Rapid Case Ascertainment in Population and Hospital-Based Studies: Notes From the Field

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Overview of Presentation

• Why Rapid Report?
• Population-Based Study
• Clinic-Based Study
  – Mayo Pancreatic Cancer Study
Why Rapid Report?

• Decrease recall bias
  – Ruminate longer to explain cause of disease
  – Confuse exposures before/after diagnosis
  – Post diagnosis changes could influence recall

• Minimize ascertainment bias
  – Systematic loss of most aggressive cases of a cancer due to early mortality
12-Month Survival (1995-2001)

Source: SEER Program (2005)
Approaches to Decrease Bias

• Include Next-of-Kin Interviews
  – Limited exposure assessment of varying validity and reliability
  – Best type of control not always clear
  – Limited collection of biologic specimens
    • Tumor tissue, but often limited for genomic DNA-based studies (and need to have sufficient tissue)

• Enroll only living patients
  – Enroll before major impact of survival
  – Enroll before initiation of therapy
NCI-SEER Interdisciplinary Case-Control Study of Non-Hodgkin Lymphoma
Goals of the study

• Environmental Risk Factors
  – Household pesticides
  – Occupational exposures (benzene)

• Medical History

• Lifestyle
  – Diet and physical activity
  – Sun exposure

• Biologic specimens
  – DNA: genetic polymorphism studies
  – Serum: Organochlorines; antibodies
# Data Collection Scheme

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Group A (AA, 50% other)</th>
<th>Group B (all other)</th>
</tr>
</thead>
</table>
| **Mail**             | • Lifetime residence & work calendar | • Family Medical Hx     | • Food Frequency Questionnaire  
|                      |                                    |                         | • Physical activity     |
| **CAPI**             | • Demographics                     | • Detailed medical hx (diseases, surgeries, antibiotics) | • Abbrev medical hx  
|                      | • Residential pesticides           | • Illicit drugs         | • Allergies            |
|                      | • Occupational history             |                         | • Hobbies             |
|                      | • Hair coloring use                |                         | • Sun exposure        |
|                      |                                    |                         | • Cell phone          |
| **Other**            | • Consent forms                    |                         |                     |
|                      | • G.P.S.                            |                         |                     |
|                      | • Blood (treatment)                |                         |                     |
|                      | • Buccal                           |                         |                     |
|                      | • Dust sample                      |                         |                     |
|                      | • Water sample                     |                         |                     |
## Data Collection Scheme

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Group A (AA, 50% other)</th>
<th>Group B (all other)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mail</strong></td>
<td>• Life work habits</td>
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<tr>
<td></td>
<td>• Education</td>
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<tr>
<td><strong>CAPI</strong></td>
<td>• Demographic</td>
<td></td>
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<tr>
<td></td>
<td>• Residence</td>
<td></td>
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<td>• Occupation</td>
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<td></td>
<td>• Hair color</td>
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<tr>
<td><strong>Other</strong></td>
<td>• Consent</td>
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<tr>
<td></td>
<td>• G.P.S.</td>
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<td>• Blood (treatment)</td>
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<tr>
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<td>• Buccal</td>
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<td></td>
<td>• Dust sample</td>
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<tr>
<td></td>
<td>• Water sample</td>
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<td></td>
<td><strong>In-Person</strong></td>
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<td><strong>In-Home Interview</strong></td>
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<td></td>
<td><strong>Pre-treatment blood</strong></td>
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<tr>
<td></td>
<td>Blood Frequency Questionnaire</td>
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<td></td>
<td>Physical activity</td>
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<td></td>
<td>Abbrev medical hx</td>
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<td></td>
<td>Allergies</td>
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<td></td>
<td>Hobbies</td>
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<td>Sun exposure</td>
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<td>Cell phone</td>
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</tr>
<tr>
<td></td>
<td>Residential pesticides</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Occupational history</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hair coloring use</td>
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</tbody>
</table>

**Group B** (all other)
Case Selection

• Eligibility
  – Aged 20 to 74 years
  – Uninfected with HIV

• Sampling scheme
  – Iowa, Seattle: all cases
  – Detroit, LA: all African-Americans and a random sample of all other

• Rapid Reporting Systems
Rapid Reporting - Iowa

• Standard Reporting
  – Begin abstracting 6 mos after diagnosis
  – 15 month lag

• Rapid Reporting
  – Registry field staff increase surveillance
    • Monthly for smaller hospitals/path labs
    • Weekly for larger facilities
  – Report in “early”
    • Laptop electronic form submitted
    • Fax path report to central registry
Iowa Cancer Registry

- Pre-HIPAA
- Temporary Number
  - Not abstracted
- Reconciliation
  - Against Iowa database
    - Is this a recurrence or transformation?
  - Other field reports
    - Concurrent (follow forward)
    - Recent past (follow back)
Iowa Cancer Registry

• Check Eligibility (IRB regulated)
  – Date of diagnosis
  – Age at diagnosis
  – Iowa residence
  – Histologically confirmed, new diagnosis of non-Hodgkin lymphoma
    • Chronic Lymphocytic Leukemia
  – (HIV/AIDS status)
Iowa Cancer Registry

• Passive Consent
  – Physician of record (oncologist > family)
  – Fax letter and form
  – Eligibility criteria
    • Asked to report any inaccuracies
    • Does patient meet eligibility
  – 14 days to respond with do not contact
  – Letter to cases:
    “Where your physician’s name was available in our database, we have contacted him or her about your participation in this study”
Rapid Reporting
Iowa Experience - First 9 Months

Reported
N=271

Eligible
N=188

Interview
N=164

10% Diagnosis date (28)
8% Age (21)
6% Previous NHL (15)
2% Not NHL (5)
1% Residence (3)

12% Deceased (23)
3% Physician refused (6)

Time to report: Median = 55 days
Mean = 77 days
Results of Full NCI Study
Case Recruitment

Eligible
N=2,248

Attempted
N=1,728

Interviewed
N=1,321

14% Deceased (320)
3% Physician refusal (57)
1% Moved (16)
6% Not located (127)

16% Refused (274)
8% Ill, impaired, etc (133)

Participation Rate = 76%
Response Rate = 59%
### Impact of Rapid Reporting

<table>
<thead>
<tr>
<th>Time from diagnosis to interview</th>
<th>Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 3 months</td>
<td>16%</td>
<td>16%</td>
</tr>
<tr>
<td>&gt;3 – 6 months</td>
<td>45%</td>
<td>61%</td>
</tr>
<tr>
<td>&gt;6 – 12 months</td>
<td>23%</td>
<td>85%</td>
</tr>
<tr>
<td>&gt;12 – 24 months</td>
<td>12%</td>
<td>96%</td>
</tr>
<tr>
<td>&gt;24 months</td>
<td>4%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Median = 5.0 months, Mean = 7.3 months
## NHL Subtype

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Number Interviewed</th>
<th>Median Time Dx to Interview</th>
<th>Participation Rate</th>
<th>Response Rate</th>
<th>Percent Deceased</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>1321</td>
<td>5.0</td>
<td>76%</td>
<td>59%</td>
<td>14%</td>
</tr>
<tr>
<td>SLL</td>
<td>161</td>
<td>4.7</td>
<td>81%</td>
<td>69%</td>
<td>8%</td>
</tr>
<tr>
<td>Mantle Cell</td>
<td>50</td>
<td>4.1</td>
<td>78%</td>
<td>66%</td>
<td>10%</td>
</tr>
<tr>
<td>Follicular</td>
<td>319</td>
<td>4.6</td>
<td>79%</td>
<td>70%</td>
<td>6%</td>
</tr>
<tr>
<td>Marginal Zone</td>
<td>106</td>
<td>5.7</td>
<td>75%</td>
<td>62%</td>
<td>6%</td>
</tr>
<tr>
<td>DLBCL</td>
<td>417</td>
<td>4.8</td>
<td>75%</td>
<td>53%</td>
<td>21%</td>
</tr>
<tr>
<td>Burkitt</td>
<td>20</td>
<td>5.4</td>
<td>80%</td>
<td>49%</td>
<td>24%</td>
</tr>
<tr>
<td>PTCL</td>
<td>20</td>
<td>4.9</td>
<td>77%</td>
<td>43%</td>
<td>42%</td>
</tr>
</tbody>
</table>
Pre-Treatment Blood Specimen

<table>
<thead>
<tr>
<th>Type of Lymphoma</th>
<th>N</th>
<th>Untreated</th>
<th>Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>%</td>
<td>med</td>
</tr>
<tr>
<td>All</td>
<td>714</td>
<td>18%</td>
<td>3.7</td>
</tr>
<tr>
<td>SLL</td>
<td>98</td>
<td>39%</td>
<td>3.8</td>
</tr>
<tr>
<td>Mantle Cell</td>
<td>33</td>
<td>18%</td>
<td>3.3</td>
</tr>
<tr>
<td>Follicular</td>
<td>191</td>
<td>23%</td>
<td>3.5</td>
</tr>
<tr>
<td>Marginal Zone</td>
<td>65</td>
<td>34%</td>
<td>3.8</td>
</tr>
<tr>
<td>DLBCL</td>
<td>198</td>
<td>3%</td>
<td>5.7</td>
</tr>
<tr>
<td>Burkitt</td>
<td>11</td>
<td>0%</td>
<td>-</td>
</tr>
<tr>
<td>PTCL</td>
<td>29</td>
<td>11%</td>
<td>3.1</td>
</tr>
</tbody>
</table>
Summary: NHL Study

- **Successful**
  - Shortened time from dx to interview
  - Real time link to physicians

- **Limitations**
  - Ascertainment bias: differential loss of aggressive NHL subtypes

- **Not Successful**
  - Pre-treatment blood
  - Frozen tumor tissue (not a rapid reporting issue on a population basis)
Overview of Presentation

• Why Rapid Report?
• Population-Based Study
• Clinic-Based Study
  – Mayo Pancreatic Cancer Study
Impact on Molecular Epidemiology Studies of Pancreatic Cancer

• Bias related to survival
  – Population-based studies of pancreatic cancer – 30-70% deceased and unable to enroll into studies (no DNA)

• Bias related to DNA source
  – Retrospective, registry-based study in Spain used tumor tissue as DNA source
    – Only 34% of 149 cases had useable tumor tissue
Mayo Clinic Pancreatic Patient Recruitment (G. Petersen, PI)

- Starting in October 2002, all consecutive patients approached
  - At diagnosis (ultra-ultra rapid recruitment)
  - By mail within 2 months (ultra-rapid recruitment)
- HIPAA (Preparatory to Research)
- Over 600 patients enrolled to date
  - 92% within 30 days of diagnosis
  - 80% consent rate
Deaths among 412 recruited subjects, Mayo Clinic Pancreatic Cancer Registry

Survival
- Less than 31 days: 3.4%
- 31 to 61 days: 7.0%
- 62 to 92 days: 8.5%
- 3+ to 6 months: 21.6%
- 6+ to 12 months: 32.3%
- More than 1 year: 27.2%

40.5% ≤ 6 mos
### Pilot Study Results

#### Allele/Genotype Frequencies

**Cases**

<table>
<thead>
<tr>
<th>Candidate Genes</th>
<th>Controls (N=62)</th>
<th>All (N=62)</th>
<th>Short (N=31)</th>
<th>Long (N=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2E1 / G1293C / (C)</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>CYP2E1 / C1053T / (C)</td>
<td>0.97</td>
<td>0.98</td>
<td>0.98</td>
<td>0.98</td>
</tr>
<tr>
<td>GSTT1 / (Null)</td>
<td>0.18</td>
<td>0.15</td>
<td>0.16</td>
<td>0.13</td>
</tr>
<tr>
<td>GSTM1 / (Null)</td>
<td>0.53</td>
<td>0.48</td>
<td>0.45</td>
<td>0.52</td>
</tr>
<tr>
<td>NQO1 / (C)</td>
<td>0.78</td>
<td>0.88</td>
<td>0.82</td>
<td>0.95</td>
</tr>
</tbody>
</table>

**Controls** (N=62)

- CYP2E1 / G1293C / (C): 0.02
- CYP2E1 / C1053T / (C): 0.97
- GSTT1 / (Null): 0.18
- GSTM1 / (Null): 0.53
- NQO1 / (C): 0.78

**Source:** Petersen GM, et al. (unpublished)

**Short:** died within 4 months of diagnosis

**Long:** survival >9 months
Surgery among 412 recruited subjects, Mayo Clinic Pancreatic Cancer Registry

No surgery 78%
Primary resection 20%
Liver resection 2%
## Pilot Study Results

### Allele/Genotype Frequencies

<table>
<thead>
<tr>
<th>Candidate Genes</th>
<th>Controls (N=61)</th>
<th>All (N=62)</th>
<th>No Surgery (N=52)</th>
<th>Surgery (N=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2E1 / G1293C / (C)</td>
<td>0.02</td>
<td>0.02</td>
<td>0.01</td>
<td>--</td>
</tr>
<tr>
<td>CYP2E1 / C1053T / (C)</td>
<td>0.97</td>
<td>0.98</td>
<td>0.98</td>
<td>1.00</td>
</tr>
<tr>
<td>GSTT1 / (Null)</td>
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<td>0.15</td>
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<td>0.60</td>
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<td>0.88</td>
<td>0.87</td>
<td>0.94</td>
</tr>
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Source: Petersen GM, et al. (unpublished)
Conclusions

• Rapid reporting critical for identifying cases quickly
  – Decrease ascertainment bias related to survival
  – Increase the percentage of cases with biologic specimens
• For some cancers, ultra-rapid reporting through hospital-based registries may be required
Acknowledgements

NHL Case-Control Study

- NCI
  - Patricia Hartge
  - Nat Rothman
  - Martha Linet
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  - Wendy Cozen
  - Leslie Bernstein

- FHCRC
  - Scott Davis

Pancreatic Cancer Study

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  - Gloria Petersen
  - Janet Olson
  - Mariza de Andrade
  - Julie Cunningham