

Cancer Genomics and Research in American Indian and Alaska Native Communities: Presentation and Discussion



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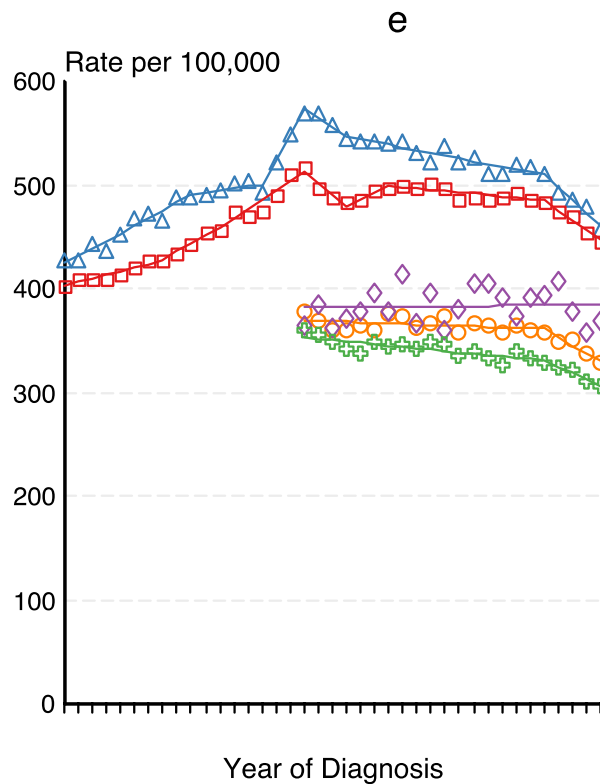
Overview

1. *Cancer Overview*
2. *Genomics*
 - *Examples of Ongoing Efforts*
3. *Precision Medicine*
 - *Examples of Ongoing Efforts*
4. *Summary*

SEER Incidence and US Death Rates

All Cancer Sites, Both Sexes

Rates for Whites and Blacks from 1975 – 2013 and for Asian/Pacific Islanders, American Indians and Alaska Natives and Hispanics from 1992-2013



Mortality

Rate per 100,000

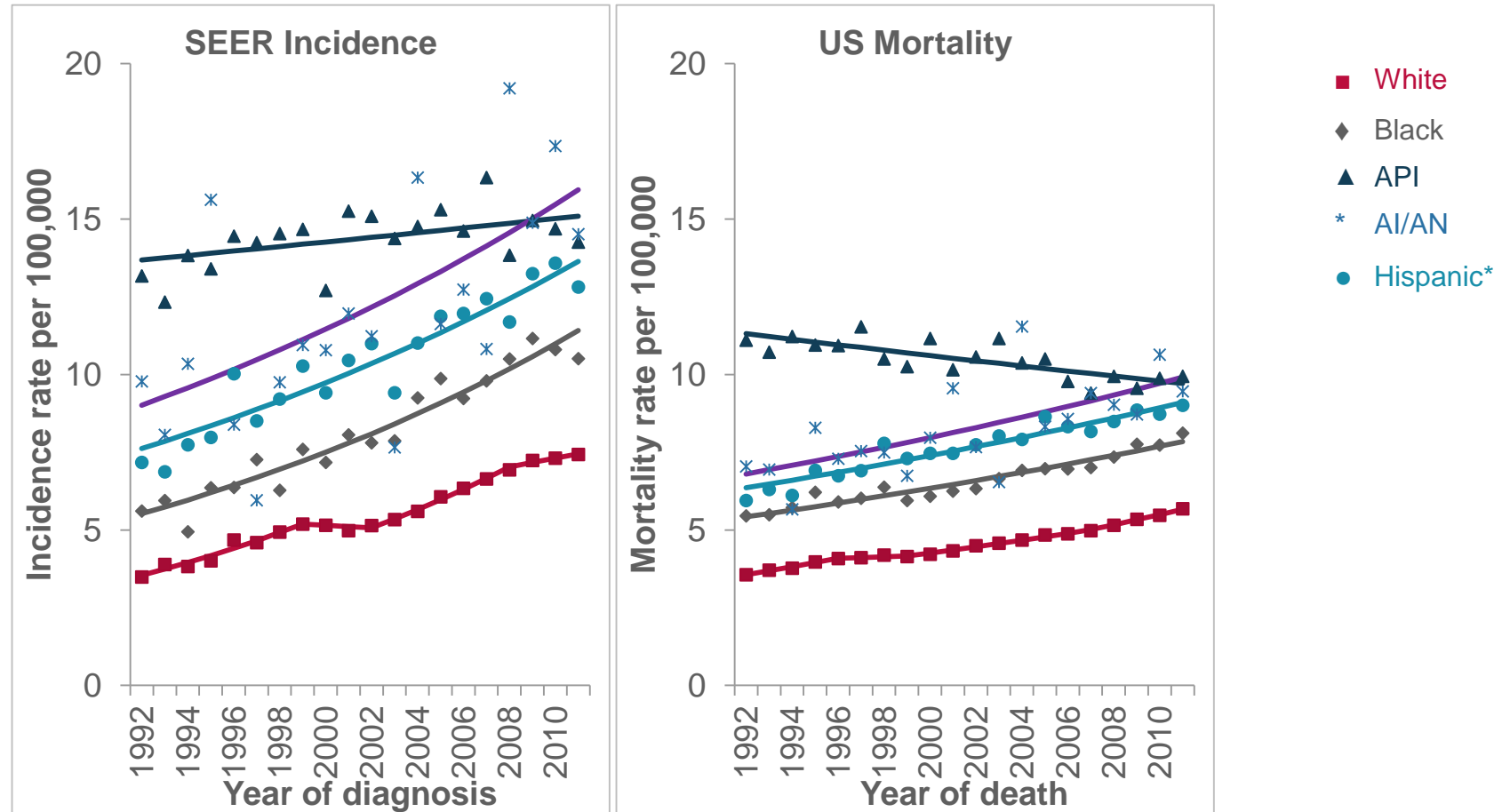
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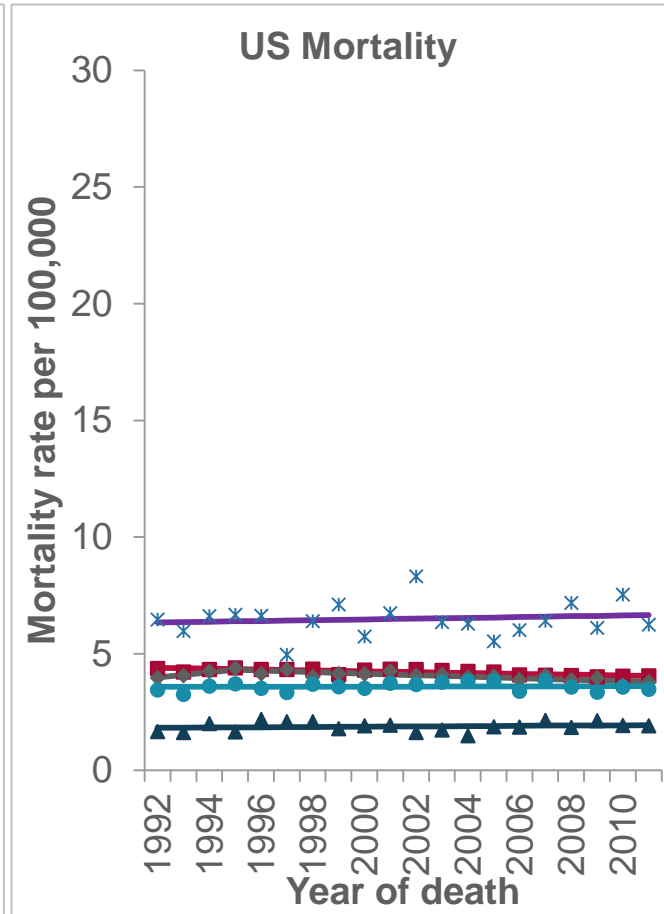
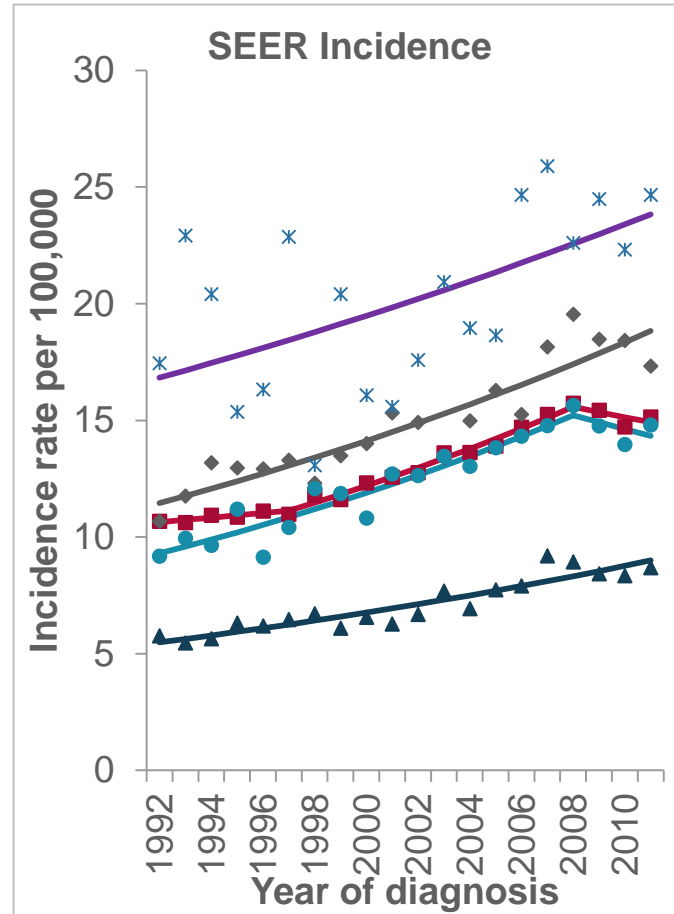
Year of Death

Liver & Intrahepatic Bile Duct



*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992–2011, Mortality data from NCHS

Kidney & Renal Pelvis



- White
- ◆ Black
- ▲ API
- * AI/AN
- Hispanic*

*Hispanic is not mutually exclusive from other groups
Incidence data from SEER 13 1992–2011, Mortality data from NCHS

Cancer is Very Complex

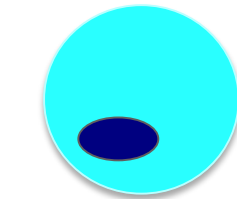
- Aided by the genomics revolution and advances in biomedical technology, the cancer research community has made many important discoveries over the past decade
 - DNA sequencing, RNA and protein expression, etc...
- Cancer is not a single disease, it is many diseases even within a single organ site
 - Therefore not all cancers can be treated uniformly
- For greater progress, more research is needed

How Does Cancer Evolve? Multiple Steps are Involved

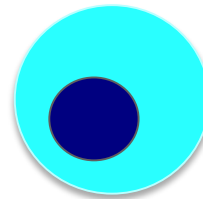
Environmental
Factors

Time/Age

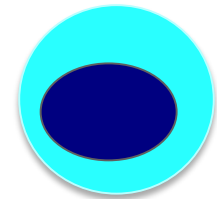
Inherited
Genetic
Alterations



Transformed cell



Premalignant cell



Malignant cell

Multiple
Genetic
Alterations

- Uncontrolled growth
- Invasion
- Metastasis

Environmental Exposure and Lifestyle Factors Linked to Cancer



Tobacco

- A factor in 20% of all cancer deaths
- Associated with 20 different kinds of cancer



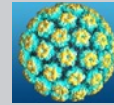
Obesity

- Risk factor for: liver, kidney, colorectal cancer, and others



Arsenic

- Exposure in contaminated groundwater, smoking



Viruses

- HBV, HCV, HPV



UV light

- Sunlight



Aflatoxin

- Corn, peanuts



Metal exposure

- Mercury, lead, cadmium, aluminum, and uranium

Genetic Alterations Influence Cancer Risk

- *Mutations* – Alterations in the DNA sequence in a cell
 - *Germline mutations* – Mutations that are inherited
 - From birth these mutations are present in every cell of the body
 - *Somatic mutations* – Mutations that are acquired in some cells as a result of:
 - Errors in DNA replication, environmental exposures (e.g., tobacco, aflatoxin, UV exposure), lifestyle (e.g., obesity/diet)
- *Normal Genetic Variation* – Often referred to as variants or polymorphisms

1. Cancer Genomics

- *Examples of Ongoing Efforts*

The Cancer Genome Atlas (TCGA)

- Initiated over a decade ago as a collaboration between NCI and NHGRI
- *Vision*: To improve our ability to diagnose, treat, and prevent cancer
- *Approach*: To accelerate our understanding of the molecular basis of cancer through genome characterization
- Research has enabled:
 - Genomic characterization of tumors to inform treatment decisions
 - Identification of mutations in tumor cells that could be targeted for the development of new therapies

TCGA data describes



33

DIFFERENT
TUMOR TYPES

...including

10

RARE
CANCERS

...based on paired tumor and normal tissue sets
collected from



11,000

PATIENTS

...using

7

DIFFERENT
DATA TYPES



www.cancer.gov

What About Underrepresented Populations?

- TCGA used convenient samples
- There was no effort to ensure minority representation with the exception of Blacks/African Americans in prostate and breast cancers
 - Several demographic groups are underrepresented:

TCGA	
Whites	77%
Blacks/African Americans	12%
Hispanics	3%
Asian Americans	2%
Native Americans/Alaska Natives	0%
Pacific Islanders/Native Hawaiians	0%

NCI Genomic Data Commons

- An expanding knowledge base for cancer that stores genomic and clinical data for use by the cancer research community
- Promotes and facilitates data sharing. The GDC collects datasets from cancer research programs
- Promotes strategies for tissue collection that ensure adequate quantity and high quality
- The will GDC offer cutting edge bioinformatics tools
- Researchers will be able to compare their data with other data using cloud computing capabilities
- Will enable data sharing while assuring ownership is respected



Expanding access to genomic and clinical data will accelerate cancer research and help improve the diagnosis and treatment of each cancer patient.

www.cancer.gov

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Cases

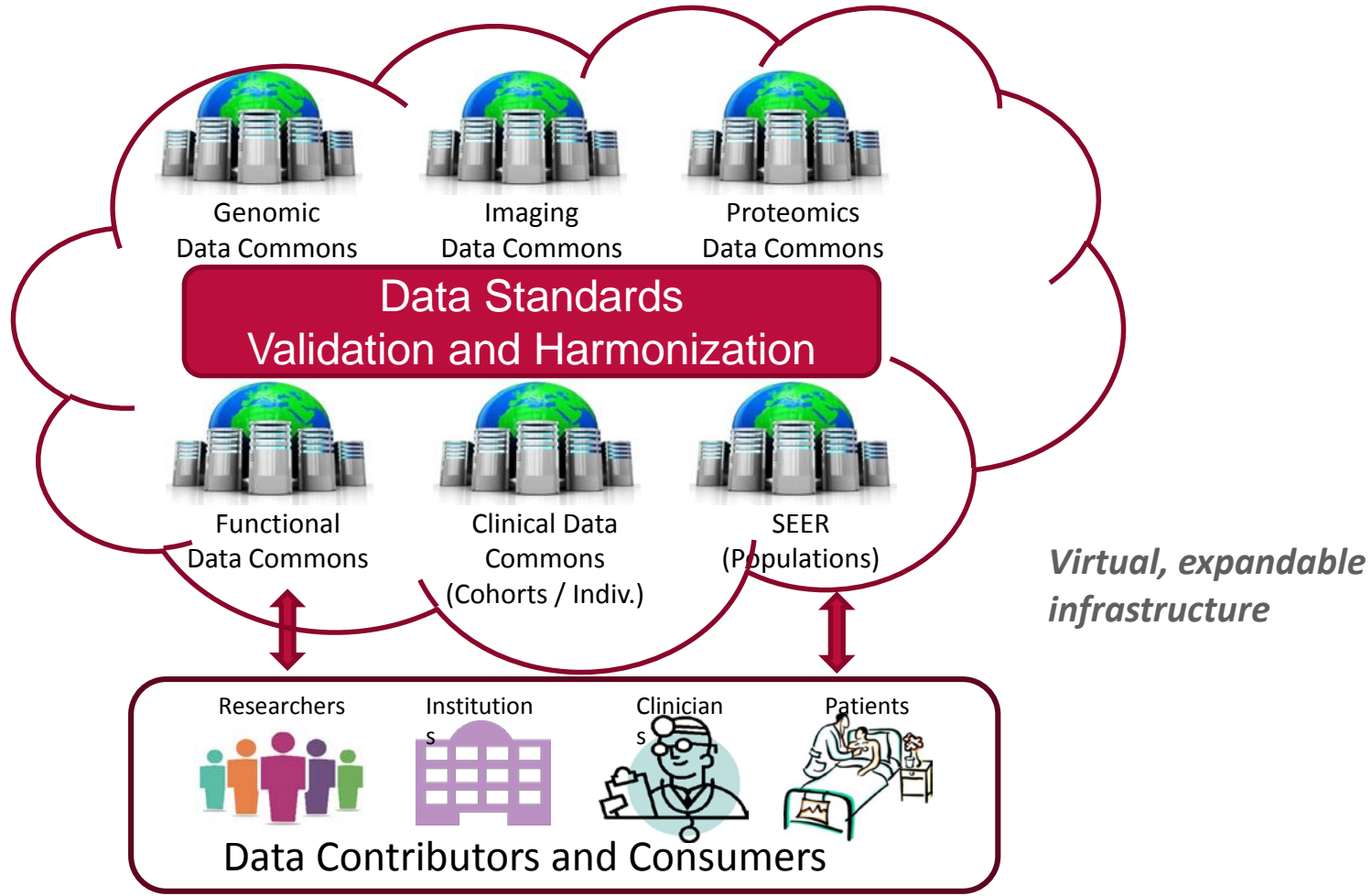
TCGA and TARGET:
14,000

Foundation Medicine:
18,000



Expanding access to genomic and clinical data will accelerate cancer research and help improve the diagnosis and treatment of each cancer patient.

NCI Cancer Research Data Ecosystem: Vision



Early-Onset Malignancies Initiative: Minority Serving NCORPs Sites

Goals:

- To investigate why certain populations are at increased risk of developing cancer at an early age, through the collection and characterization of malignancies
- To obtain genomic data from underrepresented populations
- To obtain information about treatment and response
- To develop a tissue bank for future study

Specimen collection is focused on six cancer sites from racially and ethnically diverse populations

Specimen Details



* Renal in NA and Caucasian only

Future of Genomics Research in Cancer

We can do more...


- To determine which genetic factors are playing a role in cancer
- To understand how genetic factors may be similar or different among different populations
- To understand how genes are influenced by lifestyle and exposures

What we need...

- Biospecimens with comprehensive characterization including DNA sequencing, RNA expression, protein expression, and other types of analysis (“-omics”)

Biospecimens are Critical for Advancing Cancer Research in AI/AN Populations

- What is a biospecimen and associated data?
 - Tissue/blood samples from individuals diagnosed with cancer (informed consent)
 - Information about the individuals (clinical data, exposure data, family history, etc..)
- Why is it important?
 - “-omics” technologies enable researchers to understand the sample at the molecular level which can inform individual treatment decisions, advance knowledge about cancer, and contribute to risk assessment on a population level
- What happens to the data?
 - All sources securely stored
 - Shared with the research community (guidelines in place)
 - Can be integrated with other data types and used in future studies

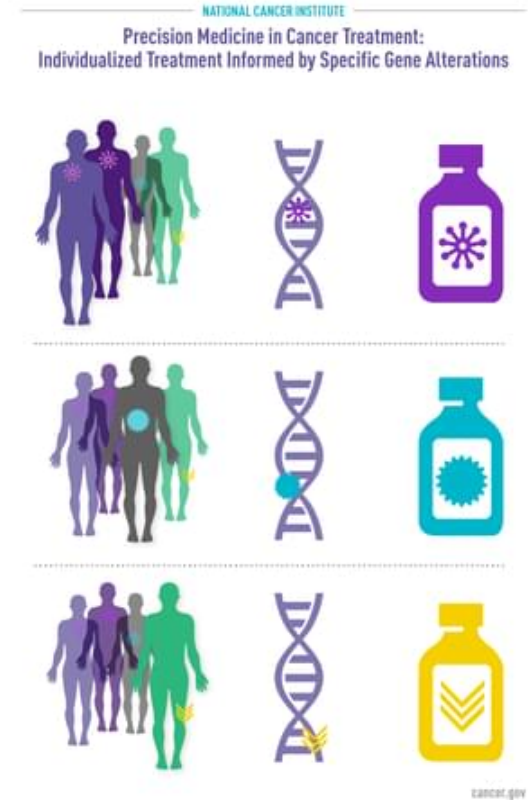


2. Precision Medicine in Oncology

- *Examples of Ongoing Efforts*

Precision Medicine for Cancer

- Interventions to prevent, diagnose, or treat cancer, based on a molecular and/or mechanistic understanding of the causes, pathogenesis, and/or pathology of the disease
- Where the *individual characteristics* of the patient are sufficiently distinct, interventions can be concentrated on those who will benefit, sparing expense and side effects for those who will not



Modified by NCI Acting Director Doug Lowy, MD from: *IOM's Toward Precision Medicine, 2011*

Precision Medicine Initiative® in Oncology

- Identify existing and new treatments that can target tumors
 - Understand and overcome resistance to cancer treatments and determine effective combination targeted therapies
 - Work with patients to collect tumor samples and use them to better understand cancer genomics and biology
 - Develop models that can be used to test therapies in development
-



[INFO](#) [SPEAKERS](#) [AGENDA](#) [HOTEL](#) [REGISTER](#)

National Meeting on Precision Medicine and Cancer in **AMERICAN INDIAN & ALASKA NATIVE COMMUNITIES:**

A Dialogue on Cancer Research

**SAVE
THE
DATE**

**NOV 10
2016**

Samis Education Center
OU Health Sciences Center
Oklahoma City, Oklahoma

<http://www.precisionmedicineandcancernationalmeeting.com/>

Advancing Precision Medicine Relies on Biospecimen Collection and Analysis

Southcentral Foundation –

A tribally owned/operated healthcare organization partnering with American Indian/Alaska Native communities in research

A Cancer Research Study Example

Tamoxifen Metabolism and Gene Variation Among Alaska Native and American Indian People (2011-2016)

Adapted from: Denise A. Dillard, Ph.D. (Inupiaq)
Director of Research, Southcentral Foundation



Alaska Native People Shaping Health Care



The Studies Before the Study

- *Ethical and Cultural Implications of Specimen Banking Among Alaska Native People (2006-2010)*
 - Clear and extensive consent
 - Important given the unclear lines between research and clinical care when research is conducted in clinical settings
 - Respectful treatment and return of specimens and data with AI/AN oversight
 - Assessment of the trustworthiness of researcher
- *Pharmacogenetics in Rural and Underserved Populations (2010-2015)*
 - *Views of Pharmacogenetics Among Alaska Native People (2010 - 2012)*

Adapted from: Denise A. Dillard, Ph.D. (Inupiaq)
Director of Research, Southcentral Foundation

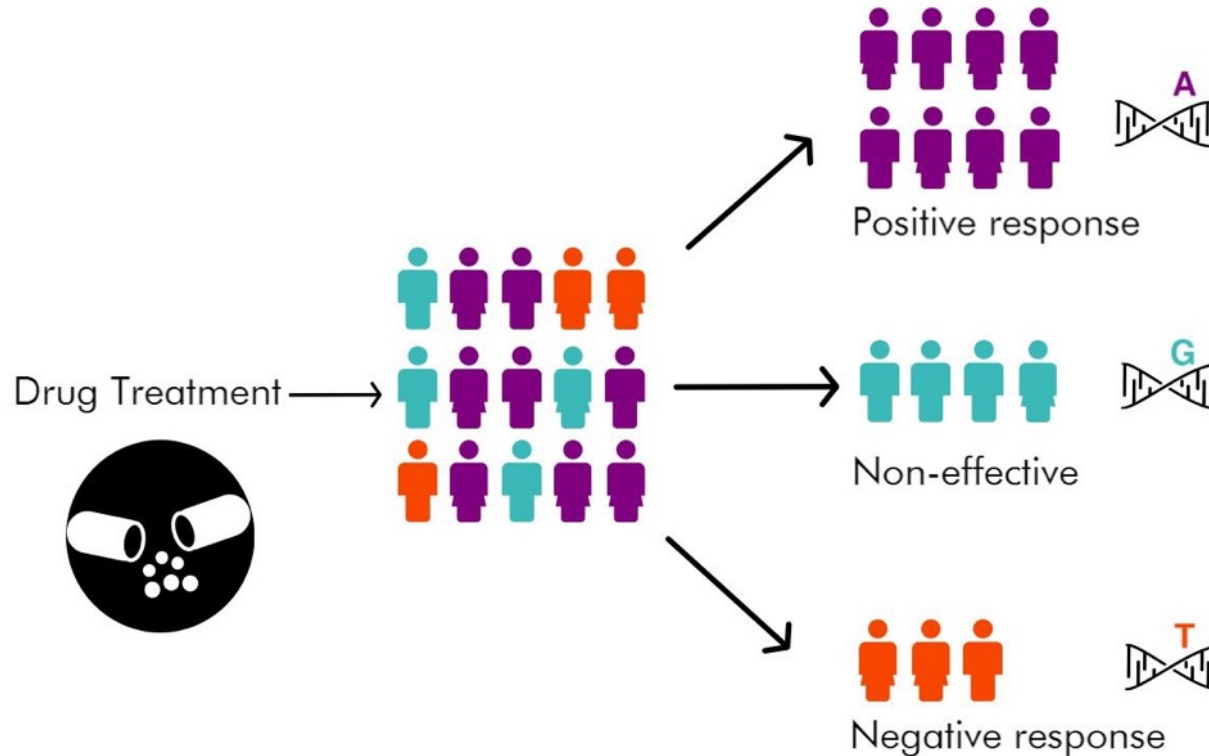


Alaska Native People Shaping Health Care



What is Pharmacogenomics (genetics)?

- The study of how a person's genes affect the way he or she responds to drugs
 - Being applied to learn ahead of time what the best drug or the best dose of a drug will be for an individual

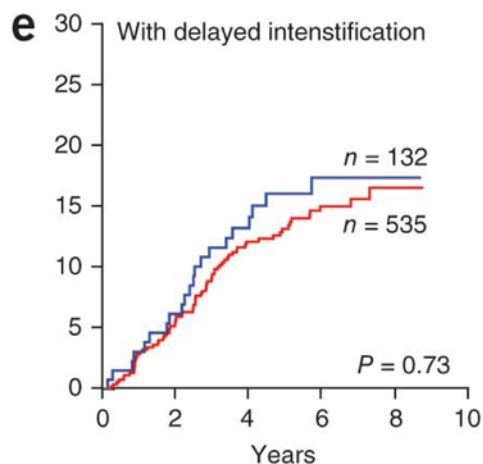
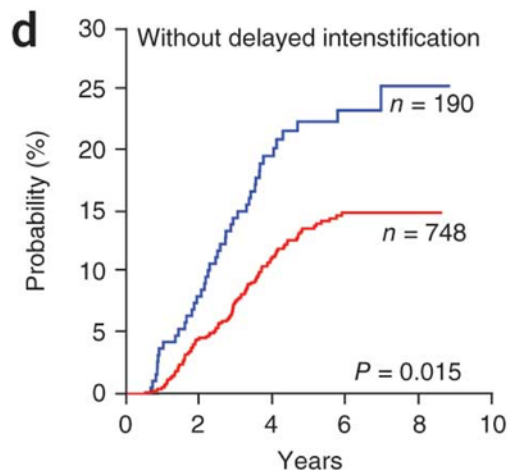
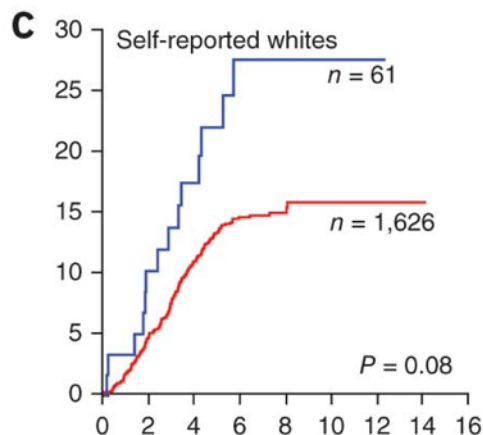
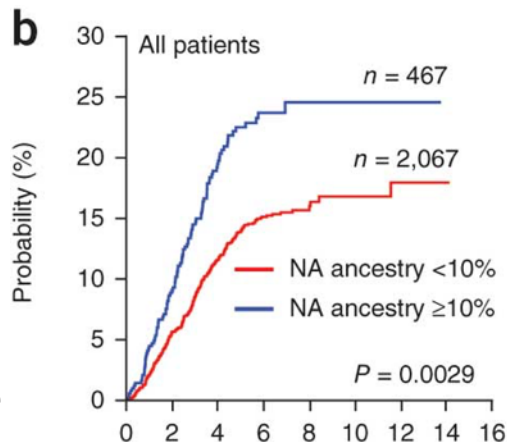


Ancestry and Relapse of Childhood Acute Lymphoblastic Leukemia

- Acute Lymphoblastic Leukemia (ALL)
 - Hispanic children have the highest incidence of this childhood leukemia, with dramatic increases in past decades
 - American Indian children have lower incidence, but poorer outcomes
- Researchers from the Children's Oncology Group (COG) sequenced patients' DNA samples who did not respond to traditional therapy
 - Researchers found many new mutations in the study samples
 - They evaluated genetic ancestry by looking at ancestry-associated DNA markers (genetic test)
 - Research showed a strong association between the degree of Native American ancestry and poorer outcomes

Association of Native American Genetic Ancestry with Risk of Relapse

Risk of relapse



- Increased probability of leukemia relapse in Native Americans, and Hispanic and non-Hispanic whites with higher degrees ($\geq 10\%$) of Native American genetic ancestry
- Additional chemotherapy can reduce the chance of relapse

Knowledge of Genetic Ancestry Resulted in Better Patient Outcomes

- Researchers learned that by giving a single extra round of chemotherapy to children with a higher percentage of Native American ancestry, they were able to achieve similar positive outcomes to individuals with a lower percentage of Native American ancestry
- One example of how ancestry and associated genetic background can play an important role in treatment decisions

Summary

- Precision Medicine Initiative® in Oncology is focused on identifying individual characteristics of patients and their tumors
- Disparities in cancer incidence and mortality result from many factors
 - Access, exposure, genetics, lifestyle
- Ancestry markers are an important tool for research
- We must continue conducting basic research to improve our ability to treat, diagnose, and prevent cancer for all populations

Rural Cancer Control: Challenges & Opportunities

May 4-5, 2017

FedEx Institute of Technology
University of Memphis

Registration: <https://emsreg.memphis.edu/ruralcancercontrolmeeting>



Are AI/AN communities willing to participate in efforts to increase our genomic understanding of cancer?

Thank you

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**NATIONAL
CANCER
INSTITUTE**

www.cancer.gov

www.cancer.gov/espanol

Extra Slides

Genetic Ancestry of 2,534 children with ALL

