



www.sciencedirect.com
www.rbmsociety.com



ORIGINAL ARTICLE

Impact of government health coverage for ART: The results of a 5-year experience in Quebec

F. Bissonnette^{a,b}, S. Phillips^{a,b,*}, J. Sampalis^c, E.M. Dahdouh^{b,d},
P. St-Michel^e, W. Buckett^{c,f}, I.J. Kadoch^{a,b}, N. Mahutte^g

^a Clinique OVO, Montreal, Quebec, Canada; ^b University of Montreal, Montreal, Quebec, Canada; ^c McGill University, Montreal, Quebec, Canada; ^d ART Center, CHU Sainte-Justine, Montreal, Quebec, Canada; ^e Procrea Clinics, Quebec, Canada; ^f MUHC Reproductive Centre, Montreal, Quebec, Canada; ^g The Montreal Fertility Centre, Montreal, Quebec, Canada

Corresponding author. E-mail address: s.phillips@cliniqueovo.com (S. Phillips).



Dr Francois Bissonnette is the Medical Director of OVO, a fertility clinic in Montreal, and a Professor in the Department of Obstetrics-Gynecology at the University of Montreal. He completed his specialty training in obstetrics and gynaecology in 1980, and was certified by the Royal College of Physicians and Surgeons of Canada in 1985. He was subsequently trained in reproductive endocrinology and infertility at the University of Louisville, Kentucky. He is a past President of the Canadian Fertility and Andrology Society, and is currently Director of the Canadian ART Registry.

Abstract An analysis of national registry data for 5 years of in-vitro fertilization (IVF) funding in Quebec, Canada was compared with the previous complete year of non-funded IVF cycles, as well as the first complete year following the end of funding. The number of cycles, livebirth rates, age group of patients treated, use of donor gametes, multiple pregnancy rates and cycle cancellation rates were assessed. The total number of IVF cycles performed increased dramatically during the funded period, averaging over 10,000 cycles per year. There was no change in the age group distribution of patients treated, but less egg donation was performed. Interestingly, funding was also associated with an increase in the IVF cycle cancellation rate (17.0% versus 34.4%, $P < 0.001$), a dramatic decline in the multiple pregnancy rate (25.6% versus 4.9%, $P < 0.001$), and a decline in the livebirth rate per fresh embryo transfer in stimulated IVF cycles (32.3% versus 25.5%, $P < 0.001$). Although the livebirth rate for stimulated IVF declined, over 9000 babies were born as a result of the coverage. Lessons learned from this experience could help develop a more fiscally responsible programme that still facilitates access to IVF care.

© 2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

KEYWORDS: IVF, public funding, multiple pregnancy rates

<https://doi.org/10.1016/j.rbms.2019.01.002>

2405-6618 © 2019 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

In August 2010, the Provincial Government of Quebec introduced public coverage for assisted reproductive technology (ART) treatment (*Gazette Officielle du Québec, 2010*). In parallel, the number of embryos that could be transferred was controlled. The law encouraged single embryo transfer (SET) in all cases, but permitted up to two embryos in women aged ≤ 36 years and up to three embryos in women aged ≥ 37 years. The results of the first few months of the programme demonstrated a dramatic decrease in the multiple pregnancy rate due to the increased use of elective SET (*Bissonnette et al., 2011*). The law covered ART treatment for all residents of Quebec via the provincial health plan. There were no exclusion criteria in terms of age, previous history of tubal ligation/vasectomy, previous pregnancies, sexuality or marital status. The coverage provided for three stimulated in-vitro fertilization (IVF) cycles including medication, along with any associated procedures such as surgical sperm retrieval or donor semen, and the frozen embryo transfers (FET) resultant from those egg retrievals. Any frozen embryos had to be used before further ovarian stimulation could be undertaken. Egg donation was covered if the egg donor herself was a holder of a valid Quebec health card, but obtaining donor eggs from out of province or from an egg bank was not covered.

An IVF cycle only counted towards the three attempts if an embryo transfer occurred. Therefore, any cycles cancelled prior to embryo transfer (poor ovarian stimulation, no eggs at retrieval, failed fertilization or no high-quality embryos available for transfer) were not counted. Furthermore, a successful live birth reset the counter.

After a little more than 5 years of operation, on 15 November 2015, the programme was terminated (*Gazette Officielle du Québec, 2015*). A new law removed the coverage of IVF, except in the case of fertility preservation for oncologic reasons, although only ovarian stimulation, oocyte retrieval and cryopreservation remained covered; fertilization by intracytoplasmic sperm injection, embryo culture and future use of the cryopreserved material were not included. Furthermore, the law increased restrictions on embryo transfer, mandating SET for all women aged < 37 years, while permitting two embryos to be transferred in patients aged ≥ 37 if written justification was provided in the patient file. In sharp contrast to IVF, intrauterine insemination (IUI) was covered to a maximum of nine attempts, including medication, monitoring, semen preparation and insemination. The purchase of donor semen for IUI was no longer covered.

Materials and methods

In Canada, professionals working in the field of assisted human reproduction meet under the auspices of the Canadian Fertility and Andrology Society (CFAS). Since 2000, CFAS has managed a registry of ART cycles performed across the country [Canadian Assisted Reproductive Technology Registry (CARTR)]. Since 2014, CARTR has been managed by the Better Outcomes Registry Network (BORN) Ontario. BORN is the province of Ontario's registry for births within the province. Although based in one province, for the ART registry, BORN manages the data from all IVF clinics across Canada. BORN does not receive any

patient identifying information from provinces other than Ontario, and is managed by very strict privacy regulations.

Data from CARTR-BORN is available upon request for research purposes. There was no direct patient involvement in this study and data were already anonymized: as such, no ethical approval was required according to Canadian Institutes of Health Research policy on ethical conduct for research involving humans. This study used CARTR-BORN data from August 2010 until November 2015, representing the period when ART was covered under Quebec provincial health insurance, and from 2009 and 2016 to compare data from years either side of the coverage when ART was within the private domain.

Data are reported as livebirth rates per embryo transfer. During the 64 months of the programme, in addition to the live births that were reported to clinics, there were an additional 1310 clinical pregnancies for which the livebirth data were not reported by patients. As these pregnancies were confirmed by ultrasound at the clinics, a 15% loss of pregnancy (*Avalos et al., 2012*) was assumed, and the remaining 85% of these lost-to-follow-up clinical pregnancies were added to the livebirth data. There were 27 similar cases in 2009 and 124 cases in 2016, of which 85% were also included in the livebirth data.

Statistical analysis was performed using Chi-squared test, and the result was considered to be significant when $P < 0.05$. No funding was obtained for this study.

Ethical approval was not required for this study according to the Canadian Tri-council Policy Statement on Ethical Conduct for Research Involving Humans, as data were obtained from a centralized anonymized databank.

Results

The total number of cycles performed per year increased dramatically once the programme became established (see *Fig. 1*). Interestingly, however, the proportion of patients treated by age was not affected by the availability of insured IVF treatments (see *Fig. 2*). The number of fresh IVF cycles started decreased dramatically in 2016, while the number of frozen-thaw cycles started remained relatively stable in 2016. It is important to note that upon termination of the programme in November 2015, all patients with

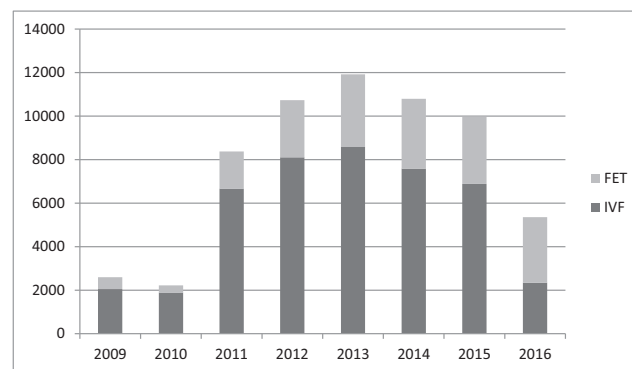


Fig. 1 Number of cycles of in-vitro fertilization (IVF) and frozen embryo transfers (FET) started per year in the province of Quebec.

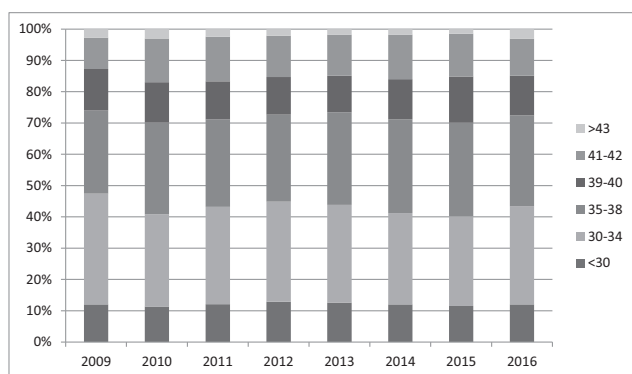


Fig. 2 Proportion of in-vitro fertilization (IVF) and frozen embryo transfer (FET) cycles by patient age over time in the province of Quebec.

cryopreserved embryos in storage from the programme still had coverage for their FET cycles until a pregnancy was obtained. In addition, all patients with a valid prescription for IVF obtained prior to 15 November 2015 were also covered for their fresh IVF attempt and all FET cycles as a result of that attempt. Thus, despite the change in the law, some fresh and frozen–thaw cycles performed in 2016 remained covered.

The overall cancellation rate for fresh IVF cycles increased from 17% in 2009/2016 (combined) to 34.4% during the programme ($P < 0.001$) (Table 1).

Use of donor gametes

During the funded period, the percentage of IVF cycles that were combined with donor sperm decreased (8.2% versus 6.2%, $P < 0.001$). The use of donor eggs in IVF also declined significantly during the insured period (4.5% versus 2.4%, $P < 0.001$), and this reduction was seen for all age groups.

Livebirth rates

The overall livebirth rate per fresh embryo transfer decreased during the funded period compared with 2009/2016 (33.9% versus 23.7% between 2010 and 2015, $P < 0.001$) (Table 2). Although significant for both fresh and frozen IVF cycles, the absolute percentage point decline was greater in fresh cycles. The complete results for stimulated cycles, natural modified cycles and FET cycles broken down by age are presented in Tables 3–5. The reduction in the livebirth rate per transfer for fresh embryo transfer following IVF with

ovarian stimulation was significant in all age groups except for 39–40 years (Table 3).

There were 9232 live births between 2010 and 2015, and although the multiple pregnancy rate was reduced significantly by the programme, as reported previously (Bissonnette et al., 2011), a small proportion of these live births involved the birth of more than one baby. Overall, more than 9232 babies were born as a result of the programme.

Use of single embryo transfer

As should be expected from a programme twinned with legislation controlling the number of embryos to be transferred, the use of SET in stimulated IVF cycles and FET cycles increased significantly (Table 6) when comparing 2009 with 2010–2015 (IVF 9.2% versus 64.3%, $P < 0.0001$; FET 10.0% versus 73.5%, $P < 0.0001$). Moreover, because the change in coverage in 2015 coincided with even tighter restrictions on the number of embryos that could be transferred, the use of SET increased further in 2016 (IVF 71.5%, FET 86.7%). Not surprisingly, there was no difference in the use of SET in the natural cycle IVF groups. Coincident with increased use of SET, the multiple pregnancy rate decreased from 25.6% in 2009 to 3.3–7% during the years of the programme, and was 4.5% in 2016 during the return to privately funded cycles (Table 7).

Discussion

There was an enormous increase in the number of cycles performed during the insured period, with total cycle numbers reaching close to 12,000 in 2013, and averaging over 10,000 per year. This represented a five-fold increase compared with the number of cycles performed in 2009, despite the fact that the proportion of patients in each age group did not change. However, this coincided with a reduction in the livebirth rate per transfer during the funded period.

Interestingly, this occurred despite an increase in the cycle cancellation rate. Although it is possible that the dramatic increase in the number of cycles performed without time to effectively increase capacity may have initially stressed the ability of IVF centres to expand and continue to provide the same high-level care, the types of patients seeking treatment also changed. Funding altered the balance between the cost of trying another cycle and the probability that the next cycle might succeed. Increasingly, patients with a poor prognosis returned for another cycle rather than considering alternatives, such as egg donation or adoption. Moreover, because government funding applied separately to ovarian stimulation, egg collection and embryo transfer, both patients and IVF centres had no real disincentive to start IVF cycles even if they were cancelled prior to retrieval, or cancelled after

Table 1 Cancellation rates of fresh in-vitro fertilization cycles between the insured period (2010–2015) and pre/post insured years (2009 and 2016).

		2009	2016	2009 and 2016	2010–2015	P-value
Overall	Total cycles started	2055	5353	7408	39,722	<0.001
	Cycles completed	1769	4380	6149	26,064	
	%	13.9%	18.2%	17.0%	34.4%	

Table 2 Livebirth rates per embryo transfer (ET) for in-vitro fertilization (IVF), modified natural cycle IVF and frozen embryo transfers (FET) between the insured period (2010–2015) and pre/post insured years (2009 and 2016) in the province of Quebec.

		2009	2016	2009 and 2016	2010–2015	P-value
IVF	Total ET	1725	1398	3123	23,765	<0.001
	<i>n</i> live births	616	395	1011	6066	
	%	35.7%	28.3%	32.3%	25.5%	
Natural IVF	Total ET	44 ^a	37 ^a	81 ^a	2062 ^a	0.03
	<i>n</i> live births	16	13	29	520	
	%	36.4%	35.2%	35.8%	25.2%	
FET	Total ET	492	2938	3430	12,924	<0.001
	<i>n</i> live births	109	765	874	2824	
	%	22.2%	26.1%	25.5%	21.9%	
Overall	Total ET	2261	3373	5634	38,955	<0.001
	<i>n</i> live births	741	1163	1904	9232	
	%	32.8%	34.5%	33.9%	23.7%	

^a <38 years old.

retrieval. Thus, it was not unusual for patients with a poor prognosis to initiate multiple stimulated IVF attempts before finally completing all of their funded embryo transfers.

The impact on the success rate per transfer in FET cycles is interesting. The data show that the proportion of SET increased even more for FET cycles than fresh IVF cycles. From 2009 to 2016, the use of blastocyst transfer increased. Coupled with the fact that cryopreservation was included in the overall cycle reimbursement, the years 2010–2015 saw more selective use of embryo cryopreservation and higher subsequent cryo–thaw transfer success rates. These factors may have mitigated the negative impact of funding on the success rates of frozen–thaw cycles compared with fresh cycles.

In terms of the use of donor gametes within IVF cycles, a decrease in donor egg use during the programme was noted for all patient age groups. In terms of the use of donor eggs in

Canada, it is important to note that, under Federal law, it is illegal to reimburse donors for their donation, and therefore almost all gametes from egg and sperm banks come from the USA. Although in the funded years, the purchase of donor sperm was covered by the programme, the purchase of donor eggs was not. Thus, those patients who may have most benefited from donor eggs had little to lose by attempting an IVF cycle using their own eggs, even when their prognosis was very poor. In a private setting, those patients may have chosen to put their money towards egg donation rather than spend it on an autologous attempt with a poor prognosis. As the data demonstrate, relatively few patients chose to spend additional money on treatments that were not covered in addition to or in place of the funded treatments. In terms of treatment age, although the law did not impose a maximum age limit, the clinics, using historical data from CARTR-BORN, applied a

Table 3 Livebirth rates per embryo transfer (ET) using in-vitro fertilization with ovarian stimulation between the insured period (2010–2015) and pre/post insured years (2009 and 2016) in the province of Quebec.

		2009	2016	2009 and 2016	2010–2015	P-value
<30 years	Total ET	197	144	341	2708	<0.001
	<i>n</i> live births	93	60	153	968	
	%	47.2%	41.7%	44.9%	35.7%	
30–34 years	Total ET	586	389	975	6754	<0.001
	<i>n</i> live births	246	140	386	2260	
	%	42.0%	36.0%	39.5%	33.5%	
35–38 years	Total ET	483	402	885	6732	<0.001
	<i>n</i> live births	179	117	296	1760	
	%	37.1%	29.1%	33.4%	26.1%	
39–40 years	Total ET	236	210	446	3288	0.12
	<i>n</i> live births	53	42	95	600	
	%	22.5%	20.0%	21.3%	18.2%	
41–43 years	Total ET	181	209	390	3839	0.017
	<i>n</i> live births	32	25	57	409	
	%	17.7%	12.0%	14.6%	10.7%	
Overall	Total ET	1725	1398	3123	23,765	<0.001
	<i>n</i> live births	616	395	1011	6066	
	%	35.7%	28.3%	32.4%	25.5%	

Table 4 Livebirth rates using in-vitro fertilization in a modified natural cycle between the insured period (2010–2015) and pre/post insured years (2009 and 2016) in the province of Quebec.

		2009	2016	2009 and 2016	2010–2015	P-value
<30 years	Total ET	10	1	11	316	0.76
	<i>n</i> live births	3	1	4	101	
	%	30.0%	100%	36.4%	32.0%	
30–34 years	Total ET	21	14	35	965	0.03
	<i>n</i> live births	10	5	15	253	
	%	47.6%	35.7%	42.9%	26.2%	
35–38 years	Total ET	13	22	35	781	0.3
	<i>n</i> live births	3	7	10	166	
	%	23.1%	31.8%	28.6%	22.2%	
Overall	Total ET	44	37	81	2062	0.03
	<i>n</i> live births	16	13	29	520	
	%	36.4%	35.2%	35.8%	25.2%	

ET, embryo transfers.

soft cut-off of 43 years of age for autologous IVF, so an increase in the use of donor eggs is seen after this age (49.2% of IVF cycles).

We have previously reported on the reduction in cost per live birth during the programme compared with previous years where a 50% tax deduction was possible in Quebec (Velez et al., 2014). It is important to note that the cost of the programme was the major reason cited for its untimely end. Although it is difficult to obtain precise details on the annual costs, they were widely presented in the media as being between \$CAN 70 and 80 million per year. If one considers that the average lifetime contribution of an individual in terms of income tax in the province of Quebec is approximately \$CAN 330,000 (StatsCanada), it can be

estimated that the 9232+ babies born as a result of the programme will contribute over \$CAN 3 billion. Therefore, at a cost of \$CAN 400 million over the 5.5 years, it suggests that, in purely financial terms, the Provincial Government of Quebec achieved close to an eight-fold return on their investment.

The design of the coverage encouraged the cancellation of cycles as only a cycle resulting in an embryo transfer counted towards the three insured cycles per patient. This is clearly demonstrated by the significant increase in cycle cancellations in all age groups. This clearly had an important impact on results as well as financially on the programme. Such a design leads to aggressive rejection of suboptimal embryos since the concept that a better outcome can be achieved in a future

Table 5 Livebirth rates using frozen embryo transfers between the insured period (2010–2015) and pre/post insured years (2009 and 2016) in the province of Quebec.

		2009	2016	2009 and 2016	2010–2015	P-value
<30 years	Total ET	77	352	429	1754	0.02
	<i>n</i> live births	15	106	121	403	
	%	19.5%	30.1%	28.2%	23.0%	
30–34 years	Total ET	194	899	1093	4388	0.04
	<i>n</i> live births	47	262	309	1105	
	%	24.2%	29.1%	28.3%	25.2%	
35–38 years	Total ET	119	904	1023	3797	0.004
	<i>n</i> live births	28	241	269	838	
	%	23.5%	26.7%	26.3%	22.1%	
39–40 years	Total ET	51	301	356	1406	0.003
	<i>n</i> live births	11	73	84	236	
	%	21.6%	24.3%	23.6%	16.8%	
41–43 years	Total ET	34	333	367	1201	0.8
	<i>n</i> live births	3	49	52	164	
	%	8.8%	14.7%	14.1%	13.7%	
Overall	Total ET	492	2938	3430	12,924	<0.001
	<i>n</i> live births	109	765	874	2824	
	%	22.2%	26.0%	25.5%	21.9%	

ET, embryo transfers.

Table 6 Proportion of use of single embryo transfers (SET) between 2009 and 2010–2015 in the province of Quebec.

		2009	2010–2015	2016	P-value
IVF	Total ET	1769	26,064	1398	<0.001
	SET	163	16,766	999	
	%	9.2%	64.3%	71.5%	
Natural IVF	Total ET	44	2299	44	0.53
	SET	42	2251	44	
	%	95.0%	97.9%	100%	
FET	Total ET	492	12,924	2938	<0.001
	SET	49	9496	2546	
	%	10.0%	73.5%	86.7%	

IVF, in-vitro fertilization; FET, frozen embryo transfers; ET, embryo transfers.

cycle leads to the desire to maximize the use of the three available embryo transfers. Furthermore, it creates pregnancy and livebirth rate per cycle data that are not comparable with other studies. Undoubtedly counting a cycle from the start of ovarian stimulation or egg collection would reduce cancellation rates. Data from 2016, when the cancellation rate returned to <20%, confirms that this increased cancellation rate was associated directly with the funding design, and not, as could have been hypothesized, by development of new technologies such as time lapse or pre-implantation genetic testing for aneuploidy which tend to 'deselect' embryos and can result in increased cancellation.

There is substantial variation from country to country regarding IVF funding. A survey of patients, professionals and the general public in Germany concluded that the majority of people supported public coverage of IVF. However, the concept of patient co-payments varied depending on which group was interviewed: 33% of patients agreed with this idea compared with 75% of professionals and the general public. At the time of publication, patients contributed 50% of the costs in Germany (Rauprich et al., 2010).

Some opponents to IVF funding have argued that infertility is a social rather than a medical issue (Hughes and Giacomini, 2001). However, infertility is defined as a disease by the World Health Organization (Zegers-Hochschild et al., 2009). Furthermore, due to an increased presence in the media as well as its inclusion as storylines in movies and television series, the use of IVF has become more widely known and understood by the general public, and the ability to access this technology is

Table 7 Multiple pregnancy rate from 2009 until 2016 in the province of Quebec.

Year	Multiple pregnancy rate
2009	25.6%
2010 (partial year)	3.7%
2011	7.0%
2012	6.0%
2013	3.3%
2014	3.4%
2015	5.2%
2016	4.5%

increasingly desired. Of course, the associated expense creates challenges for public funding.

There are certainly lessons that can be learned from Quebec's experience with regard to the best manner in which a programme can be designed to maximize its potential whilst maintaining fiscal restraints. The study data suggest that funding design can influence the clinical results, as well as encourage changes in clinical practice. Based on this analysis, it is suggested that a programme should fund a limited number of egg collections per patient, should include all resulting fresh and frozen embryos, and should have strict inclusion/exclusion criteria.

Acknowledgements

The authors wish to thank the team at CARTR-BORN, especially Holly Ockenden for providing the data from the registry used in this analysis. The authors would also like to recognize the work of all the ART clinics in Quebec for their participation in CARTR, and their hard work, particularly during the Quebec ART programme.

References

- Avalos, A., Galindo, C., Li, D.K., 2012. A systemic review to calculate miscarriage rates using life table analysis. *Birth Defects Res. A Clin. Mol. Teratol.* 94 (6), 417–423 (Jun).
- Bissonnette, F., Phillips, S.J., Gunby, J., Holzer, H., Mahutte, N., St-Michel, P., Kadoch, I.J., 2011. Working to eliminate multiple pregnancies: a success story in Québec. *Reprod. BioMed. Online* 23 (4), 500–504 (Oct).
- Gazette Officielle du Québec, 2010. An act respecting clinical and research activities related to assisted procreation (2009, c.30) – Coming into force of certain provisions of the Act. O.C. 643–2010, 7 July 2010. Vol. 142, No. 29, July 21 2010.
- Gazette Officielle du Québec, 2015. An act to enact the Act to promote access to family medicine and specialised medicine services and to amend various legislative provisions relating to assisted procreation. Chapter 25, 10 November 2015.
- Hughes, E., Giacomini, M., 2001. Funding in vitro fertilisation treatment for persistent infertility: the pain and the politics. 2001. *Fertil. Steril.* 76 (3), 431–442.
- Rauprich, O., Berns, E., Vollmann, J., 2010. Who should pay for assisted reproductive techniques? Answers from patients, professionals and the general public in Germany. *Hum. Reprod.* 25 (5), 1225–1233.
- Velez, M.P., Connolly, M.P., Kadoch, I.J., Phillips, S., Bissonnette, F., 2014. Universal coverage of IVF pays off. *Hum. Reprod.* 29 (6), 1313–1319.
- Zegers-Hochschild, F., Adamson, G.D., deMouzon, J., Ishihara, O., Mansour, R., Nygren, K., Sullivan, E., Vanderpoel, S., 2009. International Committee for Monitoring Assisted reproductive technology (ICMART) and the World Health Organisation (WHO) revised glossary of ART terminology. *Fertil. Steril.* 92, 1520–1524.

Declaration: The authors report no financial or commercial conflicts of interest.

Received 19 July 2018; refereed 19 December 2018; accepted 25 January 2019.