Addressing the Adverse Consequences of Cancer Treatment

A National Cancer Policy Forum Virtual Workshop
In Collaboration with the Forum on Aging, Disability, and Independence

Ongoing Data Collection Efforts to Fill Evidence Gaps:
Integrated Healthcare System Perspective

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Disclosures – Lawrence H. Kushi

- **No financial conflicts to disclose**
- My research funding comes from the National Institutes of Health, in particular the National Cancer Institute

The views and interpretations of data presented here are my own and do not necessarily represent those of Kaiser Permanente

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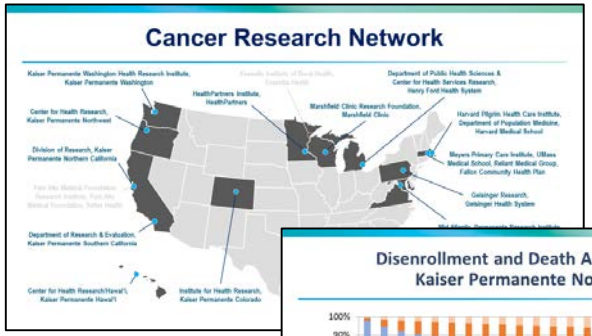
What This Talk Will Cover

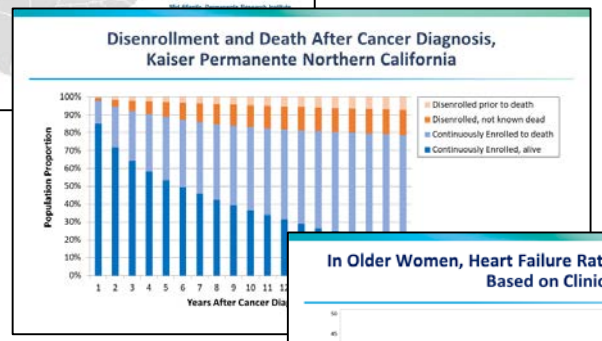
Integrated Healthcare Delivery Systems Overview

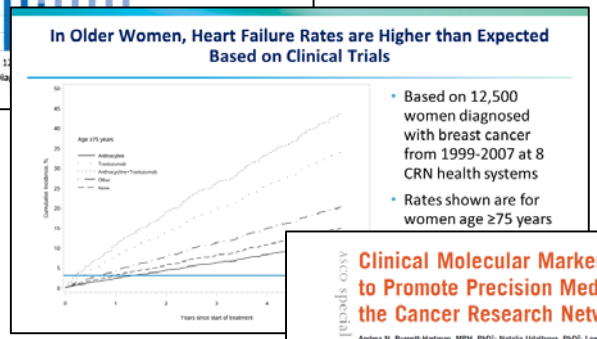
Unique Advantages of Such Settings for Research

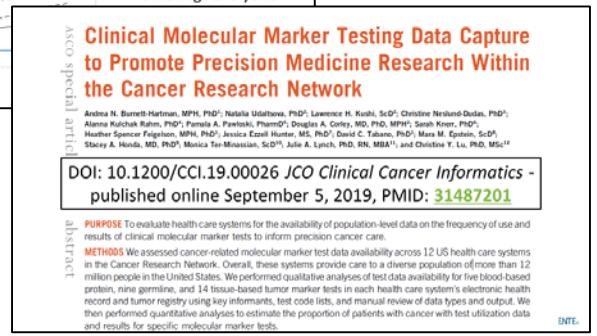
Examples of Research Related to Cancer Treatment Outcomes

Areas for Potential Improvement in Clinical Data









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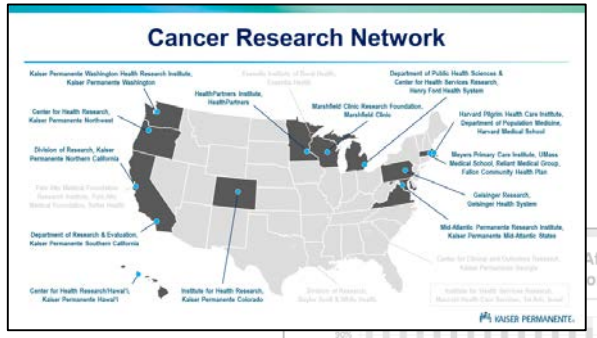

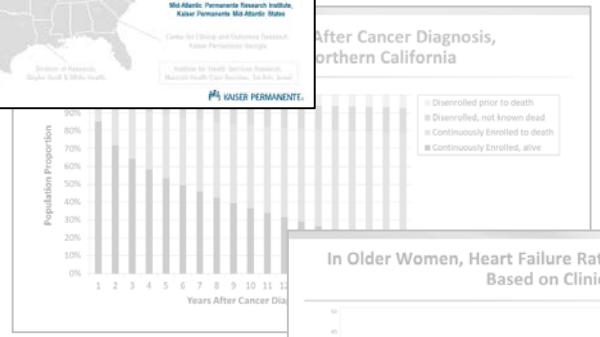

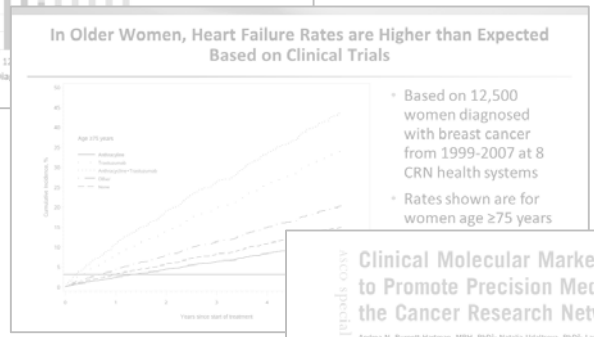

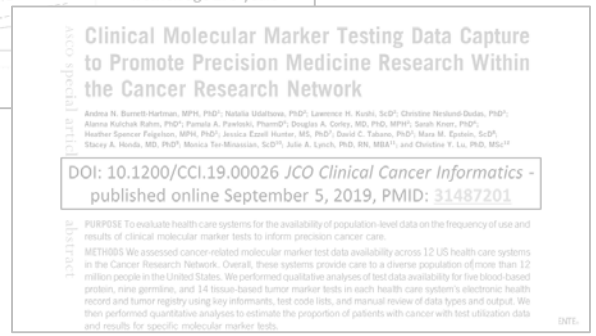

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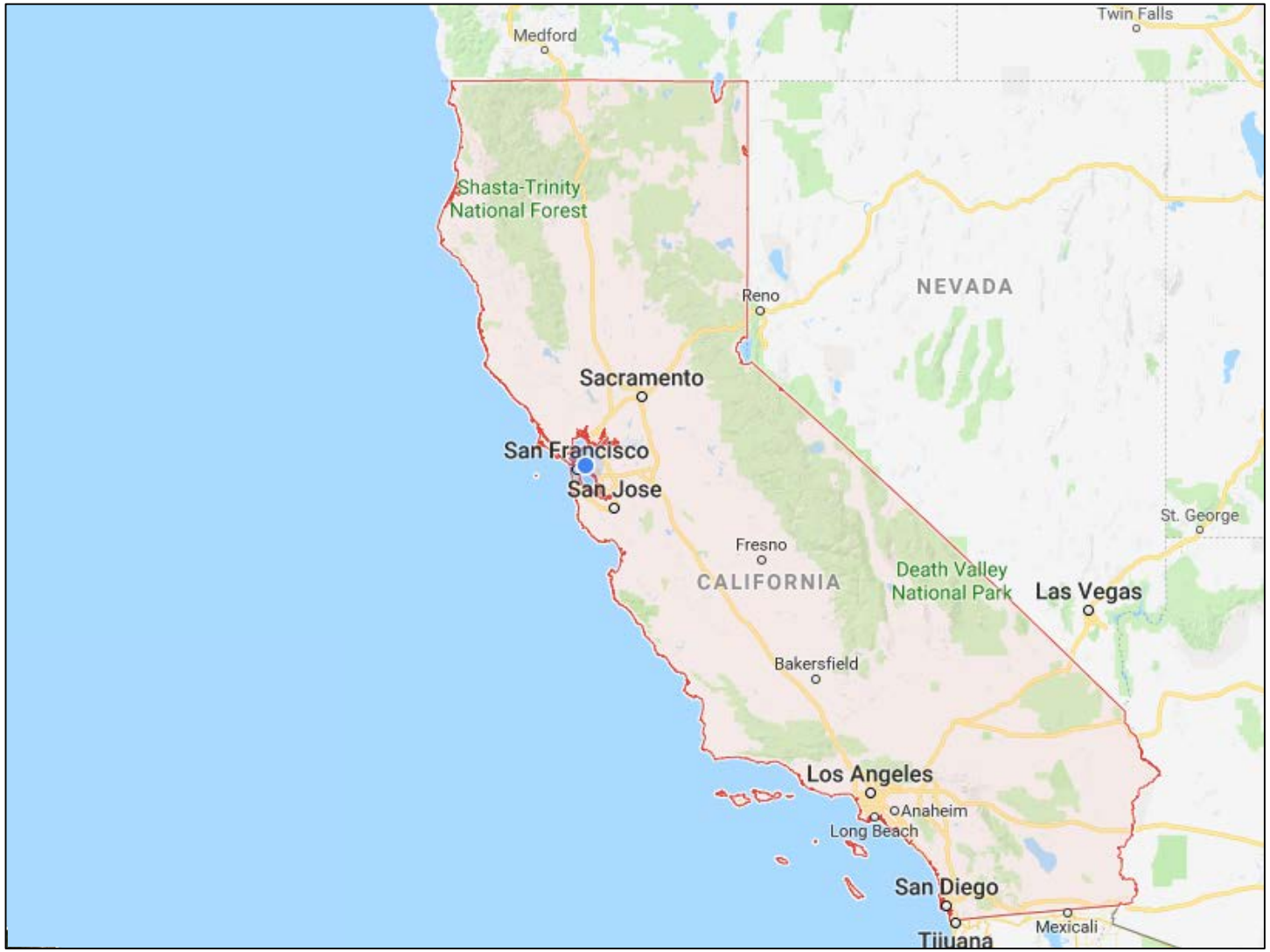

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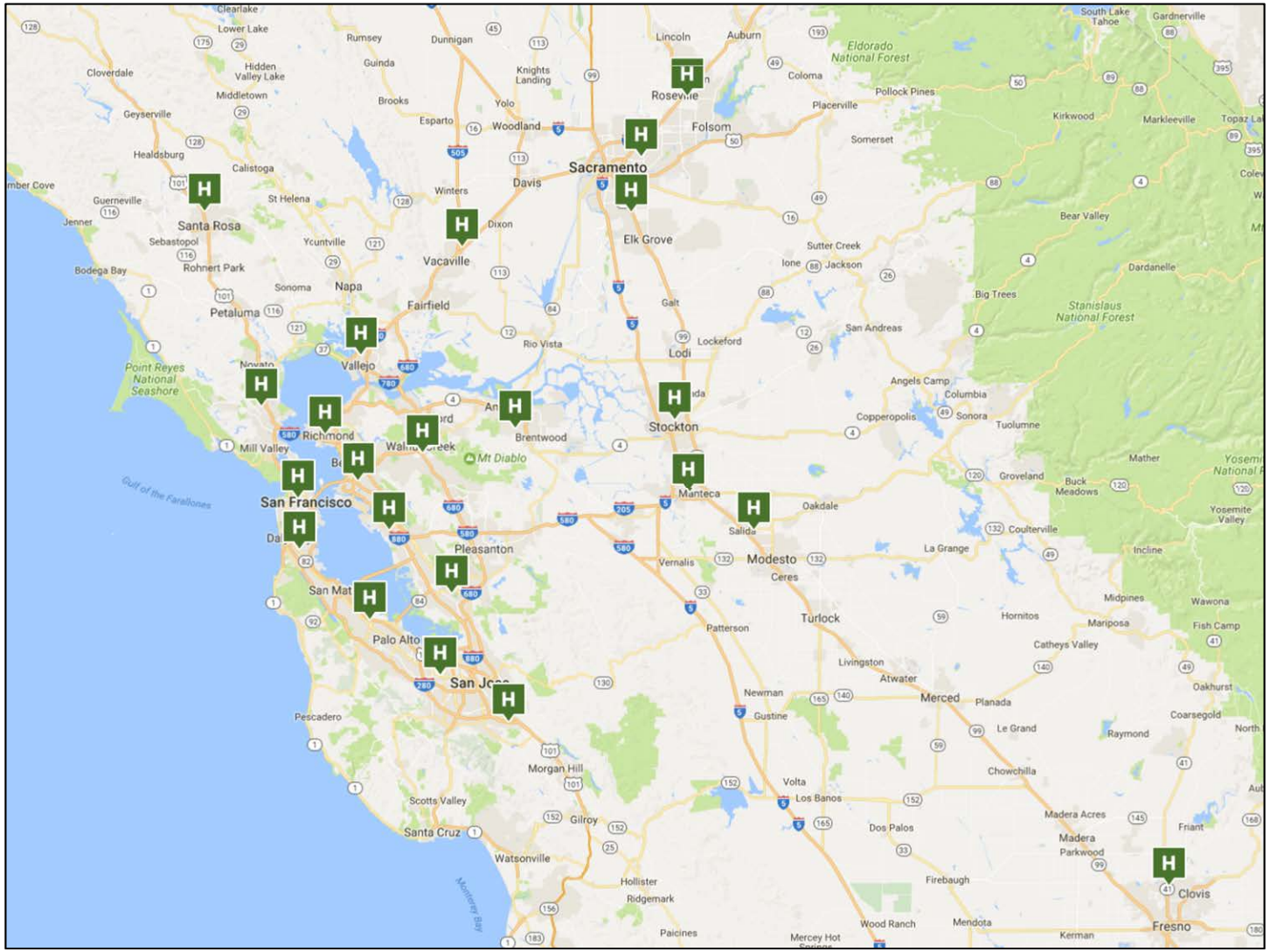

- Integrated healthcare delivery system
- 4.5 million members
- 9,368 physicians (The Permanente Medical Group)
- 21 hospitals *(shown)*
- 257 outpatient clinics
- Connected EHR
- Division of Research (~80% externally funded)

as of ~December 31, 2019

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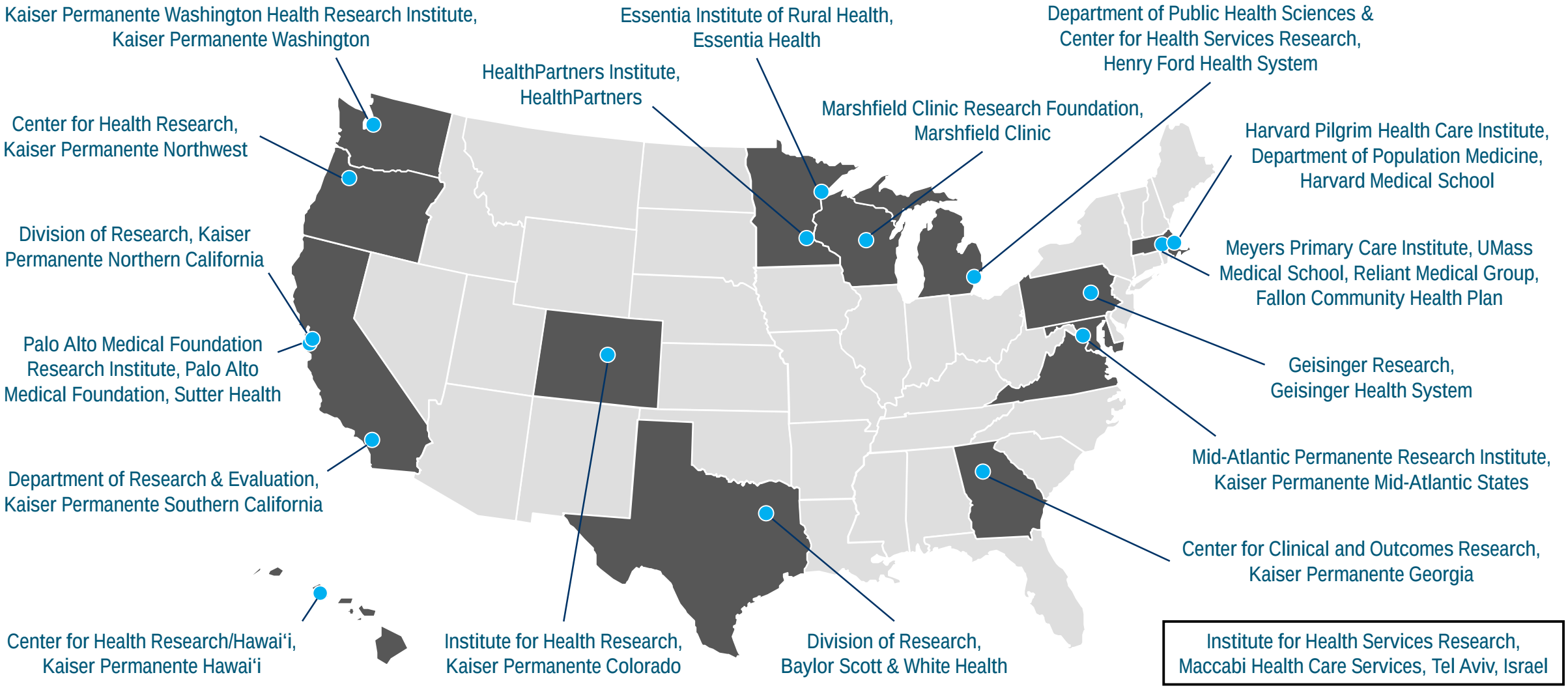
The Health Care Systems Research Network

A Consortium of Research Groups Embedded in Health Systems



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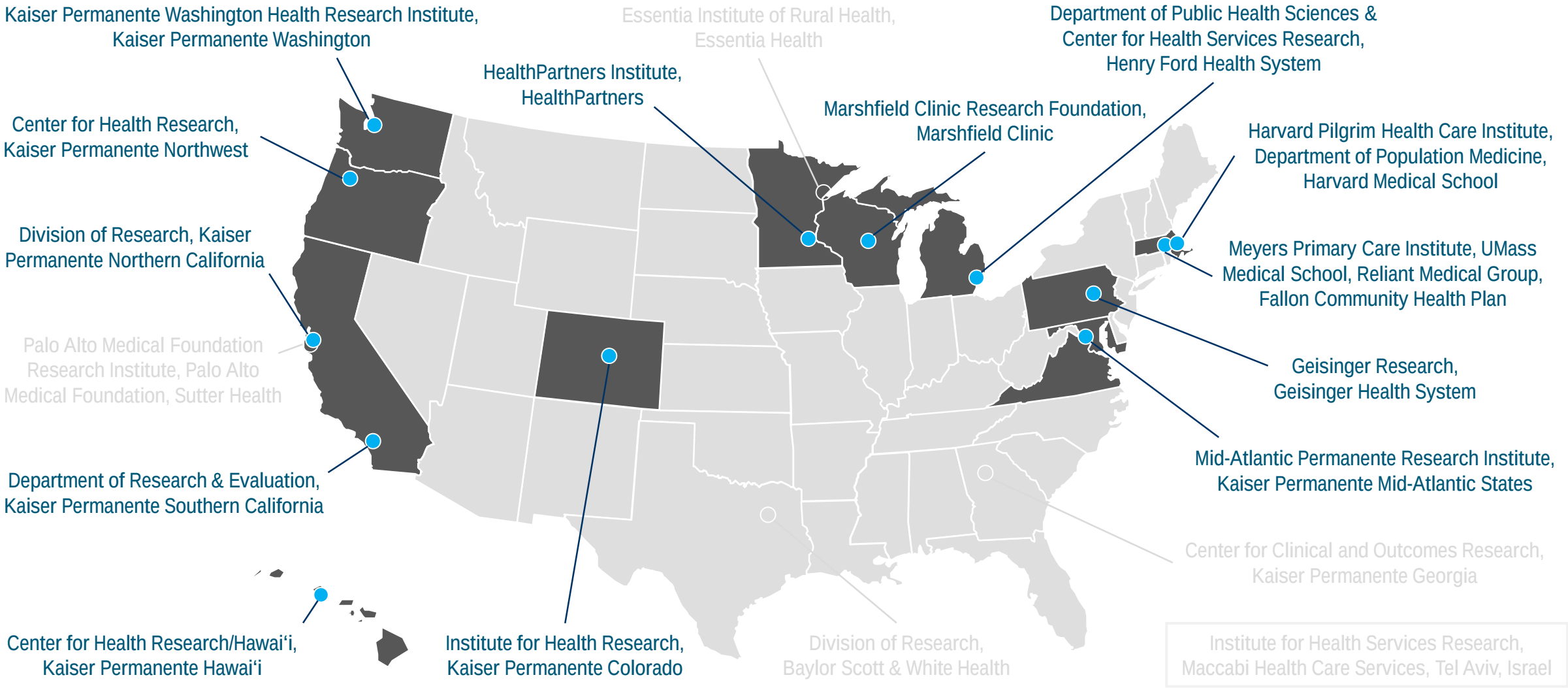
Cancer Research Network



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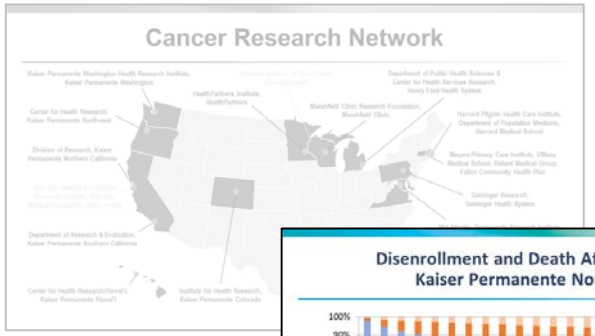

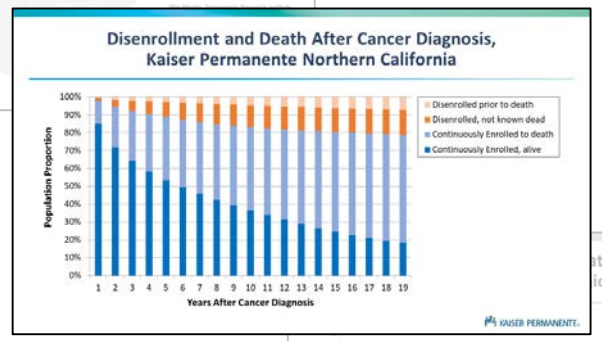

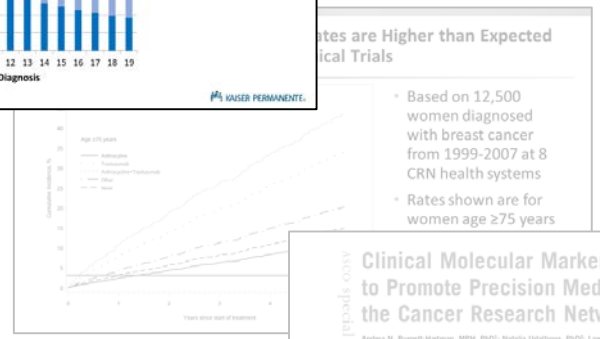

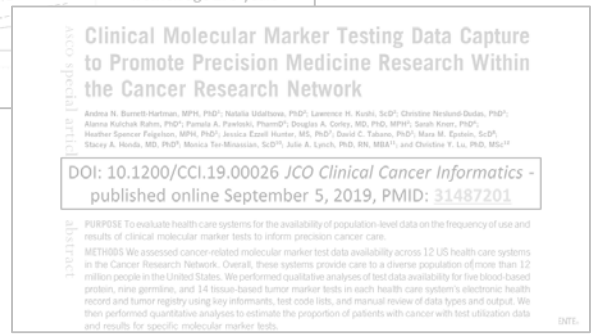

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Settings such as Kaiser Permanente provide distinct advantages for population sciences research

- **Integrated health care systems**: Most medical care is obtained within our systems
- Membership is **largely representative** of community
- **Defined membership populations** with **high retention rates**
- **Longstanding electronic health records** and other clinical or administrative databases (15+ years)
  - Not just claims data, but details of care
  - Data extracted to Virtual Data Warehouse facilitates collaborations
- **Collaborations with providers** enhances translational research and supports a learning health care system

Integrated Healthcare Systems

- **Integrated healthcare systems provide services across the whole spectrum of cancer care**
  - Primary care, preventive services, screening, cancer-related specialty care in diagnosis and treatment, surveillance, palliative care, hospice
  - Not just cancer care but care for other conditions (e.g., cardiology, metabolic diseases)
  - Some systems are largely “closed” – essentially all care provided by the healthcare system
- **Most Academic Health Centers and NCI-designated Cancer Centers do not provide a comprehensive view of clinical care:**
  - Referral or tertiary care centers with oncology specialty care and treatment; some safety net hospital affiliations; some with full-spectrum health services
  - Limited or indirect information on care prior to diagnosis, on cancer screening, or care after active cancer treatment
  - Other specialty care may not treat the same patient population as oncology services

Member Retention AFTER Cancer Diagnosis

(continuous enrollment, allowing for 60-day gap)

CRN Site	Years After Cancer Diagnosis									
	1	2	3	4	5	6	7	8	9	10
Henry Ford	0.95	0.88	0.83	0.79	0.76	0.74	0.71	0.69	0.68	0.67
KPCO	0.97	0.93	0.90	0.87	0.85	0.83	0.82	0.81	0.80	0.79
KPHI	0.97	0.92	0.88	0.86	0.84	0.82	0.81	0.79	0.78	0.77
KPMAS	0.94	0.80	0.73	0.67	0.63	0.60	0.56	0.54	0.51	0.48
KPNC	0.98	0.95	0.92	0.91	0.89	0.87	0.86	0.85	0.84	0.83
KPNW	0.97	0.93	0.89	0.87	0.85	0.83	0.81	0.80	0.79	0.78
KPWA	0.96	0.90	0.87	0.84	0.82	0.80	0.79	0.78	0.78	0.77
Marshfield	0.97	0.92	0.90	0.87	0.86	0.84	0.83	0.82	0.82	0.81

Member Retention AFTER Cancer Diagnosis

(continuous enrollment, allowing for 60-day gap)

CRN Site	Years After Cancer Diagnosis									
	1	2	3	4	5	6	7	8	9	10
Henry Ford	0.95	0.88	0.83	0.79	0.76	0.74	0.71	0.69	0.68	0.67
KPWA	0.96	0.90	0.87	0.84	0.82	0.80	0.79	0.78	0.78	0.77
Marshfield	0.97	0.92	0.90	0.87	0.86	0.84	0.83	0.82	0.82	0.81

	Years After Cancer Diagnosis						
	1	2	3	4	5	…	10
KPNC	0.98	0.95	0.92	0.91	0.89		0.83

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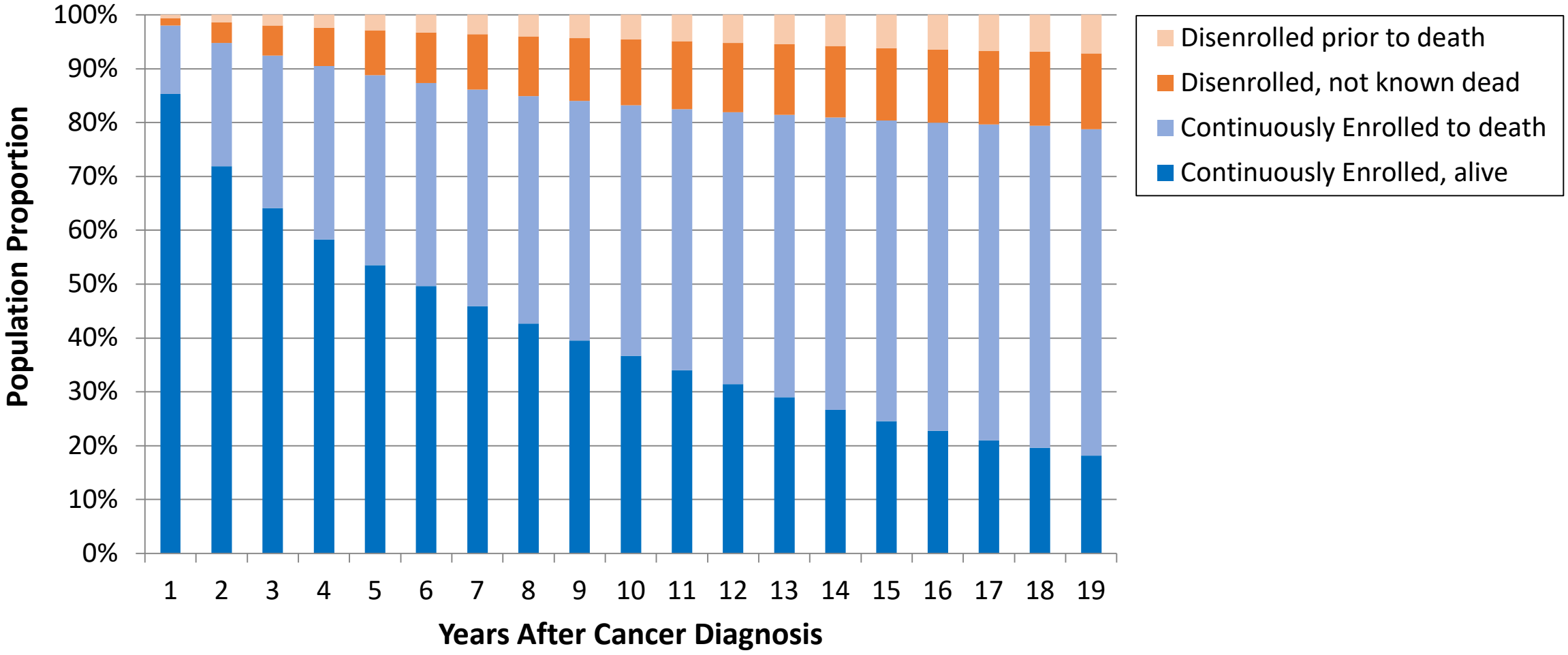
Disenrollment and Death After Cancer Diagnosis, Kaiser Permanente Northern California



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Longstanding electronic health records:
The Virtual Data Warehouse (VDW)

- The VDW is a Common Data Model: agreed upon variable names, definitions, formats, data structures
- VDW is implemented by research groups in most HCSRN health systems
- “Virtual” = data are maintained at each HSCRN Site; “Distributed” or “Federated” may be equally appropriate descriptions
- Source data (EHRs, other clinical and administrative databases) may differ from site to site and over time
- VDW data maintained as SAS datasets and Oracle databases
- Data updated on a regular (e.g., daily or monthly) basis

Data Domains in the KPNC VDW, May 19, 2020 – 1

Governance	Data Table/Domain	Number of Observations	Total Variables	VDW Common Variables	DOR-specific Variables
HCSRN	Demographics	16,811,967	29	13	16
HCSRN	Enrollment	67,832,620	32	32	0
HCSRN	Utilization	738,870,500	48	20	28
HCSRN	Diagnoses	1,876,500,667	33	12	21
HCSRN	Procedures	1,395,578,598	41	16	25
HCSRN	Provider Specialty	1,243,715	34	14	20
HCSRN	Facility	620,467	16	11	5
HCSRN	Death	1,672,567	8	5	3
HCSRN	Cause of Death	5,642,300	12	6	6
HCSRN	Tumor Registry	563,733	345	133	212
HCSRN	Laboratory Results	1,310,742,937	39	32	7
HCSRN	Census Location	34,780,900	25	11	14
HCSRN	Census Demographics	775,567	142	108	34
HCSRN	Pharmacy, Outpatient	603,618,075	30	6	24
HCSRN	Ever NDC (drug codes)	84,094	64	18	46
HCSRN	Vital Signs	732,991,700	41	20	21
HCSRN	Social History	106,528,267	55	48	7
HCSRN	Language	9,871,400	4	4	0

Data Domains in the KPNC VDW, May 19, 2020 – 1

Governance	Data Table/Domain	Number of Observations	Total Variables	VDW Common Variables	DOR-specific Variables
HCSRN	Demographics	16,811,967	29	13	16
HCSRN	Enrollment				0
HCSRN	Utilization				28
HCSRN	Diagnoses				21
HCSRN	Procedures				25
HCSRN	Provider Specialty				20
HCSRN	Facility				5
HCSRN	Death				3
HCSRN	Cause of Death				6
HCSRN	Tumor Registry				12
HCSRN	Laboratory Results				7
HCSRN	Census Location				14
HCSRN	Census Demographics				34
HCSRN	Pharmacy, Outpatient				24
HCSRN	Ever NDC (drug codes)				46
HCSRN	Vital Signs				21
HCSRN	Social History	106,528,267	55	48	7
HCSRN	Language	9,871,400	4	4	0

Adverse outcomes related to cancer treatment may be documented in:

- Diagnoses
- Procedures
- Death and Cause of Death
- Tumor Registry
- Laboratory Results
- Pharmacy
- Patient-reported Outcomes

Data Domains in the KPNC VDW, May 19, 2020 – 2

Governance	Data Table/Domain	Number of Observations	Total Variables	VDW Common Variables	DOR-specific Variables
CESR	Personal Health Record (PHR) Registration	5,843,567	6	6	0
CESR	PHR Proxy	1,822,933	5	5	0
CESR	PHR Messages	366,823,700	10	10	0
CESR	PHR Tests	299,079,300	5	5	0
CESR	PHR Activity	5,237,155,123	5	5	0
CESR	Medication Orders	572,560,049	49	46	3
CESR	Medication Orders Diagnoses	545,738,533	5	5	0
CESR	Medication Lookup	151,091	14	14	0
CESR	Infusion Medications, Administered	12,923,300	54	37	17
CESR	Infusion Medications, Dispensed	17,171,400	70	40	30
CESR	Infusion Medications, Planned	6,401,033	59	42	17
CESR	Pharmacy, Inhouse	431,840,267	21	21	0
CESR	Problem List	63,935,100	17	15	2
CESR	Pregnancy Outcomes	1,349,567	42	42	0
CESR	Pregnancy Outcomes Voided Data	8,041	5	5	0
CESR	Pregnancy Mom Baby Link	1,230,767	6	6	0

Data Domains in the KPNC VDW, May 19, 2020 – 2

Governance	Data Table/Domain	Number of Observations	Total Variables	VDW Common Variables	DOR-specific Variables
CESR	Personal Health Record (PHR) Registration	5,843,567	6	6	0
CESR	PHR Proxy	1,822,933	5	5	0
CESR	PHR Messages	366,823,700	10	10	0
CESR	PHR Tests				0
CESR	PHR Activity				0
CESR	Medication Orders				3
CESR	Medication Orders Diagnoses				0
CESR	Medication Lookup				0
CESR	Infusion Medications, Administ				17
CESR	Infusion Medications, Dispense				30
CESR	Infusion Medications, Planned				17
CESR	Pharmacy, Inhouse	431,840,267	21	21	0
CESR	Problem List	63,935,100	17	15	2
CESR	Pregnancy Outcomes	1,349,567	42	42	0
CESR	Pregnancy Outcomes Voided Data	8,041	5	5	0
CESR	Pregnancy Mom Baby Link	1,230,767	6	6	0

Cancer treatments may be documented in:

- Procedures (e.g., surgery, radiation therapy)
- Tumor Registry (SEER / NAACCR level)
- Pharmacy (oral medications)
- Infusion Medications (e.g., chemotherapy)

Data Domains in the KPNC VDW, May 19, 2020 – 3

Governance	Data Table/Domain	Number of Observations	Total Variables	VDW Common Variables	DOR-specific Variables
CESR	Patient Reported Outcomes, Types	42	7	7	0
CESR	Patient Reported Outcomes, Surveys	601	9	9	0
CESR	Patient Reported Outcomes, Survey Responses	157,989,767	11	11	0
CESR	GEMS Patient Geographic Descriptors	23,879,467	19	19	0
CESR	Referrals	5,998,633	21	21	0
CESR	Referral Diagnoses	6,439,467	6	6	0
CESR	Referral Procedures	6,109,200	6	6	0
CESR	Spirometry	170,000	50	49	1
CESR	Molecular Marker Results	619,367	12	12	0
CESR	Molecular Marker Order Results	27,973	26	26	0
CESR	Molecular Marker Variant Results	12,833	12	12	0
CESR	Benefits Members	63,834,846	23	23	0
CESR	Benefits Tiers	13,191	8	3	5
CESR	Benefits Choice	7,233,845	15	10	5
CESR	Benefits Choice RX	38,347,901	21	16	5
CESR	Bone Mineral Density (BMD) Scan Results	631,395	31	19	12
CESR	BMD Frax Score	192,005	23	20	3

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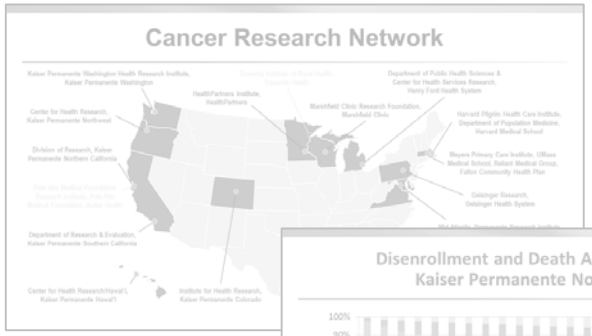

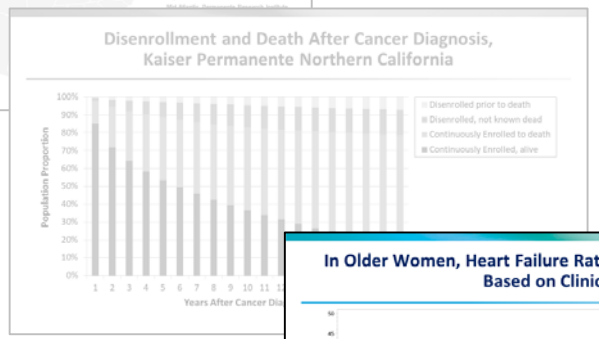

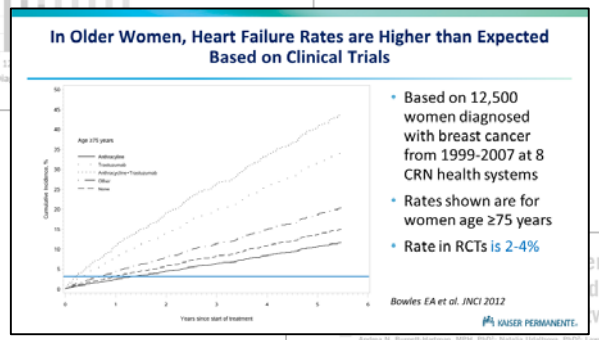

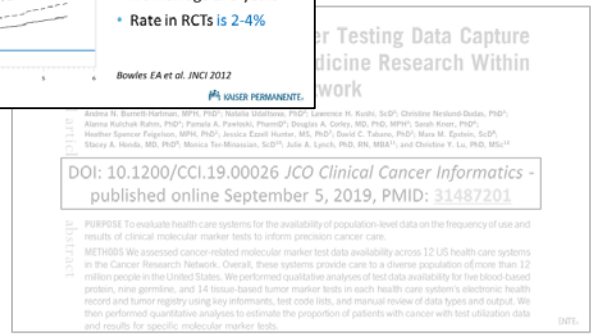

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Example of data-based research projects conducted in the Integrated Healthcare System setting

- **Comparison of "real world" to "clinical trials" experience:**
  - Clinical trials participants highly selected, tend to be relatively healthy, free of comorbidities, younger than the general patient population
  - Aiello Bowles, et al., heart failure after use of cardiotoxic therapies in breast cancer
- **Use of detailed chemotherapy data:**
  - Does obesity affect chemotherapy dosing, and might that contribute to poorer outcomes?
  - Bandera, et al., BMI, relative dose intensity, and survival in ovarian cancer

DOI:10.1093/jnci/djs317

ARTICLE

J Natl Cancer Inst 2012;104:1293-1305.

Risk of Heart Failure in Breast Cancer Patients After Anthracycline and Trastuzumab Treatment: A Retrospective Cohort Study

Erin J. Aiello Bowles, Robert Wellman, Heather Spencer Feigelson, Adedayo A. Onitilo, Andrew N. Freedman, Thomas Delate, Larry A. Allen, Larissa Nekhlyudov, Katrina A. B. Goddard, Robert L. Davis, Laurel A. Habel, Marianne Ulcickas Yood, Catherine McCarty, David J. Magid, Edward H. Wagner; for the Pharmacovigilance Study Team

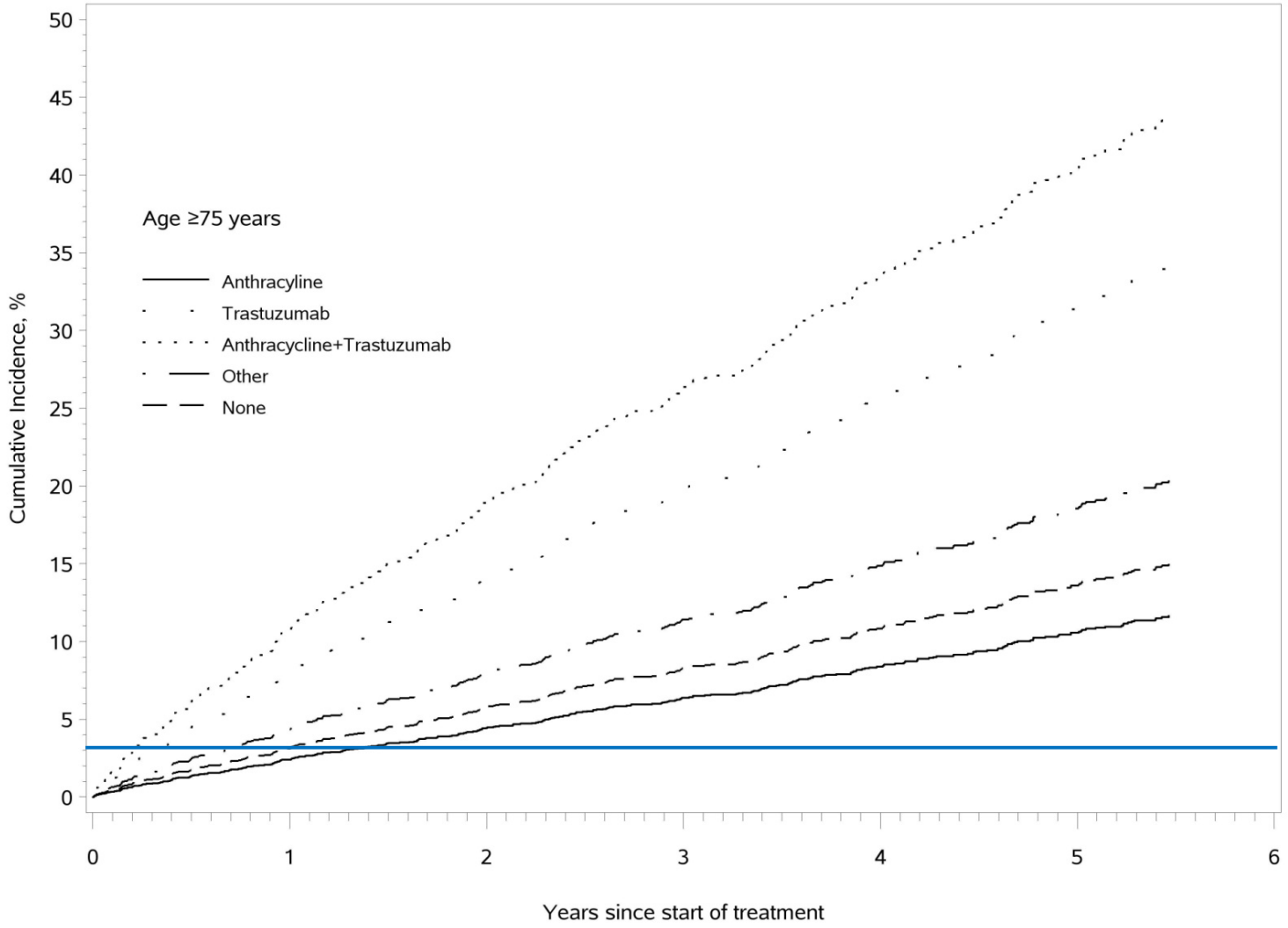
Manuscript received January 05, 2012; revised June 13, 2012; accepted June 18, 2012.

Correspondence to: Erin J. Aiello Bowles, MPH, Group Health Research Institute, 1730 Minor Ave, Ste 1600, Seattle, WA 98101 (e-mail: bowles.e@ghc.org).

Background Clinical trials demonstrated that women treated for breast cancer with anthracycline or trastuzumab are at increased risk for heart failure and/or cardiomyopathy (HF/CM), but the generalizability of these findings is unknown. We estimated real-world adjuvant anthracycline and trastuzumab use and their associations with incident HF/CM.

Methods We conducted a population-based, retrospective cohort study of 12 500 women diagnosed with incident, invasive breast cancer from January 1, 1999 through December 31, 2007, at eight integrated Cancer Research Network health

In older women, heart failure rates are higher than expected based on clinical trial findings



- Based on 12,500 women diagnosed with breast cancer from 1999-2007 at 8 CRN health systems
- Rates shown are for women age ≥75 years
- Rate in RCTs is 2-4%

Bowles EA et al. JNCI 2012

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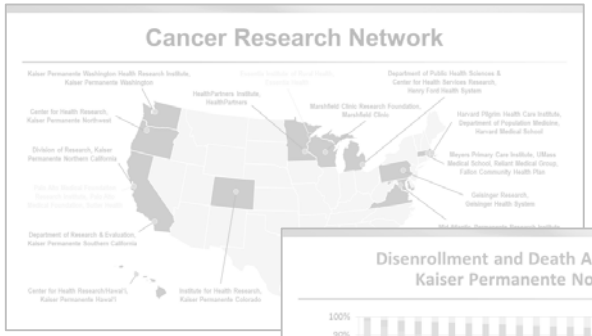

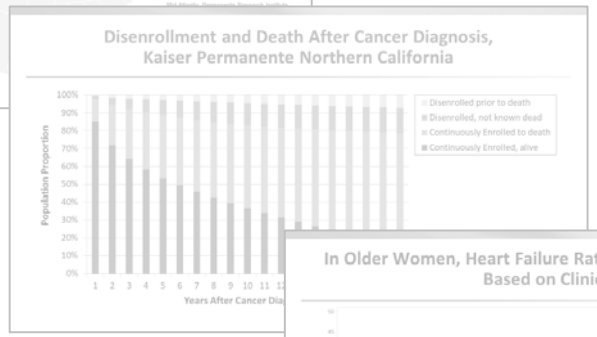

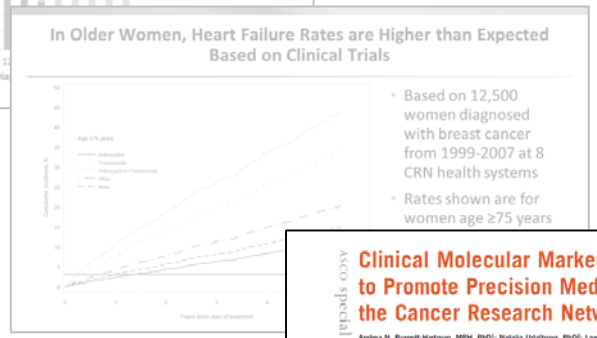

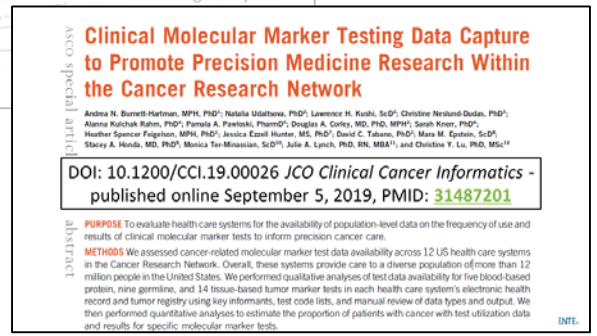
Clinical Molecular Marker Testing Data Capture to Promote Precision Medicine Research Within the Cancer Research Network

DOI: 10.1200/CCI.19.00026 *JCO Clinical Cancer Informatics* - published online September 5, 2019, PMID: 31487201

PURPOSE To evaluate health care systems for the availability of population-level data on the frequency of use and results of clinical molecular marker tests to inform precision cancer care.

METHODS We assessed cancer-related molecular marker test data availability across 12 US health care systems in the Cancer Research Network. Overall, these systems provide care to a diverse population of more than 12 million people in the United States. We performed qualitative analyses of test data availability for five blood-based protein, nine germline, and 14 tissue-based tumor marker tests in each health care system's electronic health record and tumor registry using key informants, test code lists, and manual review of data types and output. We then performed quantitative analyses to estimate the proportion of patients with cancer with test utilization data and results for specific molecular marker tests.

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There are substantial gaps in clinical data systems for addressing cancer treatments and adverse outcomes

Data domains with inadequate documentation or limitations (timeliness) include:

- **Cancer diagnosis:** routinely available in cancer registries, but information such as stage are not otherwise well documented, and thus not available in real time
- **Molecular markers:** in this rapidly evolving area, structured information on whether tests were performed, and test results, are often not available
- **Performance status:** routinely available in clinical trial setting but not clinical care
- **Radiation therapy:** detailed treatment data are available in manufacturer databases that are not linked to EHRs
- **Recurrence or Progression:** not routinely documented in structured data fields
- **Death and Cause of Death:** available from vital statistics sources, but not captured in a complete or timely manner in EHRs
- **Patient-reported Exposures and Outcomes:** For domains collected, often not systematically captured; milder symptoms may not be documented

Some Additional Thoughts re: Healthcare Systems Data

- Effective use electronic health data can continuously generate knowledge to improve health
- Such data are becoming – indeed are – widely available
- Data are relatively easy to obtain and use, but difficult to use well: easy to get an answer that is wrong with potential for harm
- Substantial limitations of clinical data:
  - NOT collected for research or analytic purposes, but for clinical or administrative purposes (e.g., billing, insurance coverage)
  - People with data available are often systematically different from people without data
  - Confounding by Indication: data are present because they have a reason for encountering the health system

Summary

Despite limitations and cautions on use and interpretation, EHR and other clinical and administrative health care data, especially in Integrated Healthcare System settings, provide a rich and outstanding opportunity to advance knowledge and improve care in cancer

Thank You

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