IVF Funding in Ontario
How Do We Define Success?

Andrea Lanes PhD
April 25, 2017
Infertility and fertility treatment

- Infertility affects a growing number of individuals in Canada
- Assisted reproductive technologies
In vitro fertilization (IVF)
FERTILITY TREATMENT CYCLES CANADA
Number of cycles and clinical pregnancies in Canada

All ART treatment cycles types

- Cycle starts
  - CARTR, 2011: 23,997
  - CARTR, 2012: 25,343
  - CARTR Plus, 2013: 28,166
  - CARTR Plus, 2015: 28,657

- Embryo transfer cycles
  - CARTR, 2011: 21,054
  - CARTR, 2012: 20,886
  - CARTR Plus, 2013: 19,787
  - CARTR Plus, 2015: 20,843

- Clinical pregnancies*
  - CARTR, 2011: 7,030
  - CARTR, 2012: 7,714
  - CARTR Plus, 2013: 7,704
  - CARTR Plus, 2014: 8,241
  - CARTR Plus, 2015: 8,236

- Ongoing clinical pregnancies†
  - CARTR, 2011: 6,368
  - CARTR, 2012: 6,982
  - CARTR Plus, 2013: 7,693
  - CARTR Plus, 2014: 8,236
  - CARTR Plus, 2015: 7,435

* Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy
† Ongoing clinical pregnancy: clinical pregnancy with ≥1 fetal heart beat on ultrasound
Type of treatment cycle, per cycle start

*All ART treatment cycles (fresh and frozen), 2015*

- **Fresh IVF – own oocytes***: 53.3%
- **Fresh IVF – donor oocytes**: 2.5%
- **Natural/modified natural IVF***: 3.3%
- **FET – own oocytes***: 33.2%
- **FET – donor oocytes**: 4.3%
- **Frozen oocyte IVF – own oocytes***: 0.3%
- **Frozen oocyte IVF – donor oocytes**: 1.5%
- Oocyte banking: 1.2%
- IVM: 0.4%

* Own oocytes exclusively
Patient age

All ART treatment cycles (fresh and frozen), 2015

<table>
<thead>
<tr>
<th>Patient age (years)</th>
<th>Percent per cycle start (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>38.9</td>
</tr>
<tr>
<td>35–37</td>
<td>23.2</td>
</tr>
<tr>
<td>38–40</td>
<td>20.8</td>
</tr>
<tr>
<td>41–42</td>
<td>9.9</td>
</tr>
<tr>
<td>≥43</td>
<td>7.3</td>
</tr>
</tbody>
</table>
Reasons for receiving fertility treatment in Canada

* Categories are not mutually exclusive
† Other reasons include: gonadotoxic therapy, no female partner and peritoneal factor or severe adhesions

Canadian Fertility and Andrology Society Annual Meeting (2016)
BIRTH OUTCOMES
CANADA
Birth outcomes success rates

All ART treatment cycles types (fresh and frozen), 2014

[Bar chart showing live births and singleton live births]

6,215 live births
5,413 singleton live births
4,553 Good perinatal outcome

* 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=353)
Distribution of birth outcomes among ongoing clinical pregnancies

**ART cycles using IVF and FET – own oocytes, 2014**

**IVF – own oocytes**
- Singleton live birth: 66.1%
- Multiple live birth: 10.6%
- Miscarriage: 18.7%
- Stillbirth: 0.7%
- Unknown: 3.8%

**FET – own oocytes**
- Singleton live birth: 65.6%
- Multiple live birth: 8.1%
- Miscarriage: 22.2%
- Stillbirth: 0.7%
- Unknown: 3.5%
ONTARIO
### Ontario treatment cycle characteristics

**All IVF and FET treatment cycles, 2013**

<table>
<thead>
<tr>
<th></th>
<th>Ontario</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total number of fresh IVF and FET cycles started</strong></td>
<td>10,441</td>
</tr>
<tr>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Fresh IVF cycles (primary cycles)</td>
<td>6,462</td>
</tr>
<tr>
<td></td>
<td>61.9</td>
</tr>
<tr>
<td>FET cycles (secondary cycles)</td>
<td>3,979</td>
</tr>
<tr>
<td></td>
<td>38.1</td>
</tr>
<tr>
<td><strong>Number of unique patients (primary and secondary cycles)</strong></td>
<td>7,015</td>
</tr>
<tr>
<td><strong>Insemination method (primary cycles)</strong></td>
<td></td>
</tr>
<tr>
<td>Cycle cancelled</td>
<td>491</td>
</tr>
<tr>
<td></td>
<td>7.6</td>
</tr>
<tr>
<td>Insemination not done (no oocytes retrieved; other reasons)</td>
<td>107</td>
</tr>
<tr>
<td></td>
<td>1.7</td>
</tr>
<tr>
<td>IVF cycles without ICSI</td>
<td>886</td>
</tr>
<tr>
<td></td>
<td>13.7</td>
</tr>
<tr>
<td>IVF cycles with ICSI</td>
<td>4,646</td>
</tr>
<tr>
<td></td>
<td>71.9</td>
</tr>
<tr>
<td>IVF cycles with and without ICSI</td>
<td>332</td>
</tr>
<tr>
<td></td>
<td>5.1</td>
</tr>
<tr>
<td><strong>Gestational carrier or surrogate (primary and secondary cycles)</strong></td>
<td></td>
</tr>
<tr>
<td>No embryo transfer</td>
<td>2,013</td>
</tr>
<tr>
<td></td>
<td>19.3</td>
</tr>
<tr>
<td>Embryo transfer – used gestational carrier</td>
<td>337</td>
</tr>
<tr>
<td></td>
<td>3.2</td>
</tr>
<tr>
<td>Embryo transfer – did not use gestational carrier</td>
<td>8,091</td>
</tr>
<tr>
<td></td>
<td>77.5</td>
</tr>
</tbody>
</table>
# Ontario treatment cycle characteristics

*All IVF and FET treatment cycles, 2013*

<table>
<thead>
<tr>
<th>Number of embryos transferred (primary and secondary cycles)</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>No embryo transfer</td>
<td>2,013</td>
<td>19.3</td>
</tr>
<tr>
<td>1 embryo</td>
<td>3,341</td>
<td>32.0</td>
</tr>
<tr>
<td>2 embryos</td>
<td>4,303</td>
<td>41.2</td>
</tr>
<tr>
<td>3 embryos</td>
<td>657</td>
<td>6.3</td>
</tr>
<tr>
<td>≥4 embryos</td>
<td>127</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Average number of embryos transferred (±SD)
(among primary and secondary cycles with ≥1 embryo transferred n=8,428)

1.7 ±0.7

<table>
<thead>
<tr>
<th>eSET or eDET (primary and secondary cycles)</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>No embryo transfer</td>
<td>2,013</td>
<td>19.3</td>
</tr>
<tr>
<td>Elective single embryo transfer (eSET)</td>
<td>1,766</td>
<td>16.9</td>
</tr>
<tr>
<td>Non-elective single embryo transfer</td>
<td>1,575</td>
<td>15.1</td>
</tr>
<tr>
<td>Elective double embryo transfer (eDET)</td>
<td>2,244</td>
<td>21.5</td>
</tr>
<tr>
<td>Non-elective double embryo transfer</td>
<td>2,059</td>
<td>19.7</td>
</tr>
<tr>
<td>3 embryos</td>
<td>657</td>
<td>6.3</td>
</tr>
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</table>
ONTARIO’S FERTILITY PROGRAM
Legislation

- July 24, 2014
- The Ontario Legislature passed *The Building Opportunity and Securing Our Future Act*
- Commitment to provide additional financial support for people in the province who want to become parents
- Established an advisory process
Advisory process

• Developed recommendations:
  1) Clinical eligibility
  2) Quality measures and oversight

• Medical experts
  – Obstetricians
  – Reproductive endocrinology and infertility
  – Embryology lab directors

• Patient representatives
Advisory process

• The MOHLTC engaged Health Quality Ontario
  – Knowledge translation of clinical evidence
  – Assisted with framing research questions
  – Performed evidence synthesis reviews

• Additional experts
  – Data collection and oversight
  – Legal
Ontario - Prior to funding

• 3 IVF cycles for patients with:
  – diagnosis of complete bilateral anatomical fallopian tube blockage
Ontario

- 18 fertility clinics that provide IVF services
  - 16 privately owned clinics
  - 2 hospital-based clinics
- Funded fertility treatment cycles
  - Commenced December 2015
  - Approximately 5,000 funded cycles per year
  - Each clinic receives a specified proportion of cycles that are eligible for funding
    - Each clinic decides how to distribute cycles
Eligibility for funding

- Ontario resident with a valid OHIP card
- Women <43 years
- Their health care provider determined IVF to be appropriate
The Fertility Program includes

- One IVF cycle per eligible patient per lifetime, including:
  - Subsequent frozen embryo transfer cycles
- One additional funded IVF cycle, if acting as a surrogate
Costs

• IVF
  – $7,000–$11,000
  – Potential additional costs of approximately $5,000
    • Medications
    • Intracytoplasmic sperm injection (ICSI)
    • Cryopreservation
Funded IVF cycles

Patients have different pathways of clinical care

The funded IVF cycle includes the one-at-a-time transfer of all viable embryos from one start point to the first end point:

Cycle Start Points

You will:
- Undergo an egg retrieval
- Have a donor undergo an egg retrieval for you
- Use previously-retrieved eggs (own or donor); or
- Use previously-created embryos (own or donor).

Cycle End Points

- Two cycle monitoring attempts with no egg retrieval
- One failed egg retrieval
- One failed surgical sperm retrieval and no alternate sperm source is chosen
- Fertilization and culture of all eggs from cycle start resulted in no viable embryos to transfer
- Thawing/culture of all frozen embryos from cycle start resulted in no viable embryos to transfer; or
- Transfers of all viable embryos (fresh & frozen) from cycle start were performed or are no longer available.

Funded IVF treatment cycles

- Reduce the multiple pregnancy rate
  - Single embryo transfers
Multiple pregnancies and births

- Increased risk of:
  - Preterm birth
  - Low birthweight
  - Respiratory distress
  - Preeclampsia
  - Placental abruption
  - Extended time in the NICU
Number of multiple pregnancies in Canada

All ART treatment cycles types

<table>
<thead>
<tr>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing clinical pregnancies*</td>
<td>6,368</td>
<td>6,982</td>
<td>7,693</td>
<td>8,236</td>
<td>7,435</td>
</tr>
<tr>
<td>Multiple pregnancies†</td>
<td>1,350</td>
<td>1,217</td>
<td>1,166</td>
<td>1,037</td>
<td>905</td>
</tr>
</tbody>
</table>

* 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 Canada

All ART treatment cycles types

<table>
<thead>
<tr>
<th>Year</th>
<th>Twin Pregnancies</th>
<th>Triplet+ Pregnancies</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARTR, 2011</td>
<td>1,278</td>
<td>72</td>
</tr>
<tr>
<td>CARTR, 2012</td>
<td>1,152</td>
<td>65</td>
</tr>
<tr>
<td>CARTR Plus, 2013</td>
<td>1,121</td>
<td>45</td>
</tr>
<tr>
<td>CARTR Plus, 2014</td>
<td>1,003</td>
<td>34</td>
</tr>
<tr>
<td>CARTR Plus, 2015</td>
<td>862</td>
<td>43</td>
</tr>
</tbody>
</table>

* Ongoing clinical pregnancy: clinical pregnancy with ≥1 fetal heart beat on ultrasound
† Multiple pregnancy: ongoing clinical pregnancy with >1 fetal heart beat on ultrasound
SUCCESS
How do we define success?

- Clinical view of success
- Surveillance view of success
- Patient view of success
Clinical outcomes

• Fertility treatment outcomes
  – Biochemical pregnancy
  – Clinical pregnancy
  – Ongoing clinical pregnancy
  – Singleton ongoing clinical pregnancy

• Birth outcomes
  – Live birth
  – Singleton live birth
  – Live birth with a good perinatal outcome
What is the denominator?

• Cycle starts
• Oocyte retrieval cycles
• Embryo transfer cycles
Stage of treatment and treatment outcomes

ART cycles using IVF – own oocytes, 2015 in Canada

- Cycle starts (CS): 15,273
- Oocyte retrieval cycles (RET): 14,275
- Embryo transfer cycles (ET): 9,075
- Clinical pregnancies*: 3,611
- Ongoing clinical pregnancies†: 3,299
- Singleton pregnancies‡: 2,872

998 cancelled: 6.5% per CS
5,200 no ET: 36.4% per RET
23.6% per CS 25.3% per RET 39.8% per ET
21.6% per CS 23.1% per RET 36.4% per ET
18.8% per CS 20.1% per RET 31.6% per ET

* Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic 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

87.1% of ongoing clinical pregnancies
Birth outcomes success rates

All ART treatment cycles types (fresh and frozen), 2014

* 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=353)
Example

- A clinic that uses Comprehensive Chromosome Screening (CCS), and starts 100 IVF cycles in women age 40 and over
- 20 cycles are cancelled prior to retrieval
- 30 cycles result in no blastocysts
- 50 cycles result in at least 1 blastocyst to biopsy
  - 20 have at least 1 euploid blastocyst to transfer
  - 20 blastocyst transfers occur
  - 10 transfers result in a pregnancy
What is the success rate?

- Does the clinic then get to report that their success rate with CCS for patients 40+ is…….
- 50% (10 pregnancies/20 embryo transfers)
- 20% (10 pregnancies/50 cycles with a biopsy)
- 12.5% (10 pregnancies/80 cycles with a retrieval)
- 10% (10 pregnancies/100 cycles started)
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

• Optimistic:
  – Assumes that women who did not return for subsequent treatment cycles had the same chance of a clinical pregnancy as those who did return for treatment

• Conservative:
  – Assumes that women who did not return for subsequent treatment cycles did not have a clinical pregnancy

Malizia BA et al., NEJM 2009; 360: 236-243
Cumulative pregnancy rate, per batch of oocytes retrieved

IVF and FET – using own oocytes, 2013, 2014 and 2015 in Canada

Clinical pregnancy: clinical intrauterine, heterotopic, or ectopic pregnancy

Optimistic: Assumes that women who did not return for subsequent treatment cycles had the same chance of a clinical pregnancy as those who did return for treatment.

Conservative: Assumes that women who did not return for subsequent treatment cycles did not have a clinical pregnancy.
Patient subgroups

- Patient age
- Types of infertility
- Body mass index
Cumulative pregnancy rate, per batch of oocytes retrieved

*IVF and FET – using own oocytes, 2013, 2014 and 2015 in Canada*

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**Optimistic cumulative pregnancy rate**

- <35 years: 42.4%, 66.6%, 81.5%, 90.1%
- ≥35 years: 31.5%, 55.7%, 72.6%, 84.1%

**Conservative cumulative pregnancy rate**

- <35 years: 42.4%, 52.8%, 55.6%, 56.2%
- ≥35 years: 31.5%, 37.7%, 39.1%, 39.4%

---

**Clinical pregnancy:** clinical intrauterine, heterotopic, or ectopic pregnancy

**Optimistic:** Assumes that women who did not return for subsequent treatment cycles had the same chance of a clinical pregnancy as those who did return for treatment.

**Conservative:** Assumes that women who did not return for subsequent treatment cycles did not have a clinical pregnancy.
Success

• Defining success is complicated
  – Clarity is imperative
  – Standard method across clinics is needed
• Accessibility of IVF treatment
• What are the long-term costs?
Limitations

• Only a predetermined number of IVF cycles funded
• Lengthy waitlists
• Each clinic determines how and who gets the funded cycles
• Characteristics of patients who received first year of funded treatment cycles may be unique
• Each clinic has specialized services
Conclusion

- Funded IVF treatment cycles are a small proportion of pregnancies in Ontario, but understanding their “success” is essential for planning their course of clinical care.
Thank you!
Andrea Lanes
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