete this particular survey (although the survey itself only took 15 minutes to complete once the data had been gathered). Further, no financial incentive was offered. Finally, almost all of the physicians targeted as respondents are in private practice, and thus have no academic infrastructure to support the collection of such data.

While the response rate achieved from the medical directors of IVF clinics was relatively high, it is important to recognize that these results may still be subject to some non-response bias given that 39% of IVF clinics did not respond to the survey. Clearly if these non-respondents differ from respondents, we cannot generalize the results of the survey to the full population of

IVF clinics in Canada. As is often the case, similarities or differences between responders and non-responders are difficult to assess, and there may be systematic differences between these two groups. For example, in relation to a scan of PGD activities in Canada, it is known to the authors and members of the committee that advised on the survey that at least one IVF unit in Canada performs embryo biopsy procedures along with genetic and molecular analysis. Our analysis suggests that any IVF unit that provides all aspects of the PGD process did not respond. Since the objective was to provide a scan of the current state of affairs of PGD in Canada, we feel it appropriate to draw attention to the likelihood of the important lack of information from such a clinic. Thus, although this report provides a fairly comprehensive description of the practices of the 17 responding clinics, including reports from a subset of these clinics on the number of patients associated with the various practices, and provides useful information about the clinics that supplied the information, it would be inappropriate to use the data to produce estimates for all of Canada.

It is of interest that the majority of PGD in Canada involves referral of embryos, blastomeres or blastocyst/trophectoderm material to another Canadian unit or to the United States for biopsy and/or cytogenetic and molecular diagnosis. Six of the 17 units who participated indicated that they did perform embryo biopsy in their unit, seven indicated that they referred embryos created in their unit to another unit in Canada for embryo biopsy, and three units referred their embryos to the United States. Although this research does not provide direct information regarding the reasons why Canadian IVF units refer their patients' embryos or related tissue to other units, one might speculate that the reasons may include lack of volume of patients requesting PGD and resulting lack of experience in embryo biopsy in most Canadian IVF units. Regionalization of PGD technology in Canada could be a way to avoid the cross

boarder transfer of embryos for embryo biopsy and cytogenetic/molecular diagnosis, as could increasing the education of Canadian clinicians and laboratory personnel regarding PGD and its technical capabilities, which may in the end allow more IVF units to offer PGD. Finally, providing information on PGD to Canadian IVF patients could add to women's choices regarding genetic testing, instead of being limited to amniocentesis and CVS. Indeed a recent Canadian citizen deliberation to create national policy on PGD suggests that Canadians see little difference between PGD and standard methods of prenatal genetic testing with regard to funding and conditions for which testing should be made available (Cox, Kazubowski-Houston & Nisker, 2009).

Although the medical directors of IVF units answered the questions regarding whether they performed embryo biopsy in their unit, or referred to another Canadian or American unit for the embryo biopsy procedure, not all the responding centres answered the questions regarding the number of patients whose embryos received biopsy in their unit or whose embryos were referred to other units for embryo biopsy. It may be that collecting this information from their records was too onerous a task.

The majority of responding centres who offer PGD utilize the services of a certified genetic counsellor for the informed choice process, about half on site and half off site. This is reassuring as there has been worry expressed that the some counsellors who are involved in the informed choice process for donor insemination and other aspects of assisted reproduction (who are generally social workers, psychologists and nurses not specifically trained in genetic counselling) might be the major source of genetic counselling regarding PGD. The results of our research indicate that genetic counselling is done by 3 of 6 health care professionals with training in genetic counseling for on-site counselling and 17 of 19 for off-site counselling.

Reflecting on why there was a good response rate from the medical directors of Canadian IVF clinics and a poor response rate from the medical directors of Canadian genetics clinics, one might hypothesize that PGD is a more important consideration for the IVF units, which daily have embryos under microscopic scrutiny, and many of whose patients, particularly due to the increasing age of women undergoing IVF (Drack, 1998; Barrett & Bocking, 2000; Elster, 2000; Adamson & Baker, 2004; Inder, Warfield, Wang, Huppi, & Volpe, 2005; Mykitiuk & Nisker, 2009), will subsequently choose to access amniocentesis or chronic villus sampling. IVF clinicians have been interested for over a decade in assisting these patients in avoiding the traumas of genetic abortion subsequent to having genetic determinations performed in the mid trimester of pregnancy (Nisker & Gore-Langton, 1995). This concern may explain that among the IVF units that indicated they do not currently offer PGD, some indicated they would be interested in doing so in the future.

One of the determinants of responses to surveys is the extent of respondent burden (time and effort) required to complete a survey (Dillman, 2007). The task of responding to this survey was challenging and time consuming in that it required clinic directors to consult other team members and/or unit records in order to provide detailed information regarding the number of patients requesting genetic analysis for particular conditions. Thus, it is fair to say that the time required to complete this survey greatly exceeded that of typical surveys sent to physicians. In spite of this, 61% of the directors of IVF clinics committed to responding to the survey. In contrast, it was suggested by communications from three directors of genetics laboratories that, as much as they would like to assist "Health Canada", they felt they did not have the time or resources to complete the survey. One director of a genetics laboratory indicated that it would be more appropriate for "Health Canada" to provide the staff to collect the information and input

the data in the genetics units than it would be for the genetics unit to dedicate their resources to such an endeavour. Such concerns were not raised by directors of IVF laboratories.

Another determinant of survey response is the salience of the topic to the targeted participants (Dillman, 2007). It is clear that the topic of PGD is a salient one for the IVF units, but perhaps not for the genetics units. The fact that topic was likely far less salient to genetics units, combined with the extensive commitment required likely came together to produce the low response rate of 39% achieved from the directors of genetics clinics.

There are other potential reasons, however, why the response rate was so much better among directors of IVF units than directors of genetics units. One might be the encouragement to complete the questionnaire at the Annual General Meeting of the Canadian Fertility and Andrology Society in November 2008 by the President of the Canadian Fertility and Andrology Society. In addition there was support from the Chair of the CFAS Medical Directors Group. Although there was support and email encouragement from the President of the Canadian Counsel of Medical Geneticists whose term ended in 2008, there was not as much opportunity for the face-to-face encouragement as occurred at the Annual General Meeting of the CFAS.

Other important reason for the lack of interest in completing the survey by directors of genetics units, might be that these units were not actively at present generally performing cytogenetic or molecular analysis of PGD embryonic tissues, or that completing the questionnaire was considered too onerous for its importance to them.

This low response rate from the directors of medical genetics units prevents us from making any meaningful conclusions about the practices of genetics clinics related to PGD. The results from responses provided by 7 genetics clinics provided as an Appendix are provided simply as an account of what this initial attempt to survey this group with the same questionnaire

used for IVF clinics produced, which may help inform a future attempt to design a survey specifically for genetics clinics. These results cannot be regarded as a valid description of genetics clinics in Canada. As a second survey is planned for obstetricians who counsel and/or perform amniocentesis or CVS, perhaps a third survey specifically for directors of genetics units, and simplified regarding particular conditions being tested for, could interest more geneticists to comment on PGD.

Although content for the questionnaire was initially informed by a survey conducted in Europe by the Institute for Prospective Technological Studies of the European Commission's Joint Research Centre, in collaboration with the European Science and Technology Observatory to describe the provision of PGD services in the European Union (Corveleyn et al., 2008), the fact that PGD has been well established in Europe for over a decade, the European questionnaire was deemed inappropriate to provide a scan of current practices and future desires particular to the practice of PGD in Canada. Further, the European survey would be time consuming if the Canadian units did not have the data required to respond to the questions in an easily accessible manner as is the case in most European clinics performing PGD, where PGD has been practised for many years and where the maintenance of accurate and up-to-date information is part of their licensure (Corveleyn et al., 2008). However, we likely did not achieve the required simplification of our survey for the Canadian context.

Further research is required to better understand why some IVF units choose to perform PGD and others do not. Additional investigation, such as by AHRC and the Medical Directors group of CFAS, is necessary to provide a better understanding in this and other areas. In addition, it is important to canvas the understanding and desires regarding PGD of the obstetricians who counsel and/or perform amniocentesis or CVS. A survey of these obstetricians,

family physicians, nurses, and counsellors who may be involved in prenatal genetic diagnosis would be important. Finally, another attempt to glean the understandings and desires of the directors of genetics units regarding PGD might be considered, using a simplified survey that would require less time to accumulate the necessary data.

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APPENDICES

Appendix I - Letter of Information

Assisted Human Reproduction Canada | Procréation assistée Canada

Preimplantation Genetic Diagnosis (PGD) and Related Genetic Counselling Activities in Canada

In partnership with the Canadian Fertility and Andrology Society, Canadian College of Medical Geneticists, Canadian Association of Genetic Counsellors, and Society of Obstetricians and Gynaecologists of Canada, Assisted Human Reproduction Canada (AHRC) has commissioned researchers at the University of Western Ontario (Drs. Jeff Nisker and Kathy Speechley) to conduct a survey of Canadian IVF clinics, genetics laboratories and genetics clinics.

You are being invited to participate in this study to collect information regarding the current and planned future practice of preimplantation genetic diagnosis (PGD) and related genetic counselling activities in Canada. Directors of IVF and genetics clinics and laboratories are being asked to complete this brief (about 15 minutes) questionnaire. We hope that your responses to the clinical, laboratory, and counselling questions will include input from relevant team members directly working in these areas. There are no known risks associated with participating in the present study. The results of this research will help Health Canada (through AHRC) plan for safe and effective delivery of health care in relation to PGD.

All information you provide will be kept strictly confidential and will be analyzed in aggregate form only and results presented in an anonymized fashion. Only a Personal Identification Number or PIN (provided below) will identify your survey. By completing and submitting this survey you indicate your consent to participate. To ensure confidentiality, the list of names and study numbers will be kept in a locked cabinet in a locked research office. Once the research has been completed, this list will be destroyed. Only Professor Speechley and the Study Coordinator, Jennifer Ryder, will have access to individual completed surveys returned. Aggregated results of the study will be distributed to partner organizations and participants (upon request).

AHRC is the federal regulatory agency responsible for protecting and promoting the health, safety, dignity and rights of Canadians who use or are born of assisted human reproduction technologies. AHRC is also responsible for promoting scientific advances that benefit Canadians, and for fostering an environment where ethical principles are applied in matters relating to assisted human reproduction.

If you have any questions about participating in this study, you may contact Professor Kathy Speechley by email at PGDstudy@uwo.ca or by telephone at 519-685-8500 ext. 52182. If you have any questions about how this study is being conducted or your rights as a research participant, you may contact the Office of Research Ethics, The University of Western Ontario at (519) 661-3036 or email at ethics@uwo.ca.

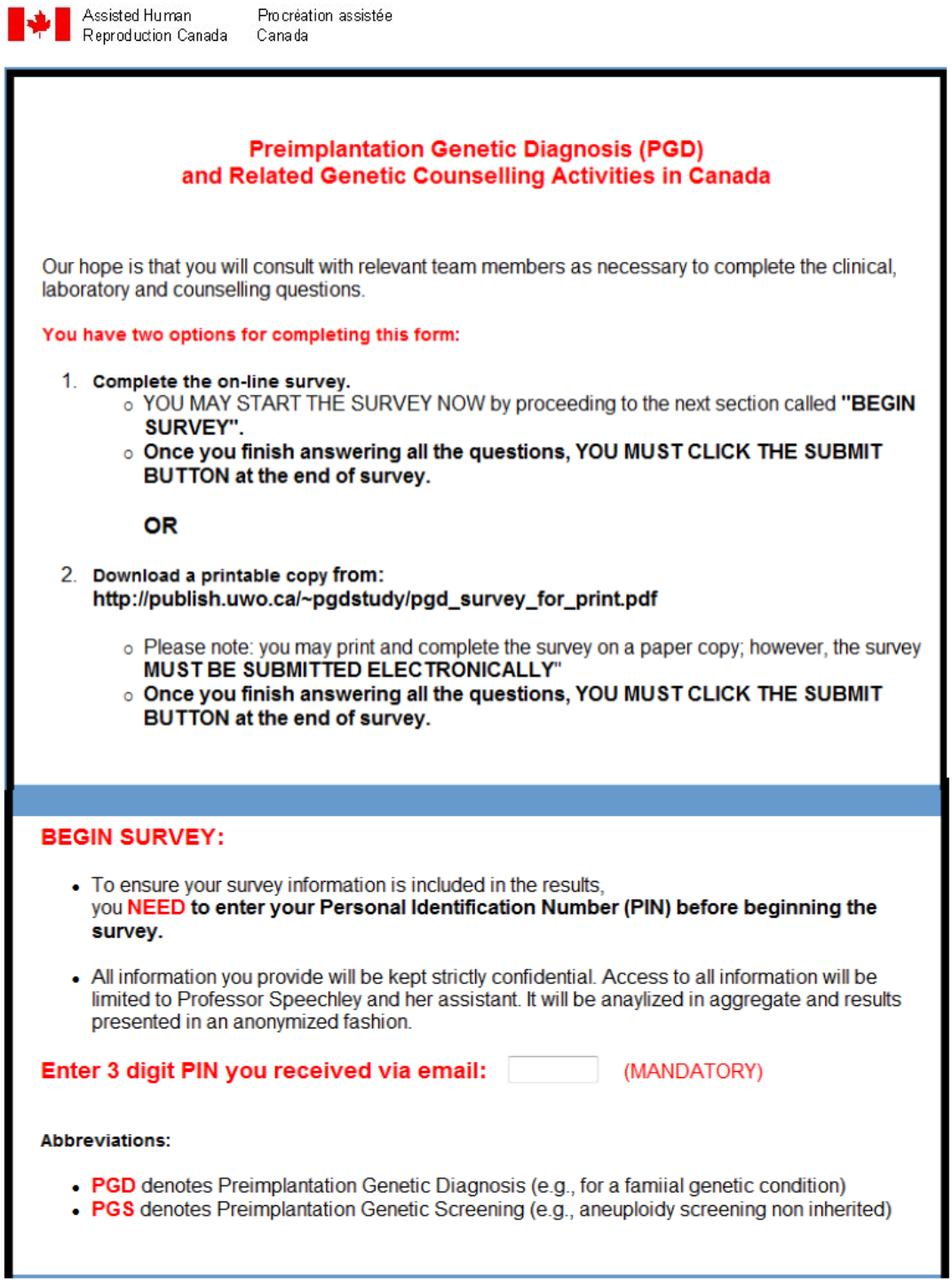
Representatives of The University of Western Ontario Health Sciences Research Ethics Board may contact you or require access to your study-related records to monitor the conduct of the

research. If the results of the study are published, your name will not be used and no information that discloses your identity will be released or published.

Access the survey directly by CTRL+ click on top of this link: http://publish.uwo.ca/~pgdstudy/
To complete the survey, enter your individual PIN: __ __ __.
Thank you for considering participating.

Sincerely,
Dr. Elinor Wilson
President, AHRC

Appendix II - Survey



Assisted Human Reproduction Canada | Procréation assistée Canada

Preimplantation Genetic Diagnosis (PGD)
and Related Genetic Counselling Activities in Canada

Our hope is that you will consult with relevant team members as necessary to complete the clinical, laboratory and counselling questions.

You have two options for completing this form:

1. **Complete the on-line survey.**
   - YOU MAY START THE SURVEY NOW by proceeding to the next section called **"BEGIN SURVEY".**
   - **Once you finish answering all the questions, YOU MUST CLICK THE SUBMIT BUTTON at the end of survey.**

   OR

2. **Download a printable copy from:**
   http://publish.uwo.ca/~pgdstudy/pgd_survey_for_print.pdf
   - Please note: you may print and complete the survey on a paper copy; however, the survey **MUST BE SUBMITTED ELECTRONICALLY"**
   - **Once you finish answering all the questions, YOU MUST CLICK THE SUBMIT BUTTON at the end of survey.**

BEGIN SURVEY:

- To ensure your survey information is included in the results, you **NEED to enter your Personal Identification Number (PIN) before beginning the survey.**
- All information you provide will be kept strictly confidential. Access to all information will be limited to Professor Speechley and her assistant. It will be anaylized in aggregate and results presented in an anonymized fashion.

Enter 3 digit PIN you received via email: (MANDATORY)

Abbreviations:

- **PGD** denotes Preimplantation Genetic Diagnosis (e.g., for a familial genetic condition)
- **PGS** denotes Preimplantation Genetic Screening (e.g., aneuploidy screening non inherited)

QUESTION 1:

Which of the following activities does your unit practice?

		NO	YES		Number of Patients: In past 5 yrs	In 2008	Anticipated in 2009
(a)	IVF	○	○	If Yes -->			
(b)	IVF & perform embryo biopsy	○	○	If Yes -->			
(c)	IVF & collect polar bodies for analysis	○	○	If Yes -->			
(d)	IVF with no PGD/PGS offered	○	○	If Yes -->			
(e)	IVF & refer to other unit in Canada for embryo biopsy	○	○	If Yes -->			
(f)	IVF & refer to unit in USA for embryo biopsy	○	○	If Yes -->			
(g)	Perform cytogenetic (e.g. familial chromosome enumeration & translocation/inversion) analysis	○	○	If Yes -->			
(h)	Perform molecular (familial gene disorder) analysis	○	○	If Yes -->			
(i)	Refer for cytogenetic analysis to another unit in Canada	○	○	In province -->			
				Out of prov. -->			
(j)	Refer for cytogenetic analysis to a unit in USA	○	○	If Yes -->			
(k)	Refer for molecular analysis to another unit in Canada	○	○	In province -->			
				Out of prov. -->			
(l)	Refer for molecular analysis to a unit in USA	○	○	If Yes -->			
(m)	Accept embryos for cytogenetic analysis	○	○	If Yes -->			
(n)	Accept embryos for molecular analysis	○	○	If Yes -->			
(o)	Accept blastomeres for cytogenetic analysis	○	○	If Yes -->			
(p)	Accept blastomeres for molecular analysis	○	○	If Yes -->			
(q)	Accept cells from blastocysts for cytogenetic analysis	○	○	If Yes -->			
(r)	Accept cells from blastocysts for molecular analysis	○	○	If Yes -->			

QUESTION 2:

If your unit performs embryo biopsy, does it do

	NO	YES
(a) Single blastomeres	○	○
(b) Two blastomeres	○	○
(c) Variation of (a) and (b)	○	○
(d) Blastocyst, trophectoderm biopsy	○	○

QUESTION 3:

	NO	YES
Does your unit recover polar bodies for analysis?	○	○

QUESTION 4:

	NO	YES
Does your unit perform genetic analysis of polar bodies?	○	○

QUESTION 5:

If your unit does not perform PDG, why not?
(Check all that apply)

- ☐ Unfamiliar with it
- ☐ No patient has requested it (no market demand)
- ☐ We would like to offer it but do not have the resources/staff/money/expertise to make it available
- ☐ PGD is considered experimental
- ☐ Not convinced it does not harm the embryo
- ☐ Not convinced it yields accurate diagnosis
- ☐ Ethical concerns about its use
- ☐ Concerned about liability
- ☐ Other

QUESTION 6:

Does your unit currently have the capacity to perform PGD testing of embryos for:

	NO	YES		
(a) Translocations	○	○	If Yes -->	☐ FISH ☐ Array CGH ☐ Other
(b) Gender testing for X linked and other conditions	○	○	If Yes -->	☐ FISH for X or Y ☐ Molecular ☐ Other
(c) Gene Disorders	○	○		
(d) HLA matching	○	○		

QUESTION 7:

Does your unit plan to perform PGD testing in the future for:

	NO	YES		
(a) Translocations	○	○	If Yes -->	☐ FISH ☐ Array CGH ☐ Other
(b) Gender testing for X linked and other conditions	○	○	If Yes -->	☐ FISH for X or Y ☐ Molecular ☐ Other
(c) Gene Disorders	○	○		
(d) HLA matching	○	○		

QUESTION 8:

What is the likelihood your unit will offer in PGD in the future?

- ○ Certain we wil offer - process is underway
- ○ Very likely
- ○ Fairly likely
- ○ Unlikely
- ○ Certain we will not offer

QUESTION 9:

Would you like to see the following services provided in Canada?

	NO	YES
(a) Embryo biopsy	○	○
(b) One cell Chromosomal enumeration and translocation/inversion testing (FISH)	○	○
(c) Gene disorder testing on blastomeres	○	○
(d) Genetic counselling with expertise in PGD	○	○

QUESTION 10:

Regarding genetic counselling and PGD, which of the following activities does your unit practice?

	NO	YES		Number of Patients: In past 5 yrs	In 2008	Anticipated in 2009
(a) Do you have genetic counselling on site	○	○				
IF YES, who does on site genetic counselling? (check all that apply) -->			Reproductive Endocrinology & Infertility (REI) physician -->			
			Nurse -->			
			Counsellor -->			
			Certified genetic counsellor -->			
			MD geneticist -->			

	NO	YES		Number of Patients: In past 5 yrs	In 2008	Anticipated in 2009
IF YES, is it recommended to all patients considering PGD?	○	○				
(b) Do you provide on site genetic counselling other than PGD?	○	○	If Yes -->			

	NO	YES		Number of Patients: In past 5 yrs	In 2008	Anticipated in 2009
(c) Do you refer off site for genetic counselling? (check all that apply) -->			Reproductive Endocrinology & Infertility (REI) physician -->			
			Nurse -->			
			Counsellor -->			
			Certified genetic counsellor -->			
			MD geneticist -->			

QUESTION 11:

Does your unit perform preimplantation genetic screening (PGS) for aneuploidy and/or plan to in the future?

		CURRENTLY			PLAN TO IN FUTURE		
		No	On Request	Routinely	No	On Request	Routinely
(a)	Of polar bodies	○	○	○	○	○	○
(b)	Of embryos	○	○	○	○	○	○
(c)	For women with recurrent pregnancy loss	○	○	○	○	○	○
(d)	For women over 35 years of age	○	○	○	○	○	○
(e)	For all women	○	○	○	○	○	○

QUESTION 12:

Does your unit freeze post PGD embryos that are not at risk of the condition?

- ○ No
- ○ Yes If Yes --> ☐ For clinical purposes
  ☐ For research purposes

QUESTION 13:

Does your unit freeze PGD embryos that ARE at risk of the condition?

- ○ No
- ○ Yes If Yes --> ☐ For clinical purposes
  ☐ For research purposes

QUESTION 14:

Does your unit confirm PGD finding by amniocentesis/CVS:

- ○ Recommended
- ○ Suggested
- ○ Varies according to situation
- ○ Not mentioned

QUESTION 15:

How often are patients referred to your genetics clinic specifically for counselling about PGD or PGS?

	PGD	PGS
Not applicable as my primary unit is not a genetics unit	○	○
Less than once per year	○	○
1-5 times per year	○	○
6-10 times per year	○	○
11-20 times per year	○	○
21-50 times per year	○	○
>50 times per year	○	○

QUESTION 16:

How often do patients request or inquire about PGD during a general genetics clinic appointment?
(Check one response that best describes your unit.)

Not applicable as my primary unit is not a genetics unit	○
Less than once per year	○
1-5 times per year	○
6-10 times per year	○
11-20 times per year	○
21-50 times per year	○
>50 times per year	○

QUESTION 17:

In your opinion, what percentage of patients who inquire actually pursue PGD or PGS?

	PGD	PGS
Less than 25%	○	○
26 – 50%	○	○
51-75%	○	○
More than 75%	○	○

QUESTION 18:

In your opinion what are the main reasons patients who are interested in PGD or PGS do NOT pursue it?
(Check all that apply.)

	PGD	PGS
Not available locally	☐	☐
Too expensive	☐	☐
Low chance of successful pregnancy outcome	☐	☐
Other, please specify	For PGD:	
	For PGS:	

QUESTION 19:

When are patients offered genetic counselling?
(Check all that apply.)

- ☐ Before PGD/PGS
- ☐ After PGD/PGS
- ☐ Never

QUESTION 20:

How often do patients request or inquire during a general genetics clinic appointment about PGS?

- ○ Not applicable as my primary unit is not a genetics unit
- ○ Less than once per year
- ○ 1-5 times per year
- ○ 6-10 times per year
- ○ 11-20 times per year
- ○ 21-50 times per year
- ○ >50 times per year

QUESTION 21: (THIS IS THE LAST QUESTION!)

Please indicate which of the following YOUR UNIT has done or plans to in the future?

	HAS DONE		PLANS TO IN THE FUTURE	
	NO	YES	NO	YES
(a) Translocations	○	○	○	○
(b) Gender testing for X linked	○	○	○	○
(c) Gender testing for other conditions	○	○	○	○

	HAS DONE		PLANS TO IN THE FUTURE	
	NO	YES	NO	YES
(d) Recessive monogenic conditions	○	○	○	○

IF YES, check all that apply

	HAS DONE	PLANS TO IN THE FUTURE
-->	☐ Cystic Fibrosis	☐ Cystic Fibrosis
	☐ β-thalassemia	☐ β-thalassemia
	☐ Sickle cell disease	☐ Sickle cell disease
	☐ Spinal Muscular Atrophy	☐ Spinal Muscular Atrophy
	☐ Steinert Myotonic Dystrophy	☐ Steinert Myotonic Dystrophy
	☐ Charcot-Marie-Tooth disease	☐ Charcot-Marie-Tooth disease
	☐ Fragile X syndrome	☐ Fragile X syndrome
	☐ Haemophilia A/B genes	☐ Haemophilia A/B genes
	☐ Duchenne/Becker Muscular Dystrophy	☐ Duchenne/Becker Muscular Dystrophy
	☐ Other, please specify	☐ Other, please specify

	HAS DONE		PLANS TO IN THE FUTURE	
	NO	YES	NO	YES
(e) Adult-onset conditions	○	○	○	○

IF YES, check all that apply

	HAS DONE	PLANS TO IN THE FUTURE
-->	☐ Huntington's	☐ Huntington's
	☐ BRCA 1 or 2	☐ BRCA 1 or 2
	☐ Alzheimer's	☐ Alzheimer's
	☐ Other, please specify	☐ Other, please specify

	HAS DONE		PLANS TO IN THE FUTURE	
	NO	YES	NO	YES
(f) HLA Matching	○	○	○	○

IF YES, check all that apply

	HAS DONE	PLANS TO IN THE FUTURE
-->	☐ in combination with genetic testing	☐ in combination with genetic testing
	☐ in absence of heritable mutation	☐ in absence of heritable mutation

Now that you have answered the questions on this paper copy:

1. **You must return to the webpage that contains the on-line version of the survey. (http://publish.uwo.ca/~pgdstudy/)**
2. Enter your "paper copy" answers on the on-line form.
3. Once you are finished completing the on-line form, **CLICK THE SUBMIT BUTTON** at the end of the survey, so that we get the results.

Thank you for taking the time to complete the survey.

Appendix III - Results for Genetics Clinics

Table III-1(Q1): Which of the following activities does your clinic practice?

	n	%		# of Patients (range)		
				Past 5 Years	2008	2009 (anticipated)
aIVF	1	14		850 n=1	170 n=1	170 n=1
b IVF & perform embryo biopsy	0	0				
cIVF & collect polar bodies for analysis	0	0				
d IVF with no PGD/PGS offered	0	0				
e IVF & refer to other unit in Canada for embryo biopsy	0	0				
f IVF & refer to unit in USA for embryo biopsy	0	0				
g Perform cytogenetic (e.g., familial chromosome enumeration & translocation/inversion) analysis	6	86		1094, 5549 n=2	1158-3200 n=3	1200, 2100 n=2
h Perform molecular (familial gene disorder) analysis	4	57		7267 n=1	1434, 5000 n=2	1500 n=1
i Refer for cytogenetic analysis to another unit in Canada	1	14	In prov.	0 n=1	0 n=1	0 n=1
			Out of prov.	38 n=1	23 n=1	20 n=1
j Refer for cytogenetic analysis to a unit in USA	3	43		140, 1227 n=2	100, 584 n=2	100, 600 n=2
k Refer for molecular analysis to another unit in Canada	6	86	In prov.	0-50 n=3	0-10 n=3	0-10 n=3
			Out of prov.	700, 875 n=2	200, 315 n=2	200, 350 n=2
l Refer for molecular analysis to a unit in USA	5	71		750, 870 n=2	220, 310 n=2	220, 340 n=2
m Accept embryos for cytogenetic analysis	0	0				
n Accept embryos for molecular analysis	0	0				
o Accept blastomeres for cytogenetic analysis	0	0				
p Accept blastomeres for molecular analysis	0	0				
q Accept cells from blastocysts for cytogenetic analysis	0	0				
r Accept cells from blastocysts for molecular analysis	0	0				

Table III-2(Q5): If your unit does not perform PGD, why not?

	n	%
Unfamiliar with it PGD is considered experimental	2	29
No patient has requested it (no market demand)	2	29
We would like to offer it but do not have the resources/staff/money/expertise to make it available	1	14
PGD is considered experimental	--	--
Not convinced it does not harm the embryo	--	--
Not convinced it yields accurate diagnosis	0	0
Ethical/moral concerns about its use	--	--
Concerned about liability	--	--
Other	5	71

Table III-3 (Q6): Does your unit currently have the capacity to perform PGD testing for embryos for:

		n	%
Translocations			
	Yes	1*	14
	No	4	57
	Blank	2	29
Gender testing for X linked & other conditions			
	Yes	1**	14
	No	4	57
	Blank	2	29
Gene Disorders			
	Yes	0	0
	No	5	71
	Blank	2	29
HLA matching			
	Yes	0	
	No	5	
	Blank	3	

*type of analysis not provided
** FISH

Table III-4 (Q7): Does your unit plan to perform PGD testing in the future for:

		n	%
Translocations			
	Yes	0	0
	No	6	86
	Blank	1	14
Gender testing for X linked & other conditions			
	Yes	0	0
	No	6	86
	Blank	1	14
Gene Disorders			
	Yes	0	0
	No	6	86
	Blank	1	14
HLA matching			
	Yes	0	0
	No	6	86
	Blank	1	14

Table III-5 (Q8): What is the likelihood your unit will offer PGD in the future?

	n	%
Certain we will offer- Process underway	0	0
Very likely	0	0
Fairly likely	0	0
Unlikely	4	57
Certain we will not offer	3	43

Table III-6 (Q9): Would you like to see the following services provided in Canada?

	n	%
Embryo biopsy	6	86
One cell Chromosomal enumeration and translocation/inversion testing (FISH)	6	86
Gene disorder testing on blastomeres	6	86
Genetic counselling with expertise in PGD	7	100

Table III-7 (Q10a): For 7 genetics centres providing genetic counselling on site, type of provider and number of patients

			# of patients (range)		
Provider	n	%	Past 5 years	2008	2009 (anticipated)
Reproductive endocrinology and infertility (REI) physician			--	--	--
Nurse	2	29	434 n=1	100 n=1	100 n=1
Counsellor	3	43	--	--	--
Certified genetic counsellor	6	86	100, 2419 n=2	25, 588 n=2	25, 630 n=2
MD geneticist	6	86	200, 5090 n=2	75, 1349 n=2	100, 1500 n=2

Of the 7 genetics centres that completed the survey, 5 reported that counselling is recommended to all patients considering PGD and 2 did not respond to this question.

Table III-8 (10b): Provision of on site genetic counselling other than PGD by Genetics Centres

			# of patients (range)		
	n	%	Past 5 years	2008	2009 (anticipated)
Yes	7	100			
No	0	0	7944	1400-4000	1400-4500
Blank	0	0	N=1	n=3	n=3

Table III-9 (Q10c): Provision of genetic counsellng off site by type of provider and number of patients

Provider	n	%	# of patients (range)		
			Past 5 years	2008	2009 (anticipated)
Reproductive endocrinology and infertility (REI) physician			--	--	--
yes	0	0			
no	5	71			
blank	2	29			
Nurse			--	--	--
yes	0	0			
no	4	57			
blank	3	43			
Counsellor			--	--	--
yes	0	0			
no	4	57			
blank	3	43			
Certified genetic counsellor			--	--	--
yes	1	14			
no	3	43			
blank	3	43			
MD geneticist			--	--	--
yes	1	14			
no	3	43			
blank	3	43			

Table III-10 (Q14): Does your unit confirm PGD finding by amniocentesis/CVS?

	n	%
Recommended	3	43
Suggested	0	0
Varies according to situation	1	14
Not mentioned	0	0
Blank	3	43

Table III-11 (Q15): How often are patients referred to your genetics clinic specifically for counselling about PGD or PGS?

	PGD		PGS	
	n	%	n	%
Not applicable as my primary unit is not a genetics unit	0	0	0	0
Less than once per year	1	14	3	43
1-5 times per year	3	43	0	0
6-10 times per year				
11-20 times per year	1	14		
21-50 times per year				
>50 times per year				
Blank	2	29	4	57

Table III-12 (Q16): How often do patients request or inquire about PGD during a genetics clinic appointment?

	PGD	
	n	%
Not applicable as my primary unit is not a genetics unit		
Less than once per year		
1-5 times per year	2	29
6-10 times per year	1	14
11-20 times per year	2	29
21-50 times per year		
>50 times per year	1	14
Blank	1	14

Table III-13 (Q17): In your opinion, what percentage of patients who inquire actually pursue PGD or PGS?

	PGD		PGS	
	n	%	n	%
Less than 25%	6	86	4	57
26-50%	0	0		
51-75%	0	0	0	0
More than 75%				
Blank	1	14	3	43

Table III-14 (Q18): In your opinion what are the main reasons parents who are interested in PGD or PGS do NOT pursue it?*

	PGD		PGS	
	n	%	n	%
Not available locally	4	57	3	43
Too expensive	5	71	3	43
Low chance of successful pregnancy outcome	3	43	2	29

* Multiple responses allowed

Table III-15 (Q19): When are patients offered genetic counselling?*

	n	%
Before PGD/PGS	5	71
After PGD/PGS	1	14
Never		

Multiple responses allowed

Table III-16 (Q20): How often do patients request or inquire during a general genetics clinic appointment about PGS?

	n	%*
Not applicable as my primary unit is not a genetics unit		
Less than once per year	4	57
1-5 times per year	1	14
6-10 times per year		
11-20 times per year		
21-50 times per year	1	14
>50 times per year		
Blank	1	14

* Percentages that do not add to 100% are due to rounding.

Table III-17 (Q21a-c): Please indicate which of the following YOUR UNIT has done or plans to do in the future?

		Has Done		Plans to in the Future	
		n	%	n	%*
Translocations					
	Yes	4	57	3	43
	No	2	29	2	29
	Blank	1	14	2	29
Gender testing for X linked					
	Yes	4	57	3	43
	No	2	29	1	14
	Blank	1	14	3	43
Gender testing for other conditions					
	Yes	2	29	1	14
	No	4	57	3	43
	Blank	1	14	3	43

* Percentages that do not add to 100% are due to rounding.

Table III-18 (Q21d): Please indicate which of the following YOUR UNIT has done or plans to do in the future?

	Has Done		Plans to in the Future	
	n	%	n	%
Recessive monogenic conditions				
Yes	4	57	2	29
No	2	29	2	29
Blank	1	14	3	43
If Yes…				
Cystic Fibrosis	3	43	2	29
B-thalassemia	1	14	1	14
Sickle cell disease	1	14	1	14
Spinal Muscular Atrophy	3	43	2	29
Steinert Myotonic Dystrophy	3	43	2	29
Charcot-Marie-Tooth disease	2	29	1	14
Fragile X syndrome	3	43	2	29
Haemophilia A/B genes	1	14	1	14
Duchenne/Becker Muscular Dystrophy	2	29	2	29
Other	2	29	1	14

Table III.19 (Q21e): Please indicate which of the following YOUR UNIT has done or plans to do in the future?

	Has Done		Plans to in the Future	
	n	%	n	%*
Adult-onset conditions				
Yes	3	43	2	29
No	3	43	2	29
Blank	1	14	3	43
If Yes…				
Huntington's	2	29	2	29
BRCA 1 or 2	2	29	1	14
Alzheimer's	1	14	1	14
Other	1	14	1	14

* Percentages that do not add to 100% are due to rounding.

Table III-22: Please indicate which of the following YOUR UNIT has done or plans to do in the future? (Q21f)

	Has Done		Plans to in the Future	
	n	%	n	%*
HLA Matching				
Yes	2	29	2	29
No	3	43	2	29
Blank	2	29	3	43
If Yes…				
In combination with genetic testing	2	29	2	29
In absence of heritable mutation	1	14	1	14

* Percentages that do not add to 100% are due to rounding.