

## Assisted reproductive technologies (ART) in Canada: 2003 results from the Canadian ART Register

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**Objective:** To present the success rates of assisted reproductive technologies (ART) cycles performed in 2003 in Canada. This is the third annual report of outcomes compiled in the Canadian Assisted Reproductive Technologies Register.

**Design:** Prospective cohort study.

**Setting:** Twenty-four of 24 ART centers in Canada.

**Patient(s):** Couples undergoing ART treatment in Canada during 2003.

**Intervention(s):** ART treatments, including in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), frozen embryo transfer, and oocyte donation.

**Main Outcome Measure(s):** Clinical pregnancy, live birth, and multiple birth rates.

**Result(s):** A total of 10,656 ART cycles was reported to the Canadian ART Register. There were 7535 IVF/ICSI cycles using the woman's own oocytes. Per cycle started, the clinical pregnancy rate was 31.2% (37.3% per embryo transfer procedure), and the live birth rate was 23.9%; the multiple birth rate per delivery was 31.3%, with a triplet birth rate of 1.6%. Of cycles with oocytes retrieved, IVF was performed in 44% and ICSI in 56%; the outcomes were similar with the two procedures. There were 462 IVF/ICSI cycles using donor oocytes. The clinical pregnancy rate was 43.9%, and the live birth rate was 31.4%; the multiple birth rate, all twins, was 36.5%. There were 2309 frozen embryo transfer cycles using the woman's own oocytes. The clinical pregnancy rate was 21.1%, and the live birth rate was 16.1%; the multiple birth rate was 27.1%, with a triplet birth rate of 1.9%. There were 350 cycles of various other ART types, including 91 cycles involving gestational carriers.

**Conclusion(s):** For 2003, the Canadian ART Register achieved 100% voluntary participation from Canadian ART centers. Success rates were higher and multiple birth rates lower in 2003 than in previous years. (Fertil Steril® 2007;88:550–9. ©2007 by American Society for Reproductive Medicine.)

**Key Words:** Assisted reproductive technology, success rates, in vitro fertilization, intracytoplasmic sperm injection, frozen embryo transfer, oocyte donation, multiple births

The Canadian Assisted Reproductive Technologies Register (CARTR) was first established in 1999 for the collection of treatment cycle data from the Canadian fertility centers that were using assisted reproductive technologies (ART), including in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), and frozen embryo transfer (FET). The IVF Directors Group of the Canadian Fertility and Andrology Society directs the CARTR program, and participation of ART centers in CARTR is voluntary.

The first complete report from CARTR, describing results from ART cycles performed in 2001, was published in 2005 (1). The CARTR results from 2002 were published the following year (2). This is the third annual published report of Canadian ART outcomes. The purpose of this paper is to re-

port the results of ART cycles performed in Canadian centers in the 2003 calendar year and submitted to CARTR.

### MATERIALS AND METHODS

As in previous years, CARTR collected data for 2003 using the Society for Assisted Reproduction Clinical Outcome Reporting System version 2 computer program, generously provided to the Canadian Fertility and Andrology Society by the Society for Assisted Reproduction. Staff at each center entered information about patient demographics, diagnosis, and obstetric history; details of treatment; and pregnancy and birth outcomes for each ART treatment cycle initiated. The completed anonymous case records were sent electronically from each ART center to the CARTR coordinating center, where they were checked for accuracy and completeness. Corrections or clarifications were requested from the centers as necessary, but no on-site data validation from source documents was performed. The records from each center were then aggregated for data analysis using the computer program

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Statistical Package for the Social Sciences (SPSS), version 13 (SPSS, Inc., Chicago, IL). The ART cycles started between January 1 and December 31, 2003 were submitted to CARTR in batch mode twice: once in mid-2004 when the pregnancy outcomes were known, for an internal interim report, and again in mid-2005 when all the birth outcomes were known, for this published report.

It was not necessary to obtain institutional review board approval for this study because data collection is one of the requirements for accreditation of centers providing ART services, as organized by the Canadian Fertility and Andrology Society in conjunction with the Canadian Council on Health Services Accreditation. Although participation in accreditation is voluntary, most of the ART centers in Canada have agreed to the process and are obliged to inform patients that such data will be collected in a manner that is anonymous. Centers that choose to avoid accreditation need not report their data to CARTR; currently, there are no consequences for nonparticipation in CARTR.

These data from CARTR for 2003 were presented to the Medical and Laboratory Directors at the annual IVF Directors' Meetings in November 2004 (pregnancy results) and October 2005 (birth results). A brief summary of the national success rates was provided to the media, with the Directors' permission, immediately after each meeting. Before submission for publication, this report was read and approved by all IVF Directors.

### Definitions of Outcomes

The definitions established by the International Committee Monitoring Assisted Reproductive Technologies (ICMART) are followed by CARTR (3). A treatment cycle is considered to have "started" when a woman undergoing ovarian stimulation receives the first dose of gonadotropins; or, in a non-stimulated cycle (e.g., for frozen embryo transfer), when a decision is made to attempt ART treatment in that cycle. A canceled cycle is one that is stopped before the oocyte retrieval procedure or thawing of embryos.

Clinical pregnancy includes intrauterine gestation (presence of a gestational sac on ultrasonography), ectopic pregnancy, and miscarriage occurring before an ultrasound examination has been done but with histologic evidence of pregnancy. Cycles with only a positive pregnancy test are not considered to have a clinical pregnancy. Implantation rate is the number of gestational sacs observed on ultrasonography, divided by the number of embryos transferred.

Pregnancy loss includes miscarriage and therapeutic abortion of a clinical intrauterine pregnancy occurring at or at less than 20 weeks' gestation. Any pregnancy termination, either spontaneous or therapeutic, occurring after 20 weeks' gestation with no liveborn infant is considered a stillbirth. A delivery is the birth of one or more infants, either living or not, after 20 weeks' gestation. A live birth is a delivery that results in at least one living infant (but, if a multiple birth, may include one or more stillborn infants). A neonatal death is the

death of an infant in the first 28 days of life. A multiple birth is the delivery of more than one infant, either liveborn or stillborn, including deliveries with all infants stillborn. High-order multiple births (triplets or more) are reported separately.

Unless otherwise noted, the clinical pregnancy rate is reported per cycle started. Cycle cancellation, ectopic pregnancy, and other complications are reported per cycle started. The miscarriage or pregnancy loss rate is reported per intrauterine pregnancy. The live birth rate is reported per cycle started, excluding from both the numerator and the denominator the cycles in which the outcome of the clinical pregnancy has not been reported. Because of these missing data, the live birth rates reported may underestimate the true live birth rates. The multiple birth rate, which includes stillbirths, is reported per delivery.

## RESULTS

### Participating Centers

All of the 24 Canadian ART centers operating in 2003 contributed to CARTR for that year (listed in the [Appendix](#)). Nine of the 24 centers performed more than 500 ART cycles in 2003, nine centers performed between 200 and 500 cycles, and six centers performed fewer than 200 cycles.

### Overall Success Rates

In total, 10,656 treatment cycles involving ART were reported to CARTR for 2003. Overall, 3128 ART cycles (29.4% of cycles started) resulted in a clinical pregnancy, at least 2346 cycles resulted in a delivery (22.4%), and at least 2324 cycles resulted in a live birth (22.2%). There were 204 cycles with ongoing pregnancies (8% of ongoing pregnancies) for which the birth outcome was not reported. Overall, there were at least 725 multiple births (30.9% of known births): 689 twin births (29.4%) and 36 triplet births (1.5%).

The various procedures and their success rates are described herein. The results of the most common procedures are summarized in [Table 1](#).

### IVF/ICSI with Own Oocytes

In vitro fertilization, including ICSI, was the most common procedure performed, with 7535 cycles reported. This category, to distinguish it from those of oocyte donation and gestational carrier cycles, includes only cycles in which the parenting woman's own oocytes are used and the same woman receives the resulting embryos. However, cycles using donated sperm are included. Because the decision to use ICSI might not be made until the sperm and oocytes are assessed in the embryology laboratory, cycles canceled before oocyte retrieval cannot be classified by type of insemination procedure; thus, results per cycle started can only be calculated for IVF and ICSI cycles grouped together.

Per cycle started, the clinical pregnancy rate was 31.2%, the live birth rate was 23.9%, and the singleton live birth

**TABLE 1****Cycle outcomes for the most common types of ART procedures.**

Outcome	IVF/ICSI	IVF/ICSI with OD	FET	FET with OD
Cycles started	7535	462	2309	171
Canceled cycles (% of cycles started)	783 (10.4)	23 (5.0)	128 (5.5)	14 (8.2)
Oocyte retrievals (% of cycles started)	6752 (89.6)	439 (95.0)	2181 (94.5) <sup>a</sup>	157 (91.8) <sup>a</sup>
Embryo transfers (% of cycles started)	6301 (83.6)	417 (90.3)	1993 (89.2) <sup>b</sup>	156 (91.2)
Clinical pregnancy (% per cycle started)	2352 (31.2)	203 (43.9)	488 (21.1)	39 (22.8)
Ectopic pregnancy (% per cycle started)	48 (0.6)	3 (0.6)	8 (0.3)	0
Miscarriage (% per IU pregnancy)	372 (16.1)	32 (16.0)	87 (18.1)	9 (23.1)
Therapeutic abortion (% per IU pregnancy)	11 (0.5)	2 (1.0)	0	0
Delivery <sup>c</sup> (% per cycle started)	1785 (24.1)	137 (31.6)	369 (16.2)	28 (16.6)
Live birth <sup>c</sup> (% per cycle started)	1766 (23.9)	136 (31.4)	367 (16.1)	28 (16.6)
Singleton live birth <sup>c</sup> (% per cycle started)	1218 (16.5)	86 (19.9)	268 (11.7)	18 (10.7)
Singleton delivery <sup>c</sup> (% of deliveries)	1227 (68.7)	81 (64.3)	264 (72.9)	18 (64.3)
Twin delivery <sup>c</sup> (% of deliveries)	530 (29.7)	50 (36.5)	93 (25.2)	9 (32.1)
Triplet delivery <sup>c</sup> (% of deliveries)	28 (1.6)	0	7 (1.9)	1 (3.6)

Note: ART, assisted reproductive technologies; FET, frozen embryo transfer; ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilization; OD, oocyte donation; IU, intrauterine.

<sup>a</sup> Cycles with embryos thawed.

<sup>b</sup> Data missing for 74 cycles.

<sup>c</sup> Cycles with unknown delivery status omitted.

Gunby. Canadian ART Register 2003. Fertil Steril 2007.

rate was 16.5%. Donor sperm was used in 3.2% of cycles with oocytes retrieved. There were 48 ectopic pregnancies (0.6%), including three heterotopic pregnancies: two of the intrauterine gestations were non-viable and one resulted in a singleton live birth. The pregnancy loss rate was 16.6% (miscarriage 16.1%, therapeutic abortion 0.5%). Of the 1785 known births (93% of ongoing pregnancies), 31.3% were multiple births (29.7% twins, 1.6% triplets). Included in these figures are 3 pregnancies and 1 singleton live birth that resulted from intrauterine insemination performed after the IVF/ICSI cycle was canceled.

Rates for IVF and ICSI separately can only be provided per successful retrieval (i.e., one or more oocytes retrieved). Of 6313 IVF/ICSI cycles with a successful retrieval, 44.3% had insemination by standard IVF, 51.0% by ICSI, and 4.8% by IVF/ICSI split (some oocytes inseminated by each method). The clinical pregnancy rates per successful retrieval were 33.3%, 35.5%, and 33.9%, respectively. Including the IVF/ICSI split cycles in the ICSI group, the clinical pregnancy rates were 33.3% for IVF and 35.4% for ICSI, and the live birth rates were 26.3 and 26.4%, respectively. The ectopic pregnancy rate was 0.7% with IVF and 0.6% with ICSI, and the pregnancy loss rates were 15.8% (miscarriage 15.5%, therapeutic abortion 0.3%) and 16.7% (miscarriage 16.2%, therapeutic abortion 0.6%), respectively. Of 735 known births after IVF, 31.4% were multiple births (30.2% twins, 1.2% triplets); of 912 known births after ICSI, 31.0% were multiple births (29.2% twins, 1.9% triplets).

### IVF/ICSI with Oocyte Donation

IVF/ICSI with oocyte donation (OD) was reported in 462 cycles in 2003. In IVF/ICSI with OD, one woman undergoes ovarian stimulation then donates some or all of the retrieved oocytes to another woman, usually anonymously. These oocytes are inseminated with sperm from the recipient's partner (or a sperm donor), and the resulting embryos are transferred to the uterus of the recipient. Information about the donor (including age) was not collected.

In OD cycles, the clinical pregnancy rate per cycle started was 43.9%, the live birth rate was 31.4%, and the singleton live birth rate was 19.9%. Donor sperm was used in 9.8% of cycles with oocytes donated. There were three ectopic pregnancies (0.6%). The pregnancy loss rate was 17.0% (miscarriage 16.0%, therapeutic abortion 1.0%). Of 137 known births (83% of ongoing pregnancies), 36.5% were multiple births (all twins).

Of 303 OD cycles with a successful retrieval, 42.0% had insemination by standard IVF, 44.4% by ICSI, and 13.6% by IVF/ICSI split. The clinical pregnancy rates per successful retrieval were 42.2%, 50.8%, and 37.5%, respectively.

### Frozen Embryo Transfer with Own Oocytes

Frozen embryo transfer involves thawing embryos created and cryopreserved in a previous IVF/ICSI cycle and transferring them to the uterus of the woman who provided the oocytes in the original cycle. In 2003, 2309 such cycles were reported.

Per cycle started, the clinical pregnancy rate was 21.1%, the live birth rate was 16.1%, and the singleton live birth rate was 11.7%. There were eight ectopic pregnancies (0.3%), including one heterotopic pregnancy that resulted in a singleton live birth. The miscarriage rate was 18.1%. Of 369 known births (94.0% of ongoing pregnancies), 27.1% were multiple births (25.2% twins, 1.9% triplets).

### **Frozen Embryo Transfer with Oocyte or Embryo Donation**

The category FET-OD includes transfer of cryopreserved embryos created from donor oocytes in a previous IVF/ICSI with OD cycle (127 cycles) and cryopreserved donated embryos (44 cycles). In the latter case, both the male and female gametes were provided by a couple other than the intended parenting couple. The thawed embryos are transferred to the woman who intends to raise the child.

In this category, the clinical pregnancy rate per cycle started was 22.8%, the live birth rate was 16.6%, and the singleton live birth rate was 10.7%. There was no ectopic pregnancy. The miscarriage rate was 23.1%. Of 28 known births (93.0% of ongoing pregnancies), 35.7% were multiple births (32.1% twins, 3.6% triplets).

### **Gestational Carrier Cycles**

There were 91 cycles in which embryos were transferred into the uterus of a woman other than the one who intended to raise the child. Gestational carriers were used in 42 IVF/ICSI and 22 FET cycles with the parenting woman's own oocytes, and 18 IVF/ICSI and nine FET cycles with donated oocytes or embryos. Donated sperm was used in two cycles.

In fresh embryo cycles using a gestational carrier, the clinical pregnancy rate per cycle started was 36.7%, the live birth rate was 15.4%, and the singleton live birth rate was 7.7%; in frozen embryo cycles, the rates were 19.4%, 13.3%, and 13.3%, respectively. Of the 28 clinical pregnancies in gestational carriers, 25.0% ended in miscarriage; there was no ectopic pregnancy. Of 12 known births (57.0% of ongoing pregnancies), 33.3% were multiple births (all twins).

### **Other Cycle Types**

Several types of ART procedures were performed in 2003 that did not fit into the categories previously described. There were 78 cycles of in vitro oocyte maturation, in which immature oocytes are retrieved from the ovaries and matured in vitro before insemination, with a clinical pregnancy rate of 26.9%, live birth rate of 17.9%, and multiple birth rate of 21.4% (all twins). Three cycles of gamete intrafallopian transfer (GIFT), in which the oocytes and sperm are transferred separately to the fallopian tube so that fertilization occurs in vivo, were reported to CARTR for 2003, with one clinical pregnancy that resulted in a singleton live birth. One cycle of zygote intrafallopian transfer (ZIFT), in which the fertilized oocytes are transferred to the fallopian tube, resulted in a miscarriage. Preimplantation genetic diagnosis was performed in five IVF/ICSI cycles, but no pregnancy resulted. There was one cycle of embryo banking.

### **Birth Outcomes for All ART Procedures**

At least 3107 infants were born from all types of ART cycles started in 2003 in Canada: 1621 singletons (52.2% of infants), 1378 twins (44.4%), and 108 triplets (3.5%). An additional 204 pregnancies had no delivery information reported. Of these pregnancies, 53 had two fetal hearts, and seven had three fetal hearts visible on ultrasonography at about 8 weeks' gestation; thus, as many as 271 additional babies may have been born.

Of the 1621 infants born as singletons, there were 11 stillbirths and seven neonatal deaths, a total perinatal mortality rate of 1.1%. The median gestational age at birth was 39 weeks (range: 22 to 43 weeks) for liveborn infants and 25 weeks (range: 21 to 39 weeks) for stillborn infants. Preterm delivery (<37 weeks) occurred in 14.1% of births and very preterm delivery (<34 weeks) in 3.9% of births. The birth weight was >2500 g for 92.8% of liveborn singletons, 2000 to 2500 g for 4.4%, 1000 to 1999 g for 2.2%, and <1000 g for 0.7%. Some type of birth defect was reported for 36 infants (2.2%).

Of the 1378 infants born as twins, there were 21 stillbirths and 28 neonatal deaths, a total perinatal mortality rate of 3.6%. The median gestational age at birth was 36 weeks (range: 21 to 43 weeks) for live births and 22 weeks (range: 21 to 26 weeks) for stillbirths. Preterm delivery occurred in 66.0% of births and very preterm delivery in 24.2% of births. Birth weight was >2500 g for 47.9% of liveborn twins, 2000 to 2500 g for 29.5%, 1000 to 1999 g for 19.0%, and <1000 g for 3.6%. Some type of birth defect was reported for 41 infants (3.0%).

Of the 108 infants born as triplets, there were eight stillbirths and three neonatal deaths, a total perinatal mortality rate of 10.2%. The median gestational age at birth was 33 weeks (range: 21 to 37 weeks) for live births and 21 weeks (range: 20 to 22 weeks) for stillbirths. Preterm delivery occurred in 97.1% of births and very preterm delivery in 64.7% of births. Birth weight was >2500 g for 10.8% of liveborn triplets, 2000 to 2500 g for 33.3%, 1000 to 1999 g for 47.3%, and <1000 g for 8.6%. Some type of birth defect was reported for three infants (2.8%).

The information provided on birth defects was limited. Overall, some type of birth defect was reported for 80 infants (2.6%): 10 cases of genetic defect (three neonatal deaths), 17 cases of cardiac defect (one neonatal death), five cases of limb defect, and 48 cases of other unspecified defects (five neonatal deaths).

The risk of a couple experiencing perinatal death was strongly related to multiplicity. Perinatal death of one or more infants occurred in 1.1% of singleton deliveries, 5.2% of twin deliveries, and 13.9% of triplet deliveries. The risk of perinatal death of all infants was 1.1%, 1.9%, and 8.3%, respectively. By type of ART procedure, perinatal death of one or more infants occurred in 2.9% of deliveries resulting from IVF/ICSI cycles (2.9% in IVF cycles and 3.2% in

**TABLE 2****Clinical pregnancy and birth results by female age for the most common ART procedures.**

Outcome/female age group	IVF/ICSI	IVF/ICSI with OD	FET
Mean female age, years (range)	35 (20–48)	41 (23–52)	35 (20–51)
Cycles started (% of cycles within procedure)			
<35 years	3338 (44.4)	66 (14.3)	1123 (48.7)
35–39 years	3045 (40.5)	94 (20.3)	870 (37.7)
≥40 years	1136 (15.1)	302 (65.4)	315 (13.6)
Clinical pregnancy (% per cycle started)			
<35 years	1263 (37.8)	27 (40.9)	265 (23.6)
35–39 years	899 (29.5)	44 (46.8)	177 (20.3)
≥40 years	179 (15.8)	127 (42.1)	45 (14.3)
Live birth <sup>a</sup> (% per cycle started)			
<35 years	998 (30.6)	18 (29.0)	201 (18.1)
35–39 years	654 (21.8)	28 (32.9)	136 (15.8)
≥40 years	104 (9.2)	90 (31.5)	30 (9.6)
Multiple birth <sup>a</sup> (% per delivery)			
<35 years	345 (34.3)	6 (37.5)	60 (30.0)
35–39 years	189 (28.5)	12 (48.0)	34 (25.8)
≥40 years	21 (20.0)	27 (31.8)	4 (13.3)

*Note:* ART, assisted reproductive technologies; FET, frozen embryo transfer; ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilization; OD, oocyte donation.  
<sup>a</sup> Cycles with unknown delivery status omitted.

*Gunby. Canadian ART Register 2003. Fertil Steril 2007.*

ICSI cycles), 1.5% from OD cycles, and 0.8% from FET cycles.

### Effect of Female Age

The clinical pregnancy and birth results for women categorized into three age groups are given in Table 2. The mean female age was 35 years in IVF/ICSI and FET cycles, and 41 years in OD cycles. The proportion of cycles in women aged 40 years and older was 15% in IVF/ICSI cycles, 14% in FET cycles, and 65% in OD cycles. In IVF/ICSI and FET cycles, the clinical pregnancy and live birth rates declined with female age, especially after age 40 years. In OD cycles, clinical pregnancy and live birth rates were similar in all age groups. The multiple birth rates declined gradually with age in IVF/ICSI and FET cycles and after age 40 years in OD cycles.

In IVF/ICSI cycles, the age-related decline in ART success can be attributed to suboptimal outcomes at several steps in the process. The proportion of started cycles with successful retrieval decreased with age (92.7% for women aged <35 years, 87.2% for those aged 35 to 39 years, and 81.5% for those aged ≥40 years), as did the mean number of oocytes retrieved (13.4, 11.3, and 9.3 respectively). In women who had one or more embryos replaced, the mean implantation rate declined with increasing female age (28.7%, 20.2%, and 8.7%), as did the clinical pregnancy rate (42.8%, 35.2%, and 21.2%), even though older women had more embryos transferred (mean 2.2, 2.4, and 2.9). The proportion of

women who had surplus embryos available for cryopreservation gradually decreased from the younger to older women (48.4%, 33.0%, and 19.3%). In women who achieved clinical intrauterine pregnancy, the pregnancy loss rate became higher as women aged (12.6%, 18.8%, and 31.1%). However, adverse birth outcomes were not found to be related to advanced female age: the risks of preterm birth (32.6%, 28.0%, and 28.5%), very preterm birth (11.7%, 10.5%, and 7.0%), and perinatal death of one or more infants (2.3%, 3.2%, and 2.1%) were similar across age groups.

### Effect of Infertility Diagnosis

In IVF/ICSI cycles, the reason for ART treatment was most commonly a single female (30% of cycles) or a single male (29%) infertility factor. Idiopathic or unexplained infertility was the diagnosis in 19% of cycles. Both female and male factors were diagnosed in 11% of cycles and more than one female factor in 3%. Clinical pregnancy rate per cycle started was highest when male factor infertility was the only diagnosis (33%) or was present in combination with a female factor (32%). Couples with idiopathic infertility had a clinical pregnancy rate of 31%. Clinical pregnancy rate was lowest in the presence of single (29%) or multiple (22%) female factors without male factor infertility.

The distribution of primary diagnostic categories was quite different in IVF and ICSI cycles (Table 3). The most common primary diagnosis for couples having IVF was tubal factor infertility, whereas for couples having ICSI it was male factor

**TABLE 3**

**Clinical pregnancy rates per successful retrieval for IVF and ICSI cycles by primary diagnostic category.**

Primary diagnosis	IVF		ICSI	
	No. of cycles (% of all IVF cycles)	No. of pregnancies (% per retrieval)	No. of cycles (% of all ICSI cycles)	No. of pregnancies (% per retrieval)
Male factor	163 (6.6)	53 (32.5)	1771 (54.6)	649 (36.6)
Tubal factor	1039 (41.8)	314 (30.2)	426 (13.1)	130 (30.5)
Idiopathic	688 (27.7)	242 (35.2)	431 (13.3)	137 (31.8)
Endometriosis	309 (12.4)	111 (35.9)	258 (7.9)	95 (36.8)
Ovulatory disorder	146 (5.9)	48 (32.9)	157 (4.8)	60 (38.2)
Other	139 (5.6)	44 (31.7)	203 (6.3)	70 (34.5)

*Note:* ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilization.

*Gunby. Canadian ART Register 2003. Fertil Steril 2007.*

infertility. The clinical pregnancy rates per successful retrieval were similar across diagnostic categories for each insemination method (see Table 3).

### Effect of Number of Embryos Transferred

The number of embryos transferred in IVF/ICSI cycles ranged from one to nine, with a mean of 2.4. A single embryo was transferred in 10% of transfer cycles. More commonly, either two (55% of cycles) or three (27% of cycles) embryos were transferred. More embryos were transferred in older women: the mean age of women receiving four or more embryos (8% of cycles) was 39 years, compared with 36 years for those receiving three embryos and 34 years for those receiving two embryos.

Overall, the clinical pregnancy rate was 37.3% per embryo transfer procedure. Clinical pregnancy and birth results by number of embryos transferred are shown in Table 4. The clinical pregnancy rate per embryo transfer procedure was low when only one embryo was transferred (17.9%). Trans-

ferring three or more embryos did not increase the clinical pregnancy rate beyond the high level observed with two embryos (41.9%); indeed, the clinical pregnancy rate declined when more than two embryos were transferred (33.9%). The mean implantation rates followed a similar pattern: 18.3% with one embryo, 28.3% with two embryos, 16.2% with three embryos, 11.1% with four embryos, and 8.5% with five or more embryos.

Twenty-six percent of two-embryo transfers were performed on day 5 after oocyte retrieval, with 65% performed on day 3. However, the clinical pregnancy rates were similar at 44.2% and 42.6%, respectively. In contrast, only 5% of three-embryo and four-embryo transfers were performed on day 5.

The total multiple birth rates were similar for two-embryo or three-embryo transfers, but were lower when more than three embryos were transferred (see Table 4). The triplet birth rate was 3.9% when three or more embryos were transferred.

**TABLE 4**

**Clinical pregnancy rate per embryo transfer procedure and multiple birth rate per known birth by number of embryos transferred in IVF/ICSI cycles.**

No. of embryos transferred	No. of cycles (% of all ET cycles)	No. of pregnancies (% per ET)	No. of births (% of all births)	No. of total multiple births (% per birth)	No. of triplet births (% per birth)
1	563 (9.5)	101 (17.9)	77 (4.7)	1 (1.3)	0
2	3267 (55.3)	1370 (41.9)	1054 (64.0)	353 (33.5)	6 (0.6)
3	1581 (26.8)	550 (34.8)	407 (24.7)	131 (32.2)	16 (3.9)
4	390 (6.6)	123 (31.5)	86 (5.2)	22 (25.6)	3 (3.5)
5 or more	103 (1.7)	31 (30.1)	22 (1.3)	6 (27.3)	1 (4.5)

*Note:* ET, embryo transfer; ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilization.

*Gunby. Canadian ART Register 2003. Fertil Steril 2007.*

## Effect of Day of Embryo Transfer

In IVF/ICSI cycles, embryo transfer was performed on day 2 (after oocyte retrieval) in 2% of transfers, day 3 in 74%, day 5 in 18%, and day 6 in 5%. The proportions varied greatly among centers. More embryos were transferred to each woman on day 2 and day 3 (mean 2.5 and 2.5) than on day 5 and day 6 (mean 2.0 and 1.9). The proportion of cycles with two embryos transferred was 37% on day 2, 48% on day 3, 81% on day 5, and 76% on day 6.

The clinical pregnancy rates per embryo transfer procedure were 21.2% on day 2, 36.7% on day 3, 41.8% on day 5, and 30.6% on day 6. The mean implantation rates were 11.6, 21.5, 29.5, and 21.7%, respectively. The multiple birth rates were 25.0, 30.7, 35.6, and 27.9%, respectively.

## Effect of Surplus Embryos for Cryopreservation

The availability of surplus embryos for cryopreservation may be an indicator of embryo quality as well as embryo number. Thus, it is interesting to compare clinical pregnancy rates within a given number of embryos transferred, for cycles with and without embryos available for cryopreservation.

In Canada in 2003, a single embryo was transferred by choice in only 81 IVF/ICSI cycles (14% of single embryo transfers and 1.4% of all transfer cycles). The clinical pregnancy rate per embryo transfer procedure was 46.9% in elective single embryo transfers, compared with 13.1% when only one embryo was available. Forty-seven percent of the two-embryo transfers had surplus embryos; thus, elective double embryo transfer was performed in 26% of all IVF/ICSI transfer cycles. In these cycles, the clinical pregnancy rate was 50.8%, compared with 34.1% when only two embryos were available. The mean implantation rate was 17.1% when all available embryos were transferred and 31.5% when surplus embryos were frozen.

## Complications and Pregnancy Reduction

Complications were reported in 168 IVF/ICSI cycles (2.4%), according to each center's own definitions. There were 145 cases of ovarian hyperstimulation syndrome (2.0% per cycle started), 50 of which (35%) required hospitalization; 19 complications related to medications (no hospitalization); and four complications related to procedures (two hospitalizations).

Of 860 multiple pregnancies from all types of ART cycles, 12.2% had spontaneous pregnancy reduction (loss of one or more but not all fetuses) and 4.3% had therapeutic pregnancy reduction, following ultrasonographic confirmation of fetal viability at about 8 weeks' gestation. Of 770 pregnancies that were originally twins, reduction to one fetus occurred spontaneously in 10.9% and therapeutically in 0.8%. Of 83 pregnancies that were originally triplets, reduction to two fetuses occurred spontaneously in 19.3% and therapeutically in 25.3%, and reduction to one fetus in 3.6% and 6.0%, respectively. Thus, only 46% of viable triplet pregnancies resulted

in a triplet birth. Of six pregnancies that were originally quadruplets, one was reduced to three fetuses and five were reduced to two fetuses, spontaneously in two cases and therapeutically in four cases. One quintuplet pregnancy was reduced therapeutically to triplets. There was no quadruplet birth.

## DISCUSSION

In this third annual report from the Canadian ART Register, we have presented the results of ART cycles performed in Canada in 2003. All of the 24 ART centers operating in Canada in 2003 contributed to CARTR, representing 100% participation, up from 95% in 2002 and 86% in 2001. One established center that joined CARTR for the first time in 2003 submitted summary data by type of ART treatment and female age group rather than cycle-specific data because of concerns relating to patient confidentiality. Therefore, cycles from that center had to be omitted from analyses involving detailed characteristics such as infertility diagnosis, insemination method, day of embryo transfer, and number of embryos transferred. Three new ART centers opened in 2003, two in Quebec and one in British Columbia. Two established centers in Ontario merged in 2003, submitting combined data to CARTR.

The trend toward increasing numbers of cycles reported to CARTR and increasing success rates that was noted from 2001 to 2002 (2) continued into 2003 (Table 5). Compared with 2002, there was a 16% increase in the total number of ART cycles reported to CARTR for 2003, from 9188 to 10,656. There was a 22% increase in the number of pregnancies resulting from all types of ART cycles, from 2556 in 2002 to 3128 in 2003, mainly because of the additional centers contributing cycles but also because of a 5.8% relative increase in clinical pregnancy rate (from 27.8 to 29.4% per cycle started;  $P < .0001$  for trend). There was a 17% increase in the number of live births reported, from 1994 in 2002 to 2324 in 2003, but only a 0.9% relative increase in live birth rate (from 22.0 to 22.2% per cycle started;  $P$  for trend .05).

The number of live births and the live birth rate are underestimates of the true figures because of pregnancies for which the outcome was not reported; the proportion of ongoing pregnancies with unknown outcome rose from 5% in 2002 to 8% in 2003. This trend of increasing rates of unknown birth outcomes is disturbing and is the main deficiency of CARTR, as it affects the accuracy of the data and the comparison of Canada's birth rates with those of other countries. Although most Canadian ART centers achieve close to complete reporting, tracking down birth outcomes is particularly difficult for centers that provide embryology services to physicians outside their center. However, these centers are taking steps to make the referring physician responsible for reporting birth outcomes. Other approaches that some centers are implementing to improve birth outcome reporting include a response card in a self-addressed, stamped envelope provided to each pregnant woman, to be filled in and returned after the birth, and computerized reminders for the clinic staff to

**TABLE 5**

**Comparison of results from the Canadian Assisted Reproductive Technologies Register (CARTR) for 2001, 2002, and 2003.**

Outcome	CARTR 2001 (1)	CARTR 2002 (2)	CARTR 2003	P for trend
No. of clinics participating (%)	19 (86)	21 (95)	24 (100)	
Total no. of ART cycles reported	7884	9188	10,656	
IVF/ICSI cycles				
No. of cycles reported	5393	6547	7535	
Cycles with ICSI (%)	56	54	56	.94
Cycles in women aged $\geq 40$ y (%)	16	18	15	.16
Cycles with $\leq 2$ embryos transferred (%)	49	60	65	<.0001
Clinical pregnancy rate per cycle (%)	28.3	29.9	31.2	.0004
Live birth rate per cycle (%)	23.1	23.8	23.9	.33
Singleton live birth rate per cycle (%)	15.5	15.7	16.5	.13
Multiple delivery rate per delivery (%)	32.8	34.8	31.3	.28
Triplet or more rate per delivery (%)	2.7	2.7	1.6	.03
FET cycles				
No. of cycles reported	1936	2083	2309	
Clinical pregnancy rate per cycle (%)	18.9	20.9	21.1	.07
Live birth rate per cycle (%)	15.4	16.3	16.1	.55
Singleton live birth rate per cycle (%)	11.5	12.2	11.7	.86
Multiple delivery rate per delivery (%)	24.9	25.2	27.1	.51
Triplet or more rate per delivery (%)	3.0	1.5	1.9	.34
OD cycles				
No. of cycles reported	301	325	462	
Clinical pregnancy rate per cycle (%)	29.2	34.8	43.9	<.0001
Live birth rate per cycle (%)	22.4	24.6	31.4	.005
Singleton live birth rate per cycle (%)	12.7	16.0	19.9	.01
Multiple delivery rate per delivery (%)	43.5	34.6	36.5	.40
Triplet or more rate per delivery (%)	7.3	1.3	0	.001

Note: ART, assisted reproductive technologies; FET, frozen embryo transfer; ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilization; OD, oocyte donation.

Gunby. Canadian ART Register 2003. Fertil Steril 2007.

telephone the couple for the birth outcome at the appropriate time. These strategies should ensure more accurate live birth rates from CARTR in future years.

Another concern relates to the overall accuracy and completeness of the data submitted to CARTR by each center. This issue was discussed in our first report (1), and the situation has not changed since that time. Because CARTR is funded solely by a small per-cycle fee charged to the participating centers and receives no government support, on-site data validation is not feasible at this time in Canada. It is expected that on-site validation will become part of the requirements of the register in the future. However, for the present, the accuracy of the CARTR report relies on the best efforts of the personnel responsible for data entry from each center.

The proportion of cycles with complications relating to the ART procedure was low at 2.4%. However, it is possible that reporting of complications was incomplete and inconsistent from center to center. At that time, CARTR had no standard

definitions for complications, and each center used its own judgment regarding which complications to include. In addition, the choices of type of complication provided by the computer program used to enter data were limited. The CARTR database is currently undergoing revision, and these problems are being addressed.

The distribution of indications for undergoing ART treatment, as designated by the primary infertility diagnosis, has remain fairly stable over the period 2001 to 2003. For IVF treatment, there has been a slight reduction in the proportion of cycles performed in couples with the main indication of tubal factor infertility (from 50% to 42%), with increases in the other diagnostic categories, in particular idiopathic infertility (from 23% to 28%). For ICSI treatment, the distribution of indications has been stable, with 55% to 58% of cycles performed in couples with the main indication of male factor infertility. Because of the relatively small number of cycles performed in each diagnostic category, clinical pregnancy rates vary somewhat from year to year for each

indication and are not statistically significantly different among categories within a given year. However, there are constant trends toward lower than average clinical pregnancy rates in couples with tubal factor infertility, in both IVF and ICSI cycles, and higher than average clinical pregnancy rates in couples with male factor infertility in ICSI cycles.

In IVF/ICSI cycles, there was a 4.3% relative increase in the clinical pregnancy rate in 2003 over the previous year (see Table 5) ( $P$  for trend .0004). This improvement can be attributed, in part, to a reduction from 18% to 15% in the proportion of cycles in women aged  $\geq 40$  years; however, another contributing factor was increased clinical pregnancy rates in the younger age groups. Unfortunately, there was also an increase in the miscarriage rate, from 13.5% to 16.1% per intrauterine pregnancy, as well as in the proportion of unreported birth outcomes; thus, the relative increase in live birth rate was only 0.4% ( $P$  for trend .33). The proportion of IVF/ICSI cycles with only one or two embryos transferred continued to rise in 2003 to 65% of embryo transfers ( $P < .0001$  for trend). As a result, there was a 5.1% relative increase in the singleton live birth rate per cycle started ( $P$  for trend .13) and a substantial 9.8% relative decrease in the overall multiple birth rate per birth ( $P$  for trend .28;  $P = .03$ , 2003 vs. 2002). Most impressively, there was a 41% relative reduction in the triplet birth rate, from 2.7% to 1.6% per birth ( $P$  for trend .03).

In FET cycles, the clinical pregnancy, live birth, and singleton live birth rates were similar in 2003 compared with the previous year (see Table 5). There were slight increases in the multiple birth and triplet birth rates. Outcomes in FET cycles did not vary in a statistically significant way across the years 2001 to 2003. At 27.1%, the multiple birth rate in FET cycles in 2003 was almost as high as that in fresh IVF/ICSI cycles (31.3%), whereas the triplet birth rate was higher (1.9% vs. 1.6%, respectively). This finding should serve as a caution to clinicians that, despite the generally lower implantation and pregnancy rates, it is just as important in FET cycles as in fresh embryo cycles to limit the number of embryos transferred to avoid high-order multiple pregnancies.

In OD cycles reported to CARTR, the clinical pregnancy, live birth, and singleton live birth rates have risen significantly over the 3-year period (see Table 5). The success rates from OD cycles are now higher than the corresponding rates from IVF/ICSI cycles using the woman's own oocytes, in line with results from other countries (4, 5). The twin birth rate from OD cycles remained high in 2003 at 36%, but there was no triplet birth. In 2002 OD cycles, a much lower live birth rate had been detected in women aged 40 years or more than in younger women. This finding was not observed in 2003; both the clinical pregnancy and live birth rates were similarly high in all three age groups (see Table 2), as would be expected.

Only a handful of cycles involving preimplantation genetic diagnosis have been reported to CARTR: three cycles in 2001, one cycle in 2002, and five cycles in 2003. This procedure was only just beginning to be provided on a clinical basis

during this time period. These few cycles represent the use of preimplantation genetic diagnosis for couples with known genetic problems. Data on the use of preimplantation genetic diagnosis to detect aneuploidy in the embryos of infertile women of older age or with multiple implantation failures were not collected by CARTR during this time period, but this is planned for the future.

Multiple birth is an issue of great concern to all providers and consumers of ART. Because the risks of preterm birth, low birth weight, and perinatal death are greatly increased in multiple births, it is essential to take steps to reduce the number of multiple pregnancies caused by ART treatment (6). Some action to do so has been taken by Canadian centers, as indicated by the 33% relative increase in the proportion of single or double embryo transfers in IVF/ICSI cycles in 2003 compared with 2001 (see Table 5). In 2003, the overall multiple birth rate in IVF/ICSI cycles reported to CARTR was lower, at 31% per birth, than in any previous year back to 1999. Most importantly, the triplet birth rate was reduced from 2.7% to 1.6% per birth.

Although triplet births were virtually eliminated when only two embryos were transferred, the twin birth rate was still unacceptably high at 33% per birth. This finding is an indication that elective single embryo transfer should be considered for more women with good prognosis. The Society of Obstetricians and Gynaecologists of Canada has recently published guidelines for the number of embryos to transfer in ART cycles (7). However, the effect on multiple birth rates of any policy changes in the ART centers in response to these guidelines will not be observed in CARTR for several years.

In summary, the Canadian ART Register has been successful, within 4 years of its inception, in recruiting 100% of Canadian centers to participate voluntarily in a compilation of ART cycles in Canada. Clinical pregnancy rates per cycle started of 31% in IVF/ICSI cycles, 44% in oocyte donation cycles, and 21% in frozen embryo transfer cycles, and live birth rates of 24%, 31%, and 16%, respectively, compare favorably with the rates around the world. Success rates were higher and multiple birth rates lower in 2003 than in previous years.

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## APPENDIX

### Canadian Centers Reporting Data to the Canadian Assisted Reproductive Technologies Register (CARTR) for 2003.

Victoria Fertility Center, Victoria, British Columbia  
University of British Columbia IVF Program, Vancouver, British Columbia  
Genesis Fertility Center, Vancouver, British Columbia  
Foothills Regional Fertility Program, Calgary, Alberta  
Assisted Reproductive Technology at University of Saskatchewan (ARTUS), Saskatoon, Saskatchewan  
Heartland Fertility Clinic, Winnipeg, Manitoba  
London Health Sciences Center, London, Ontario  
Hamilton Health Sciences Center for Reproductive Care, Hamilton, Ontario  
ISIS Regional Fertility Center, Mississauga, Ontario  
NUSTAR Fertility Center, Mississauga, Ontario  
Sunnybrook Women’s College Hospital Fertility Center, Toronto, Ontario  
Success Through Assisted Reproductive Technology (START), Toronto, Ontario  
Mt. Sinai Reproductive Biology Unit, Toronto, Ontario  
Toronto Center for Advanced Reproductive Technology (TCART), Toronto, Ontario  
IVF Canada & LIFE Program, Scarborough, Ontario  
Markham Fertility Center, Markham, Ontario  
The Fertility Center at the Ottawa Hospital, Ottawa, Ontario  
McGill University Reproductive Center, Montreal, Quebec  
Montreal Fertility Clinic, Montreal, Quebec  
OVO Fertility Clinic, Montreal, Quebec  
Procrea, Montreal, Quebec  
Procrea, Quebec City, Quebec  
Conceptia Clinic, Moncton, New Brunswick  
Reproductive Endocrine Center, Halifax, Nova Scotia

*Gunby. Canadian ART Register 2003. Fertil Steril 2007.*