

Exploring Cancer

Exploring the Role of Biology, Race, Class, and Socioeconomics



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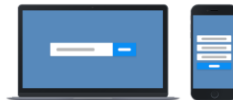
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3

Exploring Cancer

Examining the Role of Biology, Race, Class, and Socioeconomics

Fridays

11:00 - 11:50 AM EST/EDT

August 29

Welcome to Cancer(s) and Health Disparities 101 - The Introduction

September 5

Patient Navigation: The Nurse, Patient & Advocate

September 12

Achieving Excellence and Equity in Difficult Times

October 3

Breast Cancer Health Disparities

October 17

Cancer From a Public Health Perspective

October 31

The impact of Race, Ancestry and social Determinants on Black men with Prostate cancer

November 7

Health Disparities

November 14

Precision Without Representation: When the Cutting Edge Cuts Unevenly

November 21

Cancer Care for All: Challenges and Opportunities in Low-Resource Settings

4

Exploring Cancer

Exploring the Role of Biology, Race, Class, and Socioeconomics

November 14, 2025

Precision Without Representation: When the Cutting Edge Cuts Unevenly



Ugwuji Maduekwe, MD, MMSc, MPH

5



Ugwuji Maduekwe,
MD, MMSc, MPH

Ugwuji N. Maduekwe, MD, MMSc, MPH, FACS is an Associate Professor of Surgery and Director of Regional Therapies in the Division of Surgical Oncology, Department of Surgery at the Medical College of Wisconsin in Milwaukee, WI. She is the co-director of the Advancing Cancer Equity in Surgery research collaborative and is also the Deputy Director of the Advancing a Healthier Wisconsin Endowment, a role in which she is focused on supporting actionable projects focused on making Wisconsin the healthiest state. Her clinical focus is on peritoneal surface malignancies and gastric cancer while her research focuses on how variations in patterns of surgical oncologic care in gastrointestinal malignancies lead to health disparities.

Dr. Maduekwe has an undergraduate degree in molecular and cellular biology from the University of Texas at Dallas, and underwent medical training at Harvard Medical School, general surgery residency at Massachusetts General Hospital, and complex general surgical oncology fellowship at the University of Pittsburgh.

6

Professional Highlights

7

Professional Highlights

- 3.** Dr. Ugwuji Maduekwe, MD, MMSc, MPH, is a robotically trained surgeon.

8

Professional Highlights

- 3.** Dr. Ugwuji Maduekwe, MD, MMSc, MPH, is a robotically trained surgeon.
- 2.** She is a health equity researcher.

9

Professional Highlights

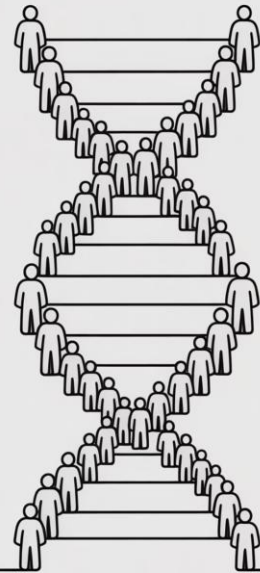
- 3.** Dr. Ugwuji Maduekwe, MD, MMSc, MPH, is a robotically trained surgeon.
- 2.** She is a health equity researcher.
- 1.** She believes that mentorship is important fuel to career trajectory.

10

Precision Without Representation: When the Cutting Edge Cuts Unevenly

Why the Future of Cancer Care Depends on Whose Data We Include

Ugwuji N. Maduekwe, MD MMSc MPH
Associate Professor of Surgery | Medical College of Wisconsin



11

The Human Cost of Uneven Progress



Chadwick Boseman

Colon Cancer, died 2020 at age 43

Black Americans are 20% more likely to develop colorectal cancer and 40% more likely to die from it.



D'Angelo

Pancreatic Cancer, died 2025 at age 51

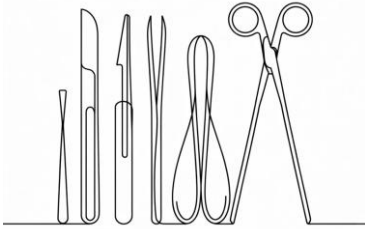
Black Americans have the highest incidence rate of pancreatic cancer among all racial and ethnic groups.

These preventable deaths underscore an urgent truth: medical breakthroughs mean nothing if they don't reach everyone equally.

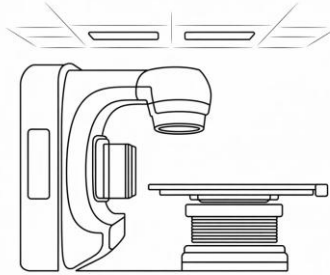
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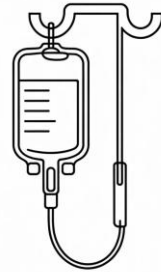
The 'Standard' of Cancer Care



Surgery



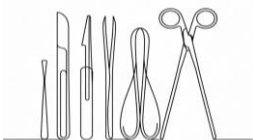
Radiation



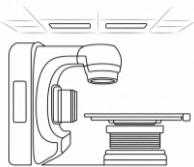
Chemotherapy

13

The 'Frontier' of Cancer Care



Surgery



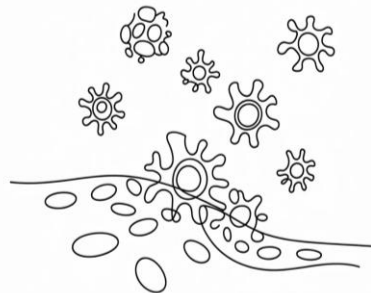
Radiation



Chemotherapy



Precision Medicine



Immunotherapy

14

What Is Research?

“A systematic investigation, including development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.”

— Centers for Disease Control



Systematic Investigation

A structured and methodical approach to inquiry and data collection.



Testing & Verification

Rigorously checking and validating hypotheses, prototypes, or processes.



Development & Design

Creating and refining new methods, tools, theories, or solutions.



Evaluation & Contribution

Assessing results and expanding the collective understanding and applicability.

15

What Is Precision Medicine? - The Basics



DNA

Your body's instruction manual.



Gene

A specific instruction or "recipe."



SNP

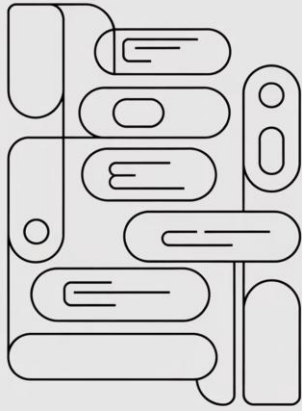
A single-letter typo (e.g., A→G).



GWAS

Scanning DNA to find relevant patterns.

16



What word comes to mind when you hear "Medical Research"?

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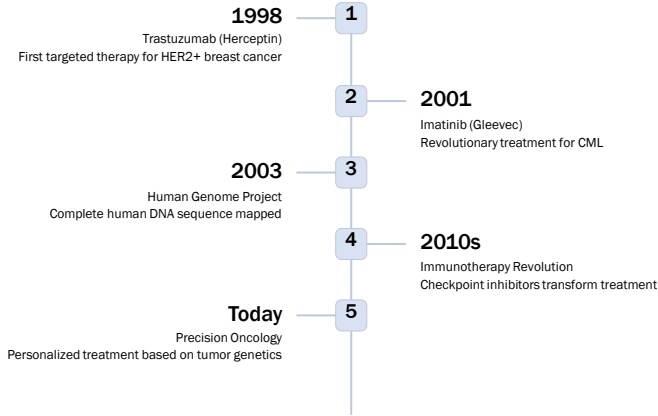
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18

Cancer Care at the Frontier of Precision



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The Proof of Precision: Imatinib (Gleevec)

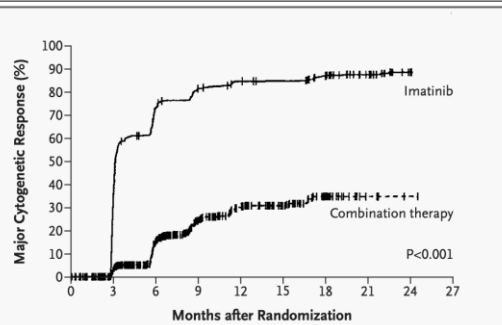


Figure 1. Kaplan–Meier Estimate of the Time to a Major Cytogenetic Response.

Major Cytogenetic Response
at 12 months

84.4%
Imatinib

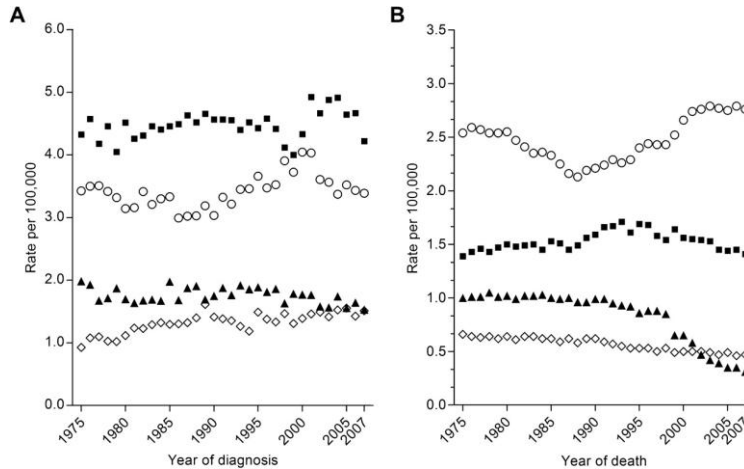
30.3%
Standard Therapy

O'Brien et al., New England Journal of Medicine, 2003

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The Effect of Precision: Imatinib



These data are consistent with data from several registries such as the Surveillance, Epidemiology, and End Results (SEER) database and show the extent to which imatinib reduced CML mortality and improved prognosis. The impact of imatinib treatment on CML survival observed in the ILTE study is probably greater than estimated.



21

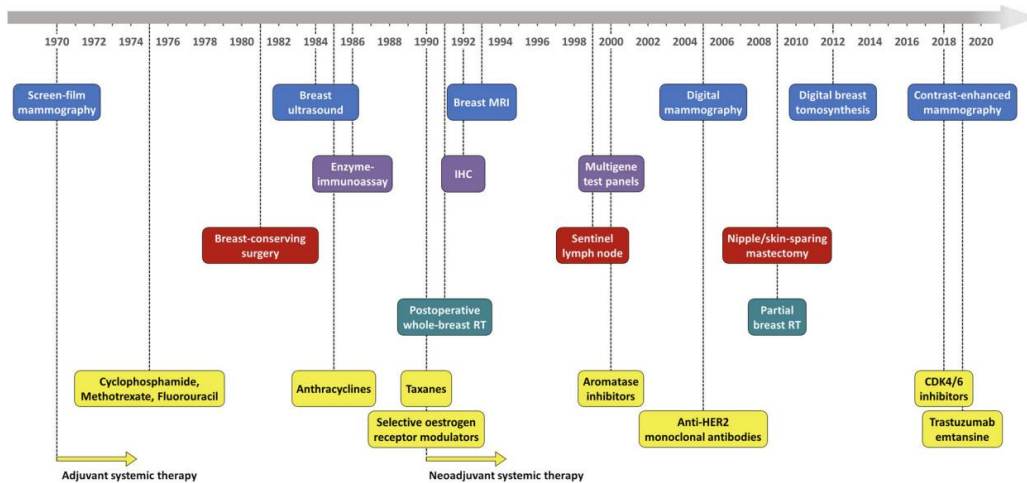


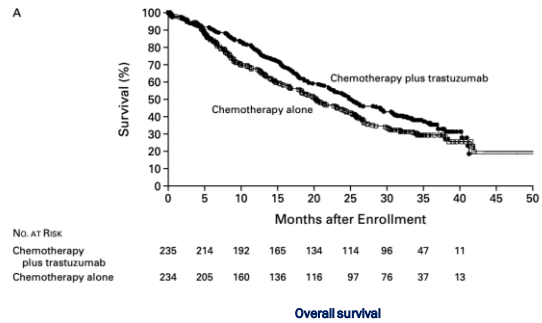
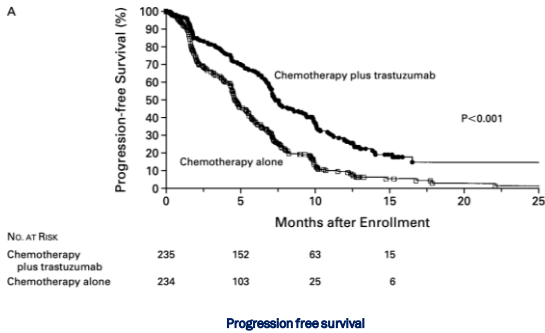
Fig. 1 Key advances in the recent history of breast cancer care (the date of introduction of each innovation was based on literature review with reference to first large studies confirming its clinical value). Specific evolutions or improvements are colour-coded. Imaging is in light blue, pathology in violet, surgery in red, radiation therapy in blue-green, systemic treatments in yellow. RT, radiation therapy; IHC, immunohistochemistry; MRI, magnetic resonance imaging; CDK4/6, cyclin-dependent kinase 4/6

Trimboli RM, Giorgi Rossi P, Battisti NML, Cozzi A, Magni V, Zanardo M, Sardaneli F. Do we still need breast cancer screening in the era of targeted therapies and precision medicine? Insights Imaging. 2020 Sep 25;11(1):105. doi: 10.1186/s13244-020-00905-3. PMID: 32975658.



22

The Proof of Precision: Trastuzumab (Herceptin)

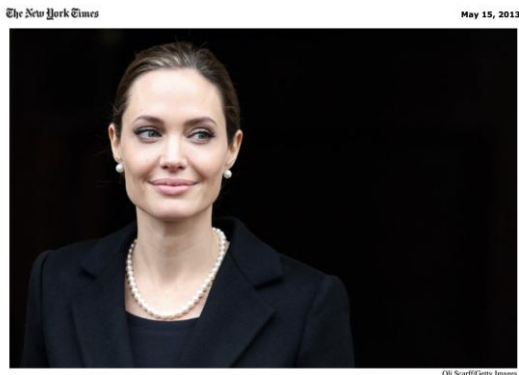


Slamon DJ, Leyland-Jones B, Shak S, Fuchs H, Paton V, Bajamonde A, Fleming T, Eiermann W, Wolter J, Pegram M, Baselga J, Norton L. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. *N Engl J Med.* 2001. Mar 15;344(11):783-92.

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Two Stories, One Gene



Angelina Jolie

- BRCA1 mutation identified through genetic testing
- Underwent preventive bilateral mastectomy in 2013
- Sparked global "Angelina Effect"
- 64% increase in genetic testing referrals worldwide



Matthew Knowles

- Diagnosed with male breast cancer, leading to discovery of BRCA2 mutation
- Highlights elevated risk in Black communities
- **Less than 1% of men aware** of their breast cancer risk
- Emphasizes gendered and racial gaps in awareness and testing

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Precision Without Representation Isn't Precision

When genomic databases lack diversity, precision tools calibrated on narrow populations become unreliable—or even dangerous—for everyone else. A drug designed using data from predominantly European populations may work differently in African, Asian, or Latin American patients due to genetic variation, metabolic differences, and environmental factors.

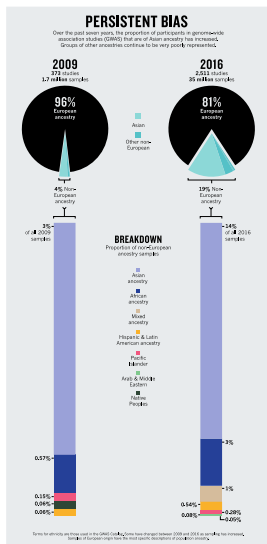
"The cutting edge becomes a cutting line—dividing those who benefit from innovation from those left behind."

Precision medicine promises personalized care, but personalization requires data from all persons. Without representative databases, we risk creating a two-tiered system: those whose genetics are well-studied receive cutting-edge care, while others face uncertainty, misdiagnosis, and ineffective treatments.

Key Insight: Genomic diversity isn't just about fairness—it's about **scientific validity**. A precision tool built on incomplete data is imprecise by definition.

Who Are We "Generalizing" From?

The foundation of precision medicine rests on massive genomic databases—repositories of genetic variants linked to disease risk, drug response, and treatment outcomes. But these databases have a serious problem: they overwhelmingly represent people of European ancestry.



Over the past decade, GWAS have been the preferred tool for discovering the genetic factors involved in common diseases. Tens of thousands of significant associations between genetic variants and biological traits have

Together, individuals of African and Latin American ancestry, Hispanic people (individuals descended from Spanish-speaking cultures in central or South America living in the United States) and native or indigenous peoples represent less than 4% of all samples analysed. Collectively, these are the most vulnerable and traditionally underserved population

Popejoy AB, Fullerton SM. Genomics is failing on diversity. Nature. 2016 Oct 13;538(7624):161-164. doi: 10.1038/538161a. PMID: 27734877; PMCID: PMC5089703.

Trastuzumab's Hidden Cost: The Cardiotoxicity Gap

Trastuzumab transformed HER2-positive breast cancer treatment, but it carries a significant side effect: cardiotoxicity (heart damage).

For many patients, this risk is manageable. But research reveals a troubling disparity:

Black women have a significantly higher probability of developing cardiotoxicity from trastuzumab compared to white women.

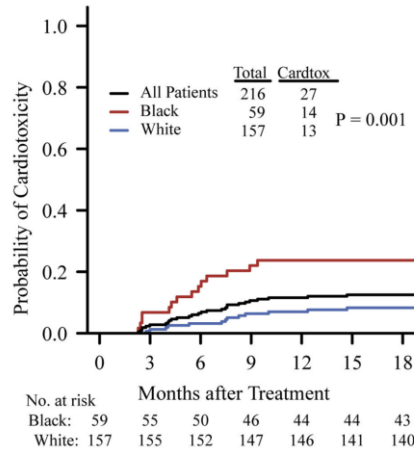


Figure 1. Cumulative Incidence of Cardiotoxicity by Race. Curves were truncated at 18 months after treatment. P-value was based on log rank test

Litvak A, Batukhali B, Russell SD, Tsai HL, Rosner GL, Jeter SC, Armstrong D, Emens LA, Fetting J, Wolff AC, Silhy R, Stearns V, Connolly RM. Racial disparities in the rate of cardiotoxicity of HER2-targeted therapies among women with early breast cancer. Cancer. 2018 May 1;124(9):1904-1911

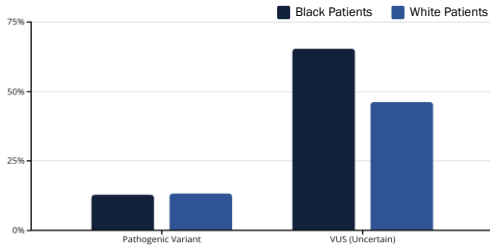
Your genetic test says "Uncertain." What does that mean?

- The test failed 0%
- You don't have a mutation 0%
- We lack data from people of your ancestry to know if this is dangerous 0%
- It's not a gene related to cancer 0%

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Case 2: When Precision Delivers Ambiguity

Genetic testing for hereditary cancer syndromes should provide clear answers: either you have a disease-causing mutation (pathogenic variant) or you don't. But for many patients, the result is neither—it's a Variant of Uncertain Significance (VUS), meaning scientists don't know whether the genetic change increases cancer risk.



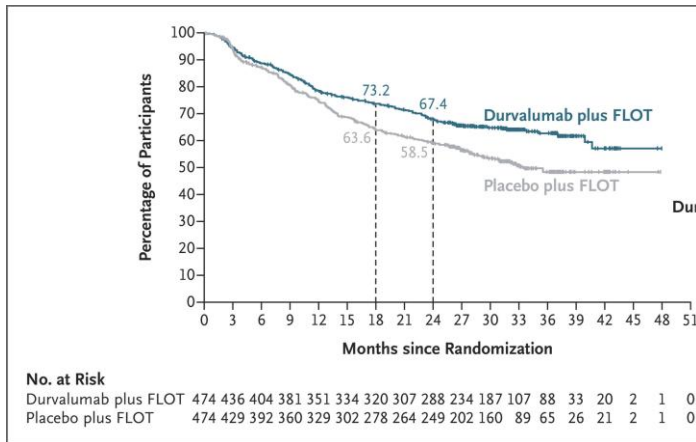
- Invitae study
 - 2894 patients across Mayo clinic centers in AZ, FL, MN, WI tested using the Invitae Multi-Cancer panel
 - Pathogenic germline variants (PGV) found in 13.3% (397) pts with shifts/clinically actionable findings in 192 (64%)
 - Variants of uncertain significance (VUS) were found in 1415 patients (47.4%)
 - Black pts: PGV rate 12.7%, VUS rate 65.5%
 - White pts PGV rate 13.3%, VUS rate 46.1%

Samadder NJ et al. Comparison of Universal Genetic Testing vs Guideline-Directed Targeted Testing for Patients With Hereditary Cancer Syndrome. JAMA Oncol. 2021 Feb

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Case 3: The MATTERHORN Trial



Janjigian YY, Al-Batran SE, Wainberg ZA, et al. Perioperative Durvalumab in Gastric and Gastroesophageal Junction Cancer. *N Engl J Med.* 2025;393(3):217-230. doi:10.1056/NEJMoa2503701

	No. of Participants with Event/ Total No. of Participants (%)	Median Event-free Survival (95% CI)
Durvalumab plus FLOT	167/474 (35.2)	NR (40.74–NR)
Placebo plus FLOT	218/474 (46.0)	32.8 (27.86–NR)

Stratified hazard ratio for event or death, 0.71 (95% CI, 0.58–0.86)
P<0.001 by stratified log-rank test

Global Incidence Pattern

Highest rates in East Asia, Eastern Europe, and Latin America—not the populations primarily studied in the trial

U.S. Disparities

Asian, Hispanic, and Black Americans have higher gastric cancer incidence than white Americans

The Generalizability Gap

Can results from a relatively homogeneous trial population apply to the diverse populations most affected by the disease?

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Case 4: Polygenic Risk Scores (PRS)

"Clinical use of current polygenic risk scores may exacerbate health disparities."

— Martin et al., Nature Genetics, 2019

Polygenic Risk Scores (PRS) represent the next frontier in precision medicine. Unlike single-gene tests (like BRCA), PRS analyze hundreds or thousands of genetic variants simultaneously to estimate disease risk. They promise to identify individuals at high risk for conditions like breast cancer, prostate cancer, or heart disease—enabling early intervention and prevention.

→ Lower Predictive Accuracy

PRS trained on European data perform poorly in African, Asian, and Latin American populations

→ Risk of Misclassification

High-risk individuals may be classified as low-risk, missing critical opportunities for prevention

→ Reinforcing Inequality

PRS may provide life-saving insights for some while offering unreliable or misleading information for others

Martin AR, Kanai M, Kamatani Y, Okada Y, Neale BM, Daly MJ. Clinical use of current polygenic risk scores may exacerbate health disparities. Nat Genet. 2019 Apr;51(4):584-591. **MCW Surgery**
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The Trust Crisis: Why Is the Data Missing?

The underrepresentation of minority populations in genomic research isn't accidental—it's rooted in a long, painful history of medical exploitation and abuse. Communities of color have legitimate reasons to distrust medical research, and understanding this history is essential to building a more equitable future.

1 1932-1972: United States Public Health Service Syphilis Study

The U.S. Public Health Service enrolled 600 Black men in a study of untreated syphilis. Participants were told they were receiving free healthcare. In reality, they were deliberately left untreated—even after penicillin became the standard cure—so researchers could study the disease's progression. Men died, went blind, or suffered severe complications. Their families were infected. The study continued for 40 years.

2

1951: Henrietta Lacks

Henrietta Lacks, a Black woman treated for cervical cancer at Johns Hopkins, had her cells taken without consent. Those cells (HeLa cells) became one of the most important tools in medicine, leading to breakthroughs in vaccines, cancer treatment, and gene mapping. Her family learned about it decades later, never compensated, while pharmaceutical companies profited billions.

3

1907-1970s: Forced Sterilization

Over **60,000 people** were forcibly sterilized in the United States under eugenics laws, disproportionately targeting Black, Indigenous, Latina, and disabled women. Many were told they were receiving routine care. California alone sterilized over 20,000 individuals. Some programs continued into the 1970s.

"Significant concern was expressed by African American and American Indian participants regarding confidentiality and autonomy, use of information, and perceived benefits from research participation."

Rosas LG, Nasrallah C, Park VT, Vasquez JJ, Duron Y, Garrick O, Hattin R, Cho M, David SP, Evans J, McClinton-Brown R, Martin C. Perspectives on Precision Health Among Racial/Ethnic Minority Communities and the Physicians That Serve Them. Ethn Dis. 2020 Apr 2;30(Suppl 1):137-148. doi: 10.18865/ed.30.51.137. PMID: 32269455; PMCID: PMC7138446.

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The Goal: Equity, Not Equality

There's a critical distinction between equality and equity, and it defines the path forward for precision medicine.

EQUALITY:

Everyone gets the same – regardless if it's needed or right for them.



EQUITY:

Everyone gets what they need – understanding the barriers, circumstances, and conditions.



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Equity in Action: A genetic test validated for one's ancestry + appropriate reference data + contextualized care = true precision medicine

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33

The Solution (Part 1): Build Better Data



1 Million+ Participants



Inclusive Recruitment



Comprehensive Data Collection



Prioritizes Underrepresented Groups

All of Us isn't just about collecting DNA—it's about understanding how genetics interact with social determinants of health, environment, and lived experience. It's designed to answer the question: *How do we build precision medicine tools that work for everyone?*

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The Solution (Part 2): Build Trust & Access

PROmoting CLinicAI Trial Engagement for Pancreatic Cancer App Study (PROCLAIM Study)

- Increase Black pancreas cancer patient enrollment in clinical trials

**LUSTGARTEN
FOUNDATION**
PANCREATIC CANCER RESEARCH



Jen Jen Yeh, MD



Ugwuji Maduekwe, MD



Marjory Charlot, MD

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What is the BIGGEST barrier to achieving health equity?

Poll Question

- A. Lack of diverse representation in research
- B. Systemic racism
- C. Mistrust
- D. Funding
- E. All of the above

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36



37

The Future of Cancer Care Depends on You

You are the next generation of researchers, clinicians, policymakers, and advocates. The future of precision medicine rests in your hands. As you move forward in your careers, I ask you to carry three questions with you:

Who is this for?

Every time you design a study, develop a drug, or implement a clinical guideline, ask: Who benefits? Whose needs are centered?

Who did we miss?

Look for the gaps. Identify the voices absent from the data, the communities excluded from trials, the patients underserved by current tools.

How do we build it for everyone?

Commit to designing systems, therapies, and research infrastructures that serve all populations from the start—not as an afterthought.

"Precision without representation isn't progress. It's a promise broken before it's made."

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38



Thank you!

39

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UNC Challenge Cancer Research

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41

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November 21
11:00 AM

Upcoming Live Webinar

Cancer Care for All: Challenges and Opportunities in Low-Resource Settings



Ashley Leak Bryant, PhD, RN, OCN, FAAN

Frances Hill Fox Distinguished Professor

Senior Associate Dean, Office of Strategy and Global Affairs

Co-Director, PAHO/WHO Collaborating Center in Quality and Safety

UNC School of Nursing

University of North Carolina at Chapel Hill

42

42

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Exploring Cancer is a webinar series taught by cancer biologists, physicians, public health experts, and other cancer specialists from **NCCU, UNC-Chapel Hill,** and **NC A&T.**

We hope to see you next time!

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