Infertility and the National Public Health Action Plan

Lee Warner, PhD, MPH
Associate Director for Science, Division of Reproductive Health
National Center for Chronic Disease Prevention and Health Promotion
Infertility Can Affect Anyone
Infertility is a Disease

- Infertility is more than a quality-of-life issue

- Infertility is considered a disease of the reproductive system according to
  - World Health Organization (WHO) in 2009
  - American Society for Reproductive Medicine (ASRM) in 2013

Practice Committee of the American Society for Reproductive Medicine, *Fertil Steril* Jan 2013.
Reproduction is a Major Life Activity

SUPREME COURT OF THE UNITED STATES

Syllabus

BRAGDON v. ABBOTT ET AL.

CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FIRST CIRCUIT


The life activity upon which respondent relies, her ability to reproduce and to bear children, constitutes a “major life activity” under the ADA. The plain meaning of the word “major” denotes comparative importance and suggests that the touchstone is an activity’s significance. Reproduction and the sexual dynamics surrounding it are central to the life process itself. Petitioner’s claim that Congress

ADA: Americans with Disabilities Act
Infertility is a Public Health Concern

- Disparities in access to care and treatment

- More infants born from use of infertility treatments
  - ~ 6% infants from ovarian stimulation treatments
  - 1.5% infants from assisted reproductive technologies (ART)

- Long-term outcomes of treatment are unknown

Infertility is a Marker of Past, Present, and Future Health

Increased Risk of High-Grade Prostate Cancer Among Infertile Men

Original Article

Semen quality, infertility and mortality in the USA

Significant medical pathology uncovered by a comprehensive male infertility evaluation

Walsh, Cancer 2010.
Eisenberg, Hum Reprod 2014.
Many Factors Contributing to Infertility Can Be Prevented

- **Infectious Diseases**
  - Sexually transmitted infections can lead to pelvic inflammatory disease (PID) and tubal factor infertility (TFI)
    - TFI accounts for 10%–40% of infertility
    - About 30% of PID is associated with gonorrhea and chlamydia

- **Environmental and Workplace Exposures**
  - Environmental and workplace exposures can affect sperm quality and disrupt menstrual function

- **Genetic and Physical Abnormalities**

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Many Factors Contributing to Infertility Can be Prevented

- Chronic Conditions and Diseases
- Medication-induced
- Behavioral factors

- Certain medications (e.g., chemotherapy) can result in infertility
  - Fertility preservation methods should be considered

- Modifiable lifestyle factors are potential causes of infertility
  - Obesity
  - Smoking
Hurdles in Defining Infertility

- **Varying case definitions used across settings and populations**
  - Reproductive outcome (e.g., absence of pregnancy or live birth)
  - Length of time without conception (e.g., 1, 2, or 5 years)
  - Type of infertility (e.g., primary or secondary)

- **Clinical definitions**
  - *Infertility* — Inability to conceive after 12 months of trying
  - *Impaired fecundity* — Difficulty getting pregnant or carrying a pregnancy to a live birth

Infertility Affects Both Women and Men

- **Couple-based impairment affecting males and females**
  - Female 33%
  - Male 20%
  - Mixed 39%
  - Unexplained 8%

- **U.S. National Survey of Family Growth, 2006–2010**
  - Women (married)
    - Infertility 6%
    - Impaired fecundity 12%
  - Men
    - Infertility 9%

Chandra A, National Health Statistics Reports; no 67, 2013.
Impaired Fecundity Increases with Age

Chandra A, National Health Statistics Reports; no 67, 2013.
A public health focus on infertility prevention, detection, and management


Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; Division of Vital Statistics, National Center for Health Statistics, Centers for Disease Control and Prevention, Atlanta, Georgia; Division of Sexually Transmitted Disease Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD and Tuberculosis Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia; Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia; and Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.


Published July 2014

Available at http://www.cdc.gov/reproductivehealth/Infertility/PublicHealth.htm
Improving the Outcome of Infertility Therapy
A Clinical Perspective

Eli Y. Adashi, MD, MS, CPE, FACOG
Professor of Medical Science
The Warren Alpert Medical School
Division of Biology and Medicine
Brown University
Goal of Infertility Therapy

The BESST Outcome is a...

Birth Emphasizing a Successful Singleton at Term

## Services Ever Used by Infertile U.S. Women

<table>
<thead>
<tr>
<th>Category</th>
<th>Service</th>
<th>Respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Treatment</td>
<td>Advice</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>Infertility Testing</td>
<td>27</td>
</tr>
<tr>
<td>Non-ART</td>
<td>Ovulation-Inducing Drugs</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Artificial Insemination</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Surgery</td>
<td>3.4</td>
</tr>
<tr>
<td>ART</td>
<td>IVF</td>
<td>3.1</td>
</tr>
</tbody>
</table>

ART: Assisted Reproductive Technology  
IVF: In vitro fertilization  
Controlled Ovarian Stimulation with Timed Intrauterine Insemination (IUI)

- Available in the U.S. since 1987
- Indicated for women diagnosed with Unexplained Ovulatory Subfertility

**Stimulation**
- Gonadotropins
- Clomiphene
- Letrozole

**Ovulation**
- hCG

**Timed IUI** (within 48 hours)
- IUI

hCG: Human chorionic gonadotropin
The Process of In Vitro Fertilization (IVF)

- Available at approximately 500 clinical sites

- Indicated for
  - Anatomic Pathology
  - Male Factor
  - Age-related Infertility
  - Unexplained Ovulatory Subfertility

Stimulation | Ovulation | Retrieval | Fertilization | Transfer
---|---|---|---|---
Gonadotropins | hCG | Oocytes | IVF | Embryo Transfer

hCG: Human chorionic gonadotropin
A Brief History of IVF

- Actualized in the UK in 1978
- Introduced into the US in 1981
- Over 5 million babies born worldwide as a result of IVF

Louise Brown, the world's first "test tube baby" with her mother Lesley. Photo taken 9 October, 1978.
The 2010 Nobel Prize
In Physiology or Medicine

Both treatments increase the incidence of multiple births, thereby increasing maternal morbidity and mortality.

Twins

- ART: 17%
- Non-ART treatments: 19%
- Natural conception: 64%

Triplet or higher order

- ART: 32%
- Non-ART treatments: 45%
- Natural conception: 23%

ART: Assisted Reproductive Technology
### Incidence (%) of major maternal complications in pregnancy

<table>
<thead>
<tr>
<th>Complication</th>
<th>Singleton</th>
<th>Twin</th>
<th>Triplet</th>
<th>Quadruplet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>6</td>
<td>10-12</td>
<td>25-60</td>
<td>&gt;60</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>3</td>
<td>5-8</td>
<td>7</td>
<td>&gt;10</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>15</td>
<td>40</td>
<td>75</td>
<td>&gt;95</td>
</tr>
<tr>
<td>Delivery &lt;37 weeks</td>
<td>10</td>
<td>50</td>
<td>92</td>
<td>&gt;95</td>
</tr>
<tr>
<td>Delivery &lt;32 weeks</td>
<td>2</td>
<td>8</td>
<td>26</td>
<td>&gt;95</td>
</tr>
<tr>
<td>Outcome</td>
<td>Singleton</td>
<td>Twin</td>
<td>Triplet</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>-----------</td>
<td>-------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>Average Gestational Age (weeks)</td>
<td>39.1</td>
<td>35.3</td>
<td>32.2</td>
<td></td>
</tr>
<tr>
<td>Average Birth Weight (gm)</td>
<td>3,358</td>
<td>2,347</td>
<td>1,687</td>
<td></td>
</tr>
<tr>
<td>Average Birth Weight</td>
<td>7 lbs 8 oz</td>
<td>5 lbs 4 oz</td>
<td>3 lbs 12 oz</td>
<td></td>
</tr>
<tr>
<td>Fetal Death (%)</td>
<td>.03</td>
<td>.09</td>
<td>.14</td>
<td></td>
</tr>
<tr>
<td>Neonatal Death (%)</td>
<td>.35</td>
<td>1.9</td>
<td>4.9</td>
<td></td>
</tr>
</tbody>
</table>


Improving Controlled Ovarian Stimulation: Recommended Prudent Practice Patterns

American Society for Reproductive Medicine (ASRM) recommendations

- Use of low-dose gonadotropin regimens
- Use of Clomiphene
- Use of Letrozole (Off-label)
  - Reduced birth plurality rates
  - Comparable per cycle pregnancy rates

Practice Committee of American Society for Reproductive Medicine, *Fertil Steril* April 2012.
Moving Towards Single Embryo Transfers

- Improvements in Embryo Selection
- Pre-implantation Genetic Screening (PGS)
  - Normal chromosomes or euploidy
  - Considered invasive
- Embryonic division analysis or morphokinetics
  - Assessing embryonic cellular fission
  - Considered non-invasive
The Future?
An “IVF-Dominant” Future?

- A more direct path (“fast track”) to IVF
  - Without antecedent controlled ovarian stimulation
  - With a focus on Single Embryo Transfers

- Limited Use of Controlled Ovarian Stimulation

- Indicated Ovulation Induction
What the “BESST” Future Should Look Like

- Infertility treatments resulting in fewer higher order (twins or greater) births
- Mothers receiving treatments face fewer medical risks
- Neonates and infants born to mothers receiving recommended procedures also have a better prognosis
- Alignment of the goals of clinical medicine with the goals of public health
Infertility from Both Male and Female Patients’ Perspective

Barbara Collura
President/CEO
RESOLVE: The National Infertility Association
The Profound Impact of the Diagnosis of Infertility

“For years I struggled with infertility. The physical and emotional toll of infertility, the monthly hope then heartbreak, the appointments with doctors and specialists, the shame and sadness, impacted our lives in ways big and small.

I lost count of how many times I cried and prayed, beseeching God to ‘fix’ me so that Nate and I could be parents.

For months, I felt broken and alone.”
"I was feeling sad, and hopeless and the 3 ½ years of trying, miscarriages and IVF had really taken its toll. I had even told my husband that I was ready to stop trying all together.

Infertility is so lonely and isolating."
Providing Support through the Journey

- **RESOLVE Support Groups**
  - Each month, 194 peer-led support groups in 42 states

- **Blogs and Social Media**
  - 3,100 blogs on infertility, adoption, and pregnancy loss
  - People use social media to connect and get support

- **Meeting the growing needs of the infertility community**
  - 25th Anniversary of National Infertility Awareness Week
    - April 20-26, 2014
  - Walks of Hope increase awareness within communities
Public Awareness About Infertility
Infertility Treatment and Insurance Coverage

- Infertility is a disease, diagnosed by a physician

- Most insurance plans, including Medicare and Medicaid, do not offer coverage, especially for IVF
  - Pre-requisites vary from plan to plan

- Affordable Care Act may not expand coverage for infertility care
Insurance Coverage at the State Level

- Only 8 states have an IVF insurance mandate:
  - AR, CT, HI, IL, MA, MD, NJ, RI
- Another 7 states mandate coverage for some infertility treatment but do not cover IVF:
  - CA, LA, MT, NY, OH, TX, WV

Pre-requisites vary from state to state.
Impact of Lack of Insurance Coverage on Decision-Making

- Out-of-pocket costs can be substantial and impact patient decision-making and risk-taking
  - Less effective treatments are pursued to lower costs
  - Precious time is wasted
  - Risks are ignored
  - Decisions not based on “best medical advice”
  - Maximize “return on investment”
  - Twins are perceived to be “less costly”

Non-ART: $200-$5,000

IVF: $10,000-$15,000

Dealing with Infertility Shouldn’t Have to Be a Life Crisis

- Access to emotional support and a sense of community can be life-changing

- Patients who receive education and information have increased awareness and manage better

- The current state of insurance coverage for infertility treatment can create incentives that lead to poor outcomes for both individual patients and for public health
  - Inequities in who gets care and who does not
  - Increased adverse health outcomes for mother and baby

- The ASRM and SART standard of care should determine insurance coverage

ASRM: American Society for Reproductive Medicine
SART: Society for Assisted Reproductive Technology
Infertility Treatments from a Public Health Perspective

Dmitry Kissin, MD, MPH

Team Lead, Assisted Reproductive Technology Surveillance and Research Team, Division of Reproductive Health National Center for Chronic Disease Prevention and Health Promotion
Multiple Birth Infants, United States, 1940-2012

Percentage of multiple birth infants

Year


0% 1% 2% 3% 4% 5%

Gonadotropins
Clomiphene
ART

ART: Assisted Reproductive Technology
Public Health Surveillance for ART

- **1981**: First ART-conceived infant born in the United States

- **1992**: U.S. Congress passed the Fertility Clinic Success Rate and Certification Act

- **1995**: CDC initiated National ART Surveillance

- All ART cycles are reported; non-ART fertility treatments are not reportable

ART: Assisted Reproductive Technology
1.5% of all infants born in the U.S. are conceived with ART

Number of ART-conceived infants

Year


1996: 20,908
1997: 24,844
1998: 28,913
1999: 30,703
2000: 35,103
2001: 40,687
2002: 45,751
2003: 48,756
2004: 49,458
2005: 52,041
2006: 54,656
2007: 57,569
2008: 61,426
2009: 60,190
2010: 61,561
2011: 61,610
2012: 65,179

Poor Perinatal Outcomes Associated with ART-conceived Infants, 2010

Sunderam S. MMWR Surveillance Summaries 2013; no 62.
Good Perinatal Outcomes Associated with Single Embryo Transfers, 2010

Good Perinatal Outcome – term, normal birth weight singleton
Increased Use of ART and Single Embryo Transfers with Insurance Coverage, 2011

- Percentage of ART infants among all infants born:
  - Mandate to cover ART: 2.9%
  - No mandate to cover ART: 1.3%

- Percentage of Single Embryo Transfers among all ART transfer procedures:
  - Mandate to cover ART: 19.7%
  - No mandate to cover ART: 14.7%

ART Practice Guidelines and Good Perinatal Outcomes

- Issued by American Society for Reproductive Medicine (ASRM) and Society for Assisted Reproductive Technology (SART) since 1998
- Recommend maximum number of embryos to transfer during ART
- Contributed to the reduction of number of embryos transferred and number of triplets and higher order multiple births
- Have not affected twin births after ART
Single, Double and Three or More Embryo Transfers, United States, 1997-2011

Percent of Total Embryo Transfers

- Single
- Double
- 3 or more

Year


All tests for trend $P<0.001$
Insurance Coverage and Practice Standards

- **Insurance coverage**
  - Increased use of ART
  - Increased the percentage of elective single embryo transfers, but only 1 in 5 chose single embryo transfer, even with coverage

- **Practice Guidelines**
  - Reduced the number of three or more embryos transferred
  - Have not reduced the number of twin gestations

- **Other countries have been able to successfully implement the restrictions on the number of embryos to transfer by offering insurance coverage**

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Single Embryo Transfer (SET) in the United States and Other Countries

Percentage of ART cycles with SET

Year

Information from National ART Surveillance Systems in Belgium, Sweden, United States, Australia and New Zealand, including unpublished data.
ART-Related Multiple Births in the United States and Other Countries

Information from National ART Surveillance Systems in Belgium, Sweden, United States, Australia and New Zealand, including unpublished data.

Infertility, Infertility Treatments, and Good Perinatal Outcomes

ART

Non-ART

Healthy Singleton
Infertility, Infertility Treatments, and Good Perinatal Outcomes

Infertility
- Medically-induced Factors
- Infectious Diseases
- Aging
- Genetic and Physical Abnormalities
- Behavioral Factors
- Environmental and Occupational Exposures
- Chronic Conditions

ART
- Medically-induced Factors
- Infectious Diseases
- Aging
- Genetic and Physical Abnormalities
- Behavioral Factors
- Environmental and Occupational Exposures
- Chronic Conditions

Non-ART

Healthy Singleton
A Call to Action

Public health strategies can

- Promote healthy behaviors to preserve fertility
- Emphasize the prevention and treatment of medical conditions that lead to infertility
- Reduce exposures to hazardous agents that affect fertility

Detection of Infertility: Public Health Opportunities

- Develop standardized case definitions

- Improve surveillance for infertility and related factors
  - Enhance information collected in existing surveillance systems
  - Expand surveillance efforts
    - Collect information about non-ART use and outcomes
Prevention of Infertility: Public Health Opportunities

- Improved understanding of the risks and causes of infertility
  - Infectious diseases
  - Chronic conditions and diseases
  - Environmental/Workplace
  - Medication-induced
  - Modifiable behavioral factors
  - Genetic and physical abnormalities

- Increase public awareness of causes of infertility and the importance of prevention
Management of Infertility: Public Health Opportunities

- Monitor safety and effectiveness of infertility treatments
  - ART: long-term outcomes unknown
  - Non-ART: short-term and long-term outcomes unknown
- Promote evidence-based guidelines and recommendations
- Increase public awareness of and eliminate disparities in access to affordable infertility services
In the End, It’s About Families

E-mail questions, comments or concerns to:

drhinfo@cdc.gov

National Public Health Action Plan for the Detection, Prevention, and Management of Infertility, July 2014. Available at: