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

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**Exploring Cancer**  
Examining the Role of Biology, Race, Class, and Socioeconomics



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**Exploring Cancer**  
 Examining the Role of Biology, Race, Class, and Socioeconomics **Fridays**  
 11:00 - 11:50 AM EST/EDT

<b>August 25</b> Welcome to Cancers and Health Disparities 101 - The Introduction	<b>October 13</b> Breast Cancer Health Disparities	<b>November 10</b> Precision Medicine and Immunotherapy
<b>September 1</b> Radiation Oncology - What is it, and What is it Good For?	<b>October 20</b> Pancreatic Cancer	<b>November 17</b> Expanding Cancer Care Quality and Delivery in Sub-Saharan Africa: a collaborative approach
<b>September 8</b> New Strategies in Treating GI Cancers	<b>October 27</b> Careers in Cancer	

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**Exploring Cancer**  
 Examining the Role of Biology, Race, Class, and Socioeconomics **November 10, 2023**

**Precision Medicine and Immunotherapy:  
 The new frontiers in cancer care?**



**Ugwuji Maduekwe, MD, MMSc, MPH**

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**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.

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**Professional Highlights**

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**Professional Highlights**

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

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**Professional Highlights**

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

**2.** She is a health equity researcher.

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**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.

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**Precision Medicine and Immunotherapy**  
*The next step in cancer care?*

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Ugwuji N. Maduekwe, MD MMSc MPH  
Associate Professor of Surgery  
Medical College of Wisconsin  
November 10<sup>th</sup>, 2023

**MCW Surgery**  
*Knowledge changing lives*

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**Cancer Treatment**

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 **Surgery**       **Radiation**       **Chemotherapy**

**MCW Surgery**  
*Knowledge changing lives*

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## Cancer Treatment




**Surgery**




**Radiation**



**Chemotherapy**



**Precision medicine**



**Immunotherapy**

**MCW Surgery**  
knowledge changing life

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What word comes to mind when you hear the term "Research"?

Nobody has responded yet.  
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### Centers for Disease Control

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

**MCW Surgery**  
knowledge changing life

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**You are a doctor in a clinic. You are walking in to see an average patient. Who is that?**

Nobody has responded yet.  
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*"Doctors have always recognized that every patient is unique, and doctors have always tried to tailor their treatments as best they can to individuals. You can match a blood transfusion to a blood type – that was an important discovery. What if matching a cancer cure to our genetic code was just as easy, just as standard? What if figuring out the right dose of medicine was as simple as taking our temperature?"*

- President Obama, January 30, 2015

https://obamawhitehouse.archives.gov/precision-medicine

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**PRESIDENT OBAMA'S PRECISION MEDICINE INITIATIVE IS DEVELOPING BETTER APPROACHES TO PREVENTIVE CARE AND MEDICAL TREATMENTS BY:**

- ▶ Helping patients gain access to their health information so they can collaborate in their own care
- ▶ Considering each individual's specifics, like genes, environment, and lifestyle
- ▶ Bringing new, effective medical technologies to market faster
- ▶ Building a research network of 1 million or more U.S. volunteers

#PrecisionMedicine    [oh.gov/PMI](http://oh.gov/PMI)

THE WHITE HOUSE



THE PRECISION MEDICINE INITIATIVE

January 20<sup>th</sup>, 2015 – Precision Medicine Initiative  
\$216 million to sign up a million person cohort

December 13<sup>th</sup>, 2016 – Congress passed the 21<sup>st</sup> Century Cures Act allocating \$1.5 billion over 10 years for the program

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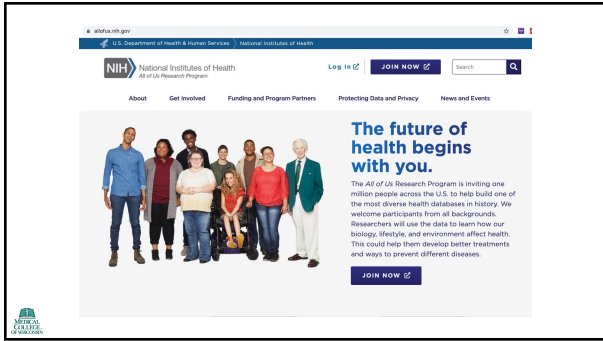
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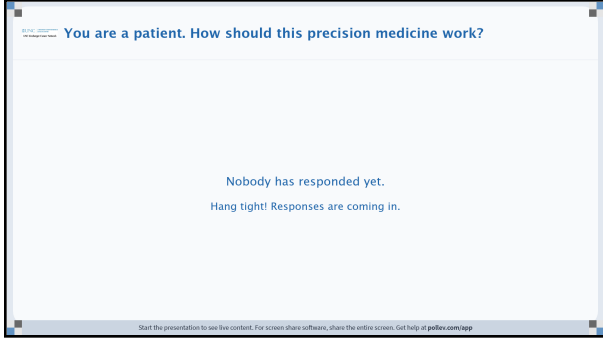
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**Glossary**

**DNA:** deoxyribonucleic acid, is the hereditary material in humans and almost all other organisms.

**Gene:** basic physical/functional unit of heredity, made up of DNA. Each chromosome contains many genes. The Human Genome Project estimated humans have 20,000 - 25,000 genes

**SNPs:** Single nucleotide polymorphism, most common type of genetic variation. Each SNP is a difference in a single DNA nucleotide. They occur almost once in every 1,000 nucleotides on average, which means there are roughly 4 to 5 million SNPs in a person's genome. These variations may be unique or occur in many individuals; scientists have found more than 100 million SNPs in populations around the world.

**GWAS:** Genome-wide association studies - searches genome for SNPs seem to be more frequent in people with a disease. Can evaluate hundreds or thousands of SNPs at a time

<https://ghr.nih.gov/genome/basic/gene>  
<https://ghr.nih.gov/genome/genome-research/>

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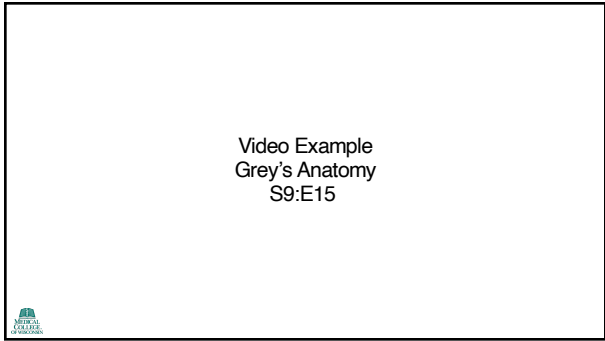
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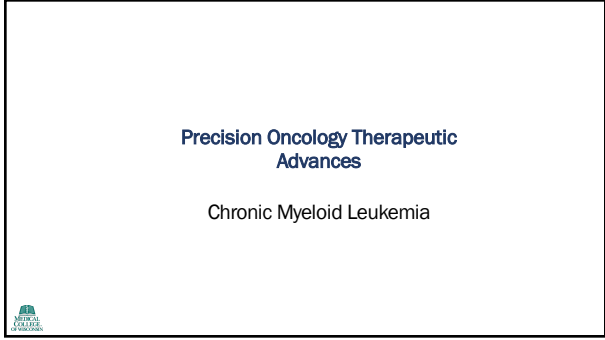
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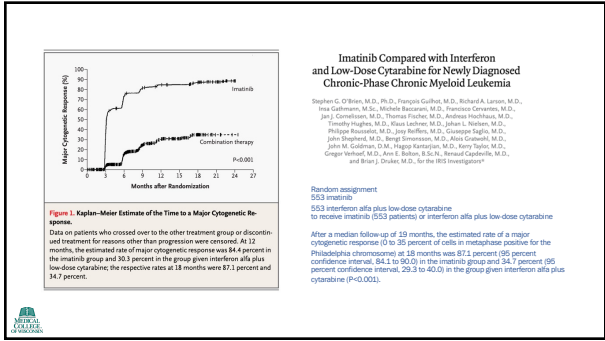
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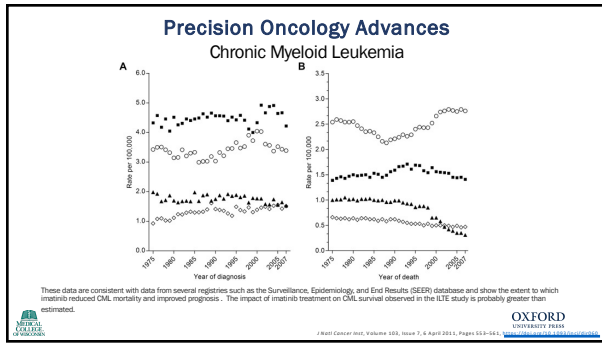
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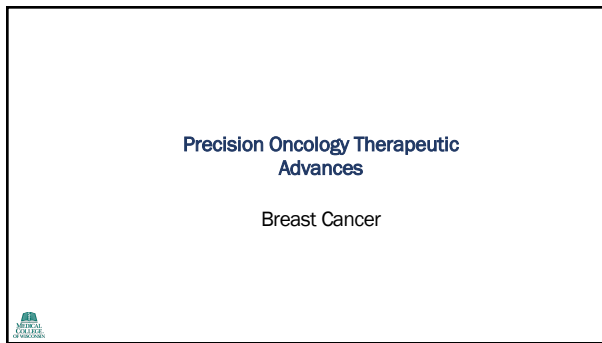
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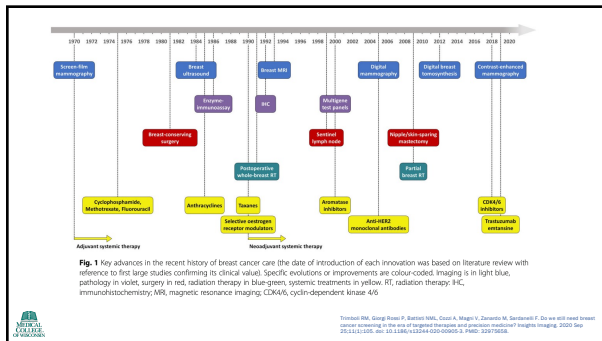
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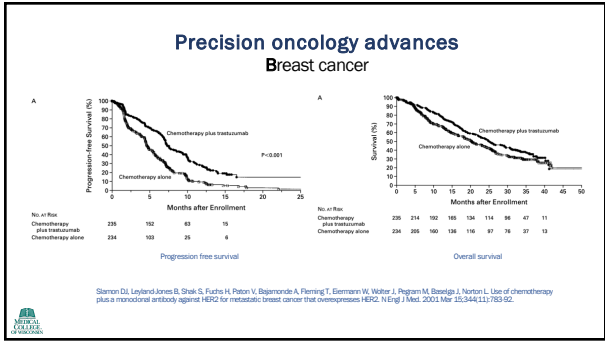
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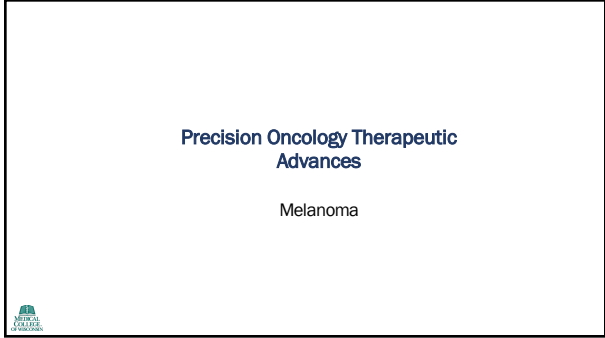
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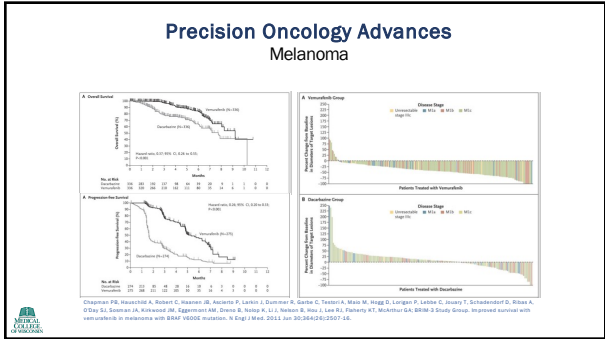
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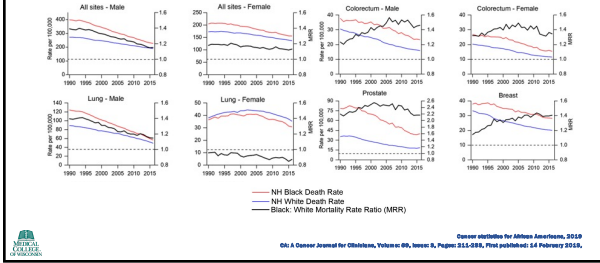
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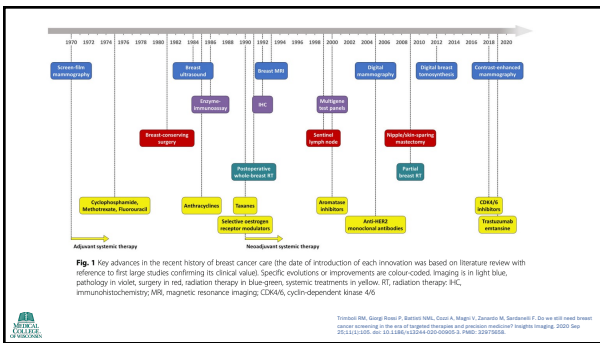
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### There is a persistent racial disparity in cancer mortality rate



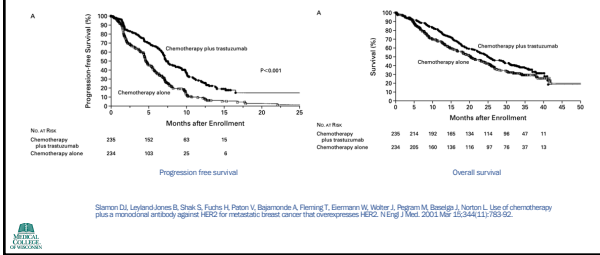
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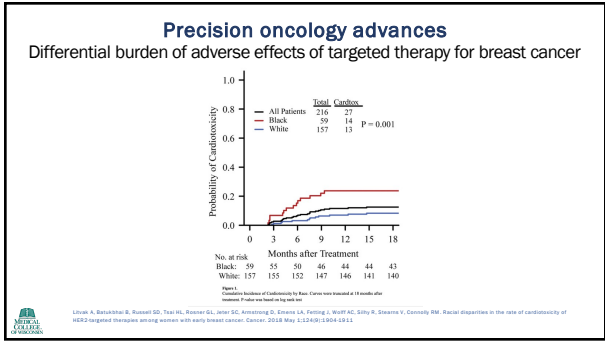


### Precision oncology advances Breast cancer



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*"Doctors have always recognized that every patient is unique, and doctors have always tried to tailor their treatments as best they can to individuals. You can match a blood transfusion to a blood type – that was an important discovery. What if matching a cancer cure to our genetic code was just as easy, just as standard? What if figuring out the right dose of medicine was as simple as taking our temperature?"*

- President Obama, January 30, 2015

<https://obamawhitehouse.archives.gov/precision-medicine>

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The strong push for inclusion also stems from the significant concern that underrepresented populations will be left behind as precision medicine research advances.

Collins RL. The Use of Racial Categories in Precision Medicine Research. *Ethn Dis.* 2019;29(5):947-91651-658. Published 2019 Dec 12.



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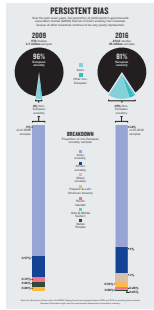
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Over the past decade, GWAS have been the preferred tool for discovering the genetic factors involved in common diseases. Tens of thousands of significant associations between genetic variants and biological traits have

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

Papayannis IG, Furlong SM. Genomics is failing on diversity. *Nature.* 2019 Oct 23;574(7624):161-164. doi: 10.1038/438181a. PMID: 31734877; PMCID: PMC6809702



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### Polygenic risk scores are not as applicable to underrepresented groups

#### Polygenic risk scores (PRS)

- predict complex traits using genetic data
- are of burgeoning interest to the clinical community as researchers demonstrate their growing power to improve clinical care, genetic studies of a wide range of phenotypes increase in size and power, and genotyping costs plummet to less than US\$50.
- Many earlier criticisms of limited prediction power are now recognized to have been chiefly an issue of insufficient sample size, which is no longer the case for many outcomes

**Underrepresentation of the people of African descent in the development cohorts mean that they are much less accurate in those patients. This is a major concern globally and especially in the U.S., which already leads other middle-and high-income countries in both real and perceived healthcare disparities**

Martin AR, Konecni 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.



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From the Field:  
Community Perspectives  
on Precision Medicine


**PERSPECTIVES ON PRECISION HEALTH  
AMONG RACIAL/ETHNIC MINORITY  
COMMUNITIES AND THE PHYSICIANS  
THAT SERVE THEM**

Lisa G. Rhee, PhD; Catherine Naranjo, MPH; Yui Tu Park, PhD, MPH;  
Jan J. Veque, MPH; Yuhel Datta, BA; Owen Garick, MD, MBA;  
Ricardo Harris, BA; Mildred Cho, PhD; Sean P. David, MD, SM, DPH;  
Jill Egan, MPH; Rhonda McClain-Brown, MPH; Christopher Martin, MD

300 community members who self-reported their race/ethnicity as American Indian (n=17), African American (n=13), Chinese (n=17), Latino (n=27), and Vietnamese (n=26), completed the survey and participated in the focus group discussions

Five cross-cutting themes were identified: 1) familiarity and attitudes toward precision health; 2) familiarity and attitudes toward genetic testing; 3) familiarity and attitudes toward precision medicine research; 4) concerns, sources of distrust and challenges; and 5) cultural norms and beliefs.

- knowledge of precision health is low in the racial/ethnic minority communities included
- some groups were enthusiastic about the approach, especially in as much as precision health considers influences on health in addition to genes (eg, environmental, behavioral, social factors).
- Significant concern was expressed by African American and American Indian participants about precision health practices and research based on past abuses in biomedical research



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**If your genes could be tested and a likelihood of future cancer determined, how high would the number have to be for you to act?**

Nobody has responded yet.  
Hang tight! Responses are coming in.

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**Does it depend on what the action would be?**

Major surgery	0%
Daily lifelong pill	0%
Having an inconvenient/uncomfortable test every year	0%

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Can we use precision medicine to PREVENT cancer?



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Video Example  
Grey's Anatomy  
S5:E17



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## Prophylactic gastrectomy is recommended for CDH1 variant carriers

Hereditary diffuse gastric cancer (HDGC) is an autosomal dominant cancer syndrome that is characterised by a high prevalence of diffuse gastric cancer and lobular breast cancer. It is largely caused by inactivating germline mutations in the tumour suppressor gene CDH1, although pathogenic variants in CTNNA1 occur in a minority of families with HDGC.

Prophylactic total gastrectomy remains the recommended option for gastric cancer risk management in pathogenic CDH1 variant carriers.

Blair VE, McLeod M, Carneiro F, Cox DG, Oshitori AL, van Den Broek JM, Harris KL, Hogenbrugge N, Oliveira C, van der Post RG, Arnold J, Bessing PG, Bessing TH, Bressanov A, Cote A, Clouston A, Schreiber AG, Grant JL, Parra MD, Fitzgerald RC, Fox JM, Gantner A, Gudi L, Lomenick RB, Karamian DG, Kauriah P, Kjafer SD, Laitinen A, Marshall FF, Nakajima T, Park S, Rissana J, Sugimura H, Szymon M, Tachibana M, Uehara T, Yamada N, Yang KH, Chapiro A, Figueiredo J, Figueiredo R, Serrano R, Saegert-Quaresima B, Breen T, Baraja S, Carreira S, Dominguez L, Foster R, Gantner S, Gatenby TD, Hesse M, Hunter B, Linton CJ, Moller EC, Muller MD, Nanni C, Nouri T, Pawlik J, Sanchez JM, Schaner C, Ribero AS, Spina A, Whitworth J, Zhang L, Zhou M, Guilford D. Hereditary diffuse gastric cancer: updated clinical practice guidelines. *Lancet Oncol*. 2019; **20**: 1032-1046.



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Opinion  
OP-ED CONTRIBUTOR  
**My Medical Choice**  
By Angelina Jolie  
May 14, 2013

Opinion  
OP-ED CONTRIBUTOR  
**Angelina Jolie Pitt: Diary of a Surgery**  
By Angelina Jolie Pitt  
March 21, 2015

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scientific reports

- The Angelina Jolie effect: Contralateral risk-reducing mastectomy trends in patients at increased risk of breast cancer
- Changes of socio-demographic data of clinic seeking genetic counseling for hereditary breast and ovarian cancer due to the "Angelina Jolie Effect"
- The Angelina Jolie effect: how high celebrity profile can have a major impact on provision of cancer related services
- Longer term effects of the Angelina Jolie effect: increased risk-reducing mastectomy rates in BRCA carriers and other high-risk women
- Are celebrity-associated cases in the US a clear manifestation of the Angelina Jolie effect?
- Evaluation of the "Angelina Jolie Effect" on Screening Mammography Utilization in an Academic Center

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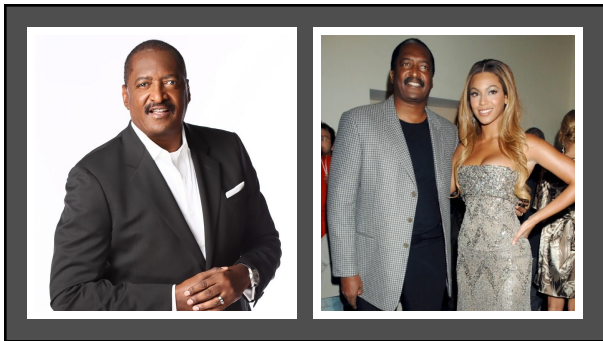
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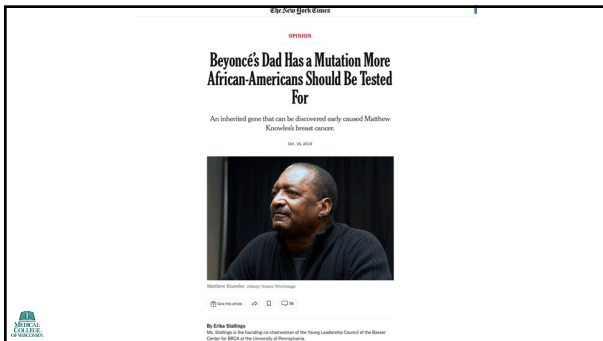
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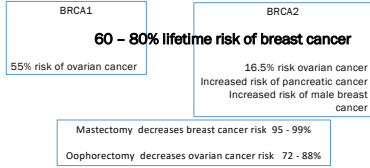
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## Risk reducing surgery should be considered for BRCA carriers



Lotheig KK, Neuman J, Butler A, Geurts JL, King AL. Risk reduction and survival benefit of prophylactic surgery in BRCA mutation carriers: a systematic review. *Am J Surg*. 2010 Oct;2(1):640-668.

Younis M, et al. Risk-reducing mastectomy in BRCA1 and BRCA2 mutation carriers: a systematic review. *Am J Surg*. 2010 Oct;2(1):640-668.



52

## Suggested Approaches to Care of Patients with Hereditary Breast and Ovarian Cancer Syndrome.

Issue	BRCA1 Carriers	BRCA2 Carriers	No Mutation Detected in Inverse Haplotype
<b>Reproductive options</b>	<p>ICSI may reduce transmission of mutation to offspring. For couples with a BRCA1 mutation, the risk of transmitting the mutation to offspring is 50% for each pregnancy. For couples with a BRCA2 mutation, the risk of transmitting the mutation to offspring is 50% for each pregnancy.</p>	<p>ICSI may reduce transmission of mutation to offspring. For couples with a BRCA2 mutation, the risk of transmitting the mutation to offspring is 50% for each pregnancy. For couples with a BRCA1 mutation, the risk of transmitting the mutation to offspring is 50% for each pregnancy.</p>	<p>ICSI may reduce transmission of mutation to offspring. For couples with a BRCA1 mutation, the risk of transmitting the mutation to offspring is 50% for each pregnancy. For couples with a BRCA2 mutation, the risk of transmitting the mutation to offspring is 50% for each pregnancy.</p>
<b>Prophylactic mastectomy</b>	<p>Consider prophylactic mastectomy. BRCA1 carriers have a 60-80% lifetime risk of breast cancer. Prophylactic mastectomy reduces this risk to 95-99%.</p>	<p>Consider prophylactic mastectomy. BRCA2 carriers have a 60-80% lifetime risk of breast cancer. Prophylactic mastectomy reduces this risk to 95-99%.</p>	<p>Consider prophylactic mastectomy. BRCA2 carriers have a 60-80% lifetime risk of breast cancer. Prophylactic mastectomy reduces this risk to 95-99%.</p>
<b>Ovarian cancer</b>	<p>BRCA1 carriers have a 55% lifetime risk of ovarian cancer. Prophylactic oophorectomy reduces this risk to 72-88%.</p>	<p>BRCA2 carriers have a 16.5% lifetime risk of ovarian cancer. Prophylactic oophorectomy reduces this risk to 72-88%.</p>	<p>BRCA2 carriers have a 16.5% lifetime risk of ovarian cancer. Prophylactic oophorectomy reduces this risk to 72-88%.</p>
<b>Prophylactic oophorectomy</b>	<p>Consider prophylactic oophorectomy. BRCA1 carriers have a 55% lifetime risk of ovarian cancer. Prophylactic oophorectomy reduces this risk to 72-88%.</p>	<p>Consider prophylactic oophorectomy. BRCA2 carriers have a 16.5% lifetime risk of ovarian cancer. Prophylactic oophorectomy reduces this risk to 72-88%.</p>	<p>Consider prophylactic oophorectomy. BRCA2 carriers have a 16.5% lifetime risk of ovarian cancer. Prophylactic oophorectomy reduces this risk to 72-88%.</p>
<b>Prophylactic salpingo-oophorectomy</b>	<p>Consider prophylactic salpingo-oophorectomy. BRCA1 carriers have a 55% lifetime risk of ovarian cancer. Prophylactic salpingo-oophorectomy reduces this risk to 72-88%.</p>	<p>Consider prophylactic salpingo-oophorectomy. BRCA2 carriers have a 16.5% lifetime risk of ovarian cancer. Prophylactic salpingo-oophorectomy reduces this risk to 72-88%.</p>	<p>Consider prophylactic salpingo-oophorectomy. BRCA2 carriers have a 16.5% lifetime risk of ovarian cancer. Prophylactic salpingo-oophorectomy reduces this risk to 72-88%.</p>
<b>Prophylactic hysterectomy</b>	<p>Consider prophylactic hysterectomy. BRCA1 carriers have a 55% lifetime risk of ovarian cancer. Prophylactic hysterectomy reduces this risk to 72-88%.</p>	<p>Consider prophylactic hysterectomy. BRCA2 carriers have a 16.5% lifetime risk of ovarian cancer. Prophylactic hysterectomy reduces this risk to 72-88%.</p>	<p>Consider prophylactic hysterectomy. BRCA2 carriers have a 16.5% lifetime risk of ovarian cancer. Prophylactic hysterectomy reduces this risk to 72-88%.</p>



53

## NATIONAL CANCER INSTITUTE THE CANCER GENOME ATLAS

### TCGA BY THE NUMBERS

TCGA produced over **2.5** PEBYTES of data

TCGA data describes **33** DIFFERENT TUMOR TYPES

TCGA data describes **10** RARE CANCERS

TCGA data describes **11,000** PATIENTS

TCGA data describes **7** DIFFERENT DATA TYPES

TCGA data describes **20** COLLABORATING INSTITUTIONS

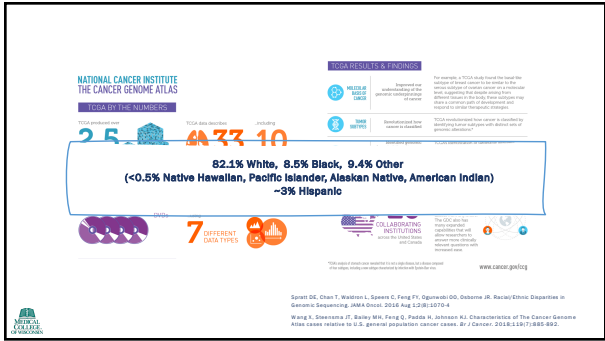
### TCGA RESULTS & FINDINGS

- WELL-TO-DO GENES**: Streamlined and standardized the genome cataloging of disease
- TUMOR SUBTYPES**: Reestablished how cancer is classified
- MARKER DRUGS**: Identified genetic characteristics of tumors that can be targeted with currently available drugs or used to help with drug development
- THE TEAM**: 20 COLLABORATING INSTITUTIONS across the United States
- WHAT'S NEXT?**: The Genome Data Commons (GDC) houses TCGA and other NCI approved data sets for research to advance cancer prevention, early detection, diagnosis, and treatment. The GDC also has many expanded capabilities that will allow researchers to answer more clinically relevant questions with increased ease.

TCGA's identification of targetable genomic alterations in lung squamous cell carcinoma led to TACT Lung 0101 Trial, which will test patients based on the specific genomic changes in their tumor.



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**What should be done to fix these disparities?**

Nobody has responded yet.  
Hang tight! Responses are coming in.

Start the presentation to see this content. For screen share software, share the entire screen. Get help at [puffin.com/opp](http://puffin.com/opp)

56

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**PROCLAIM**

**PROMoting CLinical Trial EngageMENT for  
Pancreatic Cancer App Study**

**MCW Surgery**  
*Knowledge changing life*

57

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## PROCLAIM

**01**

**DEVELOPMENT**


What do our patients need?



**02**

**TESTING**

Does this help achieve the goal?



**MCW Surgery**  
*knowledge changing life*

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58

## PROCLAIM: STUDY SCHEMA

Part 1

Consent and Screening<sup>1</sup>

↓

Interviews

↓

mHealth app Development

↓

Consent and Screening<sup>2</sup>

↓

mHealth app user testing

Part 2

Consent and Screening<sup>1</sup>

↓

Randomization (mHealth app vs control)

↓

Questionnaires and Interviews<sup>1</sup>

**MCW Surgery**  
*knowledge changing life*

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Thank you!

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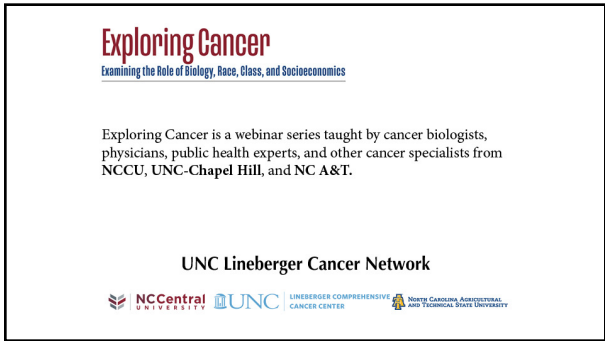
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**Exploring Cancer**  
 Examining the Role of Biology, Race, Class, and Socioeconomics  
 Upcoming Live Webinar

**Live Lecture**  
 November 17  
 11:00 AM

**Expanding Cancer Care Quality and Delivery In Sub-Saharan Africa: a collaborative approach**



**Ashley Leak Bryant,**  
PhD, RN, OCN, FAAN



**Benyam Mutneh,**  
PharmD, BCOP, CPP



**Jen Hotchkiss,**  
MSN, RN, OCN, CNL

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64

**Exploring Cancer**  
 Examining the Role of Biology, Race, Class, and Socioeconomics

**Thank you for participating!**

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