Canadian Assisted
Reproductive
Technologies Register Plus
(CARTR Plus)



Canadian Fertility and Andrology Society 65th Annual Meeting – Ottawa September 19 – 21, 2019



List of abbreviations

CS Cycle start

RET Oocyte retrieval

ET Embryo transfer

IVF In vitro fertilization

FET Frozen embryo transfer

PGT-A/PGT-M Preimplantation Genetic Testing for

Aneuploidy/Monogenic (Single Gene) Diseases

IVM In vitro maturation

OHSS Ovarian hyperstimulation syndrome

eSET Elective single embryo transfer

neSET Non-elective single embryo transfer

eDET Elective double embryo transfer

neDET Non-elective double embryo transfer



Disclaimer

- This report is based on data submitted by assisted reproductive technology clinics from across Canada to the CARTR Plus database. Although significant effort has been made to ensure the accuracy of the information presented in this report, neither the authors nor BORN Ontario nor any other parties make any representation or warranties as to the accuracy, reliability or completeness of the information contained herein.
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Suggested citations

Canadian Assisted Reproductive Technologies Registry (CARTR) Plus. Final treatment cycle and pregnancy outcome data for 2017. Better Outcomes Registry & Network Ontario. Ottawa ON, September 2019.

Canadian Assisted Reproductive Technologies Registry (CARTR) Plus. Preliminary treatment cycle data for 2018. Better Outcomes Registry & Network Ontario. Ottawa ON, September 2019.





Notes

All data current as of May 2019

- Treatment cycle outcomes for 2018 cycle starts
 - Based on 36 clinics

- Birth outcomes for 2017 cycle starts
 - Based on 36 clinics



Notes

- These slides present descriptive estimates on which no formal statistical tests have been carried out; therefore, differences across treatment cycles, patient characteristics or embryo transfer characteristics may not be statistically significant and should be interpreted cautiously
- Unless otherwise specified, denominators for birth outcomes are based on the pregnancy level





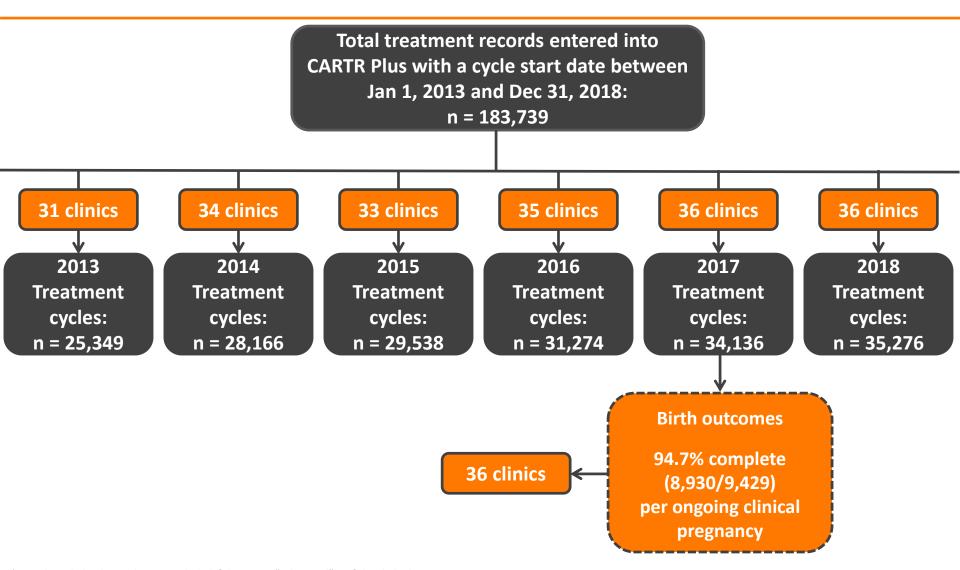
INTRODUCTION

All ART treatment cycles (fresh and frozen)



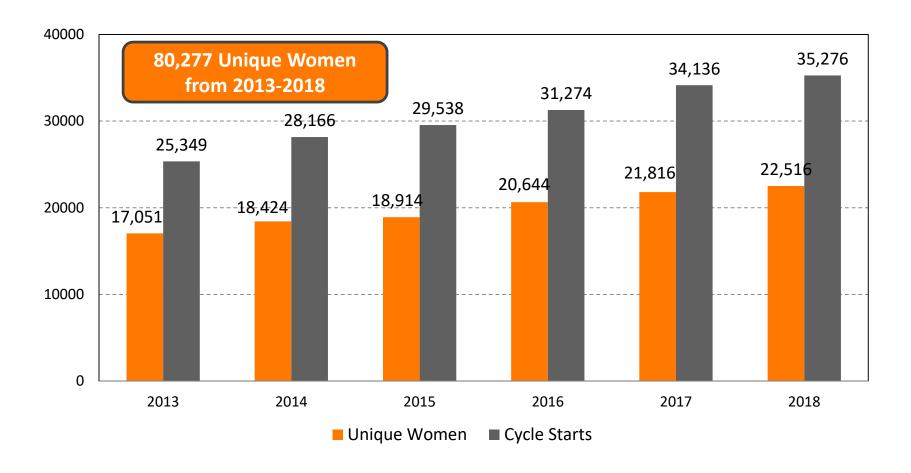
CARTR Plus records extracted May 2019





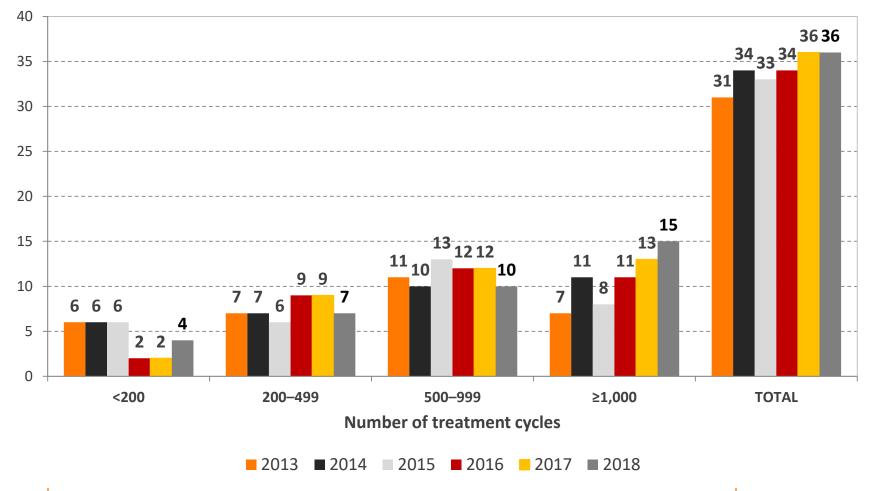
^{*} Unacknowledged records were included if they were "submitted" or if they linked to an outcome

Number of Unique Women





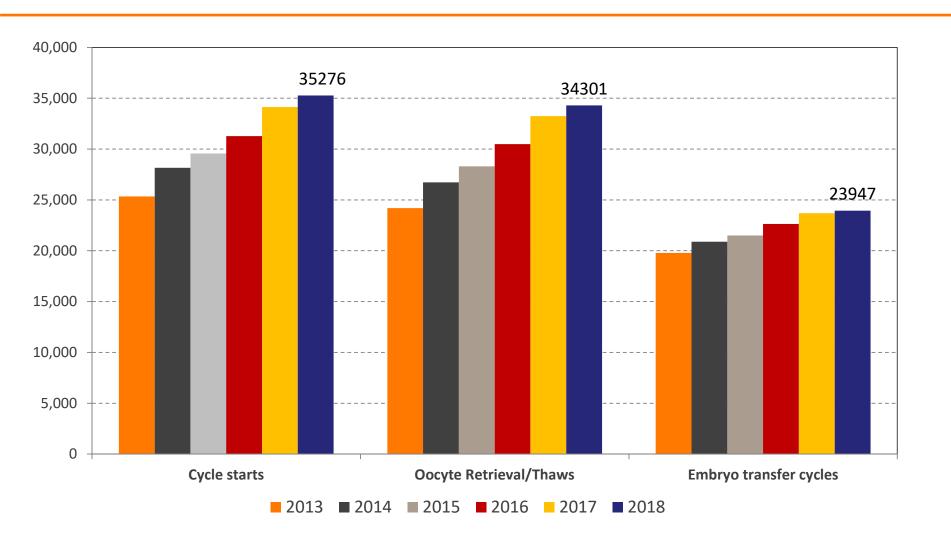
Volume of treatment cycles by clinic





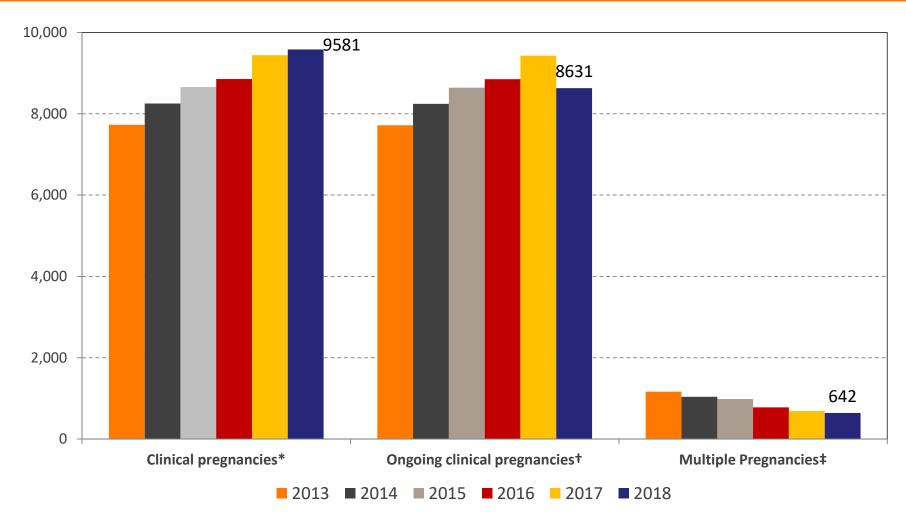
Number of cycles





Number of clinical pregnancies





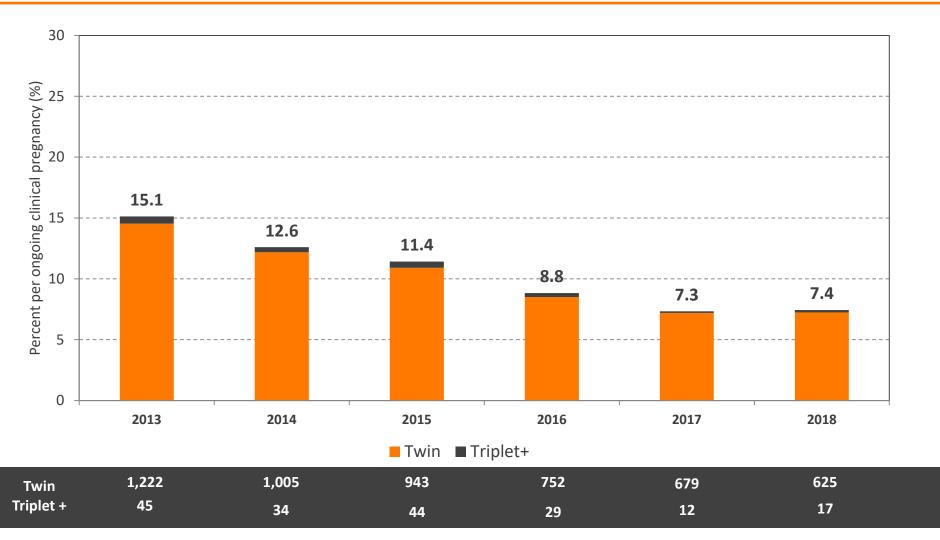
^{*} Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

[†] Ongoing clinical pregnancy: clinical pregnancy with ≥1 fetal heart beat on ultrasound

[‡] Multiple pregnancy: ongoing clinical pregnancy with >1 fetal heart beat on ultrasound

Percentage of multiple pregnancies

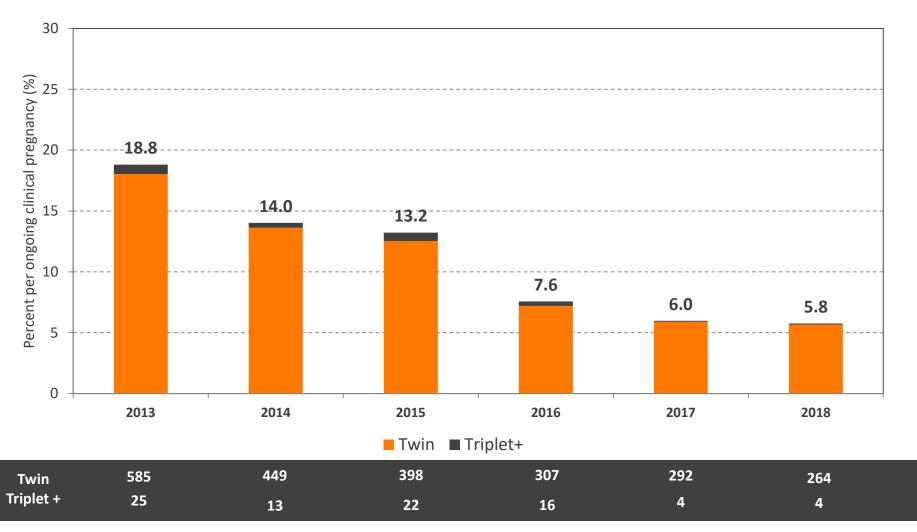
CARTR



^{*} Ongoing clinical pregnancy: clinical pregnancy with ≥1 fetal heart beat on ultrasound

[†] Multiple pregnancy: ongoing clinical pregnancy with >1 fetal heart beat on ultrasound

Percentage of multiple pregnancies in Ontario



^{*} Ongoing clinical pregnancy: clinical pregnancy with ≥1 fetal heart beat on ultrasound

[†] Multiple pregnancy: ongoing clinical pregnancy with >1 fetal heart beat on ultrasound

Specialized services

All ART treatment cycles (fresh and frozen), 2018

Description	Number of cycles
Gestational carrier	949
PGT-A/PGT-M	6,535
Oocyte or embryo banking due to cancer treatment	464
Oocyte or embryo banking due to non-cancer/non-medical reasons	611
Any use of donor oocytes or embryos	3,563
Frozen oocyte IVF	655



Oocyte or embryo freezing for non-medical reasons

2013 – 2018

Year	Oocyte Freezing	Embryo Freezing	
2013	94	40	
2014	135	40	
2015	204	80	
2016	280	52	
2017	357	64	
2018	504	108	
Overall	1,574	384	



PGT-A and PGT-M

2013 – 2018

Year	PGT-A	PGT-M	
	# Cycles	# Cycles	
2013	243	240	
2014	605	313	
2015	1,660	951	
2016	3,371	1,200	
2017	4,700	1,182	
2018	6,090	640	
Overall	16,669	4,526	



TREATMENT CYCLES FOR 2018

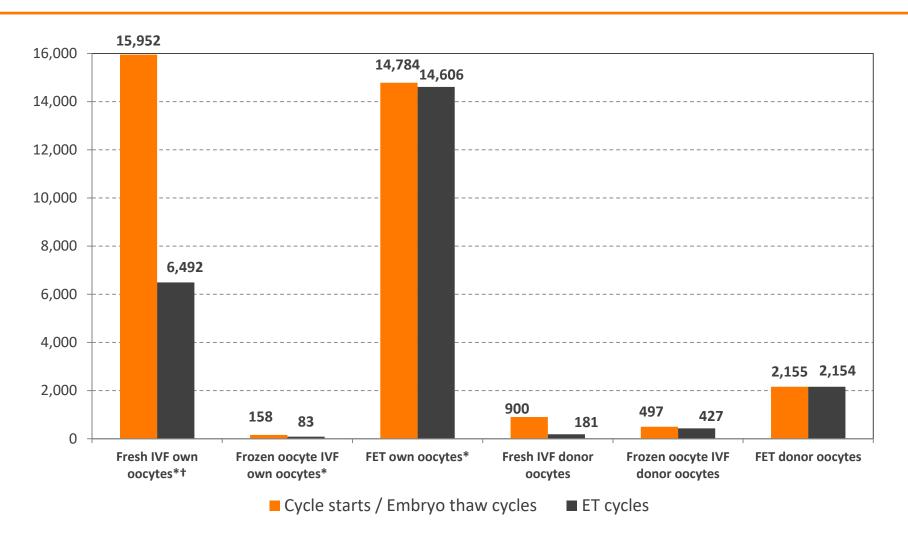
All ART treatment cycles (fresh and frozen)



Number of treatment cycles

2018





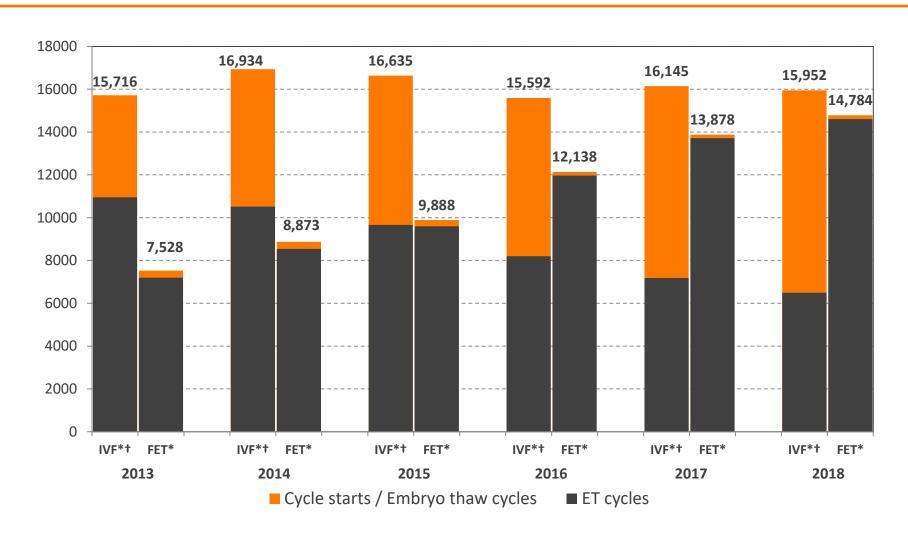
^{*} Own oocytes exclusively

[†] Includes Natural & Modified Natural IVF, own oocytes

Number of treatment cycles, by year



IVF and FET – own oocytes, 2013 – 2018



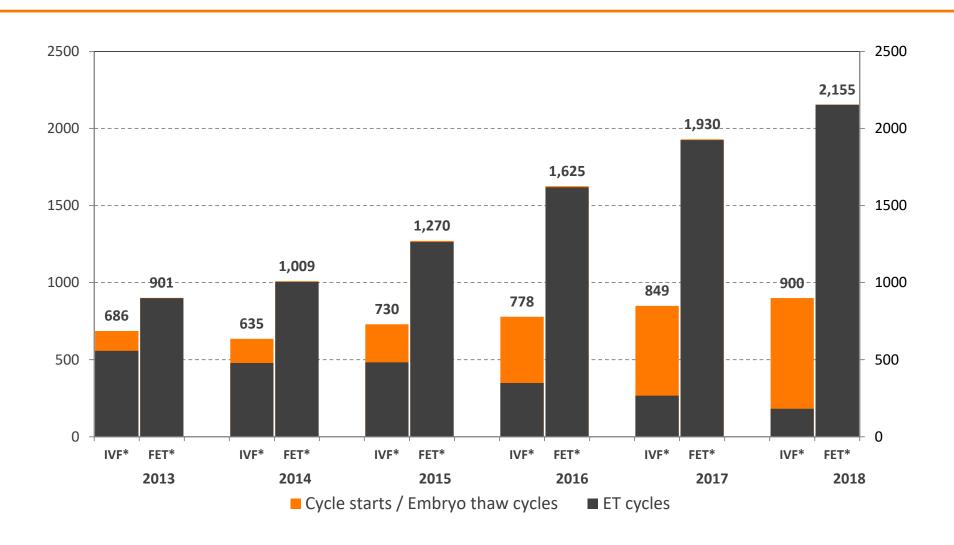
^{*} Own oocytes exclusively

[†] Includes Natural & Modified Natural IVF, own oocytes

Number of treatment cycles, by year



IVF and FET – donor oocytes, 2013 – 2018



Type of treatment cycle, per cycle start



All ART treatment cycles (fresh and frozen), 2018

Type of treatment cycle	Number	Percent
IVF – own oocytes*†	15,952	45.2
Frozen oocyte IVF – own oocytes*	158	0.5
FET – own oocytes*	14,784	41.9
IVF – donor oocytes	900	2.6
Frozen oocyte IVF – donor oocytes	497	1.4
FET – donor oocytes	2,155	6.1
Oocyte banking	817	2.3
IVM	13	0.04
TOTAL TREATMENT CYCLES	35,276	

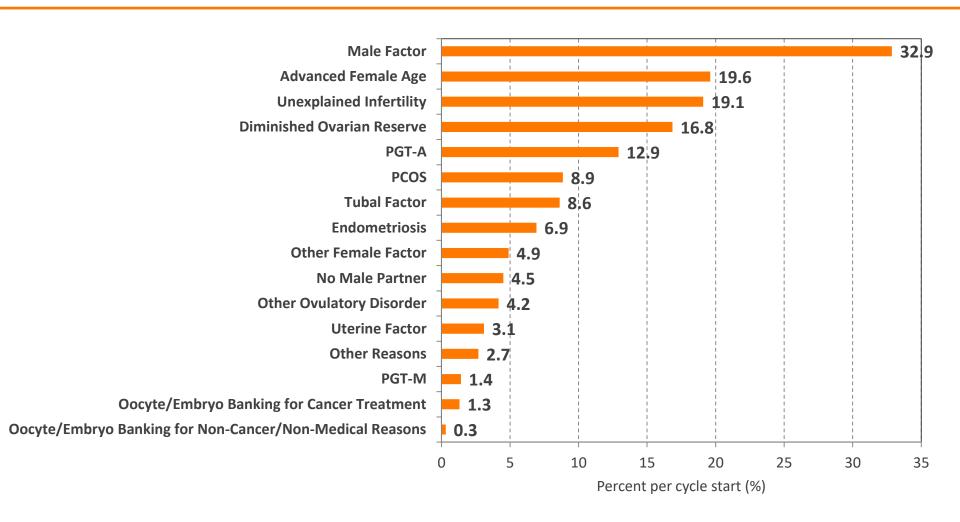
^{*} Own oocytes exclusively

[†] Includes Natural & Modified Natural IVF, own oocytes

Reasons for treatment



All ART treatment cycles (fresh and frozen), 2018



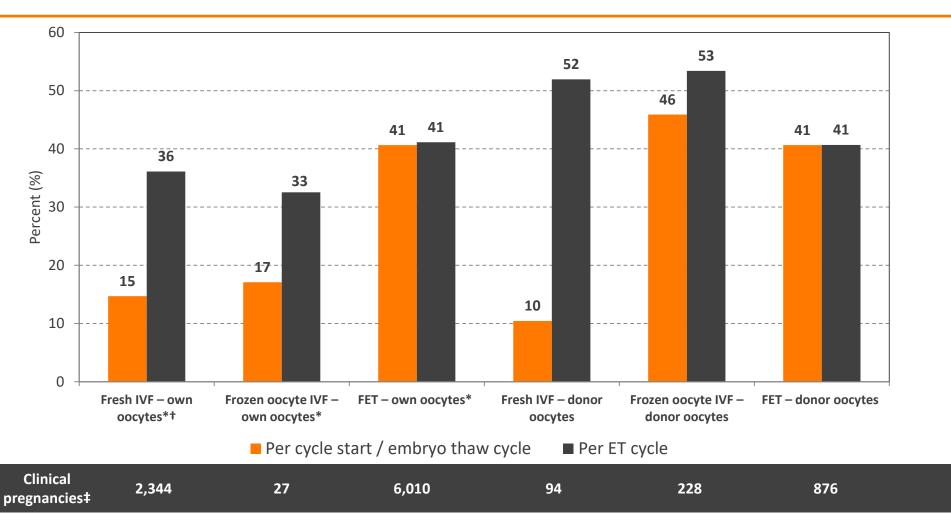
^{*} Categories are not mutually exclusive

[†] Other reasons include: gonadotoxic therapy, no female partner and peritoneal factor or severe adhesions

Clinical pregnancy by type of treatment cycle

Plus

2018



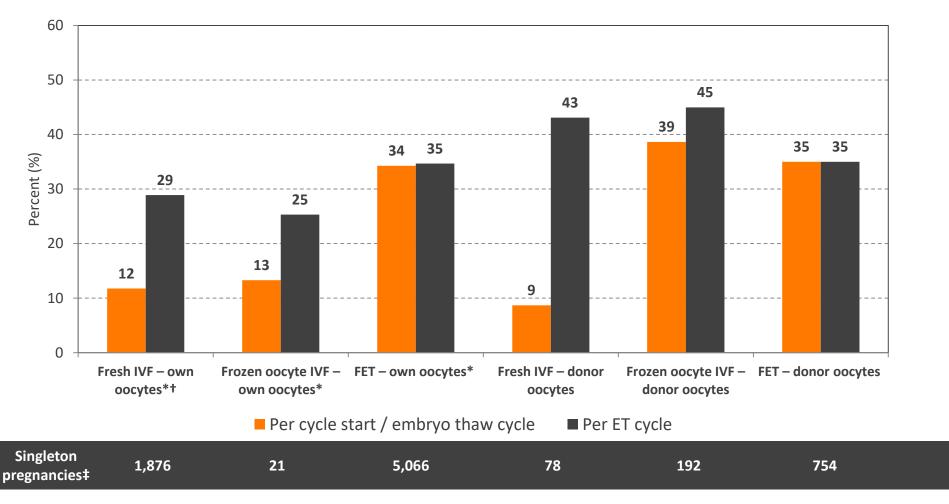
^{*} Own oocytes exclusively

[†] Includes Natural & Modified Natural IVF, own oocytes

[‡] Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

Singleton ongoing clinical pregnancy by type of treatment cycle

2018



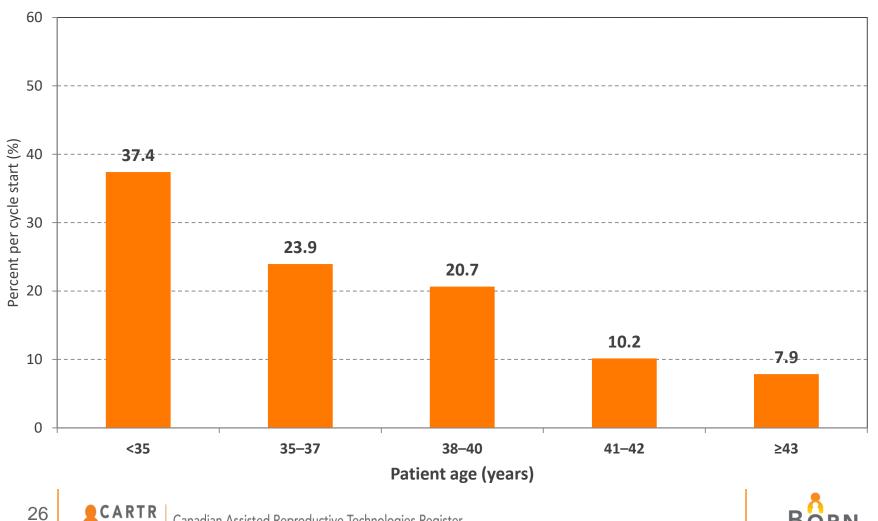
^{*} Own oocytes exclusively

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[‡] Singleton pregnancy: ongoing clinical pregnancy with only one fetal heart beat on ultrasound

Patient age

All ART treatment cycles (fresh and frozen), 2018





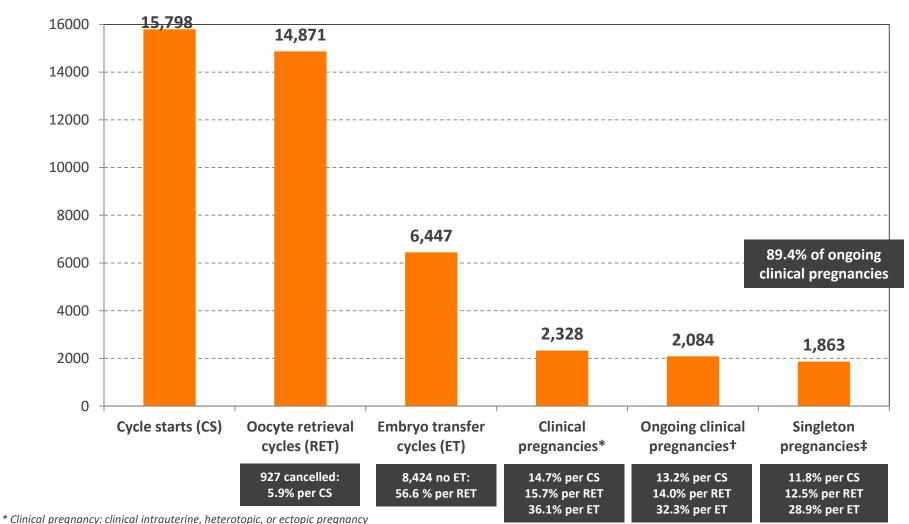
TREATMENT CYCLES FOR 2018





Stage of treatment and treatment outcomes





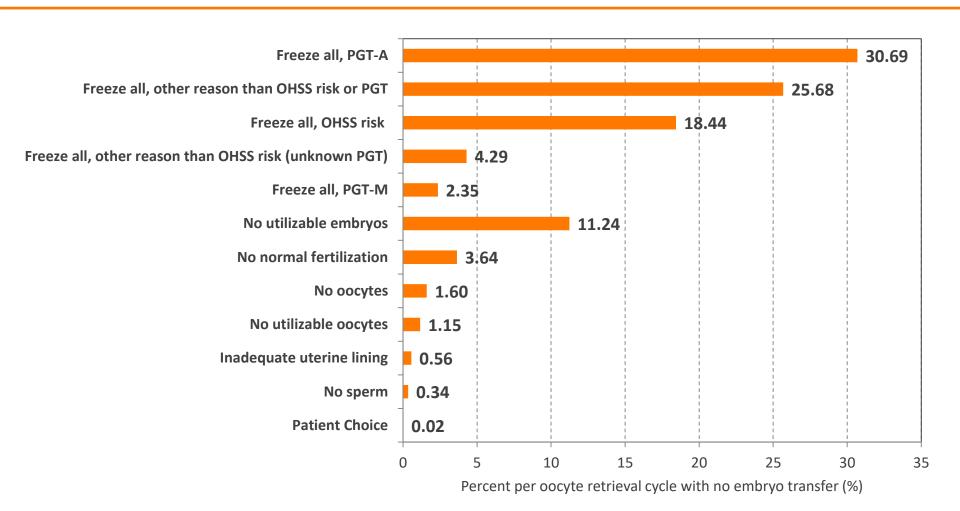
[†] Ongoing clinical pregnancy: clinical pregnancy with ≥1 fetal heart beat on ultrasound

[‡] Singleton pregnancy: ongoing clinical pregnancy with only one fetal heart beat on ultrasound

Reasons for no embryo transfer





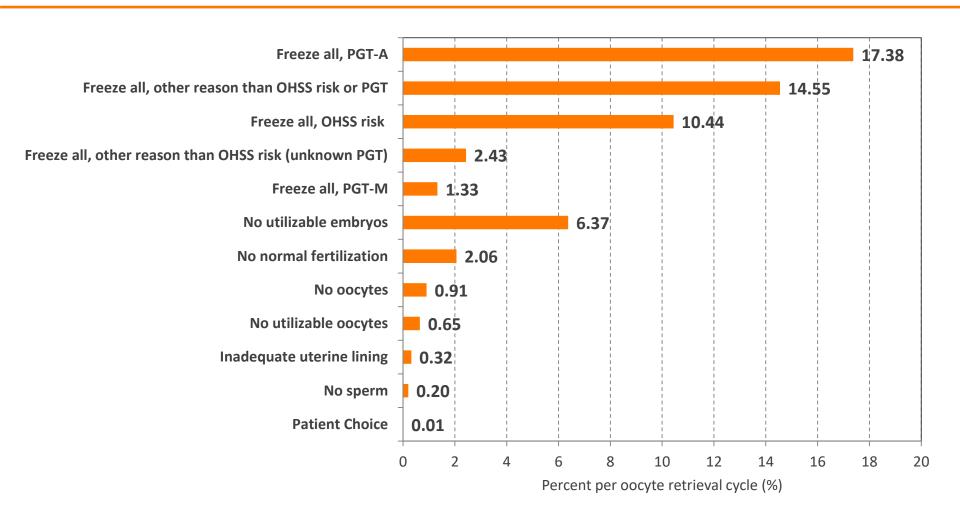


^{*} Categories are mutually exclusive

Reasons for no embryo transfer



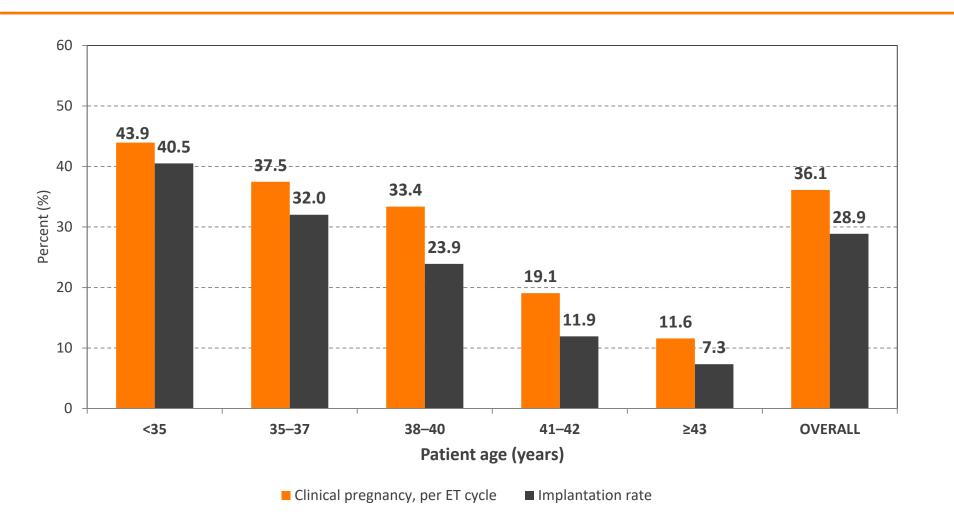




^{*} Categories are mutually exclusive

Clinical pregnancy and implantation rate



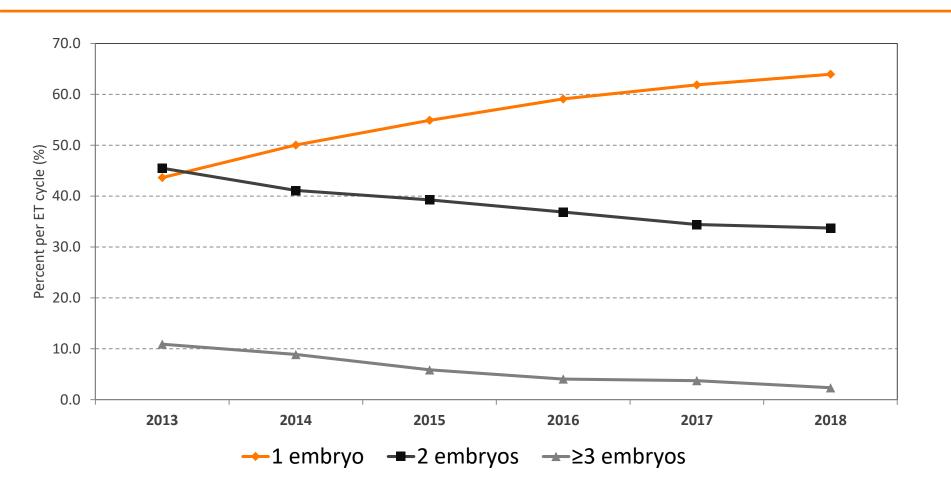


^{*} Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

[†] Implantation rate: number of gestational sacs observed on ultrasound, divided by the total number of embryos transferred

Number of embryos transferred, by year

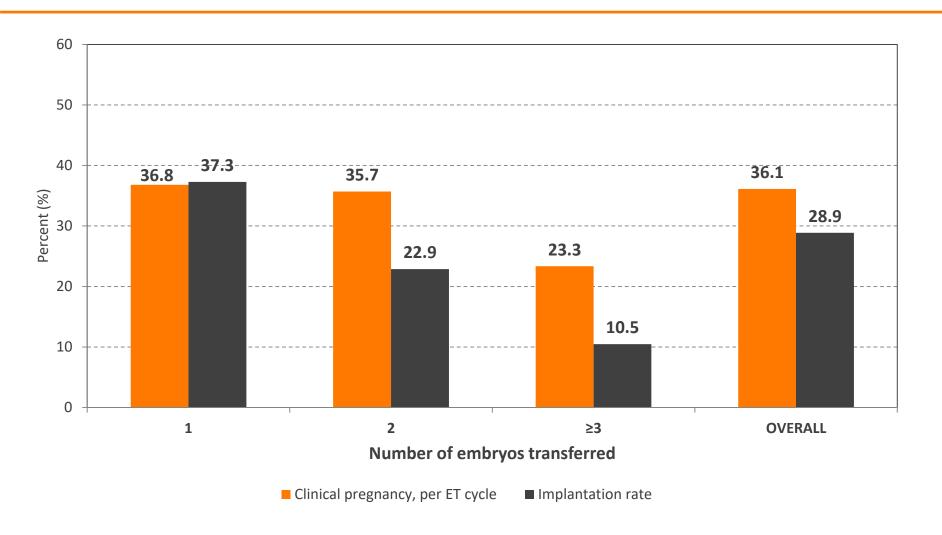




 $[\]hbox{* Excludes records with missing number of embryos transferred}$

Clinical pregnancy and implantation rate



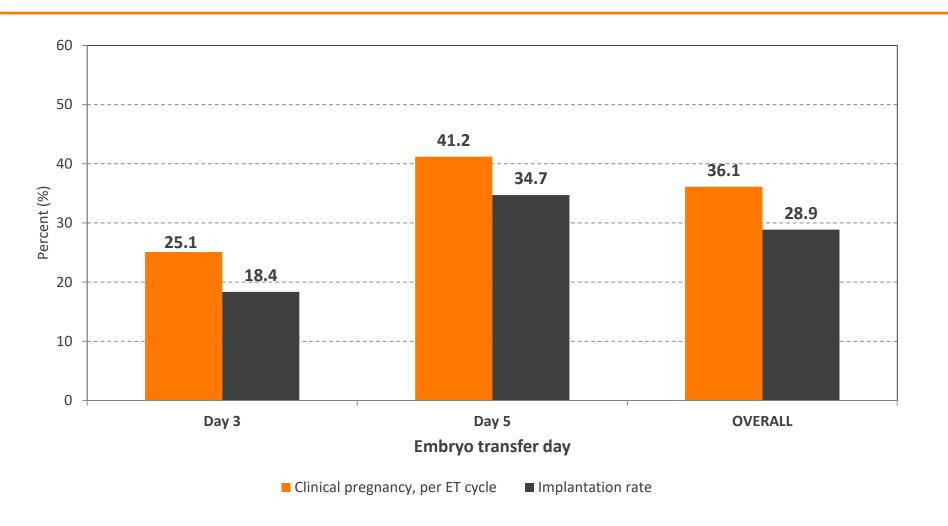


^{*} Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

[†] Implantation rate: number of gestational sacs observed on ultrasound, divided by the total number of embryos transferred

Clinical pregnancy and implantation rate



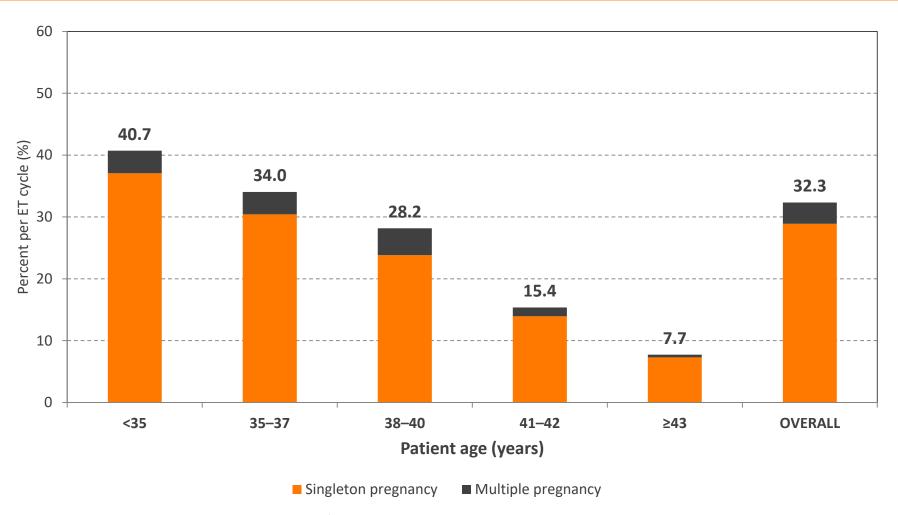


^{*} Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

[†] Implantation rate: number of gestational sacs observed on ultrasound, divided by the total number of embryos transferred

Proportion of cycles resulting in an ongoing clinical pregnancy





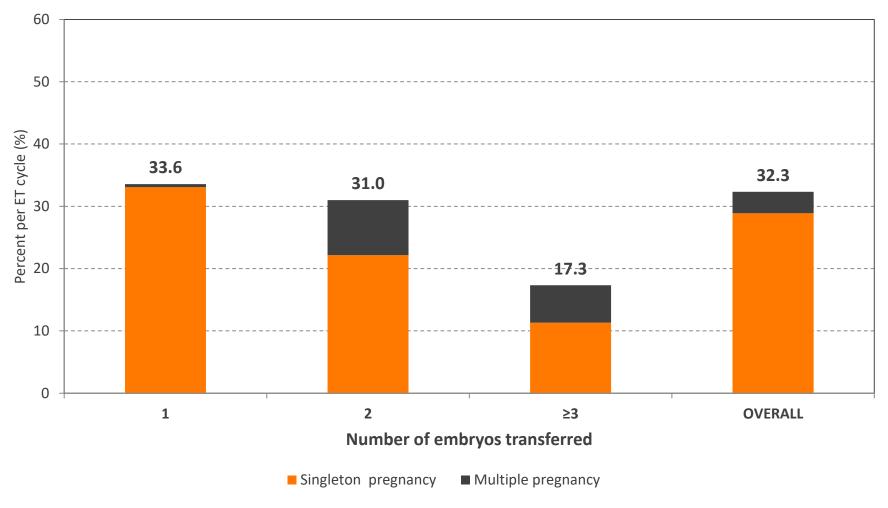
^{*} Ongoing clinical pregnancy: clinical pregnancy with ≥1 fetal heart beat on ultrasound

[†] Singleton pregnancy: ongoing clinical pregnancy with only one fetal heart beat on ultrasound; multiple pregnancy: ongoing clinical pregnancy with >1 fetal heart beat

Proportion of cycles resulting in an ongoing clinical pregnancy

ART cycles using IVF – own oocytes, 2018



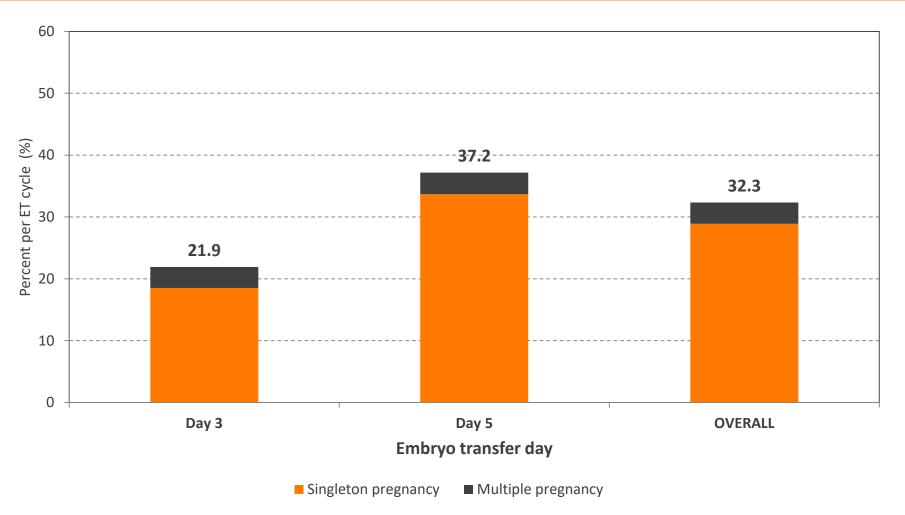


NOTE: In rare cases, a single embryo may divide and produce twins or triplets. For this reason, a small percentage of multiple pregnancies can result from a single embryo transfer * Ongoing clinical pregnancy: clinical pregnancy with ≥1 fetal heart beat on ultrasound

[†] Singleton pregnancy: ongoing clinical pregnancy with only one fetal heart beat on ultrasound; multiple pregnancy: ongoing clinical pregnancy with >1 fetal heart beat

Proportion of cycles resulting in an ongoing clinical pregnancy





^{*} Ongoing clinical pregnancy: clinical pregnancy with ≥1 fetal heart beat on ultrasound

[†] Singleton pregnancy: ongoing clinical pregnancy with only one fetal heart beat on ultrasound; multiple pregnancy: ongoing clinical pregnancy with >1 fetal heart beat

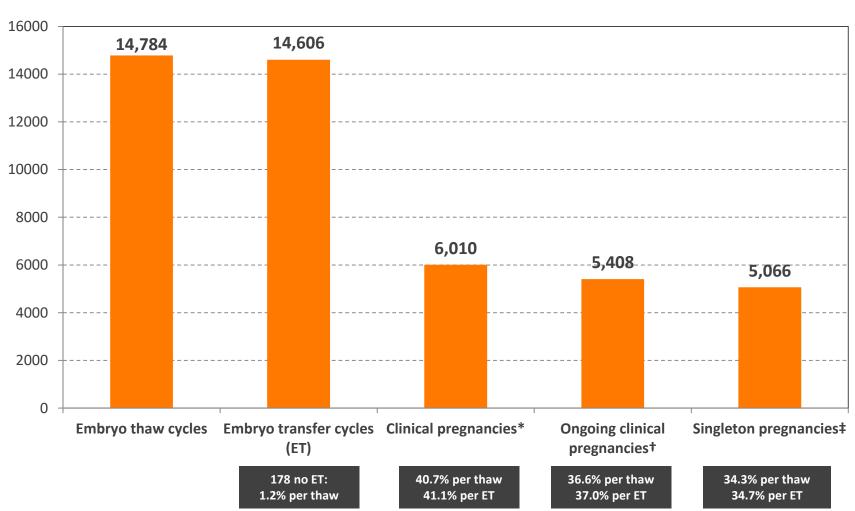
TREATMENT CYCLES FOR 2018





Stage of treatment and treatment outcomes





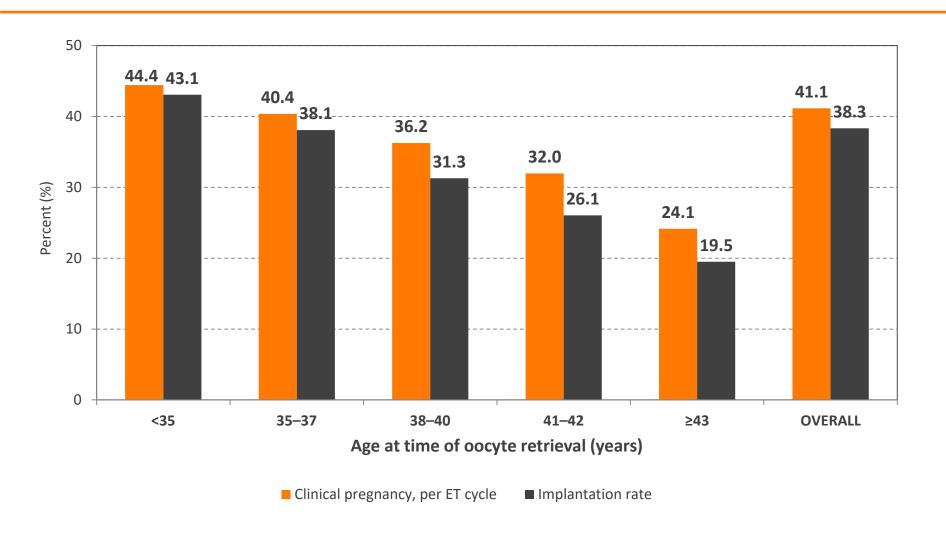
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[‡] Singleton pregnancy: ongoing clinical pregnancy with only one fetal heart beat on ultrasound

Clinical pregnancy and implantation rate



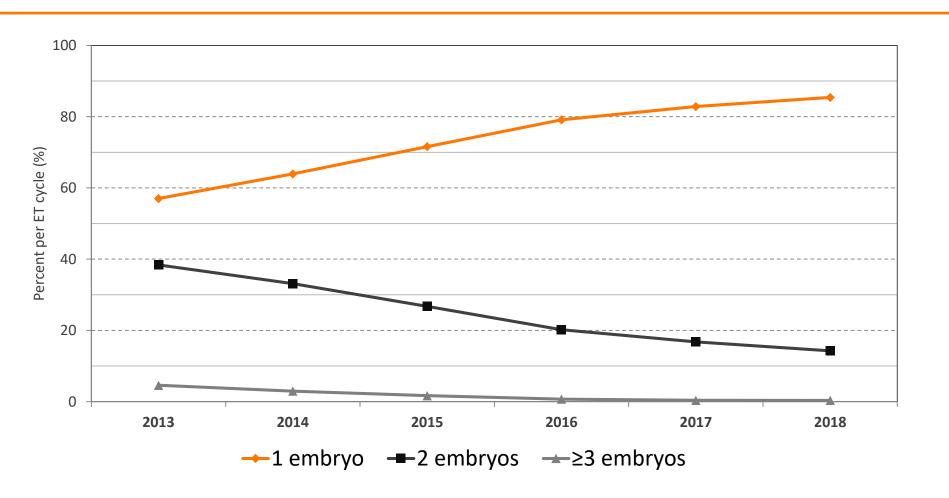


^{*} Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

[†] Implantation rate: number of gestational sacs observed on ultrasound, divided by the total number of embryos transferred

Number of embryos transferred, by year

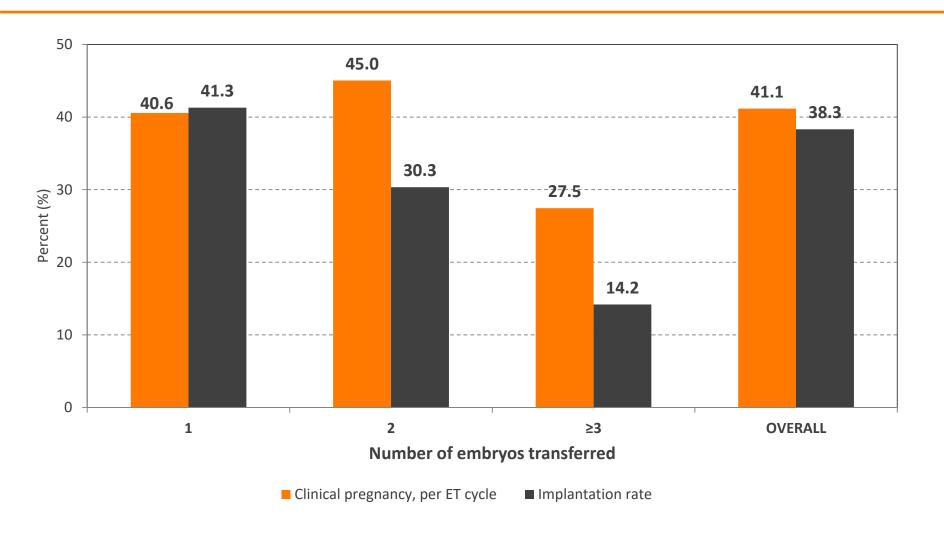




^{*} Excludes records with missing number of embryos transferred

Clinical pregnancy and implantation rate

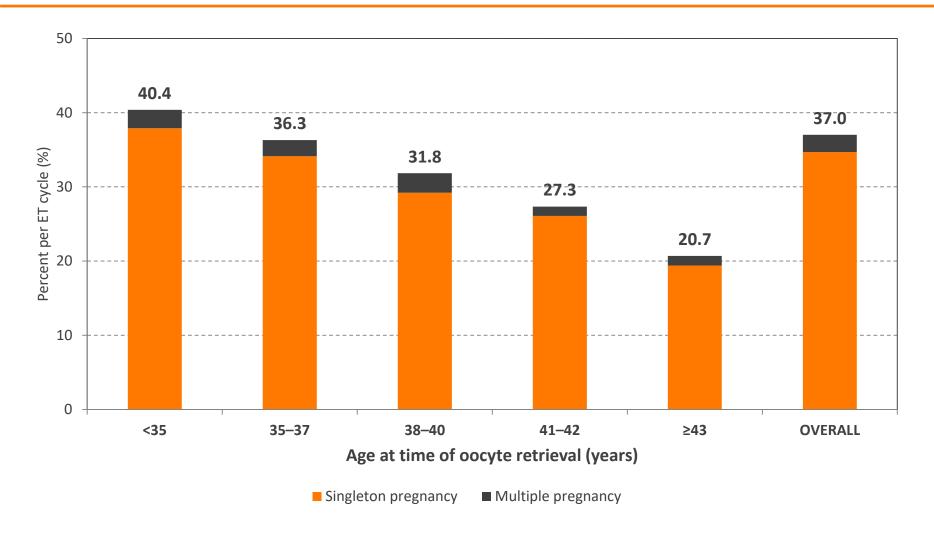




^{*} Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

[†] Implantation rate: number of gestational sacs observed on ultrasound, divided by the total number of embryos transferred

Proportion of cycles resulting in an ongoing clinical pregnancy



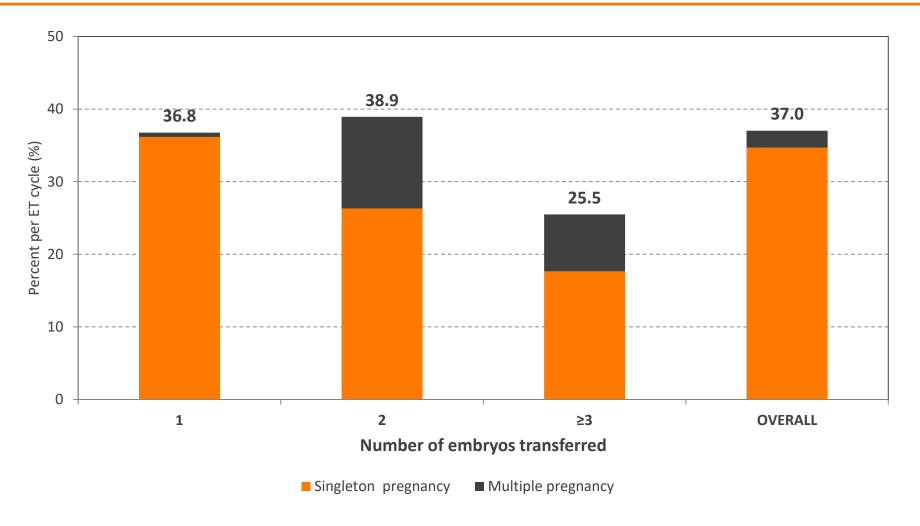
^{*} Ongoing clinical pregnancy: clinical pregnancy with ≥1 fetal heart beat on ultrasound

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Proportion of cycles resulting in an ongoing clinical pregnancy

ART cycles using FET – own oocytes, 2018





NOTE: In rare cases, a single embryo may divide and produce twins or triplets. For this reason, a small percentage of multiple pregnancies can result from a single embryo transfer * Ongoing clinical pregnancy: clinical pregnancy with ≥1 fetal heart beat on ultrasound

[†] Singleton pregnancy: ongoing clinical pregnancy with >1 fetal heart beat on ultrasound; multiple pregnancy: ongoing clinical pregnancy with >1 fetal heart beat

PRIMARY TRANSFER PREGNANCY RATE





Primary transfer rate

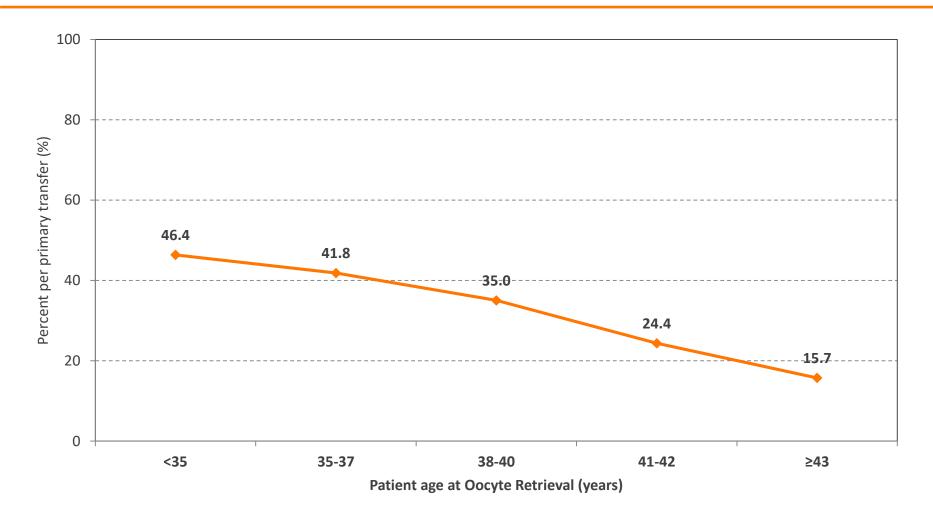
Cohort:

- Patients with first IVF cycle in CARTR Plus and no documented prior treatment cycle using own oocytes
- The first treatment cycle with an embryo transfer
 - IVF with own oocytes
 - FET with own oocytes
- Rate per patient: treatment cycle outcomes can be linked for a patient throughout the database



Primary transfer clinical pregnancy rate per patient



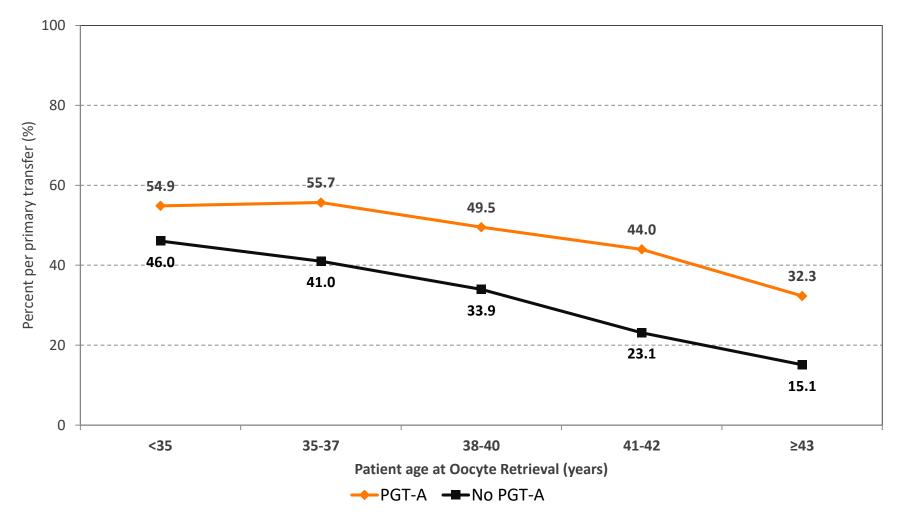


^{*} Own oocytes exclusively

[†] Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

Primary transfer clinical pregnancy rate per patient



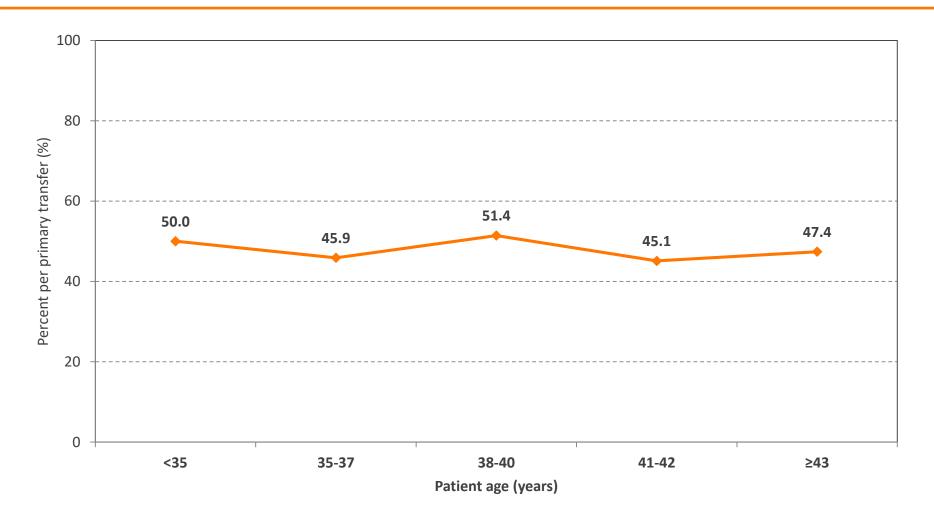


^{*} Own oocytes exclusively

[†] Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

Primary transfer clinical pregnancy rate per patient





^{*} Any donor oocytes

[†] Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

CUMULATIVE PREGNANCY RATE



Cumulative pregnancy rate

Definition:

 The number of clinical pregnancies resulting from one or more ART cycles, including the cycle when fresh embryos are transferred and all related subsequent frozen/thawed embryo transfer cycles if the fresh embryo transfer did not result in a pregnancy

Rationale:

 Estimates cumulative success with ongoing treatment, rather than success per individual stage of the treatment process



Cumulative pregnancy rate

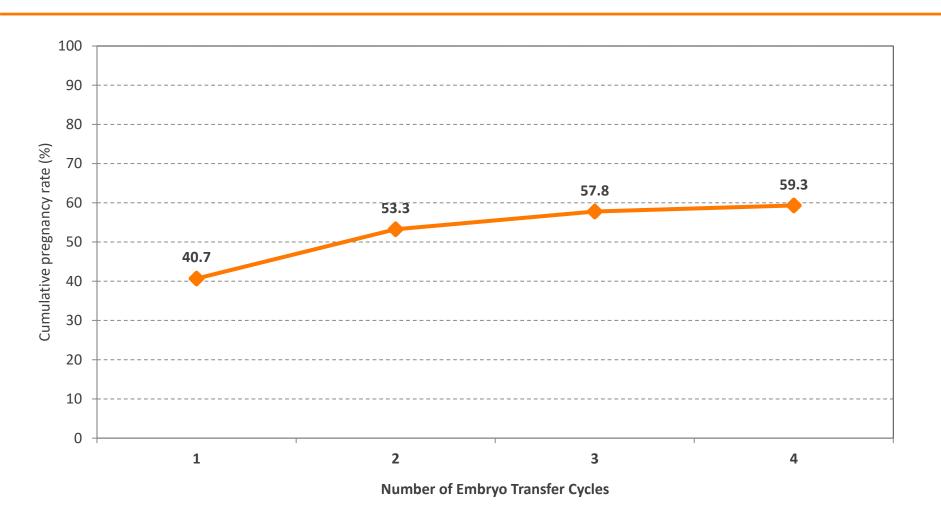
Several options for calculation:

- Per patient: treatment cycle outcomes can be linked for a patient throughout the database
- Per batch of oocytes collected: treatment cycles that used frozen oocytes or embryos can be linked to the IVF cycle where the oocytes were collected





Cumulative pregnancy rate, per patient

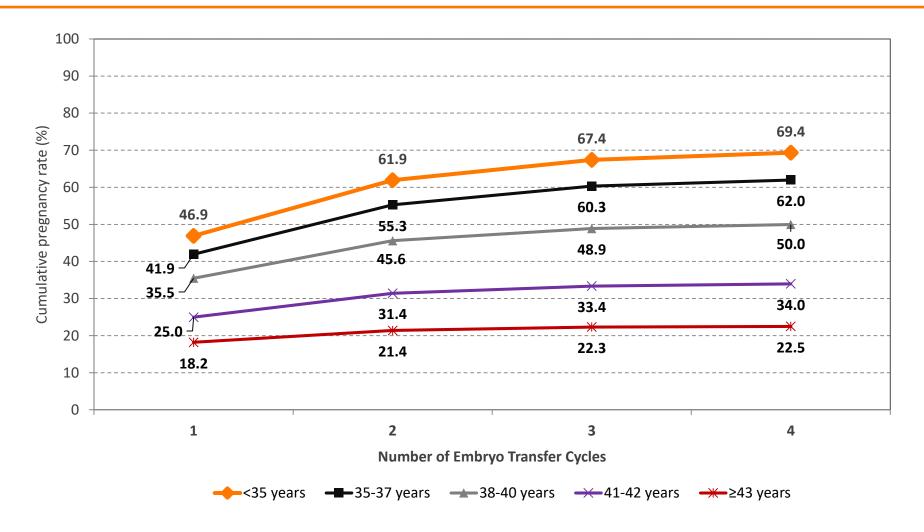


^{*} Own oocytes exclusively

[†] Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

CARTR Plus

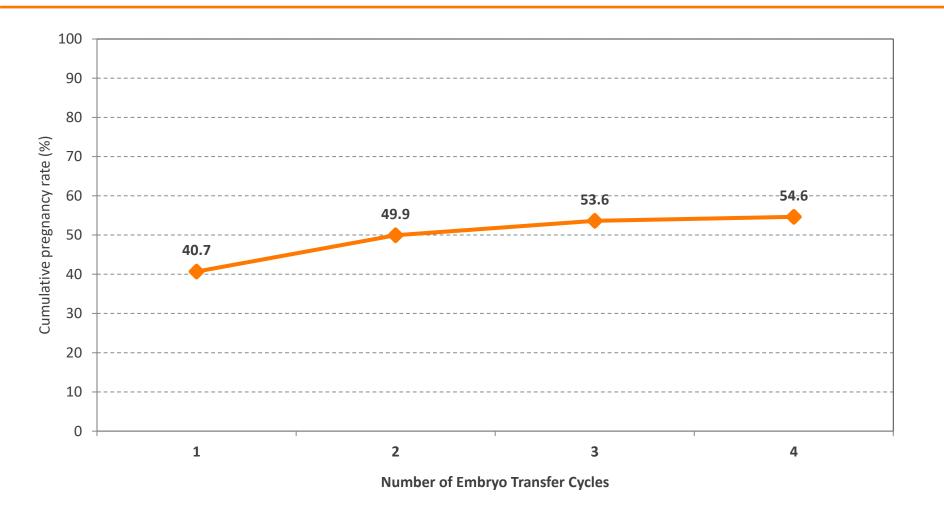
Cumulative pregnancy rate, per patient, by patient age



^{*} Own oocytes exclusively

[†] Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

Cumulative pregnancy rate, per patient, 1 year follow-up

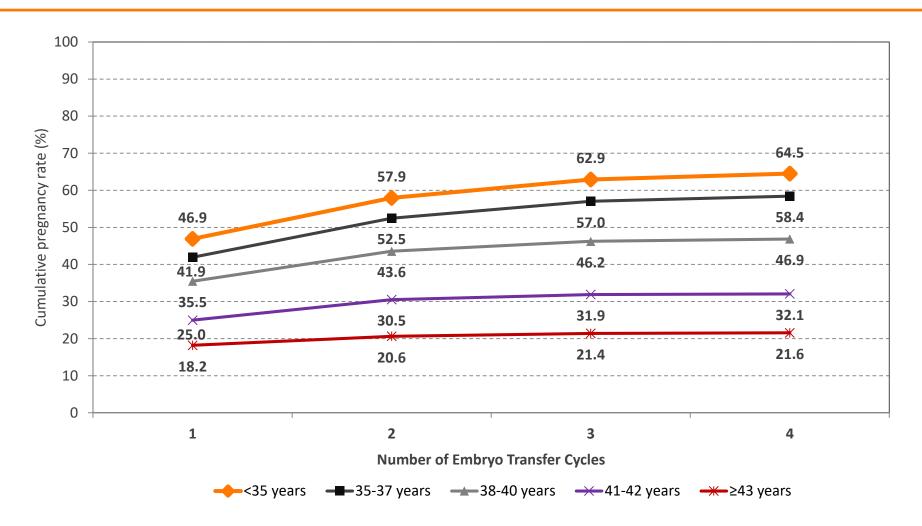


^{*} Own oocytes exclusively

[†] Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

Cumulative pregnancy rate, per patient, 1 year follow-up by patient age



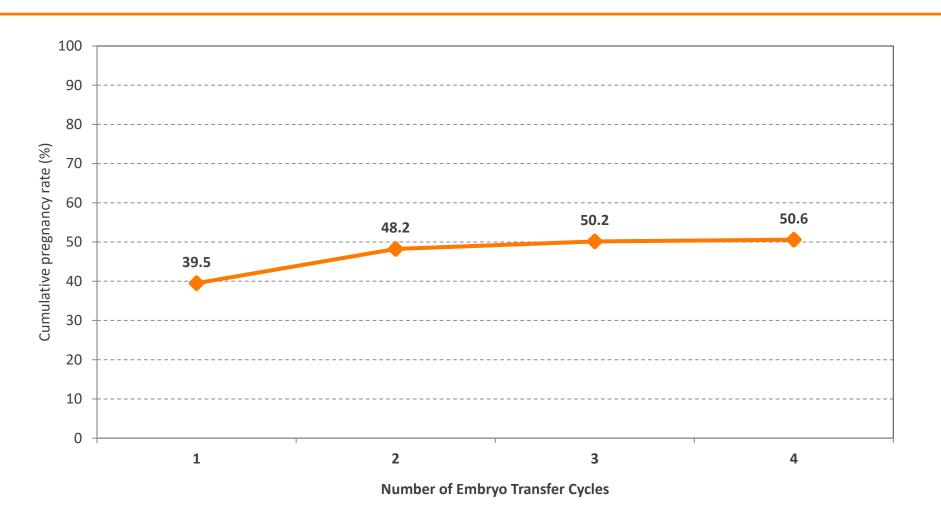


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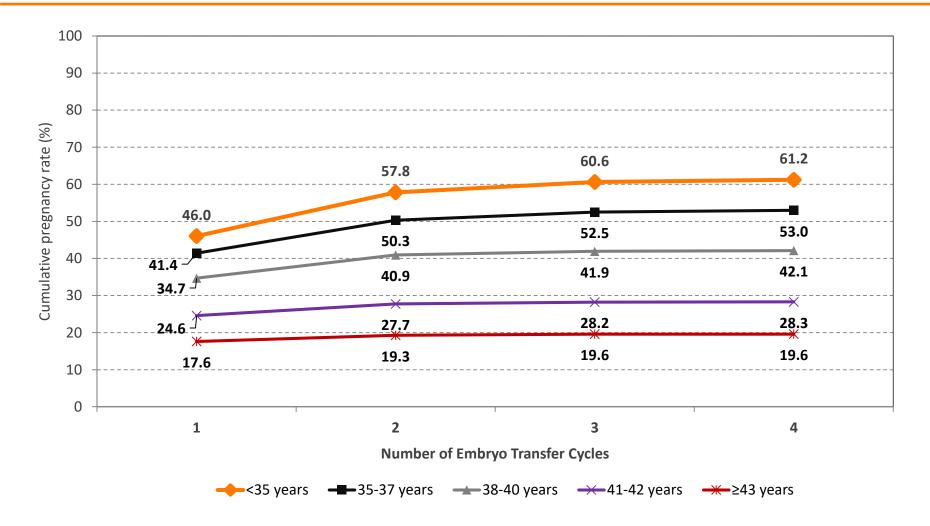
Cumulative pregnancy rate, per batch



^{*} Own oocytes exclusively

[†] Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

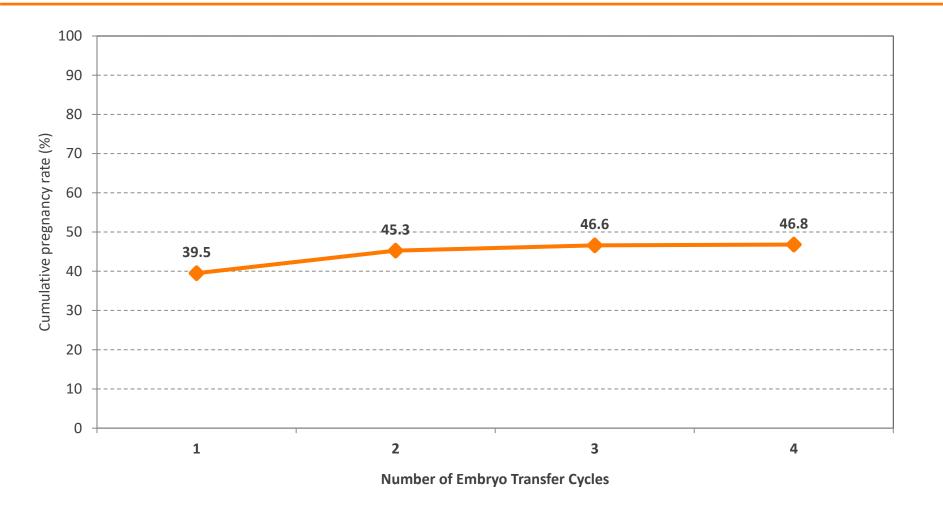
Cumulative pregnancy rate, per batch, by patient age



^{*} Own oocytes exclusively

[†] Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

Cumulative pregnancy rate, per batch, 1 year follow-up

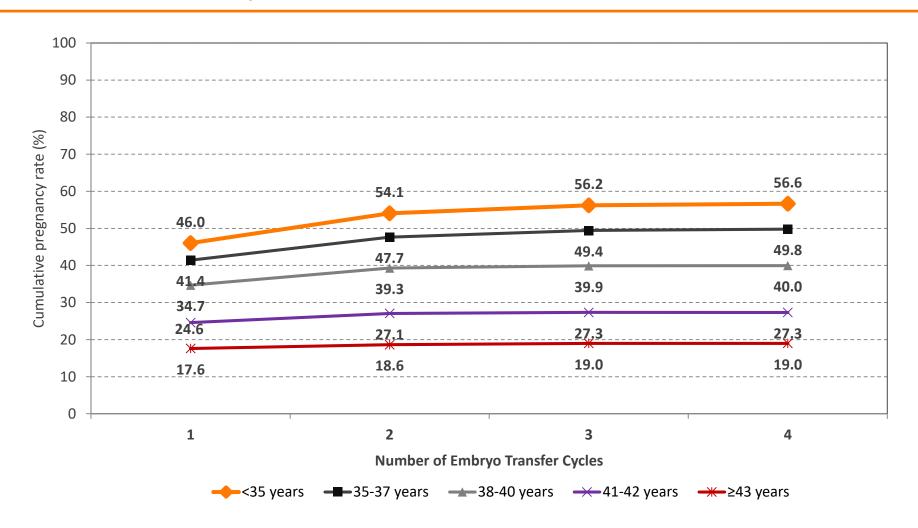


^{*} Own oocytes exclusively

[†] Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

Cumulative pregnancy rate, per batch, 1 year follow-up by patient age





^{*} Own oocytes exclusively

[†] Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

BIRTH OUTCOMES FOR 2017

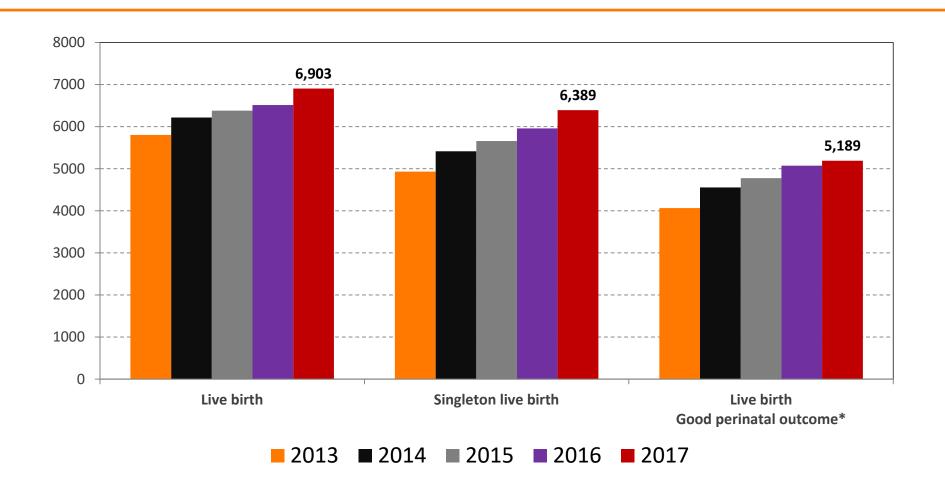
All ART treatment cycles (fresh and frozen)



Birth outcomes



All ART treatment cycles (fresh and frozen), 2013-2017



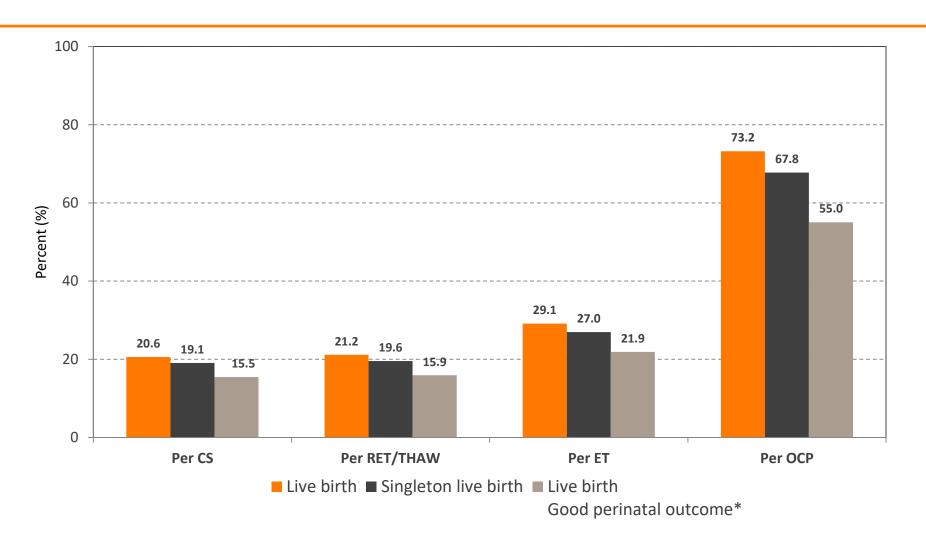
^{*} Good perinatal outcome: singleton live birth at ≥37 weeks' gestation and a birth weight ≥2,500 grams

[†] Cycle starts, oocyte retrievals/thaws and embryo transfers with an unknown birth outcome were removed from the denominator (n=501)

Birth outcome rates



All ART treatment cycles (fresh and frozen), 2017



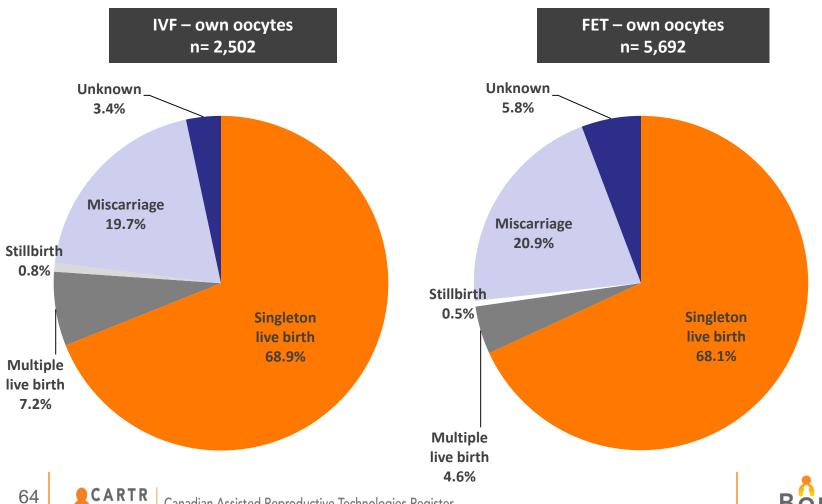
^{*} Good perinatal outcome: singleton live birth at ≥37 weeks' gestation and a birth weight ≥2,500 grams

OCP - Ongoing clinical pregnancy: a clinical pregnancy with documentation of at least one fetal heart beat on ultrasound

Cycle starts, oocyte retrievals/thaws and embryo transfers with an unknown birth outcome were removed from the denominator (n=501)

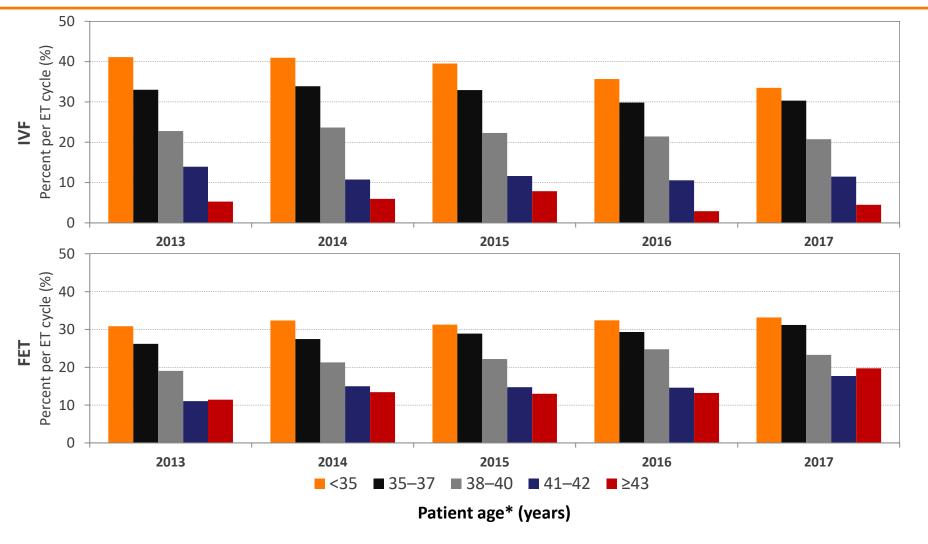
Distribution of birth outcomes among ongoing clinical pregnancies

ART cycles using IVF and FET – own oocytes, 2017



Proportion of Live Births

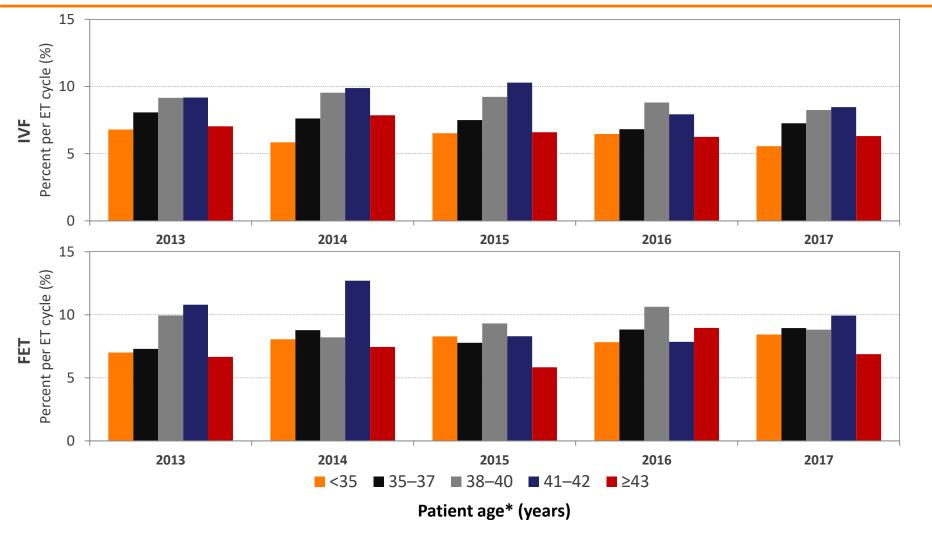




st Patient age at cycle start for IVF cycles and patient age at time of oocyte retrieval for FET cycles

Proportion of Miscarriages

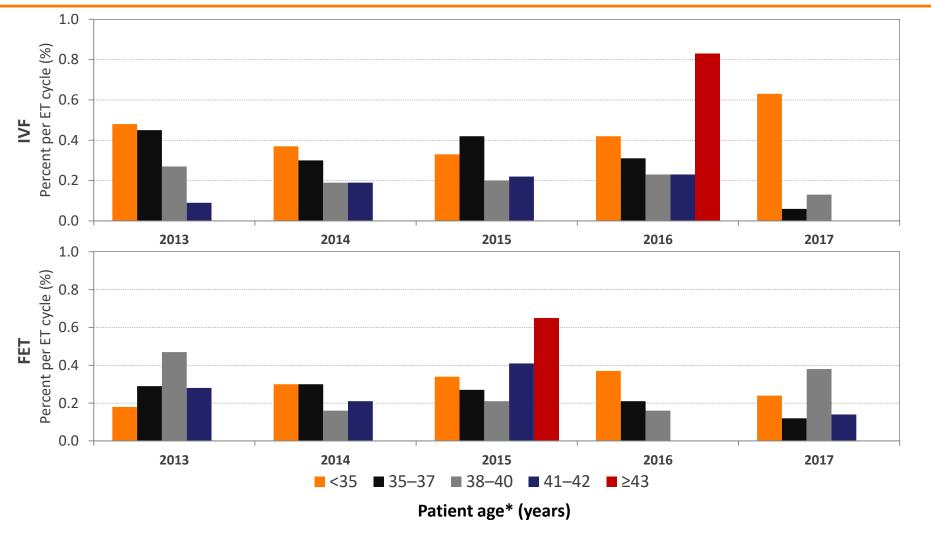




^{*} Patient age at cycle start for IVF cycles and patient age at time of oocyte retrieval for FET cycles † Miscarriage: birth outcome where all fetuses were a 'pregnancy loss' at <20 weeks' gestation

Proportion of Stillbirths



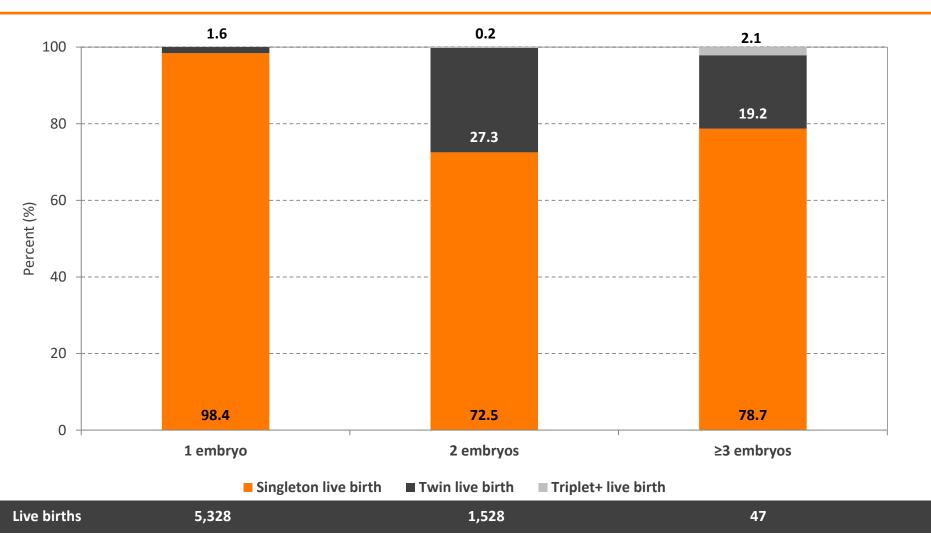


^{*} Patient age at cycle start for IVF cycles and patient age at time of oocyte retrieval for FET cycles † Stillbirths: birth outcome where no fetus(es) was born alive and at least one stillbirth at ≥ 20 weeks' gestation

Proportion of singleton and multiple live births



All ART treatment cycles (fresh and frozen), 2017



Singleton live birth: one live birth

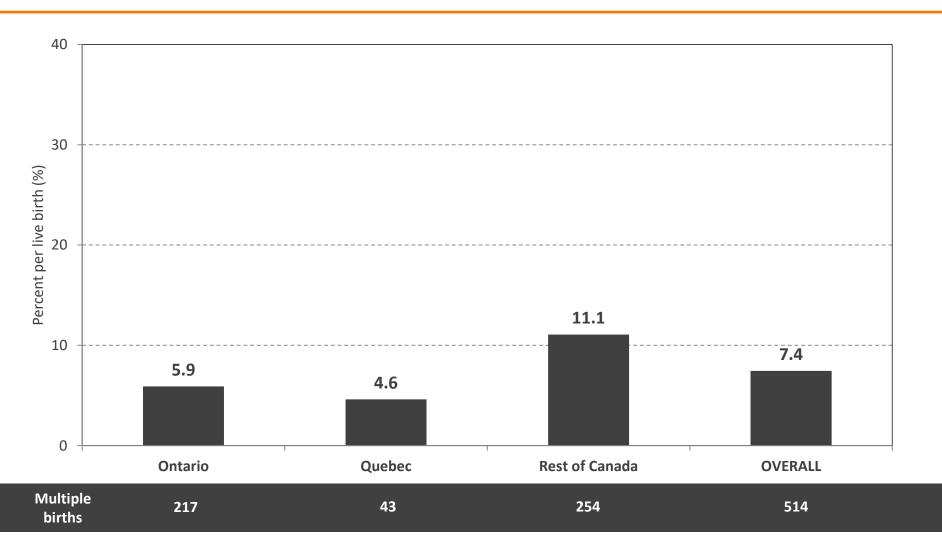
Twin live birth: two births and at least one live birth

Triplet+ live birth: three or more births and at least one live birth

Percentage of multiple live births by province



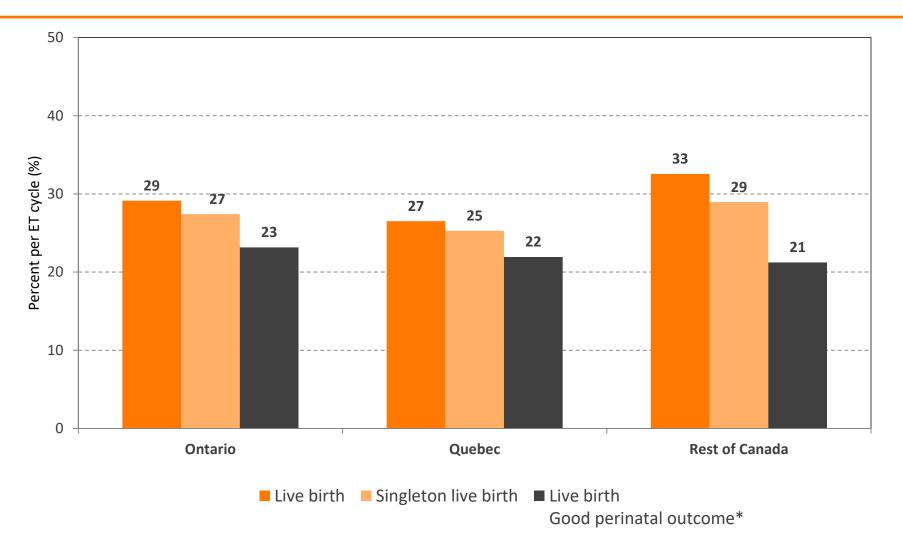
All ART treatment cycles (fresh and frozen), 2017



Birth outcomes by province



All ART treatment cycles (fresh and frozen), 2017

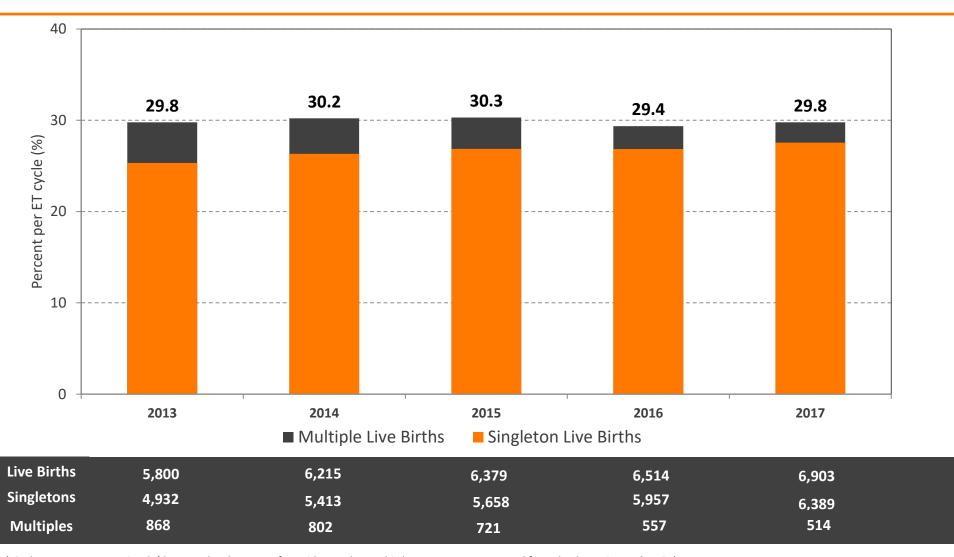


^{*} Good perinatal outcome: singleton live birth at \geq 37 weeks' gestation and a birth weight \geq 2,500 grams Cycle starts, and embryo transfers with an unknown birth outcome were removed from the denominator (n=501)

Proportion of singleton and multiple live births



All ART treatment cycles, 2013 – 2017

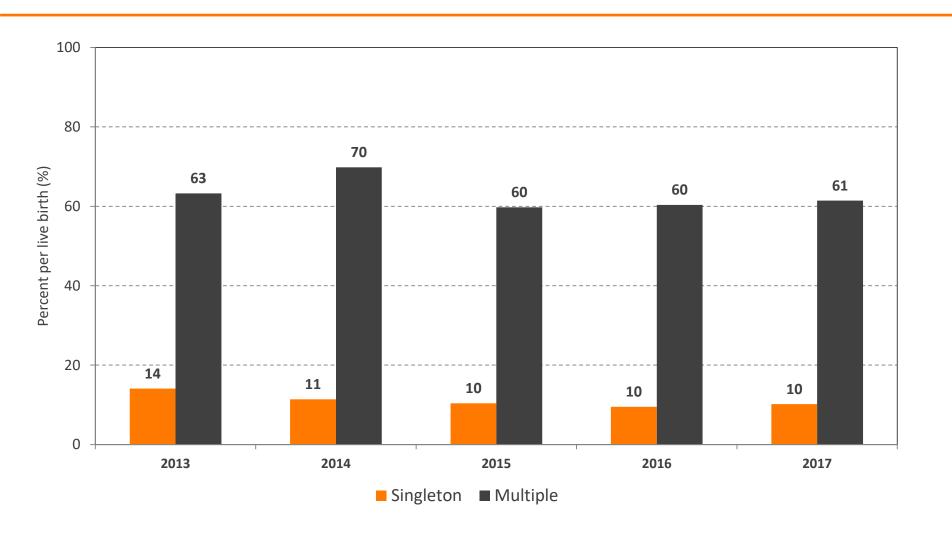


[†] Cycle starts, oocyte retrievals/thaws and embryo transfers with an unknown birth outcome were removed from the denominator (n=501)

Proportion of preterm births by plurality



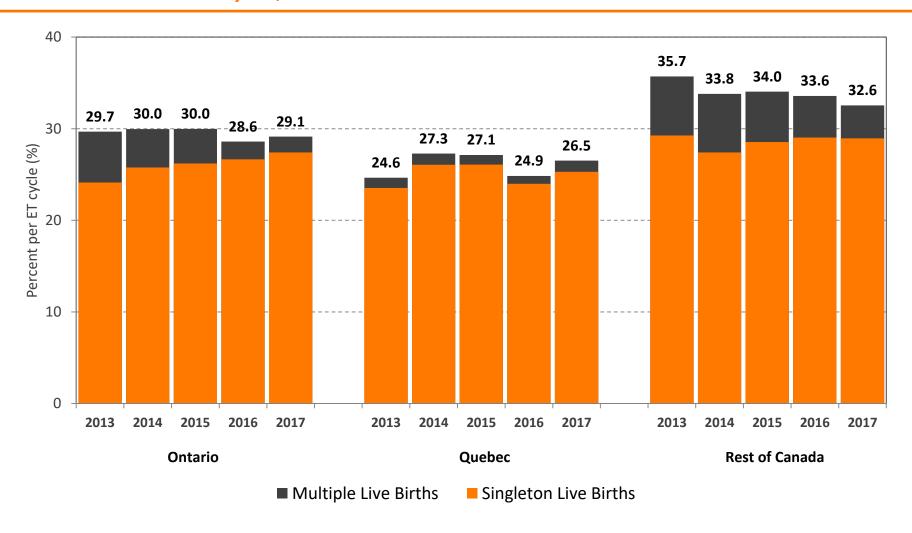
All ART treatment cycles (fresh and frozen),2013-2017



Proportion of singleton and multiple live births by province



All ART treatment cycles, 2013 – 2017



[†] Cycle starts, oocyte retrievals/thaws and embryo transfers with an unknown birth outcome were removed from the denominator (n=501)

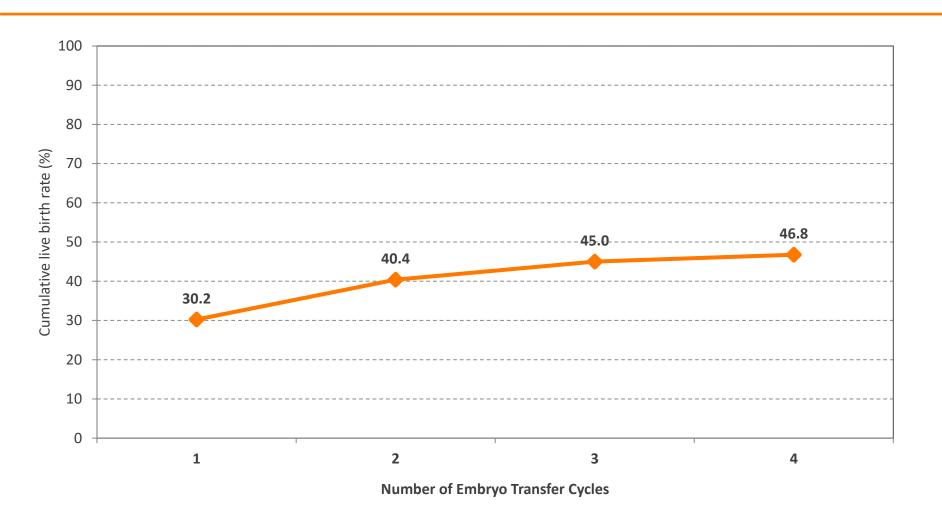
CUMULATIVE LIVE BIRTH RATE







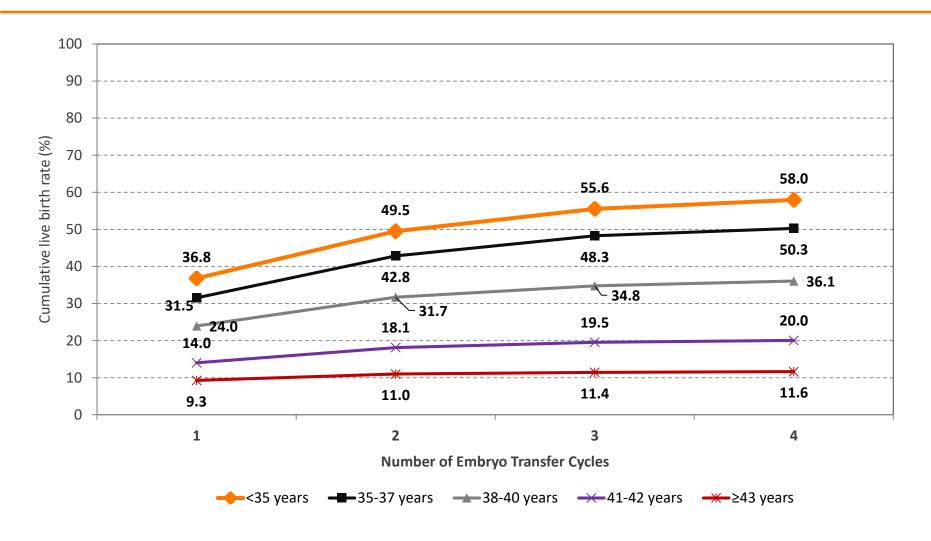
Cumulative live birth rate, per patient



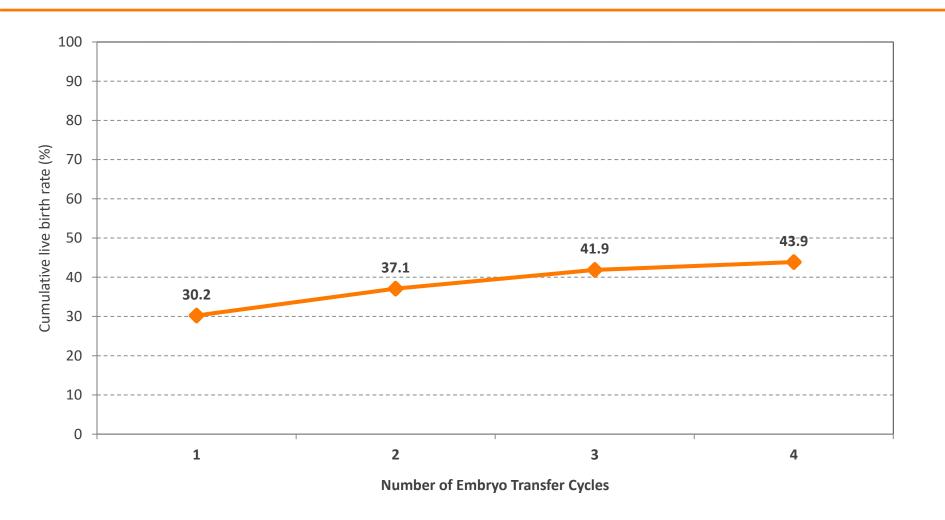
^{*} Own oocytes exclusively

CARTR Plus

Cumulative live birth rate, per patient, by patient age



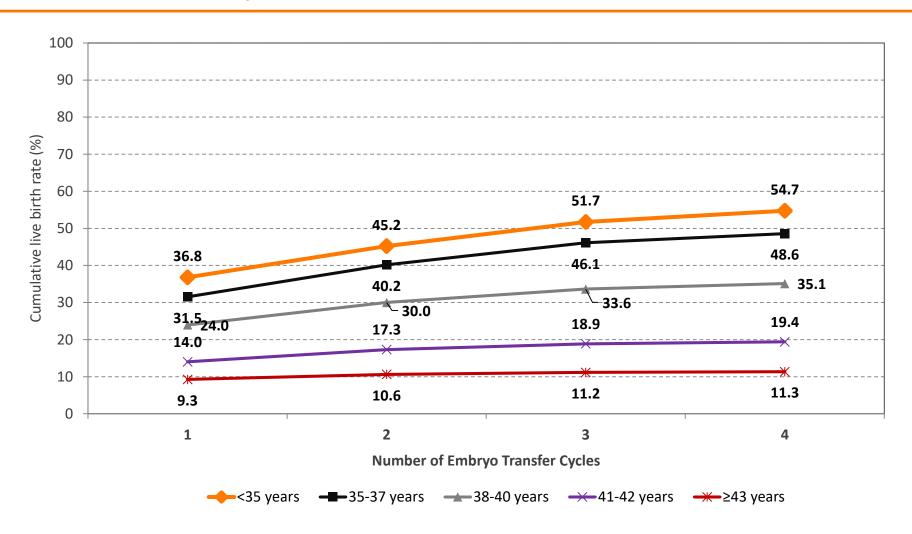
Cumulative live birth rate, per patient, 1 year follow-up



^{*} Own oocytes exclusively

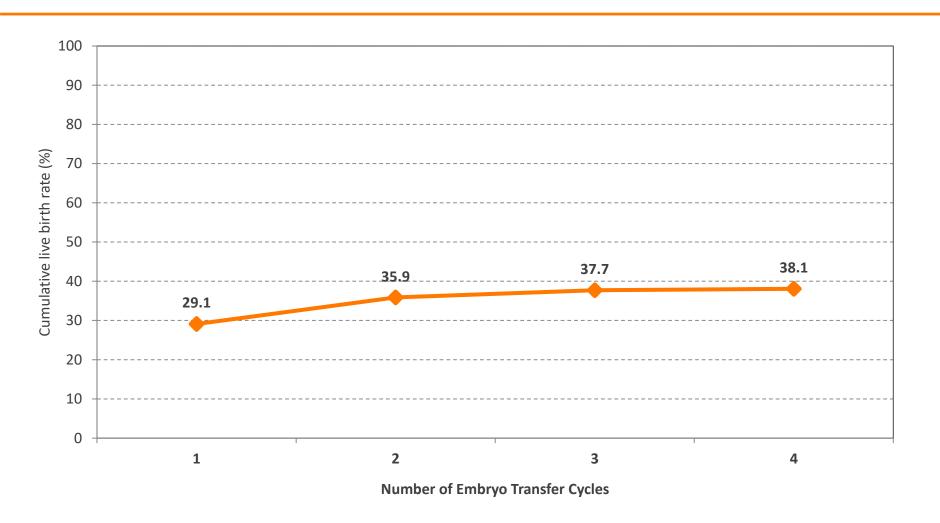
Cumulative live birth rate, per patient, 1 year follow-up by patient age







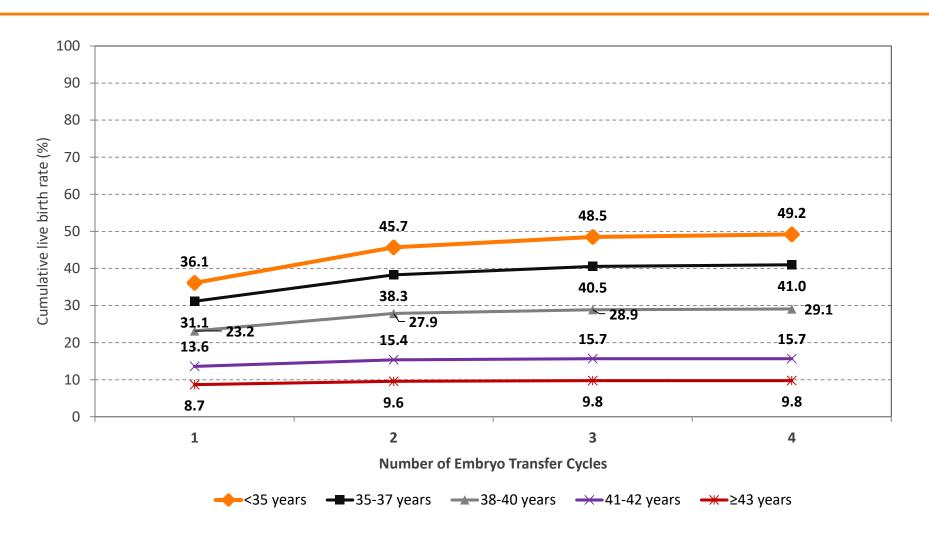
Cumulative live birth rate, per batch



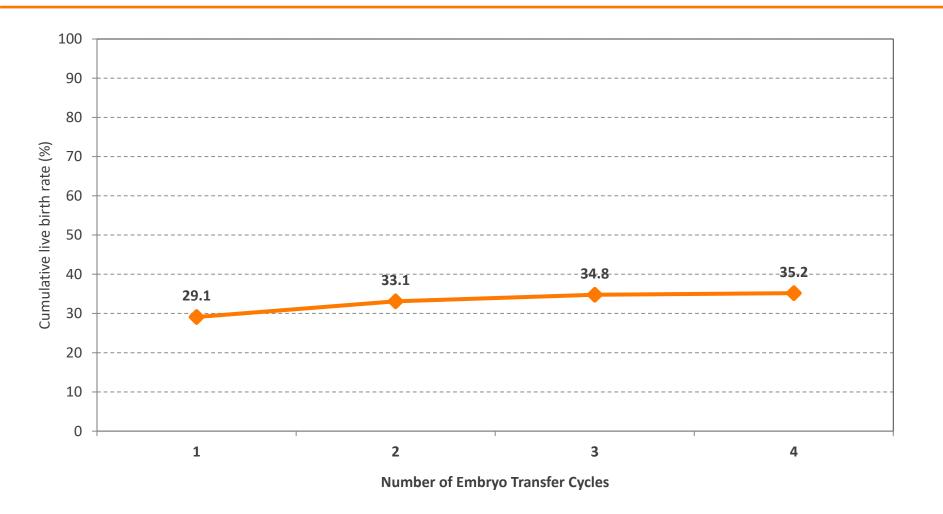
^{*} Own oocytes exclusively



Cumulative live birth rate, per batch, by patient age



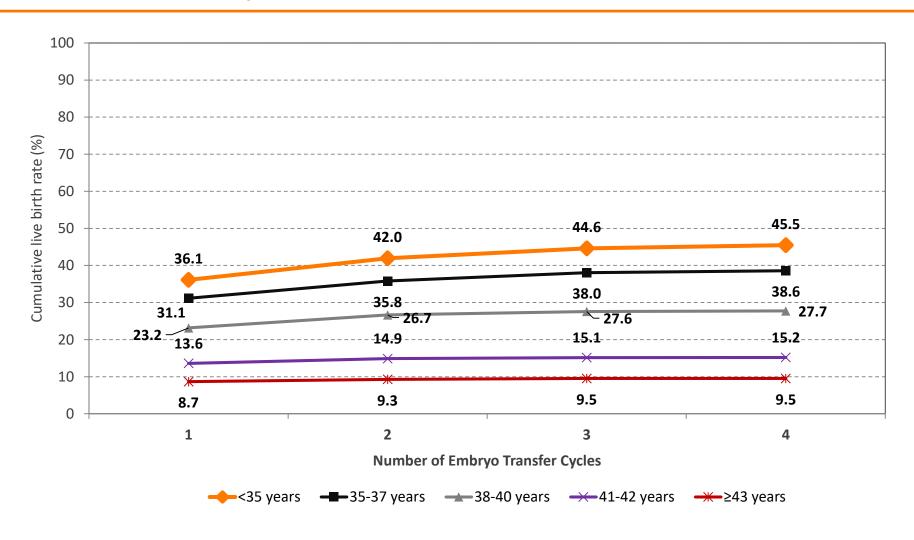
Cumulative live birth rate, per batch, 1 year follow-up



^{*} Own oocytes exclusively

Cumulative live birth rate, per batch, 1 year follow-up by patient age





ONTARIO FERTILITY PROGRAM



Ontario Fertility Program

2016

- 4,828 unique patients:
 - 4,768 IVF cycle starts
 - 60 fertility preservation cycles
- 70 gestational carrier cycles



Ontario Fertility Program

2016

• Treatment cycles:

- 5,673 IVF cycle starts
 - 0.86% cancellation rate
- 5,524 embryo transfer cycles
- 1,988 clinical pregnancies
 - 36.0% clinical pregnancy rate per ET
- 1,811 ongoing clinical pregnancy
 - 32.8% ongoing clinical pregnancy rate per ET
- 95 multiple pregnancies
 - 5.25% multiple pregnancy rate per ongoing clinical pregnancy

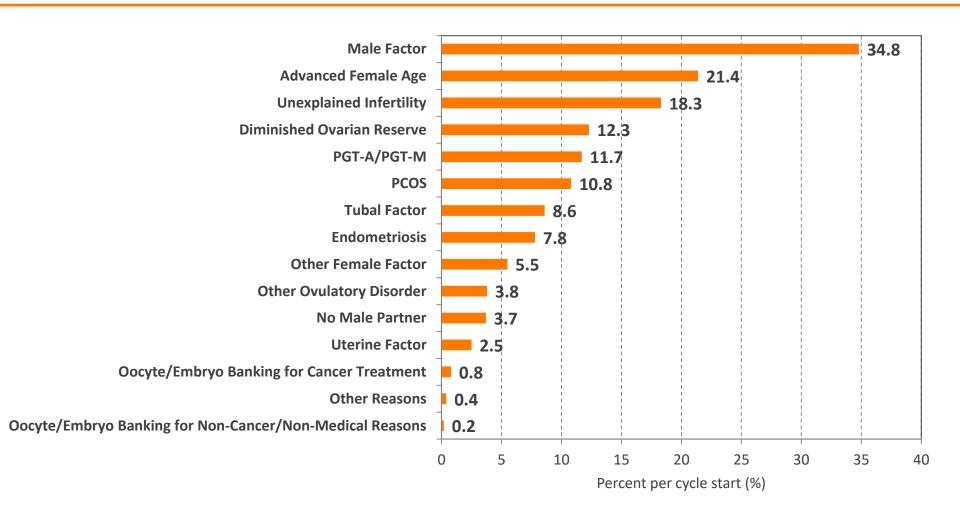




Reasons for treatment



All OFP ART treatment cycles (fresh and frozen), 2016



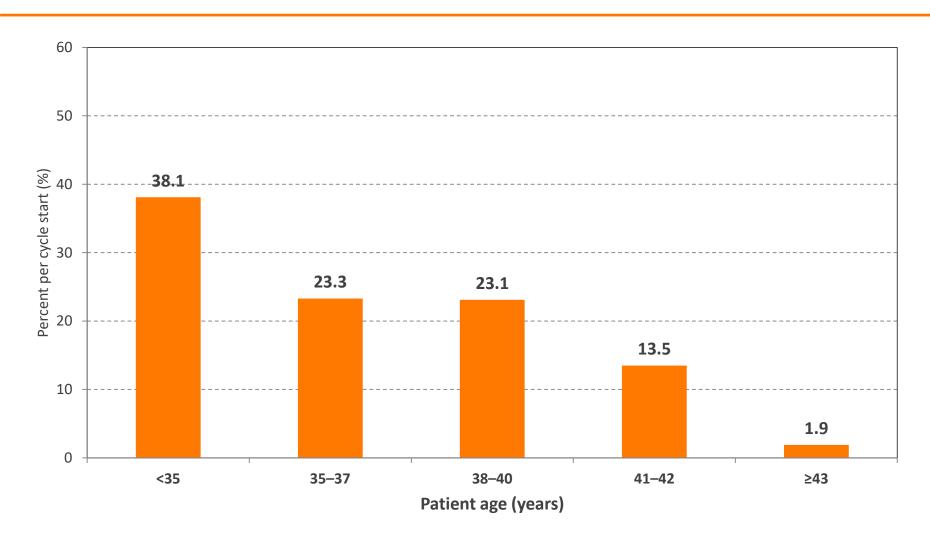
Excludes fertility preservation cycles

^{*} Categories are not mutually exclusive

[†] Other reasons include: gonadotoxic therapy, no female partner and peritoneal factor or severe adhesions

Patient age

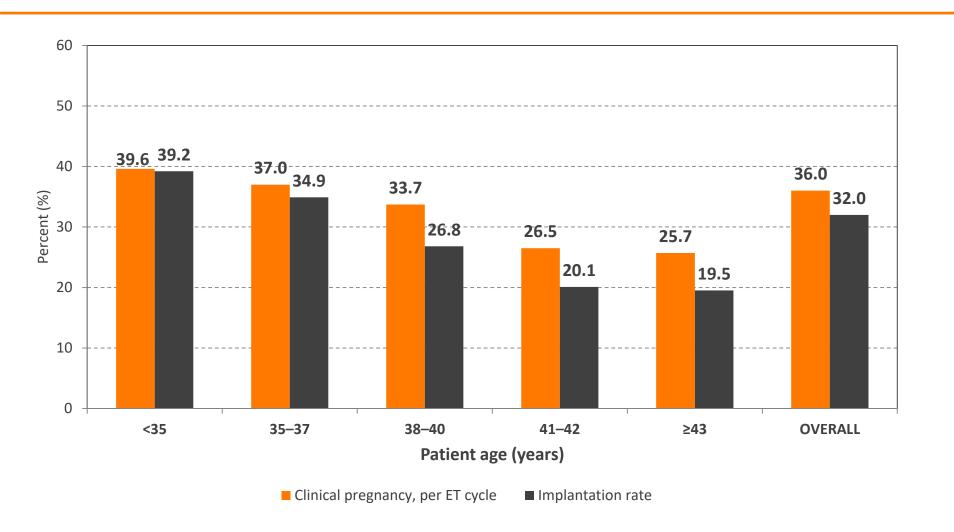
All OFP ART treatment cycles (fresh and frozen), 2016



Clinical pregnancy and implantation rate



All OFP ART treatment cycles (fresh and frozen), 2016



^{*} Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

 $^{{\}it + Implantation \ rate: number \ of \ gestational \ sacs \ observed \ on \ ultrasound, \ divided \ by \ the \ total \ number \ of \ embryos \ transferred}$

Ontario Fertility Program

2016

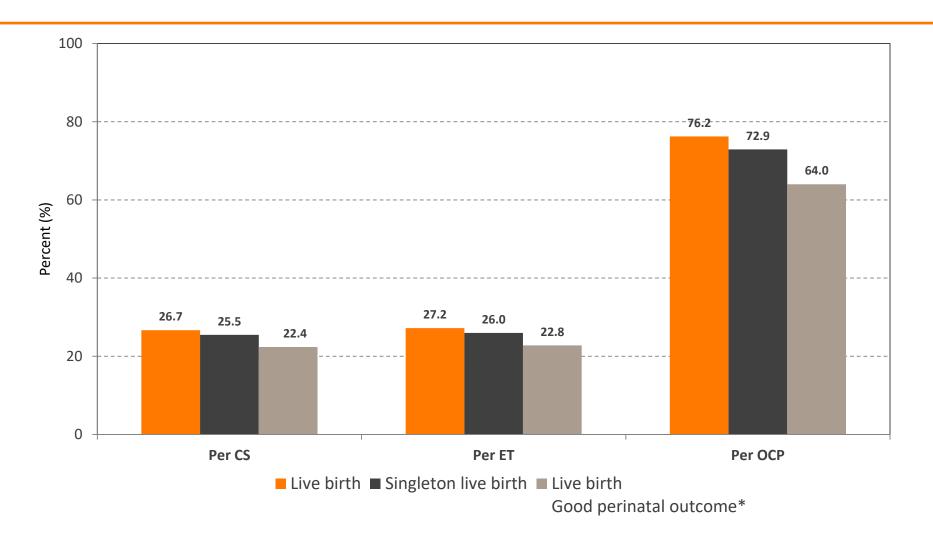
Birth outcomes:

- 1,489 live births
- 1,423 singleton live births
- 1,249 live births with a good perinatal outcome

Birth outcome rates



All OFP ART treatment cycles (fresh and frozen), 2016

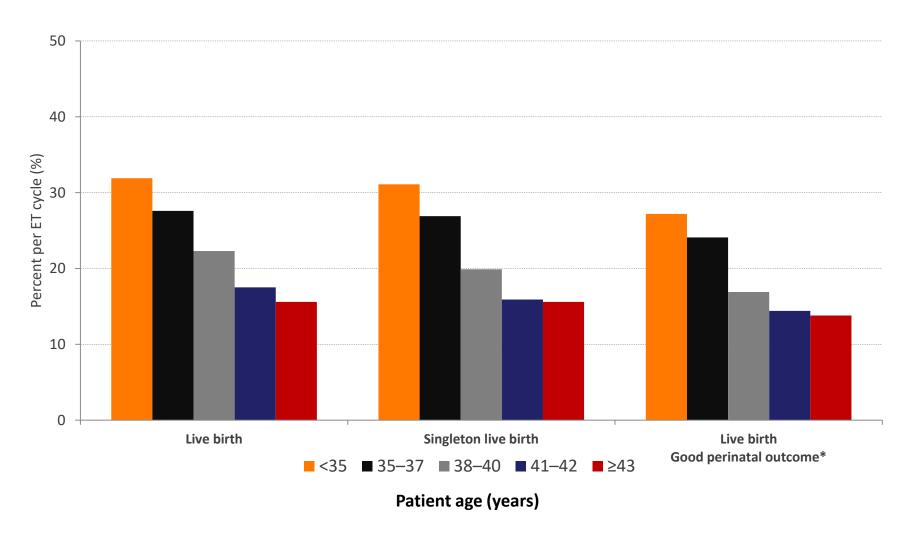


^{*} Good perinatal outcome: singleton live birth at ≥37 weeks' gestation and a birth weight ≥2,500 grams

Birth outcomes by patient age



All OFP ART treatment cycles (fresh and frozen), 2016



^{*} Good perinatal outcome: singleton live birth at ≥37 weeks' gestation and a birth weight ≥2,500 grams

GESTATIONAL AGE AT TIME OF DELIVERY

Ontario births: IVF conceptions compared to spontaneous conceptions





Preterm birth

ART vs. Non-ART Ontario – 2013 – 2017

Preterm birth:

- <37 weeks' gestation</p>
- RR = 2.16 95% CI: 2.08-2.24
- adjusted RR = 2.05 95% CI: 1.97–2.14

Singleton preterm births:

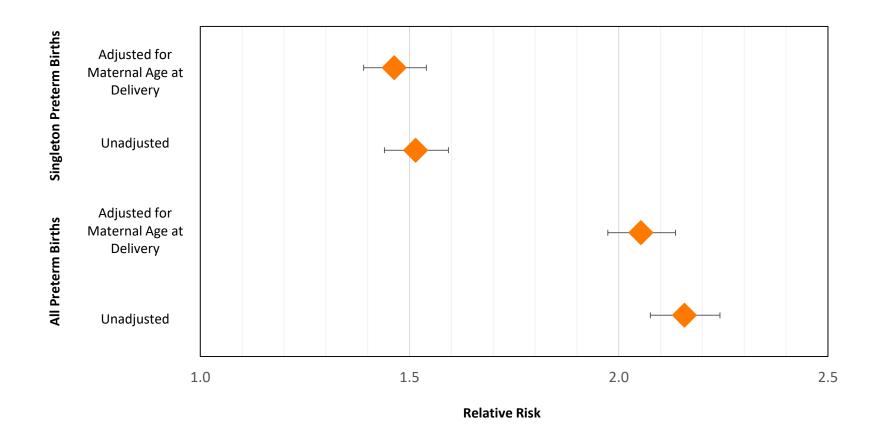
- <37 weeks' gestation</p>
- RR = 1.51 95% CI: 1.44-1.59
- adjusted RR = 1.46 95% CI: 1.39–1.54



^{*} Adjusted for maternal age at delivery.

Preterm birth in Ontario

ART vs. Non-ART Ontario – 2013 – 2017



^{*}Preterm birth is defined as live birth or stillbirth at ≤37 weeks gestation.

^{*}Error bars represent 95% Confidence Intervals



Gestational age at time of delivery

ART vs. Non-ART Ontario – 2013 – 2017



Gestational age at delivery	Total births	ART		Non-ART		RR (95% CI)	Adj. RR (95%CI)
		n	%	n	%	(0070-0.)	(527223)
<32 weeks	11,932	488	3.46	11,444	1.46	2.38 (2.17, 2.60)	2.20 (2.01, 2.41)
32 weeks	2,529	106	0.75	2,423	0.31	2.44 (2.01, 2.96)	2.33 (1.91, 2.84)
33 weeks	3,833	196	1.39	3,637	0.46	3.00 (2.60, 3.46)	2.83 (2.45, 3.28)
34 weeks	6,847	280	1.99	6,567	0.84	2.38 (2.11, 2.67)	2.26 (2.00, 2.55)
35 weeks	11,669	417	2.96	11,252	1.43	2.07 (1.86, 2.27)	2.01 (1.82, 2.21)
36 weeks	23,784	771	5.47	23,013	2.93	1.87 (1.74, 2.00)	1.79 (1.67, 1.92)
≥37 weeks	738,422	11,827	83.97	726,595	92.56	0.91 (0.90, 0.91)	0.91 (0.90, 0.92)

^{*} Adjusted for maternal age at delivery.

Gestational age at time of delivery for singleton pregnancies



ART vs. Non-ART Ontario – 2013 – 2017

Gestational age at delivery	Total births	ART		Non-ART		RR (95% CI)	Adj. RR (95%CI)
		n	%	n	%	(0010 01)	(0.2002)
<32 weeks	10,563	335	2.66	10,228	1.32	2.00 (1.80, 2.23)	1.85 (1.66, 2.07)
32 weeks	2,079	60	0.48	2,019	0.26	1.82 (1.41, 2.35)	1.75 (1.35, 2.27)
33 weeks	3,148	105	0.83	3,043	0.39	2.11 (1.74, 2.57)	1.99 (1.64, 2.43)
34 weeks	5,798	142	1.13	5,656	0.73	1.54 (1.30, 1.81)	1.48 (1.25, 1.75)
35 weeks	10,142	253	2.01	9,889	1.28	1.57 (1.38, 1.77)	1.54 (1.36, 1.75)
36 weeks	21,069	502	3.98	20,567	2.66	1.49 (1.37, 1.63)	1.46 (1.34, 1.59)
≥37 weeks	732,405	11,218	88.93	721,187	93.34	0.95 (0.95, 0.96)	0.95 (0.95, 0.96)

^{*} Adjusted for maternal age at delivery.

THANK YOU!

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