The Genetic Component of a Common Disease
The Paradigm of Cancer Genetics

Outline
- Introduce/discuss case study
- Make your plan
- Epidemiology of cancer
- ACCE
- Thinking genetically
- Revisit your plan

What other information do you want?

What level of the maternal child health pyramid do you act upon first?

What actions do you recommend?

| Lifetime Probability of Developing Cancer, by Site, Men, 2003-2005 |
|-------------------------|-----------------|
| Site                    | Risk            |
| All sites               | 1 in 2          |
| Prostate                | 1 in 6          |
| Lung and bronchus       | 1 in 13         |
| Colon and rectum        | 1 in 18         |
| Urinary bladder         | 1 in 27         |
| Non-Hodgkin lymphoma    | 1 in 45         |
| Melanoma                | 1 in 39         |
| Leukemia                | 1 in 67         |

ACS, 2009
**Lifetime Probability of Developing Cancer, by Site, Women, 2003-2005**

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>1 in 3</td>
</tr>
<tr>
<td>Breast</td>
<td>1 in 8</td>
</tr>
<tr>
<td>Lung and bronchus</td>
<td>1 in 16</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>1 in 20</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>1 in 84</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1 in 53</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1 in 58</td>
</tr>
<tr>
<td>Leukemia</td>
<td>1 in 94</td>
</tr>
</tbody>
</table>

ACS, 2009

**Will I get cancer? Why?**

- *Note that most (if not all) diseases could be plotted on a graph like this.

**Breast cancer: Alcohol use (5%), overweight and obesity (9%), physical inactivity (10%), PAF 21%**

- Will I get cancer? Why?

  - Environmental Exposures
  - Inherited Factors

**Lancet 2005;366:1784-93.**

**Will I get cancer? Why?**

- Environmental Exposures
- Inherited Factors

**Long Island Breast Cancer Study**

- Overall, modest increase in breast cancer
- Many negative environmental findings
- Family history common risk factor among cases

**See or Type**

<table>
<thead>
<tr>
<th>Site</th>
<th>Proportion of Variance 95% CI*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HERITABLE FACTORS</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.28 (0.51)</td>
</tr>
<tr>
<td>Colon</td>
<td>0.35 (0.10-0.41)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.36 (0.53)</td>
</tr>
<tr>
<td>Lung</td>
<td>0.26 (0.40)</td>
</tr>
<tr>
<td>Breast†</td>
<td>0.27 (0.44-0.51)</td>
</tr>
<tr>
<td>Gastro intestinal</td>
<td>0.00 (0.42)</td>
</tr>
<tr>
<td>Corpus</td>
<td>0.00 (0.35)</td>
</tr>
<tr>
<td>Ovary†</td>
<td>0.22 (0.41)</td>
</tr>
<tr>
<td>Prostate</td>
<td>0.42 (0.29-0.50)</td>
</tr>
<tr>
<td>Bladder†</td>
<td>0.31 (0.45)</td>
</tr>
<tr>
<td>Leukemia†</td>
<td>0.21 (0.54)</td>
</tr>
</tbody>
</table>

*CI denotes confidence interval.
Could there be a genetic link?

- 1st-degree relative → RR ~2-4
- Clinical Validity
- About 25% cancers familial, 5-10% Mendelian
- Early age
- Multiple primary cancers
- Hereditary/Syndromic pattern
- Positive genetic test

Family History as a Public Health Tool

- Note *Am J Prev Med* 2(24); Feb 2003
- From 2009 AHRQ report on assessing family history:
  - Difficult to assess clinical validity
  - Low sensitivity, but high specificity (analytic validity)
  - Impact on health behaviors uncertain (clinical utility)
  - Not psychologically harmful (ELSI)
  - Lots of research to be done

Clinical Utility

Public Health Interventions

- Primary prevention
  - ACS 5-a-day
  - Exercise
  - Prevent smoking initiation
  - Chemoprevention
  - Risk-Reducing Surgery

Hereditary Cancer

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Family History as a Public Health Tool

Cancer registries

- VDH (http://www.vdh.state.va.us/epi/cancer/index.asp)
- MACGN (www.macgn.org)
- Other initiatives
  - http://www.hhs.gov/familyhistory/
  - http://www.cdc.gov/genomics/

Public Health Interventions

- Secondary Prevention (Screening)
  - Radiology (Mammography, Colonoscopy, other)
  - Clinical and self-examinations
  - Molecular markers
Public Health Interventions

- Tertiary Prevention (Screening)
  - Prevent recurrence and/or new primary
  - Chemotherapy, radiation, surgery, screening
  - Address comorbidity and iatrogenic complications

ELSI
How Do You Help the Population?

- Cost
- Harm vs. Benefit
- Is Tailoring Worth It?

Targeting the Risk Factors

- Age
  - Initiating screening appropriately
- Diet
  - Targeted interventions (school lunches, food labeling)
- Genetics
  - Family history
  - Genetic testing

Think again about your challenge

- Cancer clusters
  - Higher-than-expected rate of cancer in geographically-defined area
- Challenges
  - It's a big country
  - Not coincidence if it happens to you
  - Media influential
  - Are we exploring all the options?
  - Question #1 – Is this a unique problem?
  - Question #2 – If so, what do you want to know?
    - i.e., What public health test/screen?

What barriers do you anticipate to promoting family history collection?

- Family communication
- Access to expert health services
- Concerns about confidentiality and/or discrimination
- Others?
Revisit Your Challenge and Think Genetically