

Priorities and Opportunities for Collaboration and Data Sharing to Promote Health Equity: Cancer Centers



**National Academies of Medicine
National Cancer Policy Forum
October 28-29, 2019**

Ken Smith, PhD, presenting for

Cornelia Ulrich, MS, PhD

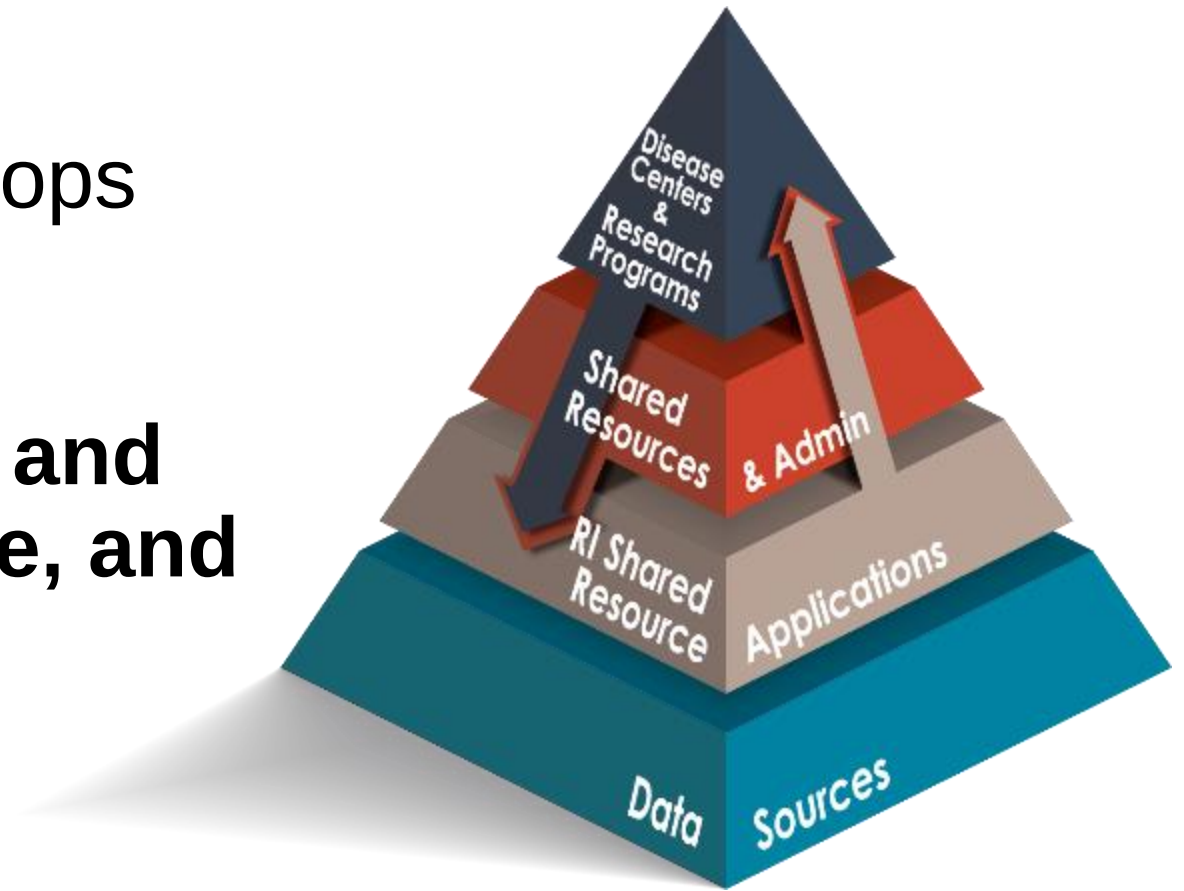
Executive Director, Comprehensive Cancer Center at Huntsman Cancer Institute
Jon M. and Karen Huntsman Presidential Professor in Cancer Research

A Uniquely Capable Shared Resource – Research Informatics



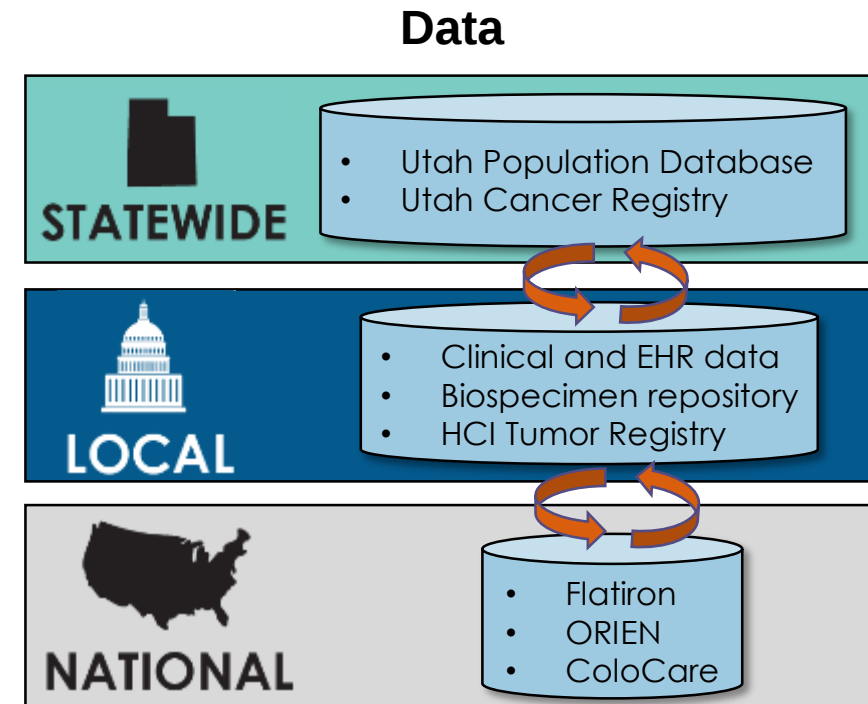
Research Informatics Shared Resource

Research Informatics develops **comprehensive software solutions** enabling Cancer Center members to **collect and mine data from local, state, and national sources.**



Partnering Statewide and Nationally in a Unique Shared Data Environment

- **Annotate disease populations** with clinical and research attributes
- **Access specimens** in patients with specific genotypic & phenotypic characteristics
- Link to **statewide tumor registry data** as well as detailed **national phenotypic** (Flatiron, ORIEN) and **genotypic** (ORIEN) datasets
- Link to **statewide pedigree, medical, health department, & census data** (UPDB)
- Query and extract **integrated datasets**



Novel Strategies for Identifying and Managing Individuals with Hereditary Cancer through the Electronic Health Record



Kaphingst
(CCPS)



Kohlmann
(CCPS)



Buys
(CCPS)



Del Fiol
(CCPS)



Kawamoto
(CCPS)



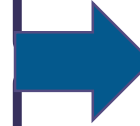
Goldgar
(CCPS)

Cancer Risk Assessment
Genetics in Med 2017

Sequence Variant Evaluation
R01CA121245, R01CA164944
Genetics in Med 2018, 2019

Communication of Genetic Risk
Patient Ed Counseling 2018
Clinical Genetics 2016

Development of Clinical Decision Support Tool
Coupling of electronic health records (EHR)
with advanced clinical decision support
U24CA204800



Targeting Genetic Services for Individuals at Familial Cancer Risk

- Randomized controlled trial comparing models for delivering genetic counseling and testing
- Automation through the Electronic Health Record

U01CA232826

IMPACT:
Effective translation of genetic discoveries to the population

I CHECKED WITH I.T. AND THEY
CONFIRMED THERE'S NO "NEGOTIATE"
BUTTON, JUST "AGREE" AND "DON'T AGREE"



LAWYERS VS. SOFTWARE UPDATES



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\$11M individuals: Utah Population Database (UPDB)



What is the Utah Population Database ?



- Linked data for the entire population (11M individuals) to conduct medical research and improve quality of care
- Medical, public health, and demographic data spanning decades
- Represents the diversity of the state
- Electronic and legal privacy protections
- Access to government, university, and private-sector* researchers

* When joined with a university team

Executive Order of the Governor of Utah (1982)

- UPDB Mandate:
- “Data resource for the collection, storage, study, and dissemination of medical and related information for

“The Purpose of Reducing Morbidity or Mortality, or for the Purpose of Evaluating and Improving the Quality of Hospital and Medical Care.”



*Rural (Kaysville) Utah 1869
(20 miles north of Salt Lake City)*

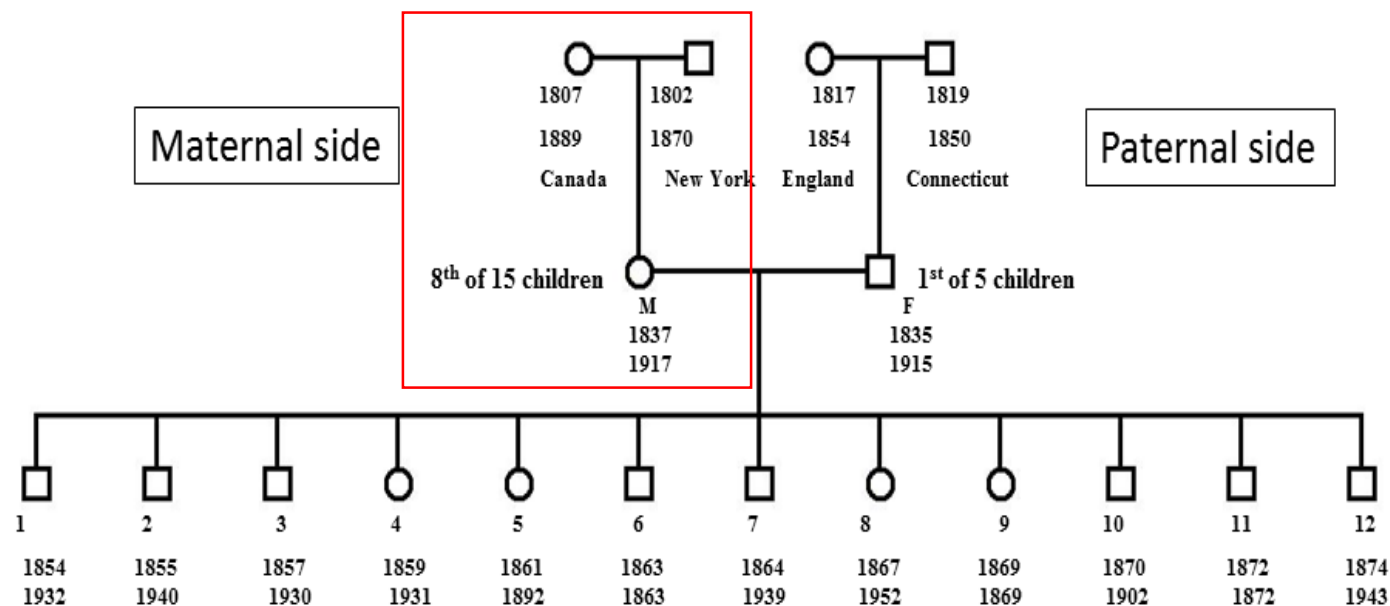
“Typical” Utah Family, Circa 1900

Common Family Structure in Utah for this Era



Shows a Father (F), Mother (M) and children by birth order
Married 1853, 12 children, 3 infant deaths

Utah Family in UPDB



Spans 11 generations from 1807 to 2015

Couple (in picture): 7,565 descendants (6,793 living; 92% BC)

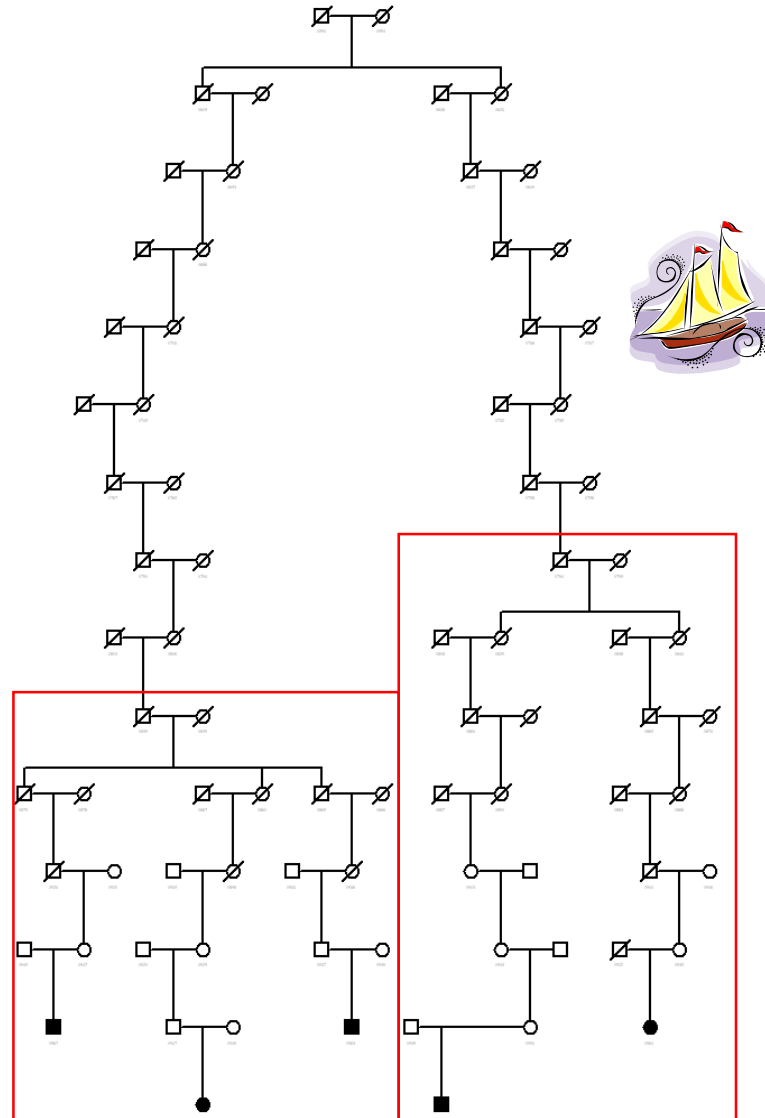
Paternal side: 11,944 descendants (10,617 living; 83% BC)

15% have genealogies from original set

Maternal side: 33,607 descendants (29,936 living; 89% BC)

17% have genealogies from original set

American Founder for Colon Cancer (AFAP APCdelAT(426-427))



1615, St. Nicholas, Somerset, England:
founders married

1624 -1640 Family emigrated to
Weymouth, Norfolk, Massachusetts

Neklason DW et al, Clin Gastro
& Hep 2008

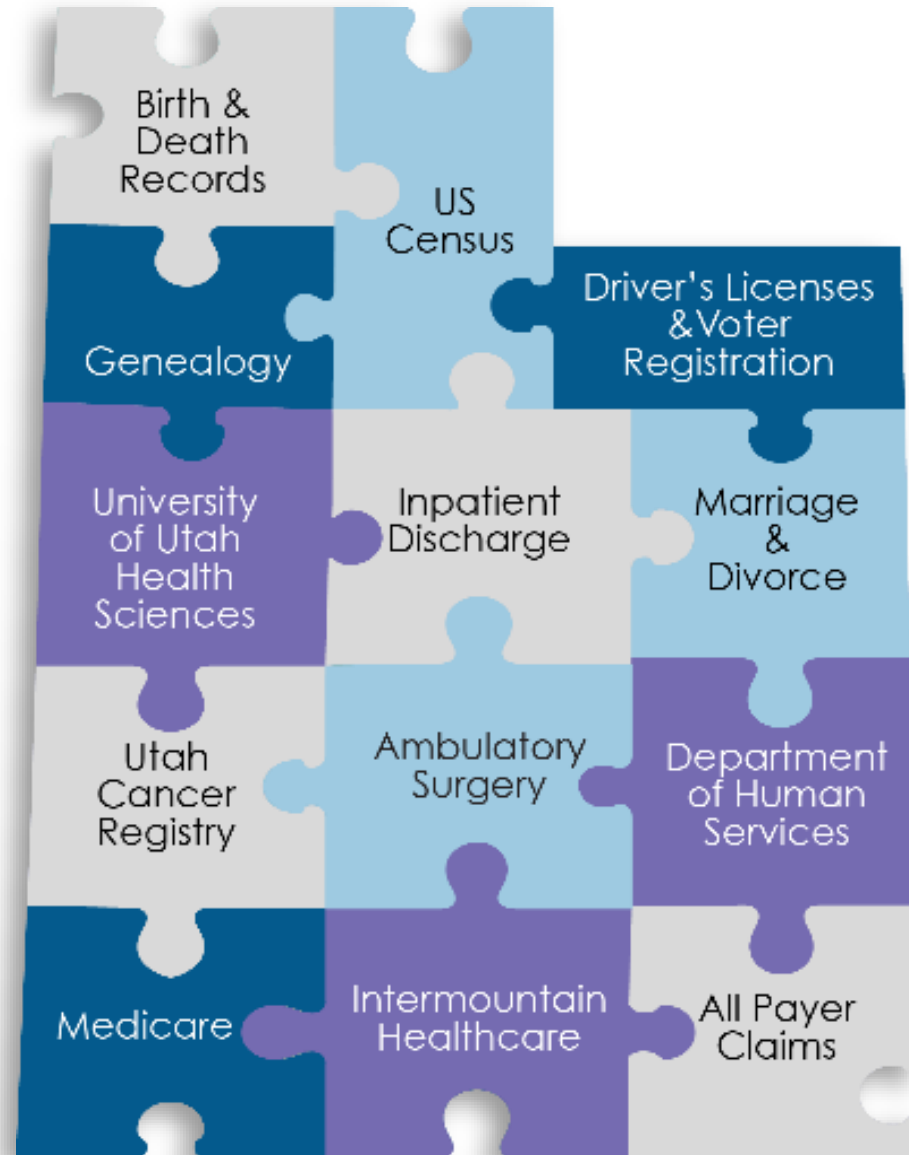
K439
New York family

Dr. William Chey

K353
Utah family

Dr. Randall Burt

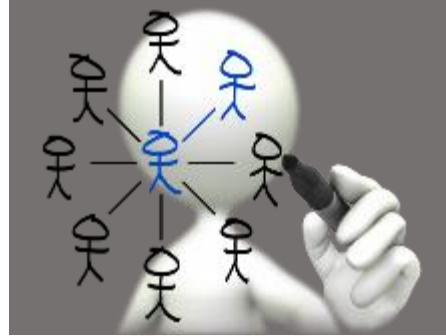
UPDB Has Evolved: Main Data Sources



Prominent Uses of UPDB



University of Utah Health Sciences Center Intermountain Healthcare Master Linkage Project



Volume of Records of Co-Morbidities Linked to UPDB

- Utah Cancer Registry (1966-present)
 - 363,844 new cases of malignant primary cancer
- Hospital Inpatient Discharge (1996-present)
 - N= 5,547,307 events
- Ambulatory Surgery (1996-Present)
 - N= 6,290,436 events
- Intermountain Healthcare (1992-present)
 - N = 4,302,801 events
- Univ of Utah Health Sciences Center (1992-present)
 - N= 2,054,424 events
- Birth Certificates (1915-21, 1933-present)
 - N= 2,929,761 births
- Death Certificates (1904-present)
 - N=864,878 decedents
- CMS/Medicare Claims (1992-2012)
 - N= 600,000 individuals





Utah Genome Project (launched 2012)

- Use the UPDB to identify families with high incidence of 15-20 target diseases
 - Well-defined diseases, accessible from UPDB-linked medical records
 - Significant public health impact and potential for translational science
 - Accelerate discovery of casual genetic variants
 - Whole exome and whole genome sequencing

Cancers
• Familial childhood cancers: Ewing sarcoma, Wilms tumor, germ cell tumors • Hematologic cancers: chronic lymphocytic leukemia, Chronic myeloid leukemia, multiple myeloma • Common cancers: breast, prostate, colorectal • Evolution of tumor mutations
Heart and Lung Diseases
• Chronic obstructive pulmonary disease • Idiopathic pulmonary fibrosis • Congenital heart disease • Familial cardiac arrhythmia
Immune Diseases
• Juvenile idiopathic arthritis • Crohn disease
Metabolism, Obesity, and Diabetes
• Genetics of extreme thinness to develop obesity interventions • Idiopathic hypogonadotropic hypogonadism • The role of brown adipose tissue in metabolic disease

Neurological
• Amyotrophic lateral sclerosis • Chiari malformations • Early infantile epileptic encephalopathy • Ataxia • Autism • Suicide
Reproductive
• Spontaneous preterm birth • Primary ovarian insufficiency
Other Conditions
• Extreme longevity • Hereditary hemorrhagic telangiectasia • Hip dysplasia • Congenital diaphragmatic hernia • Tuberous sclerosis

Who is in the UPDB?

- Broad spectrum of US and Western and Northern European populations
- Mormon founders and descendants
- Non-Mormons and descendants
- Generational depth is 17 generations at its deepest
- Recent decades have seen rising numbers of minority populations, Hispanic and Pacific Islander populations



Individuals in UPDB of Underrepresented Race/Ethnicity, (Alive in 2018)

Race/Ethnicity	N
American Indian	9,956
Asian	26,105
Pacific Islander	9,684
Black	16,619
Multiple races	56,179
Hispanic	356,214

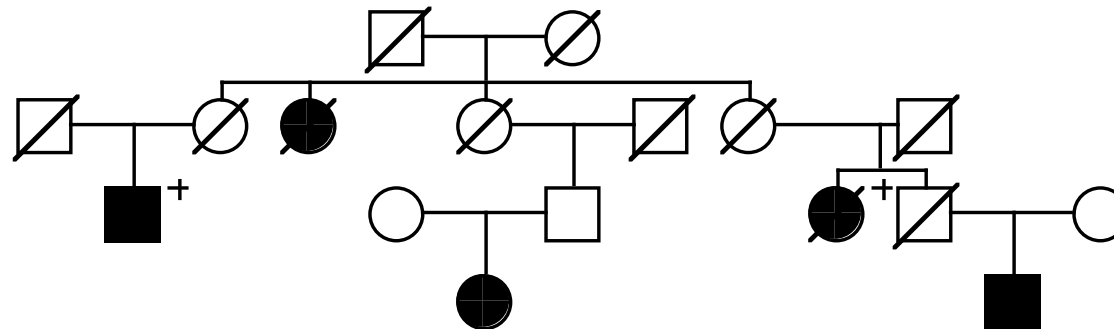
UPDB Can Support Population Sciences Research in Many Dimensions

- Identify high risk families
- Selection of controls
 - Matched General Population
 - Family-Based
 - Neighborhood-Based
- Recruitment
 - Cancer cases through Utah Cancer Registry
 - Clinic based recruitment
 - RGE based recruitment
- Population that is interested in participating in medical research
- Biospecimen collection



UPDB Research Highlight: Identification of Predisposition Genes for Cancer

- Use UPDB to test for genetic contribution to a cancer
- Use UPDB to identify high-risk pedigrees for cancer of interest
- Sample high-risk pedigree members or access stored samples in biorepositories
 - Genetic Epidemiology has 36,000 stored DNAs from high-risk cancer pedigrees
- Approach:
 - Sequence affected cousin-pairs
 - Identify rare variants shared by cousins (efficient filter for best candidate variants)
 - Validate candidate variants (association of variant with cancer risk, segregation of variant in pedigree)

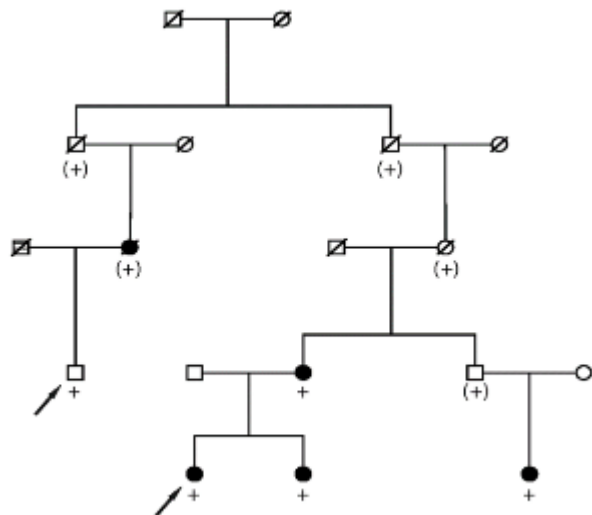


Cancer Predisposition Gene Identification

Cancer Predisposition Genes Identified Using UPDB:

<i>BRCA 1</i>	Miki et al., 1994
<i>BRCA 2</i>	Tavtigian et al., 1996
<i>CDKN2A</i>	Kamb et al., 1994
<i>GOLM1</i>	Teerlink et al., 2018

1. GOLM1 variant identified in cousins segregates to other cases



2. Case/Control Association in an independent set of melanoma cases and controls

	+	-
Case	22	469
Control	1	206

OR = 9.66 (1.29, 72.17)
Fisher p = 0.0045

Cancer Predisposition Gene Projects Analyzing Utah High-Risk Pedigrees:

- Lethal prostate cancer
- Melanoma
- Colorectal cancer
- Bladder cancer
- Small intestine carcinoid cancer
- Recurrent breast cancer
- Lung cancer
- Brain cancer

Lisa A Cannon-Albright, PhD



Craig Teerlink, PhD



UPDB Research Highlight: Cardiovascular Outcomes Among Endometrial Cancer Survivors

- **Key Question: Are endometrial cancer survivors at excess risk of cardiovascular disease?**
- Compared 2,600 endometrial cancer survivors diagnosed between 1997 and 2012 were to 10,000 age-matched unaffected women using Utah Population Database (UPDB) and the Utah Cancer Registry (UCR)
- Cardiovascular disease diagnoses were identified from electronic medical records in UPDB
- We assessed associations between endometrial cancer and risk for:
 - Hypertension
 - Cerebrovascular Disease
 - Circulatory Diseases

Mia Hashibe

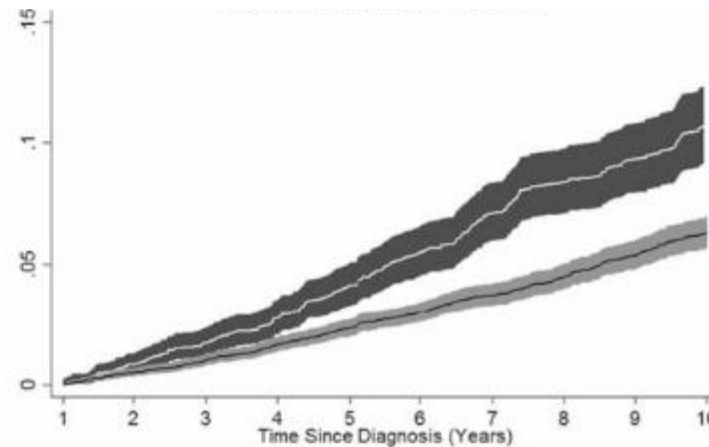
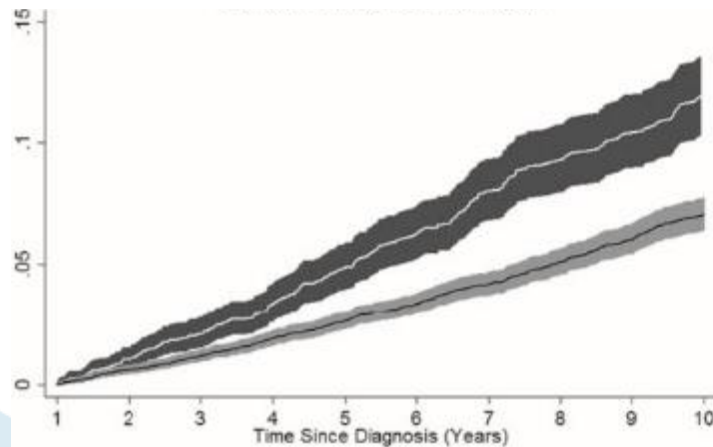


Cumulative Incidence for Cardiovascular Disease up to 10 Years After Diagnosis Between Endometrial Cancer Survivors and Matched Unexposed Women

Hypertension with complications
and secondary hypertension

Hypertensive heart and/or renal
disease

Cumulative incidence (1-10 years)



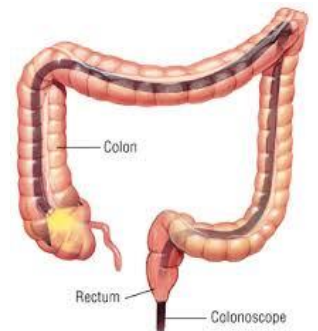
Endometrial cancer survivors

Matched unaffected women

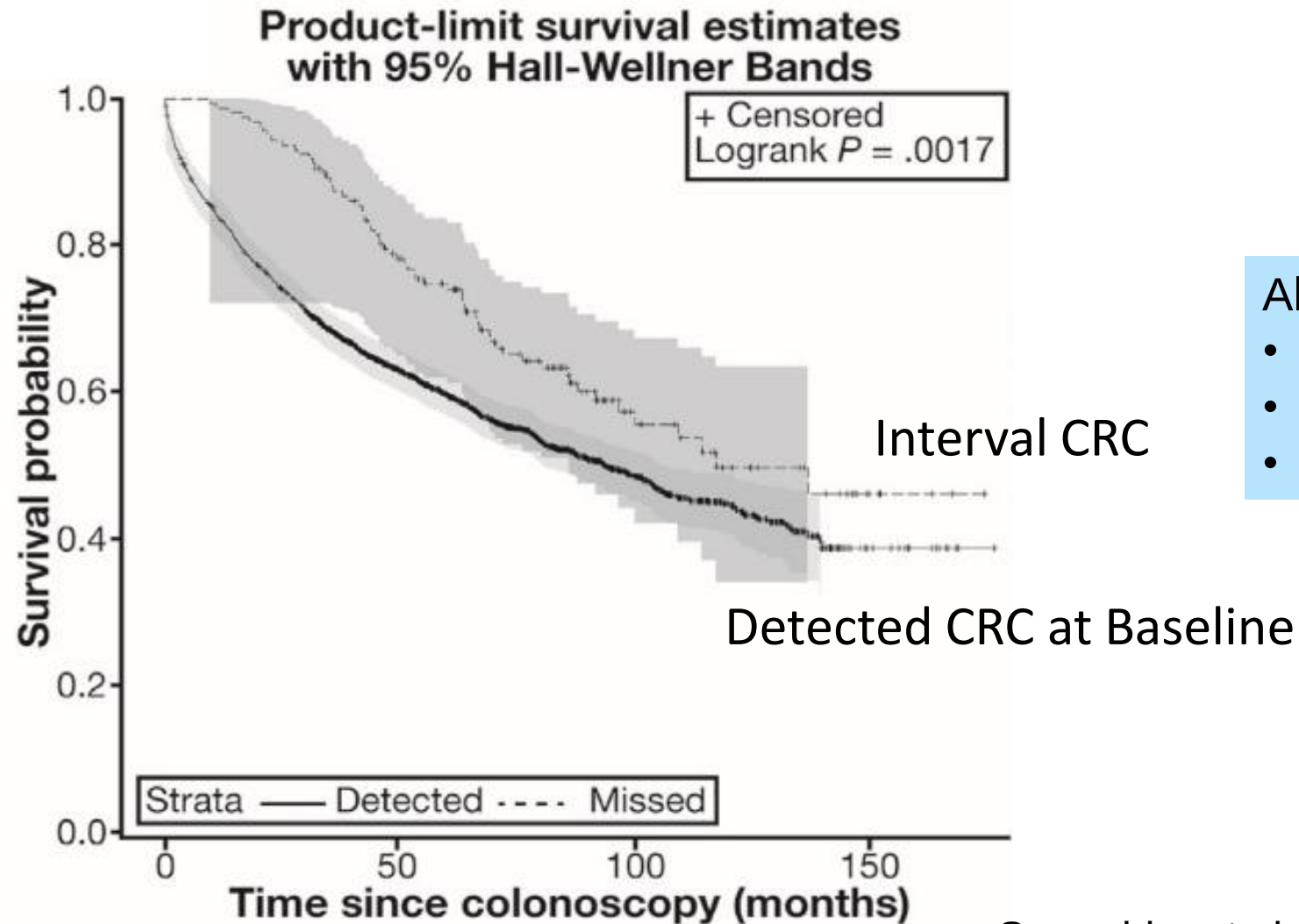
UPDB Research Highlight: Missed or Interval Colorectal Cancer and Patient Survival: A Population-Based Study

- Colorectal cancers (CRCs) diagnosed within a few years after an index colonoscopy can arise from missed lesions or the development of a new tumor. These are **interval CRCs**.
- **What are the characteristics and factors that predict interval CRCs that develop within 6-60 months of colonoscopy?**
- Colonoscopy results were linked with cancer histories from the Utah Population Database to identify patients who underwent colonoscopy 6-60 months before a diagnosis of CRC.
- Utahns were studied who had a colonoscopy from 1995 through 2009
- Factors investigated as associated with interval CRCs:

Of 126,851 patients who underwent colonoscopies, 2659 were diagnosed with CRC; 6% of these CRCs (159 of 2659) developed within 6 to 60 months of a colonoscopy.



Interval CRC Diagnoses Were Associated with Lower Risk of Death



- Also associated with
- proximal colon
 - earlier stage cancer
 - family history

Connecting to SEER: Utah Cancer Registry (UCR)



Utah Cancer Registry (UCR)

- UCR contributes data to the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program and to the CDC National Program of Cancer Registries.
- 363,844 new cases of malignant primary cancer
- UCR data are linked into UPDB.
- Cancer is a reportable disease in Utah. Data begin in 1966
- Member of the NCI SEER Program since 1973



Research Highlight: Dramatic advances in ovarian cancer classification—are there differences in patterns of survival?

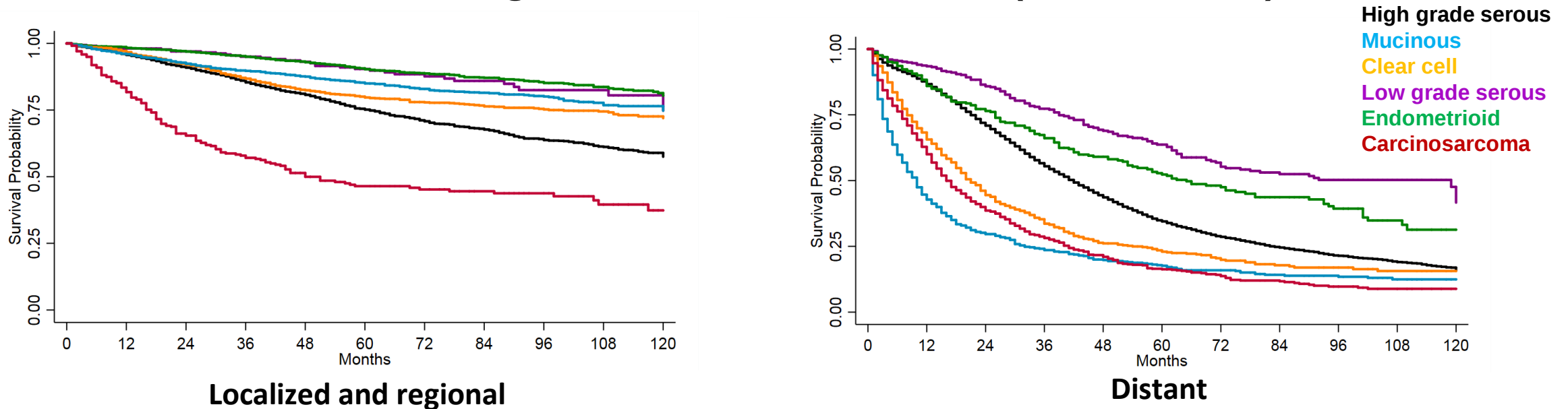
- Historically, ovarian cancer histotype classification was highly variable across pathologists
- Work over the last 15 years has shown that “Ovarian cancer represents a range of distinct diseases that share an anatomical location” (D. Bowtell)
 - Different cells of origin (e.g., fallopian tube, endometriosis, ovarian surface epithelium)
- New 2014 World Health Organization Classification refines ovarian cancer histotypes
 - Highly reproducible across pathologists
- Goals: to classify the national SEER ICD-O-3 morphology codes based on the WHO classification, and to determine whether the new guidelines impact patterns of survival
 - First comprehensive analysis of new histotype classifications, by stage

Jen Doherty



Ovarian cancer survival by histotype and stage

SEER 18 Registries, 2004-2014 (n>28,000)



- Large, population-based study demonstrates substantial differences in survival by histotype and stage
- High grade serous is NOT the most fatal
- Mucinous and clear cell have the poorest survival if diagnosed late, but do well if diagnosed early
- Ovarian cancer is a set of distinct diseases with dramatically different survival patterns by histotype and stage
- Treatments and preventive strategies must target unique features by histotype and stage to effectively to reduce ovarian cancer mortality

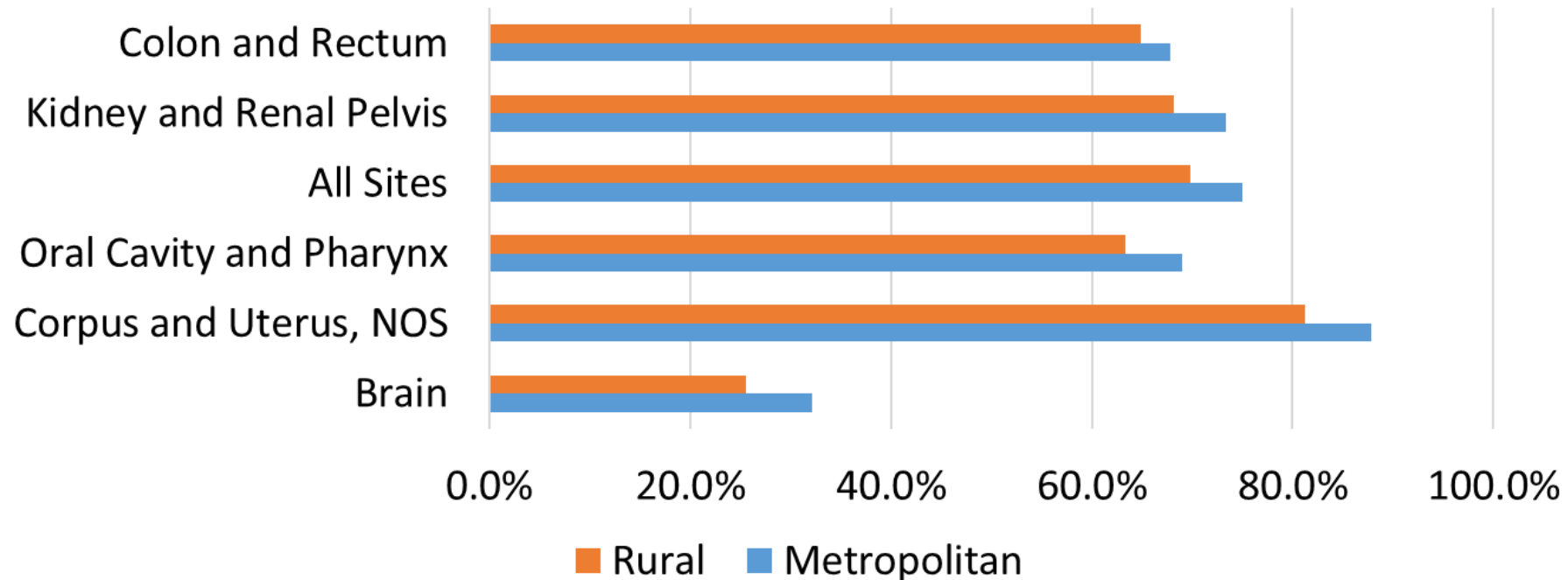
Rural Cancer Survivors in Utah



Rural Cancer Survivor Study Goals

- Over 59 million individuals in the U.S. live in rural areas where a cancer diagnosis means long travel distances to oncology centers
- Approximately 70% of Utah's 80,000 square miles has less than 7 persons per square mil
- Furthermore, only 4 of Utah's 29 counties are classified as urban (UDOH 2013)
- Study Goals: Investigate differences among cancer patients in Utah by metropolitan/urban residence for:
 - 5-year survival rates
 - Age and stage at diagnosis
 - Cancer treatment patterns

5-Year Relative Survival Rates by Residence for Cancer Patients in Utah (2004-2008)

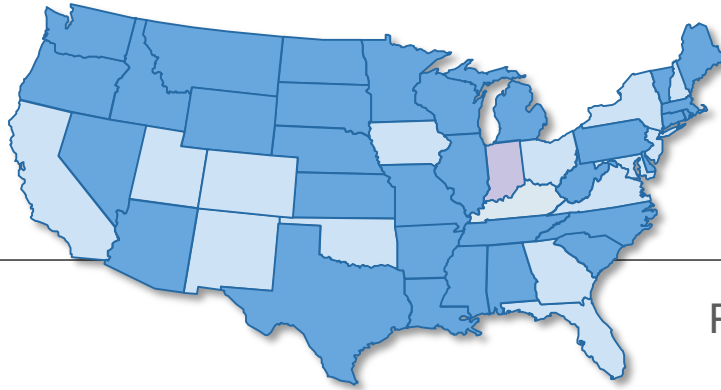


- Rural cancer patients in Utah had a lower 5-year survival (69.8%) than cancer patients residing in metropolitan areas (75.0%)
- Rural cancer patients were more likely to be diagnosed at higher stage and at an older age
- A higher proportion of rural cancer patients received no radiation or surgery for first course cancer treatment (24.2% of rural cancer patients and 21.6% of metropolitan cancer patients)

Partnering nationally: ORIEN and Flatiron



ORIEN



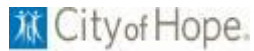
Founders:



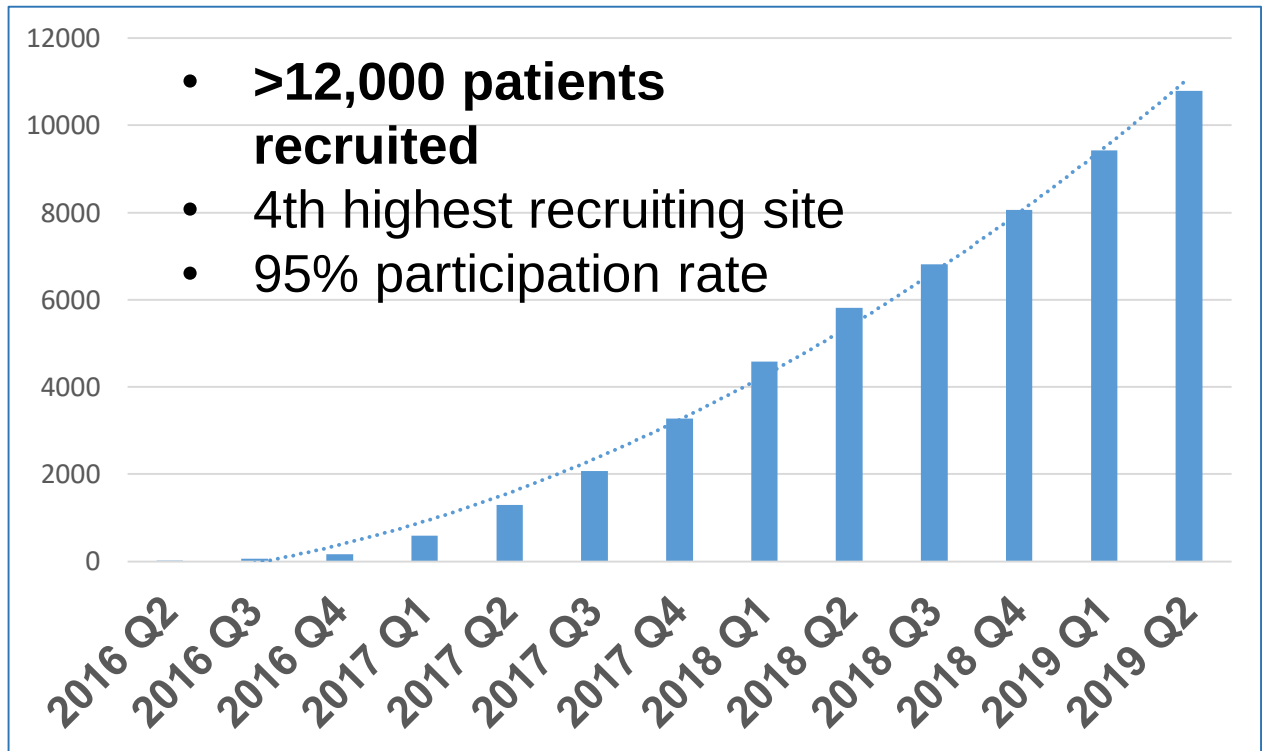
The James



THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

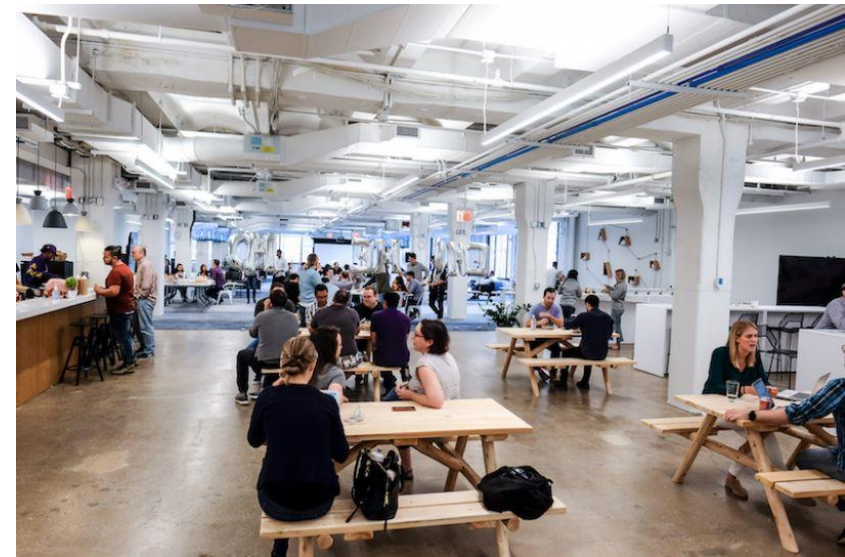


HCI - Total Cancer Care Enrollment



Connecting Nationally: HCI-Flatiron Partnership

- Established collaboration in 2014 for outcomes and quality
 - Added research component in 2016
- Data collected from introduction of EPIC at HCI in 2014
- Data on clinical outcomes abstracted by oncology professionals
 - Assisted by Flatiron technology
- Identified data returned to HCI
 - Linked to Data Warehouse
- De-identified data added to central Flatiron databases



HCI Data: Patient Reported Outcomes (PROs)

- PROs
 - Measure population outcomes (primary focus)
 - Support individual patient care (secondary focus)
- Implemented at HCI in September 2016
 - Fatigue, pain, anxiety, depression, and physical function measures from PROMIS® Computer Adaptive Tests (CAT) version
 - 2 general health questions
 - Distress thermometer
 - Additional disease-specific measures as requested by provider teams
- Measured quarterly through email link to EPIC MyChart or at clinic during check-in on tablet



HCI-Flatiron Partnership: Data Linkage



**EHR Data from
UofU Enterprise
Data Warehouse**

*Demographics, Visits, Diagnoses,
Labs, Therapies, Discharge Notes,
Physician Notes, Radiology, &
Pathology*

**Technology-enabled
EHR Data Abstraction**



**PROs collected by tablet
and Epic MyChart**

**Evaluation of
prognostic value of
PROs in advanced
cancer**
(metastatic NSCLC,
CRC, and breast)

Testing Patient Reported Outcomes in Relation to Clinical Outcomes

- Performance status is often used to stratify cancer patients for treatment and to guide supportive care
- Do PROs have prognostic value in metastatic disease, independent of physician assessment of functional status?
- Assessed associations between
 - PROs and overall survival
 - PROs and hospital-free survival
- **Goal: Identify prognostic factors in metastatic disease**
 - Clinical treatment decisions
 - Eligibility for clinical trials
 - Guide supportive care

Patient Reported Outcomes Predict Worse Survival in Metastatic Cancer Patients

Patel et al., ASCO 2018

	Probability of Survival to 12 months			Log-rank P-Value
	Low Tertile	Middle Tertile	High Tertile	
Physical Function	0.57 (0.46-0.71)	0.70 (0.61-0.81)	0.83 (0.73-0.94)	< 0.001
Pain Interference	0.72 (0.61-0.85)	0.81 (0.72-0.90)	0.54 (0.42-0.68)	< 0.001
Fatigue	0.82 (0.72-0.94)	0.69 (0.60-0.79)	0.57 (0.45-0.72)	< 0.001
Anxiety	0.73 (0.63-0.86)	0.73 (0.64-0.83)	0.67 (0.56-0.79)	0.014
Depression	0.81 (0.71-0.91)	0.70 (0.60-0.81)	0.62 (0.51-0.75)	0.002
Composite	0.77 (0.66-0.90)	0.75 (0.66-0.86)	0.59 (0.48-0.72)	< 0.001

- All individual PRO domains and a summary score were strongly associated with 12-month survival and hospital-free survival (HFS)
- **Physical function and fatigue provided the greatest discrimination**

PRO scores, independent of physician interpretation, are prognostic for overall survival and HFS and have substantial implications for patient care, treatment planning, clinical research, and financial modeling

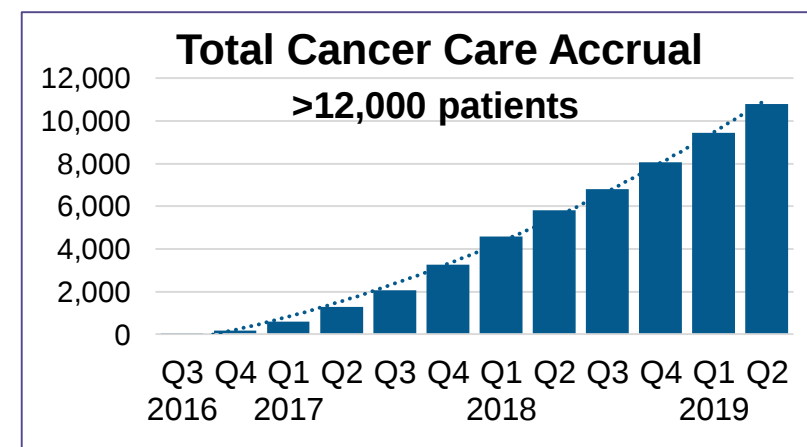
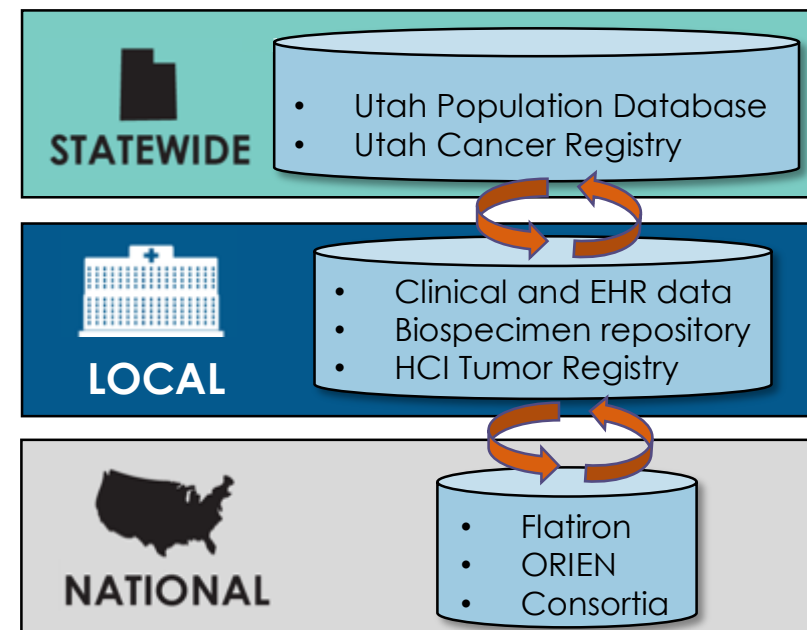
Huntsman Cancer Institute – A Paradigm for a Shared Data Environment

Huntsman Cancer Institute links data...

- Locally, statewide, and nationally for maximum data sharing and innovative research capacity
 - Utah Population Database
 - Utah Cancer Registry

National partnerships:

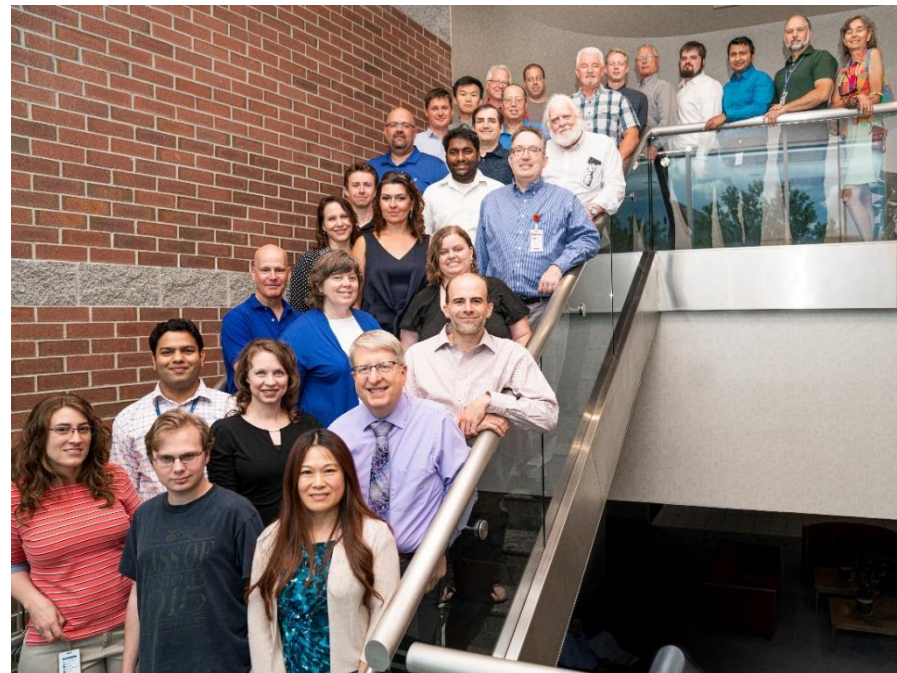
- University of Utah patient-reported outcomes data linked with Flatiron clinical endpoints
 - Demonstrated strong link between patient-reported outcomes and survival (ASCO 2018)
- Participation in ORIEN network of Cancer Centers
 - 4th highest recruiting site, 95% participation rate
 - Leadership in committees, research (>70 local and 10 ORIEN projects), and translation of genomics to the clinic



Thank you to ALL who contributed!

- Research Informatics Shared Resource
- Utah Population Database
- Utah Cancer Registry
- ORIEN
- Flatiron

... and many more who have helped to create a unique interlinked data environment at HCI & the University of Utah!





Questions?