Implications of monitoring fecundity
- or not

Joseph B. Stanford, MD, MSPH
Professor
Director, Office of Cooperative Reproductive Health
Department of Family and Preventive Medicine
University of Utah

2015 Sep 11
- Monitoring: no
- Monitoring: yes
- Approaches
- Spectrum of intervention
- Lifespan
- Timing
- Conclusions
- Proposal
Monitoring: no

- Confounding by contraception and social factors
- Treatment is getting more successful
- The next step in human evolution: medicalized reproduction?
  - Genetic selection and/or modification?
- Main issue is to monitor outcomes of treatment
Monitoring: yes

- Assess environmental impacts
- Medicalized reproduction may propagate (epi)genetic traits that would otherwise not reproduce
- Already monitoring some treatment, but gives distorted picture without additional information
- Compare and improve outcomes of all treatments
- Life course epidemiology
- Prevention of subfecundity
Approaches

- Biomarkers
- Day-specific probabilities
- Observed/expected pregnancies
- Time to pregnancy
  - retrospective
  - prospective
  - current duration
- Perinatal and subsequent health
Spectrum of intervention, fecundity

- Unexpected pregnancies
- Expected pregnancies
- Self treatment
- Complementary and alternative treatment
- Restorative treatments
- Superovulation
- Intrauterine insemination
- IVF with or without ICSI
Spectrum of intervention, fecundity

- Unexpected pregnancies
- Expected pregnancies (TTP)
- Self treatment
- Complementary and alternative treatment
- Restorative treatments
- Superovulation
- Intrauterine insemination
- IVF with or without ICSI
Spectrum of intervention

- Population based versus clinic-based
Fertility experience study: clinic and population retrospective cohorts (Utah)

- **459 Clinic** enrolled
  - First clinic visit 2000-2009
- **501 Population** enrolled
  - Corresponding index date
- Final eligibility same for both
  - Primary subfertility
  - Woman’s age 20-35 at index date

Submitted; work from NICHD R21 HD060213-01A1
Most invasive medical treatment by cohort

Population Cohort
- No Tx: 35%
- Drugs: 29%
- AI: 21%
- IVF: 15%

Clinic Cohort
- No Tx: 34%
- Drugs: 15%
- AI: 15%
- IVF: 43%
Fertility Focused Intercourse

- Monitoring CM
- Counting days
- LH-Test
- BBT
- *Any Fertility-Focused

- Month of conception (% of women having a pregnancy)
- Ever-used (% all women)

Not significantly different by cohort
The bar chart shows the percentage of women using different types of Complementary & Alternative Medicine (CAM) during conception. The chart includes:

- **Acupuncture**: Not significantly different by cohort.
- **Herbs**: Not significantly different by cohort.
- **Vitamins**: Not significantly different by cohort.
- **Any CAM**: Not significantly different by cohort.

The chart indicates that the use of any CAM is not significantly different by cohort, with specific data points for acupuncture, herbs, vitamins, and any CAM being presented in a visual format.
Across the lifespan
Subfecundity

Couple’s condition
  - Difficulty getting pregnant
Subfecundity

- Couple’s condition
  - Difficulty getting pregnant
  - Health of the baby
  - Health of the mother in pregnancy
  - Long-term health of the mother
  - Long-term health of the father
  - Long-term health of the child
Subfecundity

Couple’s condition
- Difficulty getting pregnant
- Health of the baby
- Health of the mother in pregnancy
- Long-term health of the mother
- Long-term health of the father
- Long-term health of the child
- Fecundity of the next generations
- Health of the next generations
"We are looking ahead...to make sure and to make every decision that we make relate to the welfare and well-being of the seventh generation to come. . . ."

Oren Lyons, Onondaga Nation (Iroquois; 1930-)
Is treatment about

- Achieving desired timing?
- Achieving desired family size?
- What are tradeoffs in outcomes?
  - Subfertility related outcomes
  - Treatment-related outcomes
Achieving desired family size, simulation

- To achieve one-child family, start at
  - 32 years (female) without IVF option
  - 35 years (female) with IVF option

- Two children
  - 27 years (female) without IVF option
  - 31 years (female) with IVF option

- Three children
  - 23 years (female) without IVF option
  - 28 years (female) with IVF option

Habbema JDF et al., *Hum Reprod* 2015
Cumulative pregnancies, simulation

Linkage for UCRM (UU), 2000-2005

- Initial consultations for infertility
  - 7214 unique patients
- SART treatment data
  - 1568 unique patients (2253 IVF cycles)
- Artificial insemination data
  - 2842 unique patients
- De-identified data file for analysis
Cumulative births by treatment

Nelson-Aalen cumulative hazard estimates

- iui
- art
- ucrm alone

Analysis time in months
Preterm birth and low birthweight by fertility treatment: FL, MD, UT, 2004-2008

## Preterm birth by fertility treatment

**FL, MD, UT, 2004-2008**

<table>
<thead>
<tr>
<th>Analysis; referent group</th>
<th>ART</th>
<th>IUI &amp; OS</th>
<th>OS</th>
<th>Other</th>
<th>Spont after tx</th>
<th>TTC no tx</th>
</tr>
</thead>
<tbody>
<tr>
<td>All births, women trying to conceive</td>
<td>6.2</td>
<td>2.1</td>
<td>1.4</td>
<td>0.9</td>
<td>1.3</td>
<td>ref</td>
</tr>
<tr>
<td></td>
<td>(4.2,9.2)</td>
<td>(1.2,3.6)</td>
<td>(1.0,1.9)</td>
<td>(0.5,1.6)</td>
<td>(0.8,2.0)</td>
<td>na</td>
</tr>
<tr>
<td>All births, subfertile spontaneous</td>
<td>3.2</td>
<td>1.2</td>
<td>0.7</td>
<td>0.5</td>
<td>ref</td>
<td>na</td>
</tr>
<tr>
<td></td>
<td>(1.7,6.0)</td>
<td>(0.6,2.5)</td>
<td>(0.4,1.3)</td>
<td>(0.2,1.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Singletons, women trying to conceive</td>
<td>3.3</td>
<td>1.3</td>
<td>0.9</td>
<td>0.9</td>
<td>1.3</td>
<td>ref</td>
</tr>
<tr>
<td></td>
<td>(1.7,6.2)</td>
<td>(0.6,2.5)</td>
<td>(0.7,1.4)</td>
<td>(0.5,1.6)</td>
<td>(0.8,2.0)</td>
<td></td>
</tr>
<tr>
<td>Singletons, subfertile spontaneous</td>
<td>1.7</td>
<td>0.7</td>
<td>0.5</td>
<td>0.5</td>
<td>ref</td>
<td>na</td>
</tr>
<tr>
<td></td>
<td>(0.8,3.7)</td>
<td>(0.3,1.8)</td>
<td>(0.2,1.0)</td>
<td>(0.2,1.1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Odds ratios adjusted for age, education, federal poverty level, BMI, parity, race, ethnicity, insurance, marital status, smoking

Conclusions

- We should monitor fecundity
  - Across the full spectrum of intervention
  - Across the lifespan of impact
  - With a portfolio of approaches

- For the sake of the seventh generation, and beyond
Proposal

- A dashboard or portfolio to track over time
- Existing, enhanced, and new components
Fecundity dashboard, longitudinal

- Unintended pregnancy
  - Pregnancy intentions, fertility behaviors, contraceptive mix
- Current duration
- Prospective TTP with field ovulation markers
  - Other TTP studies with targeted biomarkers
- TTP on all birth certificates
- Outcomes of full spectrum of fertility treatments
  - Birth certificates and registry
Office of Cooperative Reproductive Health