

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

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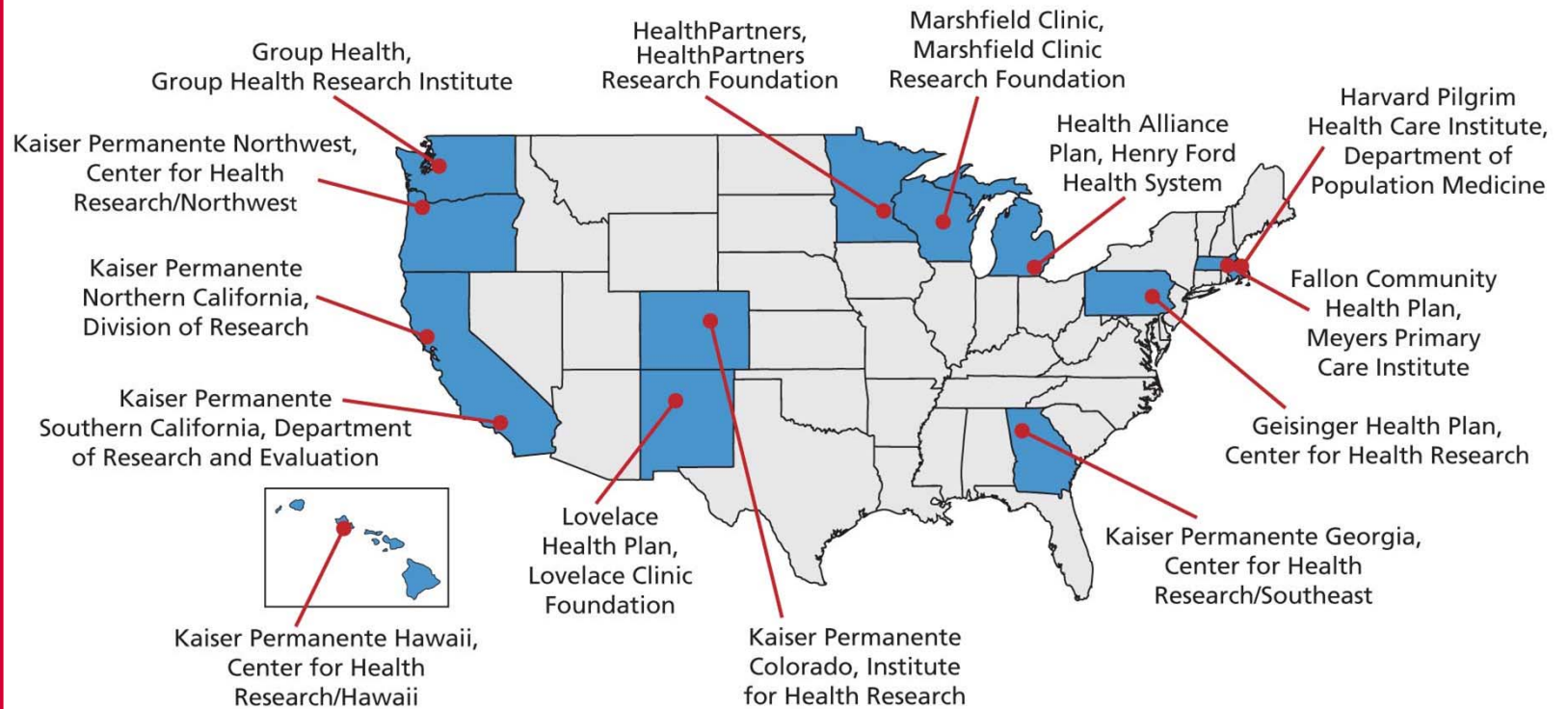


Cancer Research Network (CRN)

- 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



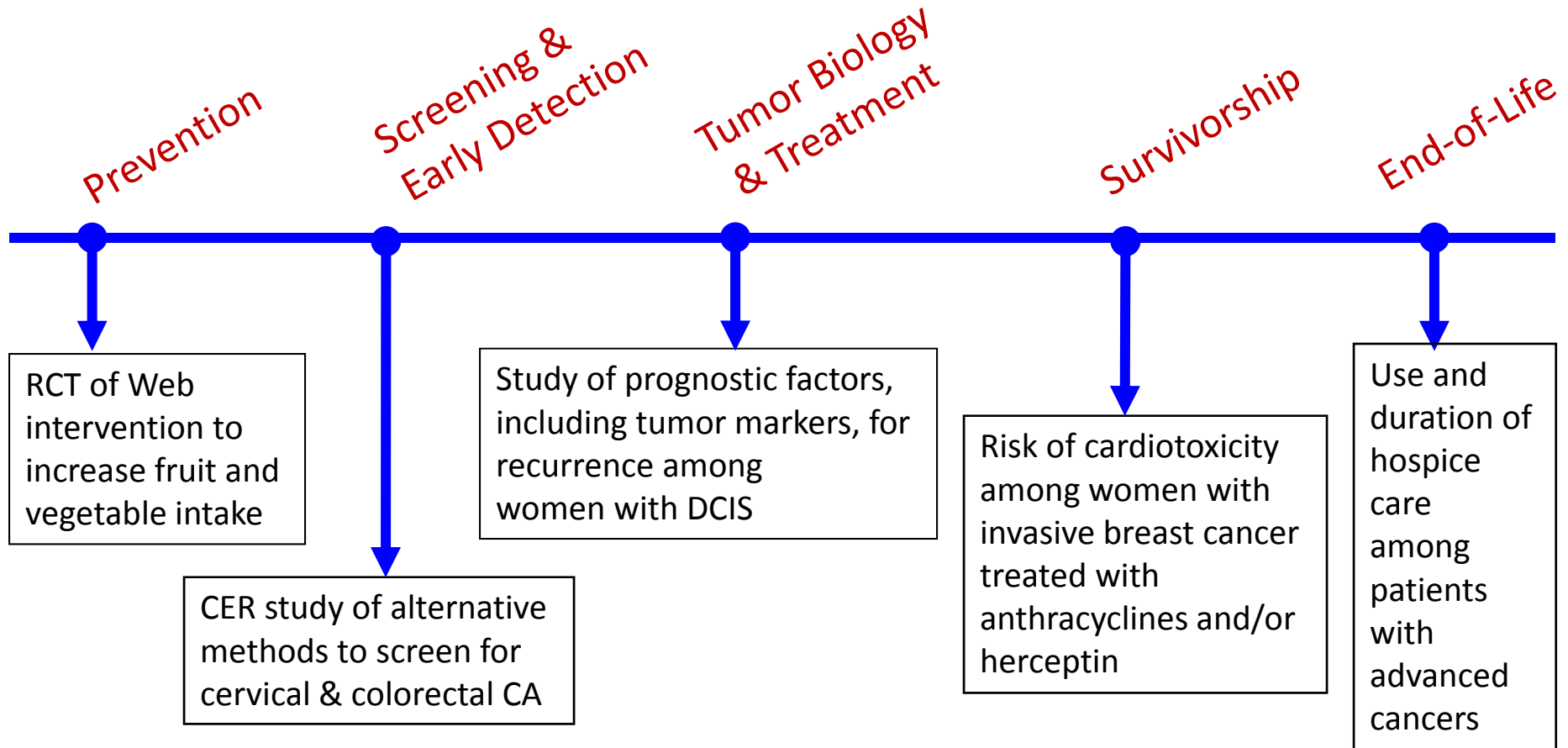
~11 million enrollees (3% of US population)



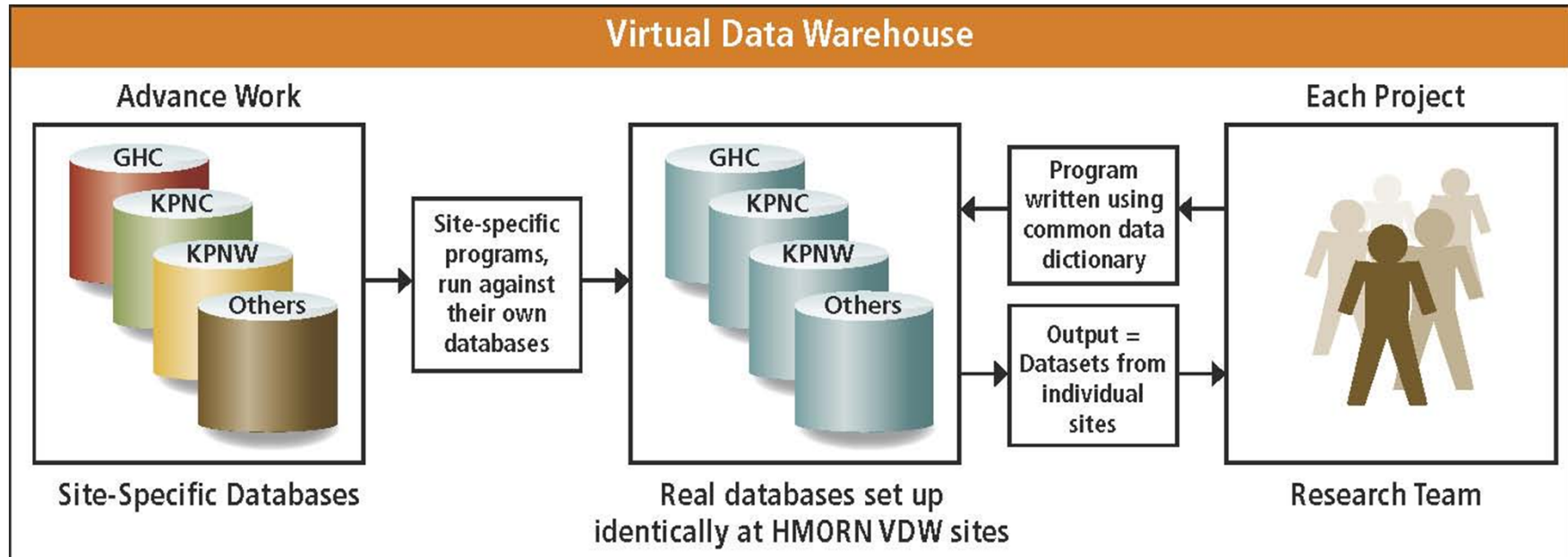
CRN Research Themes

- 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



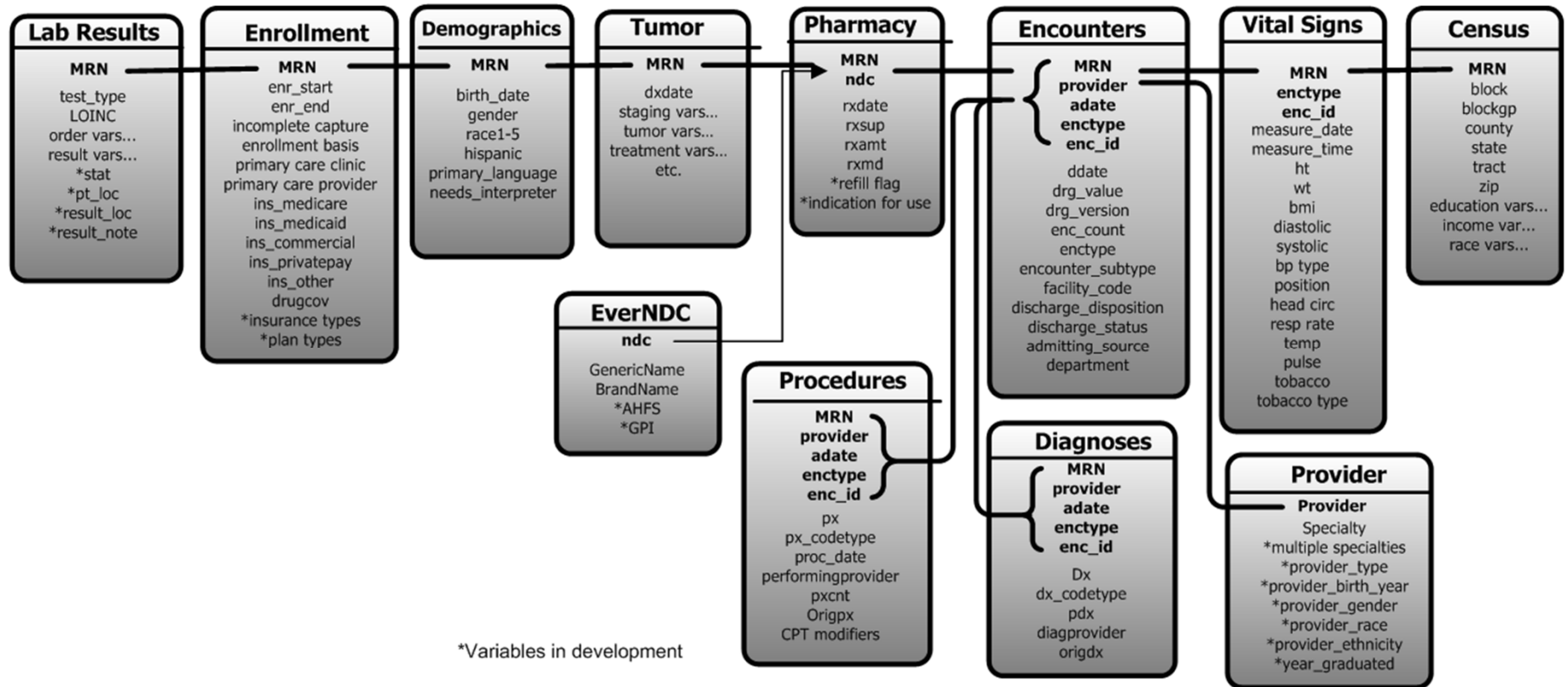
Virtual Data Warehouse (VDW)



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

- Tumor registry
- Enrollment
- Demographics
- Pharmacy
- Utilization
- Geocoding
- Laboratory
- Chemotherapy
- Radiology
- Pathology

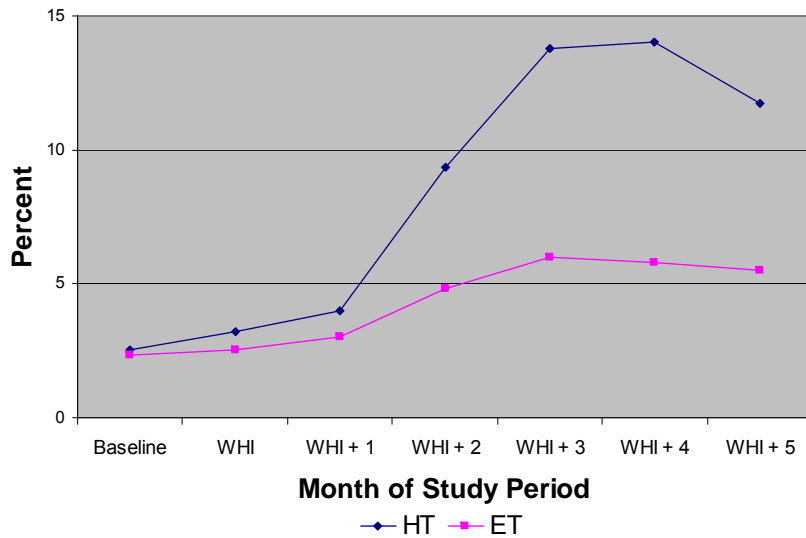
Scale and Scope of CRN Data



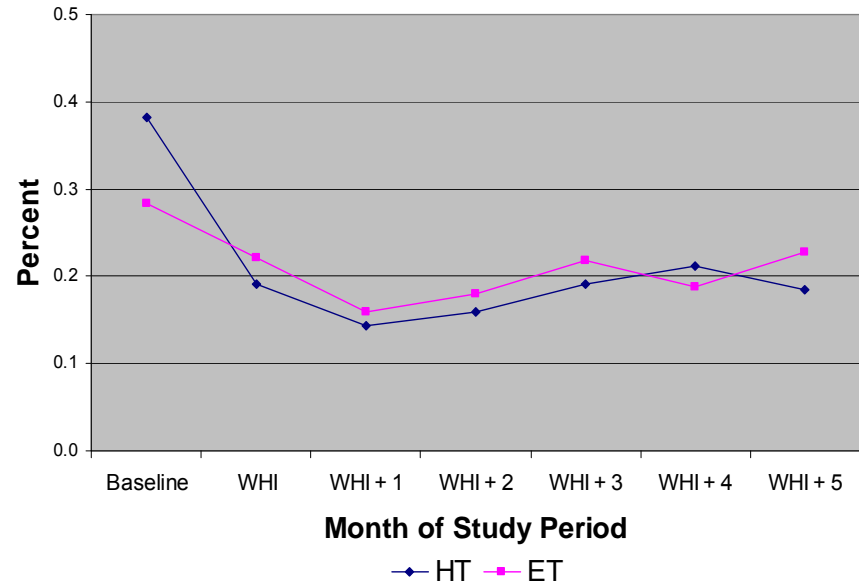
- ~11,000,000 total enrollees
- 505 patient clinics across the 14 CRN sites
- ~100,000 incident cancers per year
- ~69,000,000 Rx fills per year
- 8 of 14 CRN sites have active collaborations with Cancer Centers

Rapid Declines in HRT Use Documented with CRN Pharmacy Data

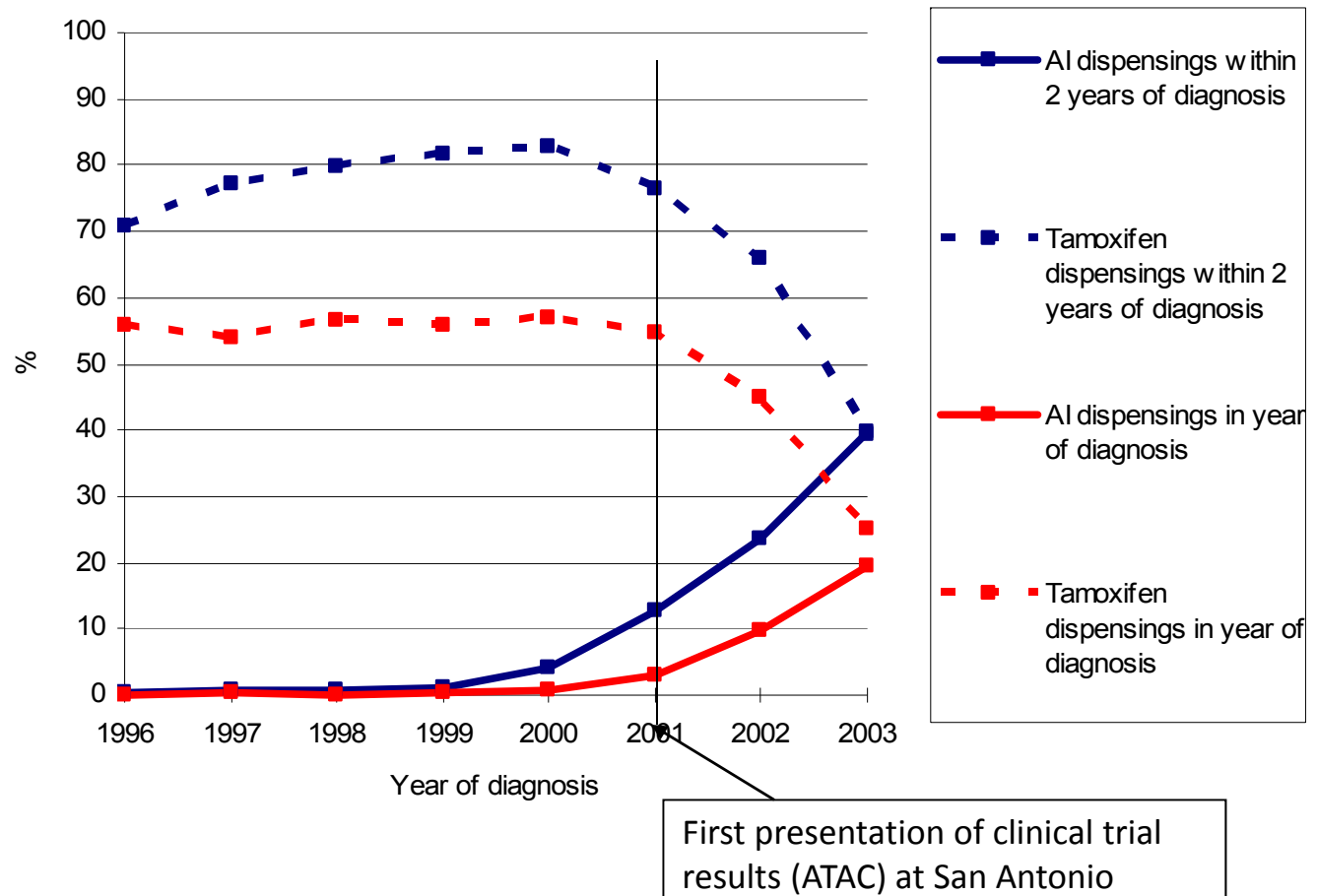
Percent of HT and ET Users that Discontinue by Study Month



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



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

Cancer Counter- Case Selection - Windows Internet Explorer

https://www.kpchr.org/crn/apps/CancerCounter/ACCCases.aspx

File Edit View Favorites Tools Help

Cancer Counter- Case Selection

CRN Cancer Counter

Case Selection: ICD 0 Third Edition

STEP 1. Pick your restrictions from the lists below (1 - many).
STEP 2. Click the "View Counts" top or bottom button.
Your selections are listed at the bottom of this page.
Dark gray boxes in the top-down lists indicate your selection.

STEP 3. Click **Review Your Selections** Data last updated: 4/22/2010

Primary Tumor Count: 984,790 **View Counts**

Create frequency tables **1-Way** **2-Way**

Primary Site- ICDO Max # Selections 20 [\[Morphologic Groups \]](#)

Count All

- C000-C009 Lip
- C010-C019 Base of tongue
- C020-C029 Other and unspecified parts of tongue
- C030-C039 Gum
- C040-C049 Floor of mouth

Behavior

Count All

- Benign
- In situ
- Malignant, primary site
- Metastatic site
- Uncertain behavior

Individual Morphology Max # Selections 20 [\[Morphologic Groups \]](#)

Count All

- 8000/0 NEOPLASM, benign
- 8000/1 NEOPLASM, uncertain whether benign or malignant
- 8000/2 Description Not Available
- 8000/3 NEOPLASM, malignant
- 8000/6 NEOPLASM, metastatic

CRN Plan Max # 4

Count All

- 1
- 2
- 3
- 4
- 5

Ethnicity

Count All

- White
- Black
- American Indian
- Chinese
- Japanese

General Summary Stage Max # Selections 7

Count All

- Distant Metastasis
- In situ
- Localized
- Regional both direct extension, lymph nodes
- Regional by direct extension

AJCC Max # 20

Count All

- 0
- 0A
- 0IS
- 1
- 1A

Vital Status

Count All

- ALIVE
- DEAD
- UNKNOWN

Gender

Count All

- Female
- Male
- Other
- Transsexual
- Unknown

RaceHispanic

Count All

- Non-Spanish
- Mexican
- Puerto Rican
- Cuban
- South/Central American

Dx Year

Beginning of year **Count All** Through year ending **Count All**

Age at Dx >90 aggregate with 90

Include age(s) **Count All** Through **Count All**

Cancel **Clear** **View Counts**

Review Your Selections:

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

Primary Tumor Count: 984,790

Behavior: All

ACCCases.aspx Trusted sites 100%

Breast Cancer: Race by Stage

Cancer Counter- 2-way report - Windows Internet Explorer

https://www.kpchr.org/crn/apps/CancerCounter/ACC2wayFrequency.aspx

File Edit View Favorites Tools Help

Cancer Counter- 2-way report

Page Tools

•--- BACK **Important Note:** Click the CRN Cancer Counter button to *clear the data set* and return to the Case Selection page. Click back to retain your selections and return to the previous page.

2-Way Frequency Results
((X: Stage), (Y: Race))

Race	In Situ	Localized	Reg by direct ext	Reg to lymph nodes	Reg both direct ext lymph nodes	Reg NOS	Dist Metastasis	Staging scheme not applicable	Unstaged unknown unspec
1 - White	44	69,083	1,563	26,152	2,650	1,633	4,358	≤5	8,330
2 - Black	≤5	6,947	208	3,324	433	371	715	≤5	512
3 - American Indian	≤5	125	6	41	10	≤5	8	≤5	17
4 - Chinese	≤5	1,462	25	546	45	13	61	≤5	47
5 - Japanese	≤5	1,238	24	366	38	11	43	≤5	36
6 - Filipino	≤5	2,230	43	942	80	9	120	≤5	51
7 - Hawaiian	≤5	605	14	239	19	≤5	25	≤5	14
8 - Korean	≤5	199	≤5	89	7	≤5	≤5	≤5	7
9 - Asian Indian	≤5	272	≤5	138	13	≤5	19	≤5	15
95 - Southeast Asian	≤5	285	≤5	122	9	≤5	16	≤5	7
96 - Other Asian	≤5	616	6	252	24	6	35	≤5	31
97 - Pacific Islander (except Hawaiian)	≤5	114	≤5	62	≤5	≤5	8	≤5	6
98 - Other	≤5	129	≤5	59	≤5	13	9	≤5	20
99 - Unknown	≤5	784	16	262	32	7	70	≤5	1,159

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

Done Trusted sites 100%

Pancreatic Cancer: Gender by Health Plan

Cancer Counter- 2-way report - Windows Internet Explorer

https://www.kpchr.org/crn/apps/CancerCounter/ACC2wa

File Edit View Favorites Tools Help

Cancer Counter- 2-way report

CRN Home Cancer Counter Case Selection ▶

•--- BACK **Important Note:** Click the CRN Cancer Counter button to *clear the data set* and return to the Case Selection page. Click back to retain your selections and return to the previous page.

2-Way Frequency Results
((X: Gender), (Y: CRN Plan))

CRN Plan	Female	Male	Other	Trans	Unknown
CRN Plan 1	584	502	≤5	≤5	≤5
CRN Plan 2	623	616	≤5	≤5	≤5
CRN Plan 3	3,058	3,252	≤5	≤5	≤5
CRN Plan 4	2,181	2,243	≤5	≤5	≤5
CRN Plan 5	269	321	≤5	≤5	31
CRN Plan 6	336	366	≤5	≤5	≤5
CRN Plan 8	229	258	≤5	≤5	≤5
CRN Plan 10	666	651	≤5	≤5	≤5
CRN Plan 11	22	37	≤5	≤5	≤5
CRN Plan 13	701	854	≤5	≤5	≤5

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

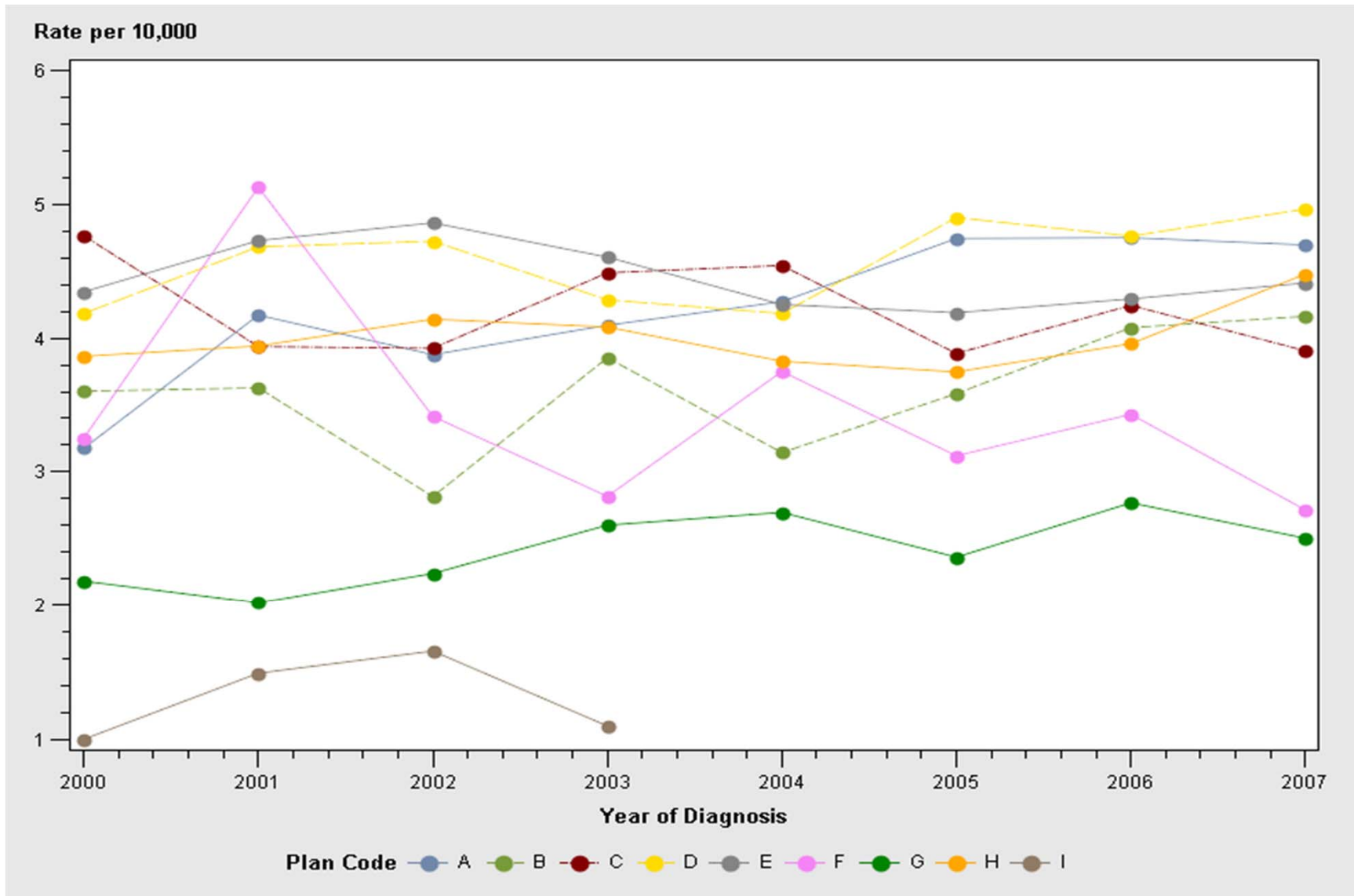
Individual Morphology:
Note - Query is limited to the first 20 selections listed:
All

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

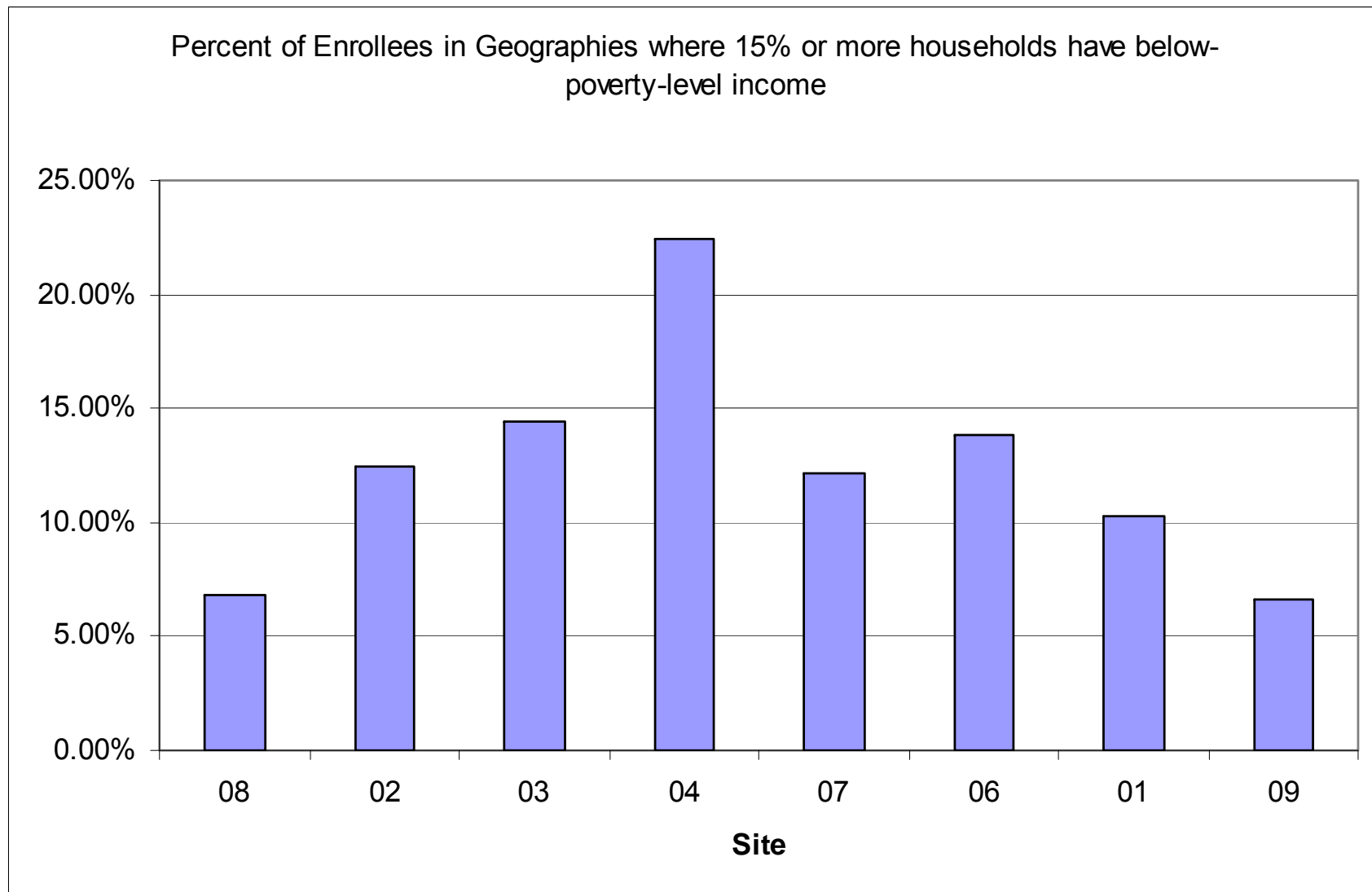
Vital status:

Done Trusted sites 100%

Colorectal Cancer Rates



Economic Diversity: Census and Geospatial Data Links



Validation of Neighborhood Socio-Economic Status (SES) Index

		Percent (by Row) of Self-Reported Education				N of Survey Respondents
		≤ HS Grad	Some College	College Grad	Post-College	
Overall Self-Reported		17.8%	33.8%	20.0%	28.4%	2,134
SES Quartile	Lowest SES	30.5%	39.3%	14.7%	15.6%	512
	Lower Middle SES	18.4%	37.4%	19.3%	24.9%	559
	Upper Middle SES	15.1%	31.2%	22.9%	30.8%	484
	Highest SES	8.3%	27.8%	23.0%	40.9%	579
		Percent (by Row) of Self-Reported Annual Household Income				N of Survey Respondents
		<\$50,000	\$50,000 - \$74,999	\$75,000 - \$99,000	≥\$100,000	
Overall Self-Reported		30.7%	28.4%	17.5%	23.4%	2,082
SES Quartile	Lowest SES	55.1%	27.7%	10.3%	6.9%	505
	Lower Middle SES	32.4%	33.6%	17.6%	16.5%	547
	Upper Middle SES	23.0%	30.4%	19.7%	26.9%	473
	Highest SES	13.6%	22.1%	22.1%	42.2%	557

- % 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

The screenshot displays the i2b2 Query & Analysis Tool interface. The main window is titled "i2b2 Query & Analysis Tool" and includes navigation links for "Find Patients", "Admin", "Analysis Tools", "Message Log", "Help", and "Log".

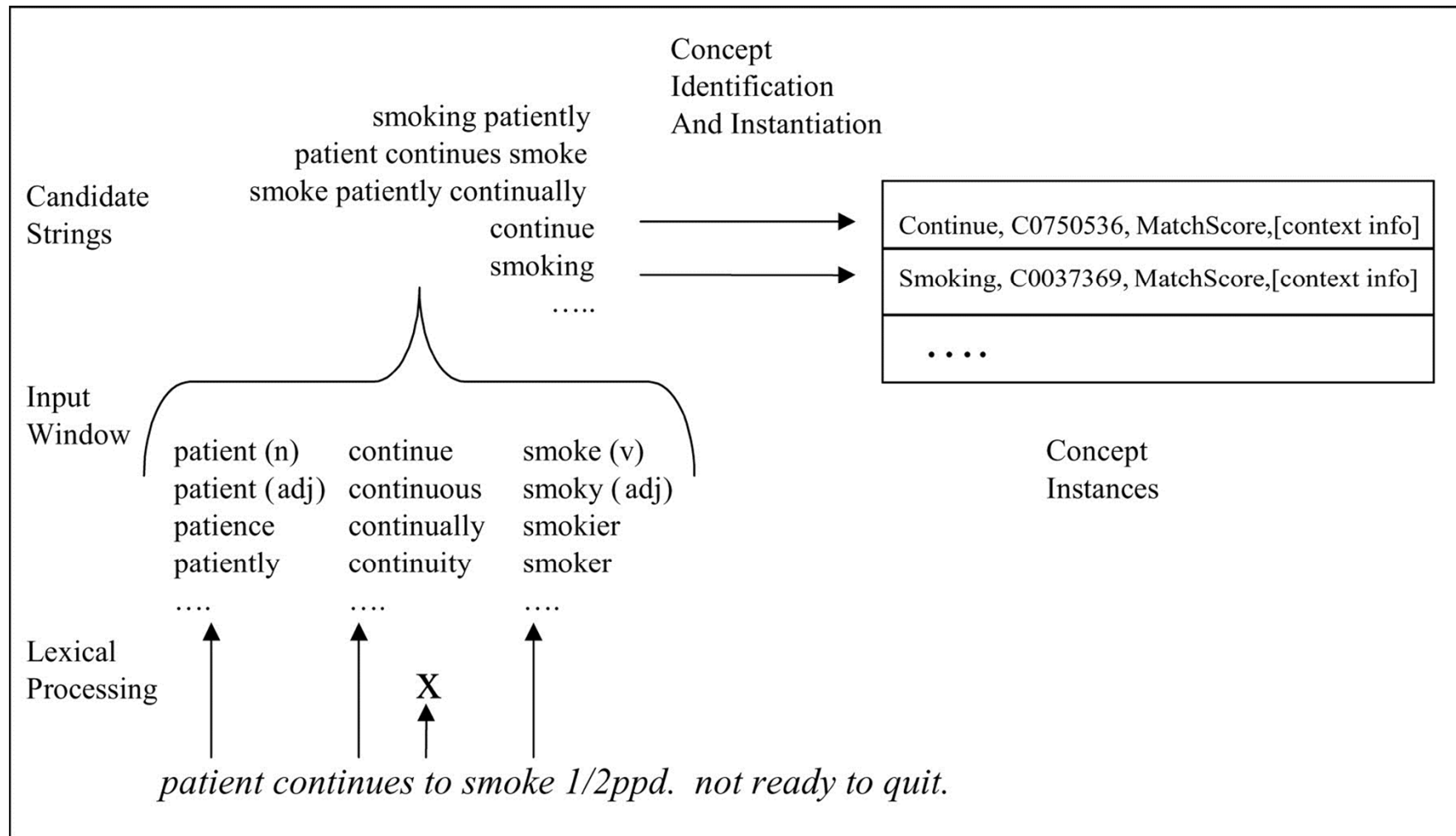
Left Panel:

- Navigate Terms / Find Terms:** A hierarchical tree of medical terms. The root is "BLOOD PRODUCTS/MODIFIERS/VOLUME EXPANDERS". Other categories include "CARDIOVASCULAR MEDICATIONS", "CENTRAL NERVOUS SYSTEM MEDICATIONS", "ANALGESICS", "ANESTHETICS", "ANTICONVULSANTS", "ANTIDEPRESSANTS", "ANTIPARKINSON AGENTS", "ANTIPSYCHOTICS", "ANTIPYRETICS", "ANTIVERTIGO AGENTS", "CNS MEDICATIONS, OTHER", "CNS STIMULANTS", "LITHIUM SALTS", "SEDATIVES/HYPNOTICS", and "DENTAL AND ORAL AGENTS TOPICAL".
- Workplace:** A workspace area containing folders for "hartje2" and "SHARED".
- Previous Queries:** A list of recent queries, including "C500 -Stage-ANTID@17:31:26 [10-22-2010] [hartje2]", "C500 -Stage-ANTID@17:30:35 [10-22-2010] [hartje2]", "250-ANT-Fem->= @15:53:47 [10-18-2010] [hartje2]", "250-ANT-Fem->= @15:53:07 [10-18-2010] [hartje2]", "250 -ANTINEO@15:51:47 [10-18-2010] [hartje2]", and "C500 -Fem-C500-17:31:26 [10-22-2010] [hartje2]".

Right Panel:

- Query Tool:** A panel for constructing queries. It features a "Query Name:" field and three groups (Group 1, Group 2, Group 3). Each group has columns for "Dates", "Occurs > 0x", and "Exclude".
 - Group 1:** Contains "C500 Breast".
 - Group 2:** Contains "Stage 2", "Stage 2B", "Stage 2C", and "Stage 2A".
 - Group 3:** Contains "ANTIDEPRESSANTS".
- Logic:** Below the groups, there are three green boxes labeled "one or more of these" connected by blue "AND" buttons.
- Buttons:** "Run Query", "New Query", "3 Groups", and "New Group".
- Query Status:** A panel showing the status of the query: "Finished Query: 'C500 -Stage-ANTID@17:31:26'", "Patient Count - 510 patients", and "FINISHED [8.4 secs]".

Natural Language Processing in MediClass



Oncology Chemotherapy Interface

Springboard Report

[Snapshot](#)
[Springboard Report](#)
[Chemo Treatment Plan](#)
[CONDENSED CP](#)
[CONDENSED SP](#)
 Report: [Springboard Report](#)

Testrx Ncalhctestjz **ONCA NSCLC CARBOPLATIN PEMETREXED**

Current Cycle	Treatment Dates	Created By	Created On	Status	Updated By	Updated On
1 of 6 cycles	6/10/2010 to 9/23/2010	Isabel Chong	6/10/2010	Active	Isabel Chong	6/11/2010

Protocol
[ONCA OVARIAN CARBOPLATIN - PRL239](#)

Reference Links
[Link](#)

Original protocol backbone is permanent and can be seen in Springboard

Related Active Treatment Plans

	Type
ONCA SUPPORTIVE PAMIDRONATE/STANDING BLOOD TRANSFUSION	ONCOLOGY SUPPORTIVE CARE

Associated Problems

	Stage
DM 2 [250.00H]	
DIHYDROPTERIDINE REDUCTASE DEFICIENCY [270.1A]	
POLST FORM ON FILE FOR LIFE SUSTAINING TX [V62.9C]	

Dosing Weight and BSA

	Weight	BSA	
Treatment plan	1 kg	0.22 m ²	Documented weight as of 5/24/10 10:00 AM, height of 179.2 cm as of 5/21/10 1:53 PM
Most recent	1 kg	0.22 m ²	Documented weight as of 5/24/10 10:00 AM, height of 179.2 cm as of 5/21/10 1:53 PM
Difference	none	none	Weight warning threshold is 10 %, BSA warning threshold is 10 %

Flowsheets
[Go to Flowsheets](#)

Day 1, Cycle 1 (21-day cycle) 6/10/10, Planned

	Dose	Route	Frequency	Signed By
Provider Reminders				
Abbreviated Protocol Description				
Comments: CARBO(AJC 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 \Leftrightarrow 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:**

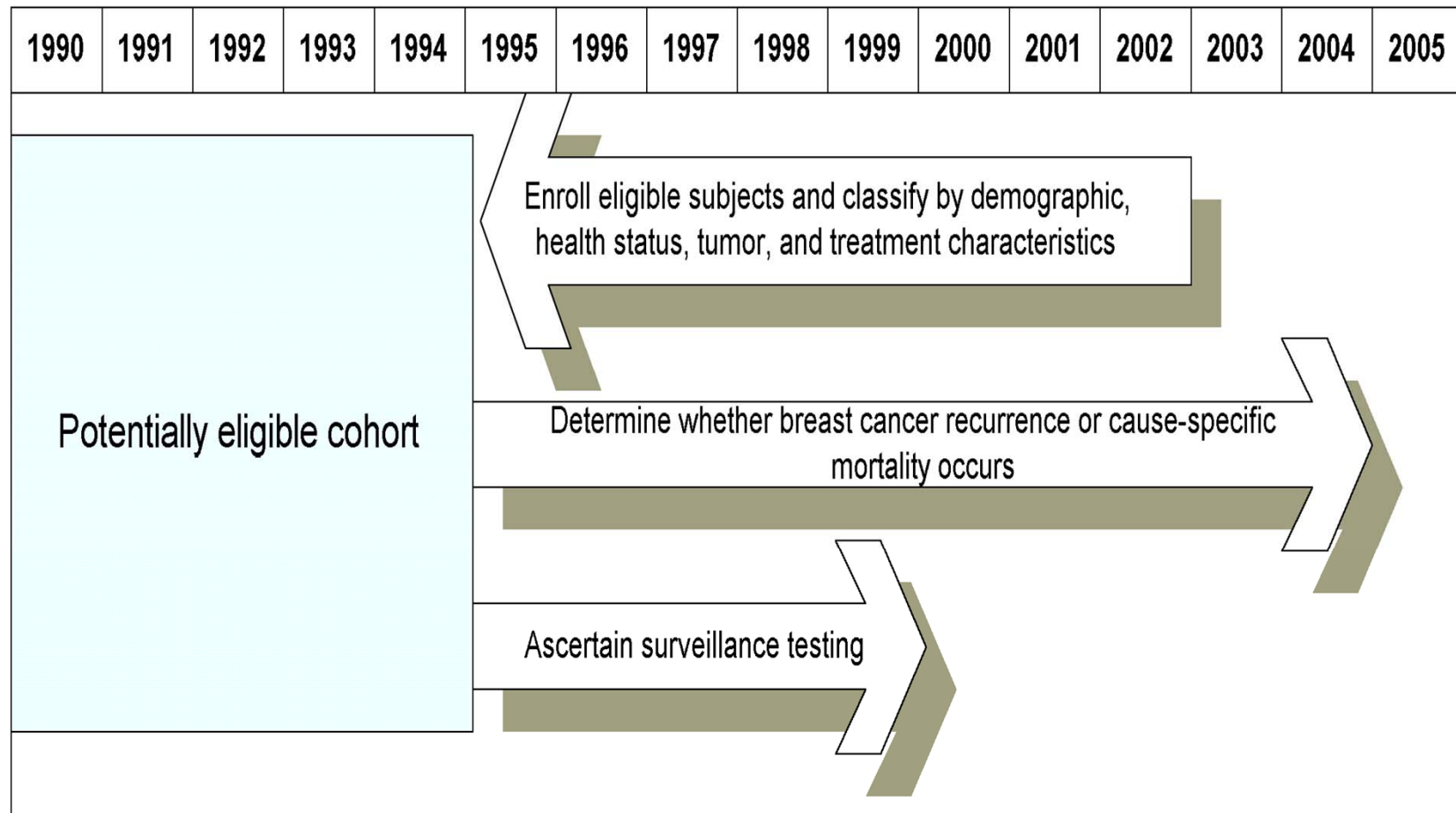
- Older women disproportionately bear the burden of breast cancer incidence and mortality
- Older women are less likely to receive standard care
- Older women are underrepresented in clinical trials
- Observational studies performed in integrated health care delivery systems offer the best opportunity 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





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

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

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

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

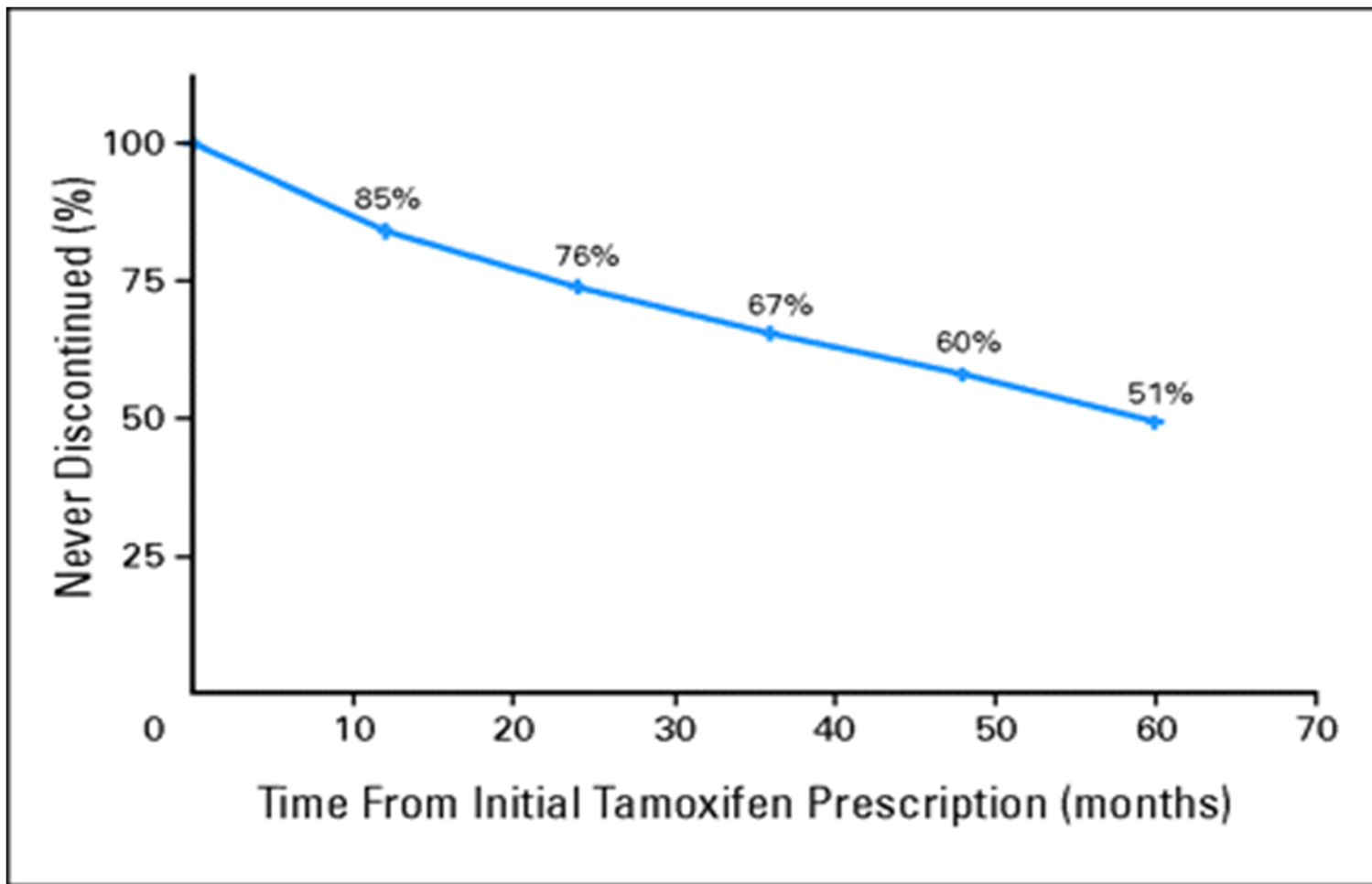
Tamoxifen Adherence and Breast Cancer Mortality in Women with Hormone Responsive Tumors

Tamoxifen Use	Breast Cancer Mortality HR (95% CI)
<1 year	6.26 (3.10 – 12.64)
1-1.9 years	4.12 (1.90 – 8.93)
2-4.9 years	1.31 (0.73 – 2.33)
≥5 years	Ref

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

# of Surveillance Mammograms	Breast Cancer Mortality OR (95% CI)
0	Ref
1	0.67 (0.39 – 1.10)
2	0.52 (0.25 – 1.10)
3	0.36 (0.13 – 0.99)
4 or more	0.12 (0.01 – 1.10)

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

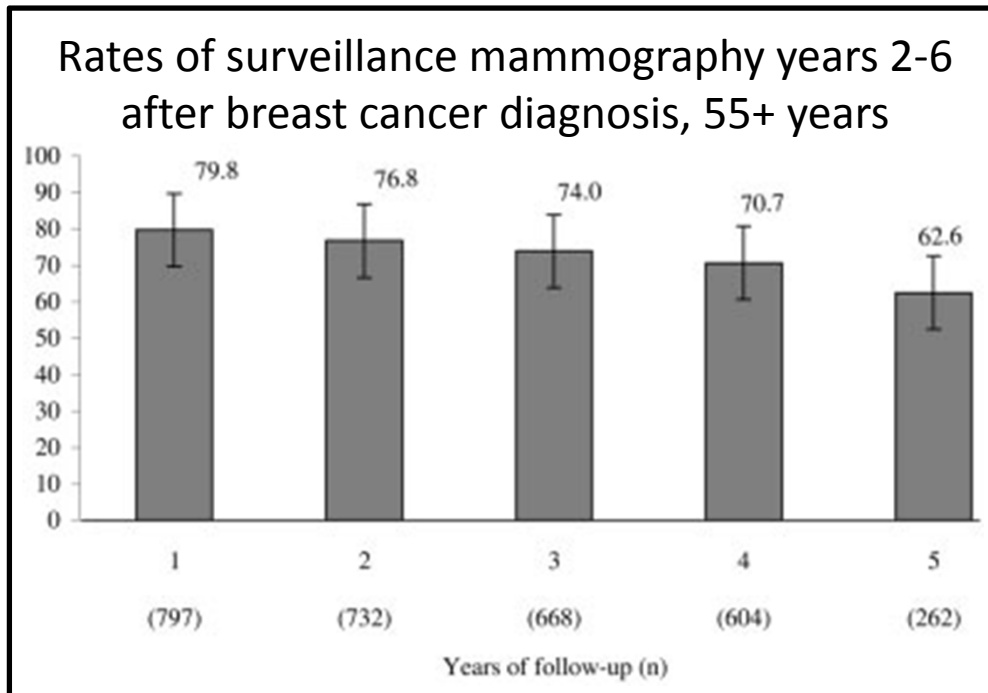
- **Investigator training programs**
 - CRN Scholars Program
 - Research support (pilot funds and PI officer)
 - Workshops, Networking and Mentoring
- **Multiple linked sources of data on the continuum of cancer care on a large and stable populations base**
 - Study multiple outcomes from delivery and 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)**
 - 2007-2009: **CRN pilot project** - “Socioeconomic Diversity in Integrated Healthcare Delivery Systems”
- **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 , $n=797$



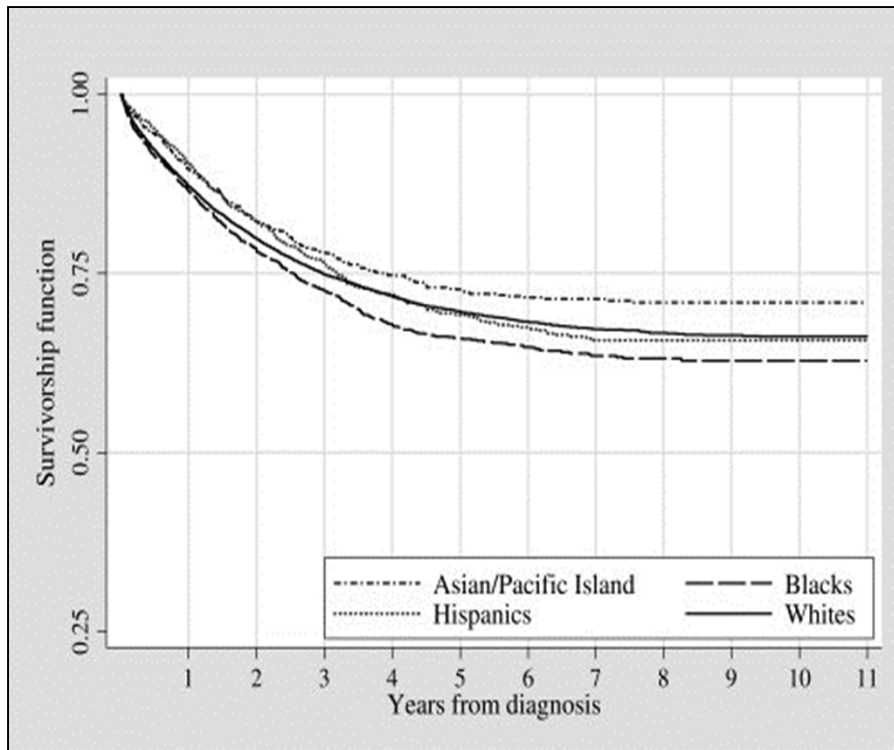
Relationships with receipt of surveillance mammography

	OR (95% CI)
<i>Other MDs</i>	<i>Ref</i>
<i>Visits with PCP</i>	2.21 [1.73-2.82]
<i>Visits with GYN</i>	3.49[2.55-4.79]

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

Racial/Ethnic Disparities for Colorectal Cancer-Specific Deaths in Insured Populations, n=13958

Unadjusted Survival Probability Plot



- Diagnosed 1993-1998
- Followed through 2003

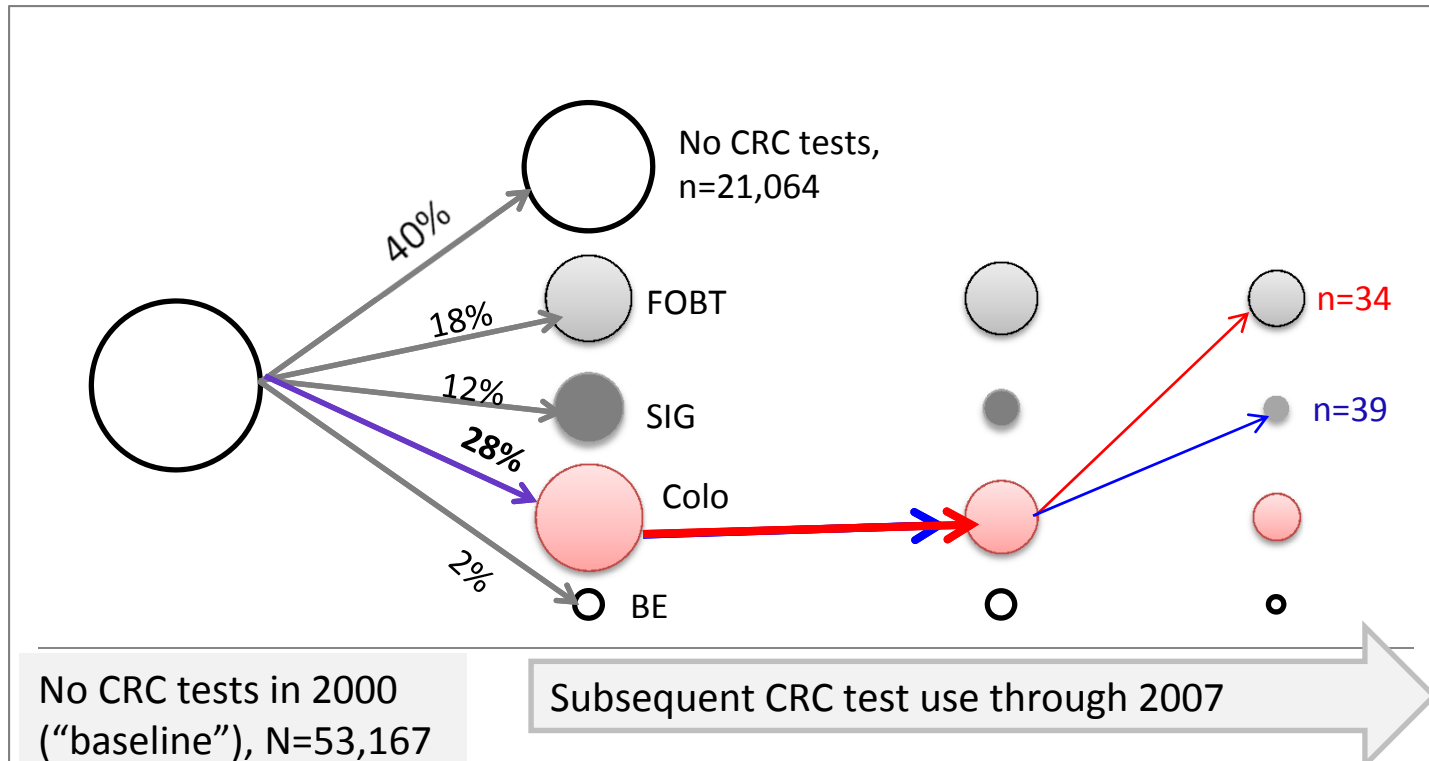
Hazard ratios (95% CI) for non-Hispanic blacks compared to whites

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
 Doubeni et al. Cancer 2007;109:612-20

Sequence of Colorectal Cancer Test Use 2000-2007



- 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



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

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



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

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2009-2010, visiting Scientist NCI, Radiation Epidemiology Branch, Division of Cancer
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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 (GHC) 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

Background: Safety from CT

- 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

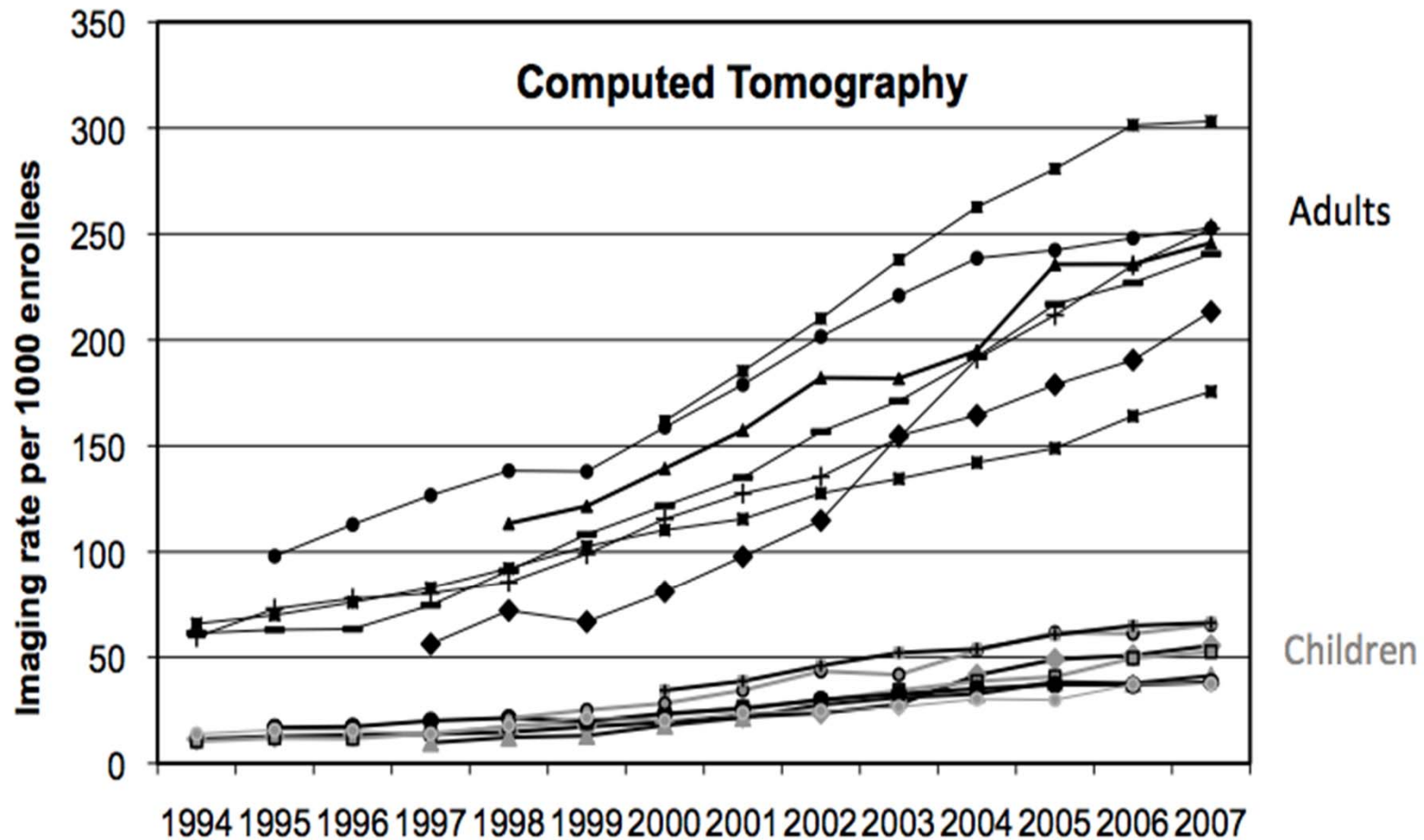
- Cancers from radiation take >5-10 years to develop and radio-sensitive cancers are uncommon
- To study the risks of imaging related radiation need:
 - A large diverse population (millions of patients), including people across all ages
 - Capacity to comprehensively / accurately assess imaging & dose
 - *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

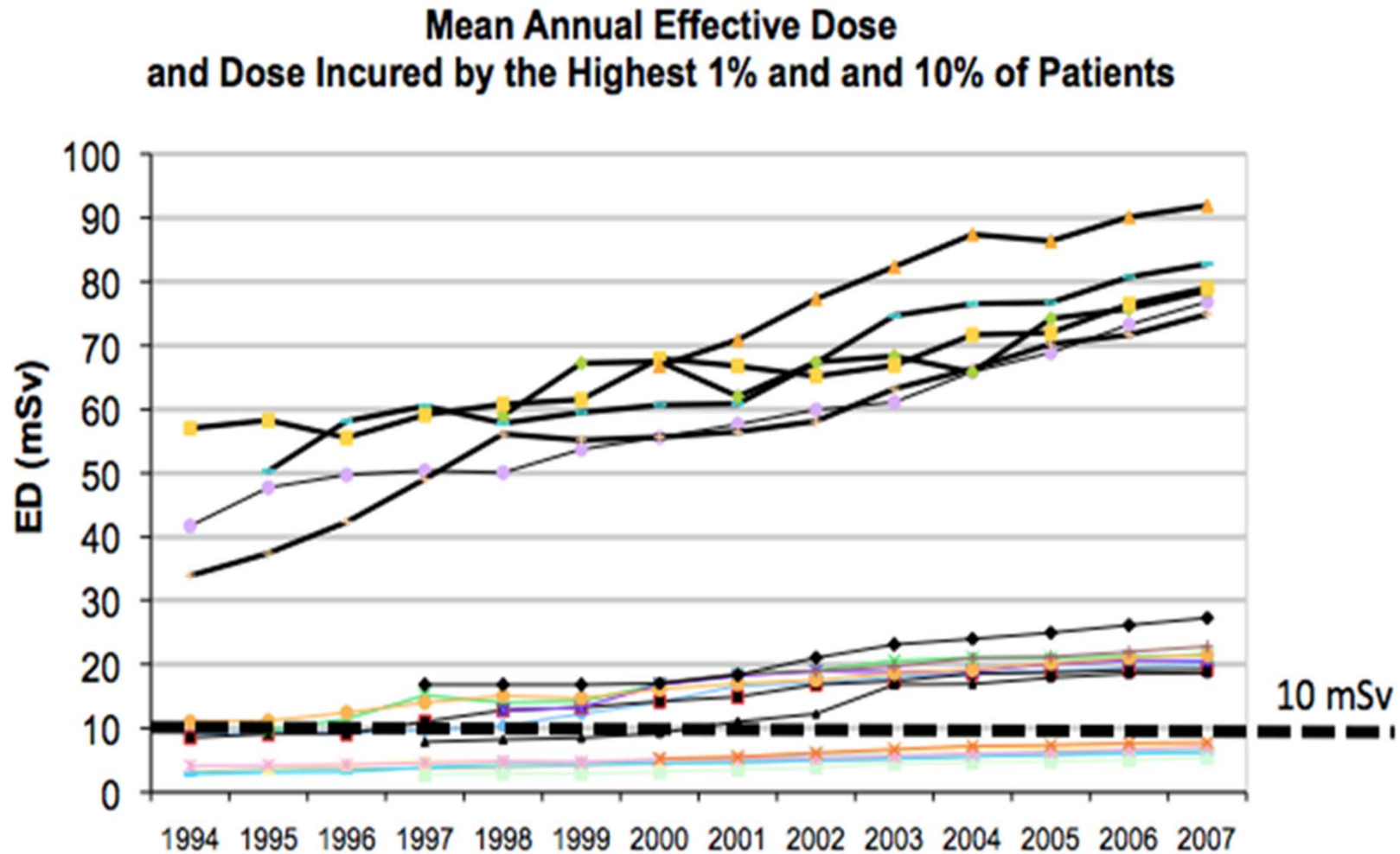
- I approached several CRN sites to conduct pilot study
- CRN sites with necessary data to assess imaging, cancer and outcomes were approached – very supportive/collaborative
- Scientific Aims of the Pilot
 - Patterns and variability of medical imaging over time
 - Patterns of radiation exposure associated 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



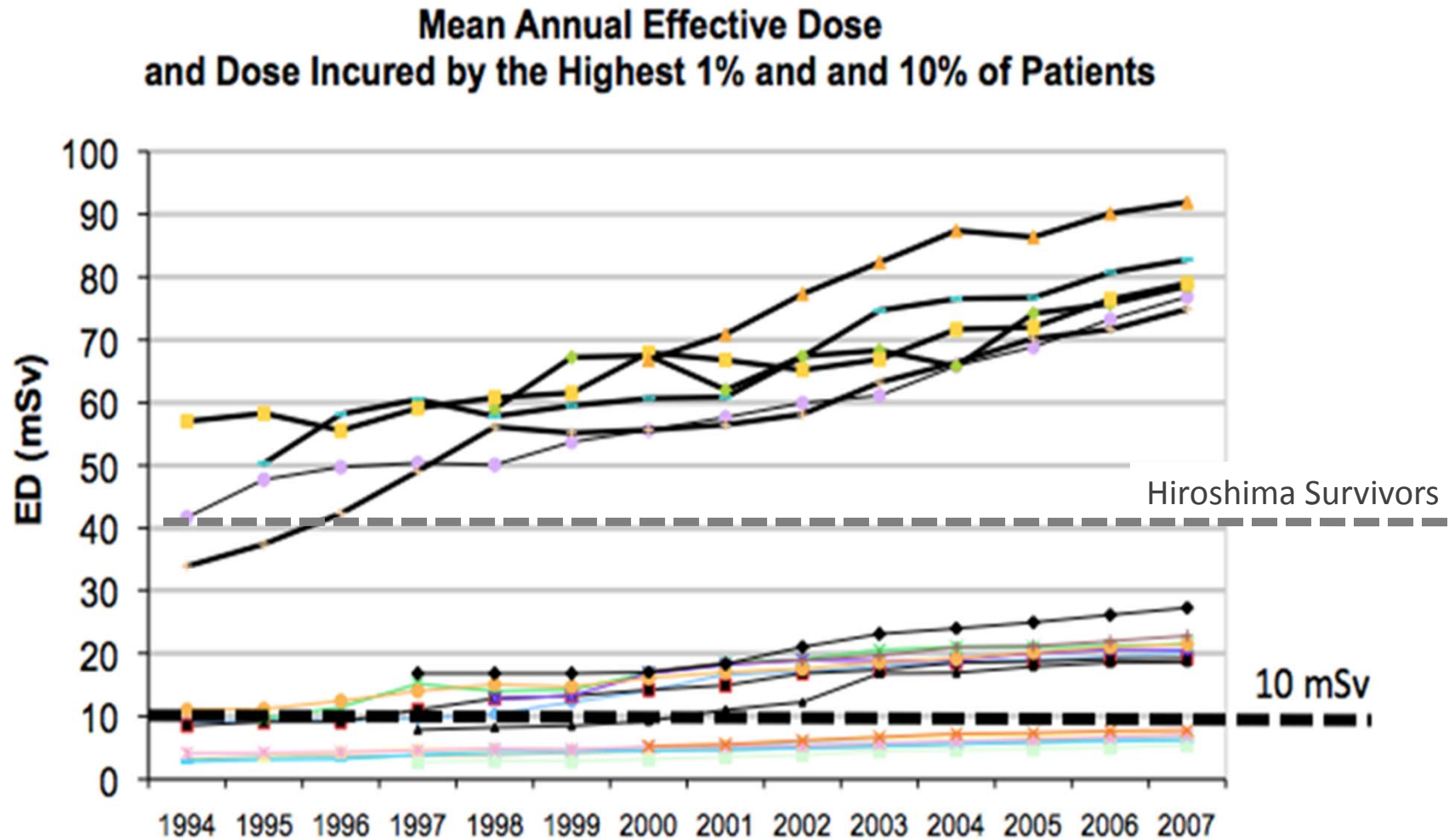
Results based on 2.5 million enrollees per year, including 30 million imaging examinations of all types and over 3 million CTs

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