Scientific Update to the BSA: HMO Cancer Research Network (CRN)

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Division of Cancer Control and Population Sciences

November 1, 2010
Cancer Research Network (CRN)

- Started in 1999; most recently funded in 2007
- Cooperative Agreement/Research Network Grant (U19)
- Network members are 14 research organizations affiliated with large integrated healthcare systems (HMOs) covering nearly 11 million individuals
- CRN is model for similar initiatives at NHLBI, NIMH, and NIH Common Fund
14 Research Sites in the CRN

Cancer Research Network Sites

- Group Health, Group Health Research Institute
- Kaiser Permanente Northwest, Center for Health Research/Northwest
- Kaiser Permanente Northern California, Division of Research
- Kaiser Permanente Southern California, Department of Research and Evaluation
- Kaiser Permanente Hawaii, Center for Health Research/Hawaii
- HealthPartners, HealthPartners Research Foundation
- Marshfield Clinic, Marshfield Clinic Research Foundation
- Health Alliance Plan, Henry Ford Health System
- Harvard Pilgrim Health Care Institute, Department of Population Medicine
- Fallon Community Health Plan, Meyers Primary Care Institute
- Geisinger Health Plan, Center for Health Research
- Kaiser Permanente Georgia, Center for Health Research/Southeast
- Lovelace Health Plan, Lovelace Clinic Foundation
- Kaiser Permanente Colorado, Institute for Health Research

~11 million enrollees (3% of US population)
CRN Research Themes

• Cancer Epidemiology, Prevention, and Health Promotion
• Dissemination and Implementation
• Health Care Delivery, Quality and Outcomes
• Cancer Communication and Decision-Making
• Psychosocial Factors and Burden of Cancer
• Health Insurance Benefit Designs and Patterns of Care
CRN Research: Examples Across the Cancer Control Continuum

**Prevention**
- RCT of Web intervention to increase fruit and vegetable intake
- CER study of alternative methods to screen for cervical & colorectal CA

**Screening & Early Detection**
- Study of prognostic factors, including tumor markers, for recurrence among women with DCIS

**Tumor Biology & Treatment**
- Risk of cardiotoxicity among women with invasive breast cancer treated with anthracyclines and/or herceptin

**Survivorship**
- Use and duration of hospice care among patients with advanced cancers

**End-of-Life**
Virtual Data Warehouse (VDW)

The VDW is populated by automated data from the following sources:

- Tumor registry
- Enrollment
- Demographics
- Pharmacy
- Utilization

- Geocoding
- Laboratory
- Chemotherapy
- Radiology
- Pathology
Scale and Scope of CRN Data

- ~11,000,000 total enrollees
- 505 patient clinics across the 14 CRN sites
- ~100,000 incident cancers per year
- ~69,000,000 Rx fills per year
- 8 of 14 CRN sites have active collaborations with Cancer Centers
Rapid Declines in HRT Use Documented with CRN Pharmacy Data

Percent of HT and ET Users that Discontinue by Study Month

Percent of HT and ET Non-users that Initiate by study month Starting 9/1999 and Ending 12/2002

Rapid Changes in Adjuvant Hormonal Therapy for Breast Cancer Documented with CRN Pharmacy Data

First presentation of clinical trial results (ATAC) at San Antonio

Scientific Accomplishments: Funding

• Since 2006, CRN and affiliated investigators have received competitive funding for
  – 17 NIH grants as well as several smaller contracts
  – 8 projects funded by other agencies (e.g. AHRQ, DoD, IOM)

• Research areas include:
  – Comparative Effectiveness of Screening, Treatment and Genomic Medicine
    – Breast, cervical, colorectal, and late stage cancers
  – Survivorship
    – Breast, colorectal and prostate cancers
  – Pharmaco-epidemiology
    – Breast and lymphoid cancers
  – Cancer Communication
  – Healthcare Delivery System Informatics
  – Using Healthcare Systems to Increase Participation in Clinical Trials
Scientific Accomplishments: Publications

- **Over 100 scientific publications since 2006:**
  - **Epidemiology**
    - American Journal of Epidemiology, Journal of Clinical Epidemiology, Nature Genetics and others
  - **Clinical Medicine**
    - Journal of the National Cancer Institute, Journal of Clinical Oncology, Archives of Internal Medicine and others
  - **Public Health**
    - American Journal of Public Health, Public Health Genomics, Medical Care, Health Affairs and others
CRN Scholars & Development Programs

• CRN Pilot Research Program
  – 17 research pilot projects funded involving academic researchers (will fund 3-5 more)
  – Led to multi-site R21s and R01s, K and other training awards, and manuscripts

• CRN Scholars Development Program
  – 28 Scholars/Junior Investigators
  – 12 Scholars either lead or co-lead CRN pilot research projects
  – Hands-on mentorship and networking opportunities with NIH scientists which have led to funded R, GO and Challenge grants, training awards and manuscripts
CRN Scientific Presentations

• **CRN Informatics R&D**
  – **Mark Hornbrook**, PhD, Chief Scientist, Kaiser Permanente Northwest Center for Health Research

• **Breast Cancer Research in the CRN**
  – **Rebecca Silliman**, MD, PhD, Professor, Boston University School of Medicine

• **Career in Cancer Research in the HMO CRN**
  – **Chyke Doubeni**, MD, MPH, Assistant Professor, Family Medicine and Community Health, University of Massachusetts Medical School

• **UCSF Collaborative Study on Medical Radiation and Cancer Risk**
  – **Rebecca Smith-Bindman**, MD, Professor, Departments of Radiology, Epidemiology/ Biostatistics, Obstetrics and Gynecology, UC San Francisco
CRN Informatics R&D

Mark C. Hornbrook PhD
Chief Scientist
The Center for Health Research, Northwest/Hawaii/Southeast
Kaiser Permanente

Investigator and Co-PI, CRN
Key Informatics Resources

- CRN can rapidly summarize clinical data to assess study feasibility and inform study design and logistics
- CRN can link Census and other geospatial information with HMO clinical data to test environmental factors
- CRN is on the cutting edge of assessing the usefulness of and implementing emerging informatics tools, such as Natural Language Processing and Distributed Research Networks
- CRN HMOs are on the cutting edge of implementing oncology EMR systems and adapting them for research purposes
CRN Cancer Counter Query Tool
## Breast Cancer: Race by Stage

### 2-Way Frequency Results

((X: Stage), (Y: Race))

<table>
<thead>
<tr>
<th>Race</th>
<th>In Situ</th>
<th>Localized</th>
<th>Reg by direct ext</th>
<th>Reg to lymph nodes</th>
<th>Reg both direct ext &amp; lymph nodes</th>
<th>Reg NOS</th>
<th>Dist</th>
<th>Staging scheme</th>
<th>Unstaged</th>
<th>unknown</th>
<th>Unspecified</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - White</td>
<td>44</td>
<td>69,083</td>
<td>1,563</td>
<td>26,152</td>
<td>2,650</td>
<td>1,633</td>
<td>4,358</td>
<td>≤5</td>
<td>≤5</td>
<td>8</td>
<td>3,330</td>
</tr>
<tr>
<td>2 - Black</td>
<td>≤5</td>
<td>6,947</td>
<td>208</td>
<td>3,324</td>
<td>433</td>
<td>371</td>
<td>715</td>
<td>≤5</td>
<td>≤5</td>
<td>512</td>
<td>17</td>
</tr>
<tr>
<td>3 - American Indian</td>
<td>125</td>
<td>6</td>
<td>41</td>
<td>10</td>
<td>≤5</td>
<td>8</td>
<td>≤5</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 - Chinese</td>
<td>≤5</td>
<td>1,462</td>
<td>25</td>
<td>546</td>
<td>45</td>
<td>13</td>
<td>61</td>
<td>≤5</td>
<td>≤5</td>
<td>47</td>
<td>13</td>
</tr>
<tr>
<td>5 - Japanese</td>
<td>≤5</td>
<td>1,238</td>
<td>24</td>
<td>366</td>
<td>38</td>
<td>11</td>
<td>43</td>
<td>≤5</td>
<td>≤5</td>
<td>36</td>
<td>11</td>
</tr>
<tr>
<td>6 - Filipino</td>
<td>≤5</td>
<td>2,230</td>
<td>43</td>
<td>942</td>
<td>80</td>
<td>9</td>
<td>120</td>
<td>≤5</td>
<td>≤5</td>
<td>51</td>
<td>14</td>
</tr>
<tr>
<td>7 - Hawaiian</td>
<td>≤5</td>
<td>605</td>
<td>14</td>
<td>239</td>
<td>19</td>
<td>≤5</td>
<td>25</td>
<td>≤5</td>
<td>≤5</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>8 - Korean</td>
<td>≤5</td>
<td>199</td>
<td>≤5</td>
<td>89</td>
<td>7</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
<td>7</td>
<td>≤5</td>
</tr>
<tr>
<td>9 - Asian Indian</td>
<td>≤5</td>
<td>272</td>
<td>≤5</td>
<td>138</td>
<td>13</td>
<td>≤5</td>
<td>19</td>
<td>≤5</td>
<td>≤5</td>
<td>15</td>
<td>≤5</td>
</tr>
<tr>
<td>95 - Southeast Asian</td>
<td>≤5</td>
<td>285</td>
<td>≤5</td>
<td>122</td>
<td>9</td>
<td>≤5</td>
<td>16</td>
<td>≤5</td>
<td>≤5</td>
<td>7</td>
<td>≤5</td>
</tr>
<tr>
<td>96 - Other Asian</td>
<td>≤5</td>
<td>616</td>
<td>6</td>
<td>252</td>
<td>24</td>
<td>6</td>
<td>35</td>
<td>≤5</td>
<td>≤5</td>
<td>31</td>
<td>17</td>
</tr>
<tr>
<td>97 - Pacific Islander (except Hawaiian)</td>
<td>≤5</td>
<td>114</td>
<td>≤5</td>
<td>62</td>
<td>≤5</td>
<td>8</td>
<td>≤5</td>
<td>6</td>
<td>≤5</td>
<td>8</td>
<td>≤5</td>
</tr>
<tr>
<td>98 - Other</td>
<td>≤5</td>
<td>129</td>
<td>≤5</td>
<td>59</td>
<td>13</td>
<td>9</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
<td>20</td>
<td>≤5</td>
</tr>
<tr>
<td>99 - Unknown</td>
<td>≤5</td>
<td>784</td>
<td>16</td>
<td>262</td>
<td>32</td>
<td>7</td>
<td>70</td>
<td>≤5</td>
<td>≤5</td>
<td>1,159</td>
<td>≥5</td>
</tr>
</tbody>
</table>

### Case Selection

**Primary Tumor Count:** 139,842

**CRN Plan:**
- Note - Query is limited to the first 4 selections listed:
  - All

**Primary Site - ICDO:**
- Note - Query is limited to the first 20 selections listed:
  - 1. C500-C509 Breast

**Individual Morphology:**
- Note - Query is limited to the first 20 selections listed:
  - All

**AJCC:**
- Note - Query is limited to the first 20 selections listed:
  - All

**Vital status:**
- All
Pancreatic Cancer: Gender by Health Plan

2-Way Frequency Results

<table>
<thead>
<tr>
<th>CRN Plan</th>
<th>Female</th>
<th>Male</th>
<th>Other</th>
<th>Trans</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRN Plan 1</td>
<td>584</td>
<td>502</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
</tr>
<tr>
<td>CRN Plan 2</td>
<td>623</td>
<td>616</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
</tr>
<tr>
<td>CRN Plan 3</td>
<td>3,058</td>
<td>3,252</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
</tr>
<tr>
<td>CRN Plan 4</td>
<td>2,181</td>
<td>2,243</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
</tr>
<tr>
<td>CRN Plan 5</td>
<td>269</td>
<td>321</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
</tr>
<tr>
<td>CRN Plan 6</td>
<td>336</td>
<td>366</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
</tr>
<tr>
<td>CRN Plan 7</td>
<td>229</td>
<td>258</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
</tr>
<tr>
<td>CRN Plan 8</td>
<td>666</td>
<td>651</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
</tr>
<tr>
<td>CRN Plan 11</td>
<td>22</td>
<td>37</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
</tr>
<tr>
<td>CRN Plan 13</td>
<td>701</td>
<td>854</td>
<td>≤5</td>
<td>≤5</td>
<td>≤5</td>
</tr>
</tbody>
</table>

Case Selection

Primary Tumor Count: 17,801
CRN Plan:
Note - Query is limited to the first 4 selections listed:

All

Primary Site - ICDO:
Note - Query is limited to the first 20 selections listed:

1. C250-C259 Pancreas

Individual Morphology:
Note - Query is limited to the first 20 selections listed:

All

AJCC:
Note - Query is limited to the first 20 selections listed:

All

Vital status:
Colorectal Cancer Rates
Economic Diversity: Census and Geospatial Data Links

Percent of Enrollees in Geographies where 15% or more households have below-poverty-level income
### Validation of Neighborhood Socio-Economic Status (SES) Index

<table>
<thead>
<tr>
<th>SES Quartile</th>
<th>Percent (by Row) of Self-Reported Education</th>
<th>N of Survey Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ HS Grad</td>
<td>Some College</td>
</tr>
<tr>
<td>Overall Self-Reported</td>
<td>17.8%</td>
<td>33.8%</td>
</tr>
<tr>
<td>Lowest SES</td>
<td>30.5%</td>
<td>39.3%</td>
</tr>
<tr>
<td>Lower Middle SES</td>
<td>18.4%</td>
<td>37.4%</td>
</tr>
<tr>
<td>Upper Middle SES</td>
<td>15.1%</td>
<td>31.2%</td>
</tr>
<tr>
<td>Highest SES</td>
<td>8.3%</td>
<td>27.8%</td>
</tr>
</tbody>
</table>

### Percent (by Row) of Self-Reported Annual Household Income

<table>
<thead>
<tr>
<th>SES Quartile</th>
<th>Percent (by Row) of Self-Reported Annual Household Income</th>
<th>N of Survey Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ $50,000</td>
<td>$50,000 - $74,999</td>
</tr>
<tr>
<td>Overall Self-Reported</td>
<td>30.7%</td>
<td>28.4%</td>
</tr>
<tr>
<td>Lowest SES</td>
<td>55.1%</td>
<td>27.7%</td>
</tr>
<tr>
<td>Lower Middle SES</td>
<td>32.4%</td>
<td>33.6%</td>
</tr>
<tr>
<td>Upper Middle SES</td>
<td>23.0%</td>
<td>30.4%</td>
</tr>
<tr>
<td>Highest SES</td>
<td>13.6%</td>
<td>22.1%</td>
</tr>
</tbody>
</table>

- % of households with income below the poverty level
- % of households receiving public assistance
- % of households with annual income below $30,000
- % of working age adult males not in the labor force
- % of adults ≥25 years with a high school education or less
- Log of median household income
- Log of median value of single family homes
i2b2 Data Query Tool Interface
Natural Language Processing in MediClass

Candidate Strings

Input Window

Lexical Processing

patient (n) patient (adj) patience patiently continue continuous continually continuity smoke (v) smoky (adj) smoker smokier smoker

smoking patiently patient continues smoke smoke patiently continually continue smoking

Concept Identification And Instantiation

Continue, C0750536, MatchScore,[context info]
Smoking, C0037369, MatchScore,[context info]

......

Concept Instances

patient continues to smoke 1/2ppd. not ready to quit.

Hazlehurst B et al. JAMIA 2005;12:517-529
Oncology Chemotherapy Interface

Springboard Report

Testrx Ncalhctestjz

ONCA NSCLC CARBOPLATIN PEMETREXED

Protocol
ONCA OVARIAN CARBOPLATIN - PRL239

Reference Links

Original protocol backbone is permanent and can be seen in Springboard

Related Active Treatment Plans
ONCA SUPPORTIVE PAMIDRONATE STANDING BLOOD TRANSFUSION
Type ONCOLOGY SUPPORTIVE CARE

Associated Problems
DM 2 [250.00H]
DIHYDROPTERIDINE REDUCTASE DEFICIENCY [270.1A]
POLS FORM ON FILE FOR LIFE SUSTAINING TX [V52.9C]

Dosing Weight and BSA

<table>
<thead>
<tr>
<th>Weight</th>
<th>BSA</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 kg</td>
<td>0.22 m²</td>
<td>Documented weight as of 5/24/10 10:00 AM, height of 179.2 cm as of 5/21/10 1:53 PM</td>
</tr>
<tr>
<td>1 kg</td>
<td>0.22 m²</td>
<td>Documented weight as of 5/24/10 10:00 AM, height of 179.2 cm as of 5/21/10 1:53 PM</td>
</tr>
<tr>
<td>None</td>
<td>None</td>
<td>Weight warning threshold is 10 %, BSA warning threshold is 10 %</td>
</tr>
</tbody>
</table>

Flowsheets
Go to Flowsheets

Day 1, Cycle 1 (21-day cycle)

Provider Reminders

Abbreviated Protocol Description
Comments: CARBO(AUC 5) PEMETREXED (500), q21d
CRN Research Resources

- Defined populations
- Ambulatory EMR data
- Health plan administrative/utilization data
- Patient Web portals
- Distributed research methods
- Emerging opportunities
  - Hospital EMRs
  - FDA Mini-Sentinel Drug Safety Surveillance
  - Biospecimen Repositories ↔ EMR-based phenotypes
Breast Cancer Research in the CRN

Rebecca A. Silliman, MD, PhD
Professor
Departments of Medicine and Epidemiology
Boston University Schools of Medicine and Public Health

Academic Liaison Committee, CRN
CRN Collaborator
CRN Breast Cancer Research Vision

• To use CRN population, data resources, and access to biological specimens to address key breast cancer research questions regarding:
  – Risk prediction and early detection
  – Prognosis
  – Treatment and its complications
  – Survivorship and Long-term outcomes

• Recent areas of emphasis:
  – Diffusion and comparative effectiveness of new technologies
  – Role of biomarkers in prognosis and treatment planning
  – Quality of care in relation to mammography, surgery, and patient experiences
Features of CRN Breast Cancer Studies

- Use representative community-based populations with large numbers of breast cancer events
- Draw comparison groups from identifiable sampling frames
- Use complementary data sources: electronic, medical record, and cancer registry data
- Involve three-six health plans
- Have substantial scholarly productivity
Notable CRN Breast Cancer Research

• **Studies of Prophylactic Mastectomy (PM)**
  – Contralateral PM after a breast cancer diagnosis
  – Bilateral PM in those with an elevated breast cancer risk

• **Predictors of DCIS Recurrence**

• **Outcomes in Older Women**
Breast Cancer in Older Women (BOW)

• **Background:**
  – Older women disproportionately bear the burden of breast cancer incidence and mortality
  – Older women are less likely to receive standard care
  – Older women are underrepresented in clinical trials
  – Observational studies performed in integrated health care delivery systems offer the best opportunity for studying the comparative effectiveness of therapies in this population

• **Question:**
  – Is less than standard care a risk factor for bad outcomes?
Study Design

Figure 1. STUDY DESIGN


Potentially eligible cohort

- Enroll eligible subjects and classify by demographic, health status, tumor, and treatment characteristics
- Determine whether breast cancer recurrence or cause-specific mortality occurs
- Ascertain surveillance testing
Prevalence of Outcomes Through 10 Years of Follow-up

N=1859

• Unique recurrences/second primaries: 351 (19%)
  – 295 recurrences
  – 56 second primaries

• Mortality: 746 (40%)
  – 295 breast cancer
  – 451 other causes

• Disenrollment: 190 (10%)
# Breast Cancer Recurrence and Mortality

<table>
<thead>
<tr>
<th>Primary Therapy</th>
<th>Local / Regional Recurrence HR (95% CI)</th>
<th>Breast Cancer Mortality HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mastectomy</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>BCS + RT</td>
<td>0.70 (0.40 – 1.30)</td>
<td>1.10 (0.80 – 1.51)</td>
</tr>
<tr>
<td>BCS only</td>
<td>3.50 (2.00 – 6.00)</td>
<td>2.19 (1.51 – 3.18)</td>
</tr>
</tbody>
</table>

BCS = Breast Conserving Surgery; RT = Radiation Therapy
N=1837

Recurrences and mortality were 2-3.5 fold higher in women treated with BCS alone

Tamoxifen Adherence and Breast Cancer Mortality in Women with Hormone Responsive Tumors

<table>
<thead>
<tr>
<th>Tamoxifen Use</th>
<th>Breast Cancer Mortality HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year</td>
<td>6.26 (3.10 – 12.64)</td>
</tr>
<tr>
<td>1-1.9 years</td>
<td>4.12 (1.90 – 8.93)</td>
</tr>
<tr>
<td>2-4.9 years</td>
<td>1.31 (0.73 – 2.33)</td>
</tr>
<tr>
<td>≥5 years</td>
<td>Ref</td>
</tr>
</tbody>
</table>

N=1837

Women who received <2 years of tamoxifen had a 4-6 times greater hazard of dying of breast cancer

Tamoxifen Discontinuance

N= 961

**Breast Cancer Mortality by Number of Surveillance Mammograms**

<table>
<thead>
<tr>
<th># of Surveillance Mammograms</th>
<th>Breast Cancer Mortality OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Ref</td>
</tr>
<tr>
<td>1</td>
<td>0.67 (0.39 – 1.10)</td>
</tr>
<tr>
<td>2</td>
<td>0.52 (0.25 – 1.10)</td>
</tr>
<tr>
<td>3</td>
<td>0.36 (0.13 – 0.99)</td>
</tr>
<tr>
<td>4 or more</td>
<td>0.12 (0.01 – 1.10)</td>
</tr>
</tbody>
</table>

N=1846

What are the Next Steps?

- Are there efficient ways to confirm the persistence of age-associated variations and outcomes?
- What would be the intervention targets if they persist?
  - Improved clinical assessment of older women?
  - Oral therapy adherence?
  - Identification and tracking of those in need of surveillance mammography?
A Career in Cancer Research in the HMO CRN

Chyke A. Doubeni, MD, MPH
Assistant Professor
Department of Family Medicine and Community Health
University of Massachusetts Medical School,
Fallon/Meyers Primary Care Institute

Investigator, CRN
Strengths of the CRN for Training the Next Generation of Cancer Researchers

- **Investigator training programs**
  - CRN Scholars Program
  - Research support (pilot funds and PI officer)
  - Workshops, Networking and Mentoring

- **Multiple linked sources of data on the continuum of cancer care on a large and stable populations base**
  - Study multiple outcomes from delivery and receipt of cancer screening to cancer mortality

- **Partnering with clinical, policy, and administrative leadership at the health plans:**
  - Enhances the relevance and rapid diffusion of innovation
  - Allows to influence policy and screening practices
A Career of Cancer Prevention Research Training in the CRN

• **Career Development (Center to Reduce Cancer Health Disparities)**
  – 2004-2007: Research supplement for under-represented minorities (CRN)
  – 2007-2012: **KO1** - “Understanding Racial and Ethnic Differences in Survival from Colorectal Cancer”
  – 2009-2010: **KO1 ARRA** Administrative Supplement

• **CRN Scholars Program (DCCPS)**

• **Independent Research Awards (DCCPS)**
  – 2009-2011: **RC2** - Cancer Screening Effectiveness and Research in Community-based Healthcare
  – 2010-2015: **RO1** - Effectiveness of Screening Colonoscopy in Reducing Deaths from Colorectal Cancer
Patterns and Predictors of Mammography Utilization Among Breast Cancer Survivors, n=797

Rates of surveillance mammography years 2-6 after breast cancer diagnosis, 55+ years

<table>
<thead>
<tr>
<th>Years of follow-up (n)</th>
<th>Rates of Surveillance Mammography (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (797)</td>
<td>79.8</td>
</tr>
<tr>
<td>2 (732)</td>
<td>76.8</td>
</tr>
<tr>
<td>3 (668)</td>
<td>74.0</td>
</tr>
<tr>
<td>4 (604)</td>
<td>70.7</td>
</tr>
<tr>
<td>5 (262)</td>
<td>62.6</td>
</tr>
</tbody>
</table>

Relationships with receipt of surveillance mammography

<table>
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<tr>
<th>Predictor</th>
<th>OR (95% CI)</th>
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<tbody>
<tr>
<td>Other MDs</td>
<td>Ref</td>
</tr>
<tr>
<td>Visits with PCP</td>
<td>2.21 [1.73-2.82]</td>
</tr>
<tr>
<td>Visits with GYN</td>
<td>3.49 [2.55-4.79]</td>
</tr>
</tbody>
</table>

Cancer survivors with visits to gynecologists or primary care physicians had a higher likelihood of having mammograms

Minority Supplement – CRCHD/NCI
Doubeni et al. Cancer 2006;106:2482–8
Racial/Ethnic Disparities for Colorectal Cancer-Specific Deaths in Insured Populations, n=13958

Unadjusted Survival Probability Plot

- Diagnosed 1993-1998
- Followed through 2003

Hazard ratios (95% CI) for non-Hispanic blacks compared to whites

|Adjusted for demographics| 1.17 [1.06-1.30] |
|Adjusted for receipt of treatment, stage | 1.06 [0.96-1.17] |

- Showed CRC mortality disparities among insured populations

Career Development (KO1) – CRCHD/NCI
- Historical cohort, 3 HMOs
- Age 50-75 yrs in 2000
- Followed through 2007

- Shows our ability to study
  - Patterns of use
  - Underuse, overuse and misuse

CRN Pilot Project/Scholars Program – DCCPS/NCI
Cancer Screening Effectiveness and Research in Community-based Healthcare

• **Goal:** Generate and disseminate scientific knowledge about effective cancer screening strategies in real-world settings

• **Aims:**
  – Create a multi-disciplinary, multi-site center for cancer screening comparative effectiveness research (CER)
  – Develop methodological capacity for population-based CER studies
  – Conduct two Proof of Principle studies:
    – Effectiveness of colonoscopy relative to other screening strategies in preventing advanced forms of colorectal cancers
    – Screening yield by liquid-based (Thin-Prep) cytology relative to conventional PAP test

Independent Research Award (RC2) – DCCPS/NCI
Effectiveness of Screening Colonoscopy in Reducing Deaths from Colorectal Cancer

• **Background:**
  – No direct evidence on the effectiveness of screening colonoscopy in reducing death from right colon cancers

• **Primary aim:**
  – Estimate the effectiveness of screening colonoscopy for preventing death from colon cancer particularly for cancers in the right colon

• **Secondary aims:**
  – Assess the impact of the quality of colonoscopy on its effectiveness
  – Evaluate the effectiveness of colonoscopy relative to sigmoidoscopy

Independent Research Award (RO1) – DCCPS/NCI
CRN as an Environment for Career Development

The access to unique data systems on a stable and diverse population base along networking, collaborations, mentorships and opportunities to partner with health plan leaders afforded by the CRN positions it uniquely to train the next generation of population-based cancer researchers.
UCSF Collaborative Study
Medical Radiation and Cancer Risk

Rebecca Smith-Bindman, MD
Professor Departments of Radiology,
Epidemiology and Biostatistics
Obstetrics, Gynecology, and Reproductive Medicine
University of California, San Francisco
2009-2010, visiting Scientist NCI, Radiation Epidemiology Branch, Division of Cancer Epidemiology and Genetics

CRN Collaborator
Areas of Interest

• **Research Focus**
  - Broadly on the utilization, interpretation, accuracy and outcomes associated with medical imaging

• **Goals**
  - To understand whether patients are helped or harmed by undergoing different imaging tests
  - To quantify risks and benefits of imaging
  - To develop concrete guidelines about when and how to image patients in different clinical settings
Background: Utilization of Imaging

- Utilization of new imaging technology (CT, MRI, PET) has increased dramatically last 20 years
- There are many drivers of increased imaging – including improvements in technology, strong financial incentives and patient and physician generated demand
- Group Health Cooperative (CHC) study demonstrated 10-20% annual increase in imaging using these new technologies*
- At GHC, the dramatic rise in imaging was associated with a doubling of imaging related costs during last 10 years*

* Smith- Bindman, Health Affairs, 2008
CT has become a mainstay of medical imaging

Radiation dose associated with CT are higher and more variable than widely known*

Doses in the same range as a single CT have been associated with cancer, but no study has directly assessed CT

- Data is from Hiroshima survivors, accidental exposures to radiation, and medical exposures to radiation for benign and malignant disease

The absence of direct assessment of CT has led to dismissing of the results and known associations of radiation with cancer

* Smith- Bindman, Archives of Internal Medicine 2010
Setting to Study Safety of Imaging

• Cancers from radiation take >5-10 years to develop and radio-sensitive cancers are uncommon

• To study the risks of imaging related radiation need:
  – A large diverse population (millions of patients), including people across all ages
  – Capacity to comprehensively / accurately assess imaging & dose
    – Studies that ask subjects to recall imaging are biased
  – Ability to follow patients for many years after imaging to see if cancer develops
  – Ability to link patients to population based cancer registries to learn about cancers many years after exposure
CRN Pilot Project

- I approached several CRN sites to conduct pilot study
- CRN sites with necessary data to assess imaging, cancer and outcomes were approached – very supportive/collaborative
- Scientific Aims of the Pilot
  - Patterns and variability of medical imaging over time
  - Patterns of radiation exposure associated with imaging over time
  - Variation in radiation exposure associated with CT examinations
- We rapidly designed study, applied and received pilot funding, and completed project – extremely efficient
- The results have since influenced several aspects of care at participating sites within extremely short time frame
Even in the Setting of Integrated Health Plans
Use of Imaging has Soared

Results based on 2.5 million enrollees per year, including 30 million imaging examinations of all types and over 3 million CTs
Radiation Exposure Has Increased Dramatically

For each patient, each year, we summed radiation from all imaging examinations and described the distribution in dose among those with the highest annual exposure.
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Pilot Results: Dose and Cost

• Costs of imaging across the CRN have tripled over 15 years

• There are dramatic differences within and between health plans in use of different tests and costs – desperately calling for some comparative effectiveness work to tease apart what imaging is appropriate and effective and cost effective

• There are dramatic differences in radiation dose for the same study across settings – desperately calling for work to standardize dose to appropriate levels
Planned Future Work

• We have planned a Program Project grant to focus several integrated research efforts on medical imaging

• **ARISE: Appropriate Radiology Imaging for Safety and Effectiveness**

• The projects take advantage of the CRN: VDW to assess imaging, ability to retrieve imaging studies from 15 years ago to quantify dose, capacity to follow enrollees for many years to assess cancer

• The study includes 70 million person years of follow up, 150,000 cancers, allowing definitive answers to broad range of questions

• The projects also take advantage of the health plan leadership so we will rapidly disseminate results and improve care
Importance of this Work

• Imaging is increasing dramatically
  – Fastest growing area of medical costs

• Radiation dose associated with medical imaging in the range where there is substantial evidence that it is carcinogenic:
  – Exposure to medical radiation has increased 5-10 times in the past 20 years

• Topic is timely as numerous organizations have called for this research: IOM, CMS, FDA, U.S. Congress, Professional Societies

• **CRN is the only context in the US where such a study is feasible**

• CRN provides opportunity to assess care, rapidly study the cost and effectiveness of that care, quantify harms, and to rapidly disseminate results to improve care