Epidemiology of Endometriosis and Pelvic Pain

Stacey A. Missmer, ScD
Department of Obstetrics, Gynecology, and Reproductive Biology
Michigan State University

Department of Epidemiology, Harvard T.H. Chan School of Public Health
Boston Center for Endometriosis

Disclosures

• Academic and Professional Society Affiliations
  • Faculty – Michigan State University, Harvard University, Boston Children’s Hospital
  • Scientific Director – Boston Center for Endometriosis
  • Treasurer – World Endometriosis Society
  • Secretary – World Endometriosis Research Foundation, America
  • Chair-elect – ASRM EndoSIG
  • NIH RMN DSMB
  • Statistical Editor – Human Reproduction

• Industry Affiliations
  • Advisory Boards Member – AbbVie
  • Advisory Board Member – Celmatix
  • Unfunded collaborator – Oratel Diagnostics

• Research Funders
  • NIH
  • Marriott family foundations
Prevalence / Incidence of Endometriosis

• Conventional wisdom = 10%

• Nurses’ Health Study 2 (N = 116,430)
  • Prevalence in 1989 = 5% (5,299)
  • Prevalence in 2009 = 9% (10,529)
  • Incidence = 2.8 / 1000 woman-years

• ENDO Study (N = 131 general population)
  • Prevalence = 11% (MRI)

Endometriosis and Public Health

• 3rd leading cause of gynecologic hospitalizations

• U.S. Interview Survey (n = 31,617)
  • Annual prevalence = 7 / 1000 women
  • Mean number of “bed” days = 18 / year
Menstrual Cycle

PREVALENCE OF ENDOMETRIOSIS DURING LAPAROSCOPY BY INDICATION FOR SURGERY

<table>
<thead>
<tr>
<th>Condition</th>
<th>Total N</th>
<th>N with Endometriosis</th>
<th>% with Minimal/Mild Disease</th>
<th>Range in %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelvic pain</td>
<td>2400</td>
<td>588</td>
<td>24.5</td>
<td>4.5–82.0</td>
</tr>
<tr>
<td>Infertility</td>
<td>14,371</td>
<td>2812</td>
<td>19.6</td>
<td>2.1–78.0</td>
</tr>
<tr>
<td>Tubal sterilization</td>
<td>10,634</td>
<td>433</td>
<td>4.1</td>
<td>0.7–43.0</td>
</tr>
</tbody>
</table>

Endometriosis and pelvic pain

• Does NOT correlate with rASRM stage / visualized disease

Mild Disease

Severe Disease
What is endometriosis???

- Lesion appearance (red, yellow, clear, white, blue/black)

D. Martin, 1997
Health Across the Lifespan

GSWH Symptoms

Women undergoing incident laparoscopy (n=1,418 women in ten countries)

- 65% of women with endometriosis had pain

Nnoaham, Fertil Steril 2011
GSWH QOL Impact

Activities negatively impacted by symptoms (n=2,753 women in eight countries)

- Sexual life: 50%
- Relationship: 36%
- Family: 35%
- Performance at work/school/university: 34%
- Housekeeping: 32%
- Attendance at work/school/university: 29%
- Social activities: 21%
- Sports: 9%
- Other:

Adolescent QOL

**SF-36**: Girls with endometriosis did not differ on mental health domains, except for Social Functioning which was significantly lower than the norm.

Gallagher, J Pediatr Adolesc Gynecol 2016
Case Heterogeneity

- What were presenting symptoms?
- Functional Status and Quality of Life
- Varying risk factors?

### Cigarette Smoking and Endometriosis

<table>
<thead>
<tr>
<th>Smoking Category</th>
<th>Pain Sx</th>
<th>Infertility Work-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never Smoker</td>
<td>1.0 (referent)</td>
<td>1.0 (referent)</td>
</tr>
<tr>
<td>Current Smoker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-14 per day</td>
<td>1.1 (0.8-1.4)</td>
<td>0.8 (0.5-1.3)</td>
</tr>
<tr>
<td>15-24 per day</td>
<td>1.5 (1.2-1.9)</td>
<td>0.7 (0.4-1.2)</td>
</tr>
<tr>
<td>25-34 per day</td>
<td>1.9 (1.3-2.7)</td>
<td>0.4 (0.1-0.7)</td>
</tr>
<tr>
<td>35+ per day</td>
<td>1.4 (0.7-2.7)</td>
<td>0.6 (0.1-4.2)</td>
</tr>
</tbody>
</table>

**p₁ < 0.0001**  **p₁ = 0.049**

Missmer, Am J Epidemiol 2004
## aHealthy Eating Index and Endometriosis

<table>
<thead>
<tr>
<th>aHEI-2010 score</th>
<th>Relative Risk (95% CI)</th>
<th>Pain Sx</th>
<th>Infertility Work-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quintile 1</td>
<td>1.00 (referent)</td>
<td>1.00 (referent)</td>
<td></td>
</tr>
<tr>
<td>Quintile 2</td>
<td>0.86 (0.77-0.96)</td>
<td>1.12 (0.84-1.49)</td>
<td></td>
</tr>
<tr>
<td>Quintile 3</td>
<td>0.94 (0.84-1.05)</td>
<td>1.19 (0.90-1.58)</td>
<td></td>
</tr>
<tr>
<td>Quintile 4</td>
<td>0.85 (0.75-0.95)</td>
<td>1.11 (0.83-1.48)</td>
<td></td>
</tr>
<tr>
<td>Quintile 5</td>
<td>0.84 (0.74-0.94)</td>
<td>1.15 (0.86-1.53)</td>
<td></td>
</tr>
</tbody>
</table>

$p_t = 0.01$ $p_t = 0.34$

Dougan, WCE2017 poster; under review
Breastfeeding and lower risk of endometriosis

For every 3-months: 3% reduction in risk:
RR: 0.97 (0.96-0.98)

Linear trend: ≥ 36 months RR: 0.60 (0.50 to 0.72)

< 1 month: 1.00 (ref)
Impeding Endometriosis Discovery

- Disease heterogeneity
- Varying paths to diagnosis
- Diagnostic bias

Paths to Diagnosis / Lost Patients
Paths to Diagnosis / Lost Patients

- Pain → Silence
- Pain → PCP → Dismissed
- Pain → PCP → OCs → Dismissed
- Pain → PCP → OCs → Success
Paths to Diagnosis / Lost Patients

Pain → Silence
Pain → PCP → Dismissed
Pain → PCP → OCs → Dismissed
Pain → PCP → OCs → Success
Pain → PCP → Specialist → Wrong DX

Pain → PCP → Specialist → Surgical DX
Paths to Diagnosis / Lost Patients

Pain → PCP → OCs → Dismissed → Silence
Pain → PCP → OCs → Success
Pain → PCP → Specialist → Wrong DX

Pain → PCP → Specialist → Surgical DX

??
Pain → PCP → Specialist → Surgical DX
MISSED – HOW MANY WOMEN? WHO?
Complexity of Endometriosis and Pelvic Pain

- Family history
- Genetics
- Environment
  - Lifestyle
  - Epigenetics
  - Biochemistry
- Wellness
- Illness

Onset and types of symptoms:
- Fertilization Birth
- Menarche
- Adulthood
- Menopause

1st visit primary care...
Surgical Dx
Medical and/or surgical treatments
Recurrence of symptoms and/or disease

Endometriosis Research Funded by NIH
FY 2001 – FY 2016

Fiscal Year

Amount (Millions of US$)


Total NICHD Extramural ~ $900 million

Funding Sources

- Governmental
- Foundations
- Philanthropy
- Industry

Courtesy of Dr. Katie Terry; adapted from Walker and Stewart. Science 2005
What epidemiologists need most is courage and persistence and energy, because answers are not obvious or easy.

~ Zena Stein, 2003
Thank you!