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

Learn more, register for courses, and sign up for our mailing list at **www.exploringcancer.org**

A collaboration between

NCCentral University | UNC Lineberger Comprehensive Cancer Center | North Carolina Agricultural and Technical State University

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Exploring Cancer

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

Fridays
11:00 - 11:50 AM EST/EDT

August 25
Welcome to Cancer(s) and Health Disparities 101 - The Introduction

September 1
Radiation Oncology - What Is It, and What Is It Good For?

September 8
New Strategies in Treating GI Cancers

October 13
Breast Cancer Health Disparities

October 20
Pancreatic Cancer

October 27
Careers in Cancer

November 10
Precision Medicine and Immunotherapy

November 17
Expanding Cancer Care Quality and Delivery in Sub-Saharan Africa: a collaborative approach

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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

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 Medicine and Immunotherapy
The next step in cancer care?

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

MCW Surgery
knowledge changing life

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Cancer Treatment

Surgery

Radiation

Chemotherapy

MCW Surgery
knowledge changing life

12

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.

Hang tight! Responses are coming in.

Start the presentation to see live content. For screen share software, share the entire screen. Get help at **pollev.com/app**

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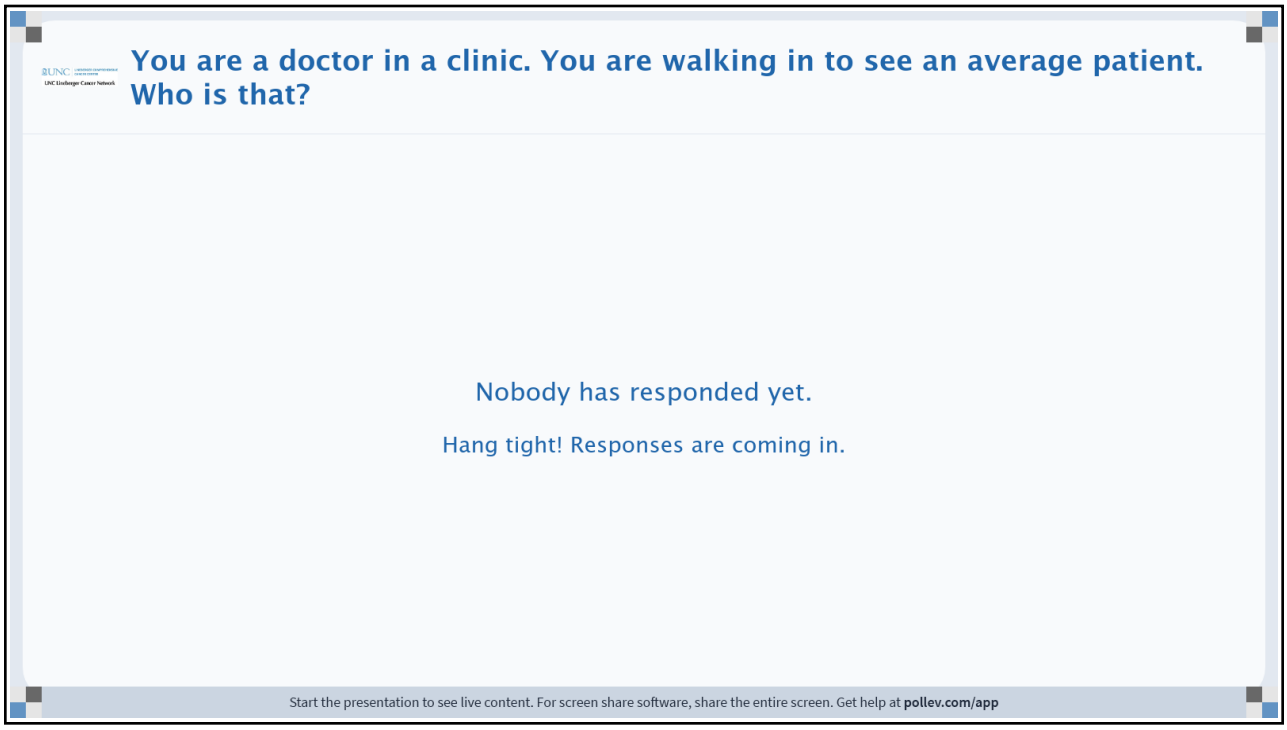
Centers for Disease Control

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

MCW Surgery
knowledge changing life

15

15



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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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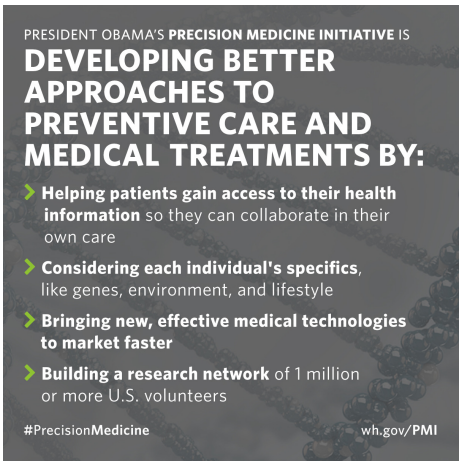

THE WHITE HOUSE

THE PRECISION MEDICINE INITIATIVE

January 20th, 2015 – Precision Medicine Initiative $216 million to sign up a million person cohort

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

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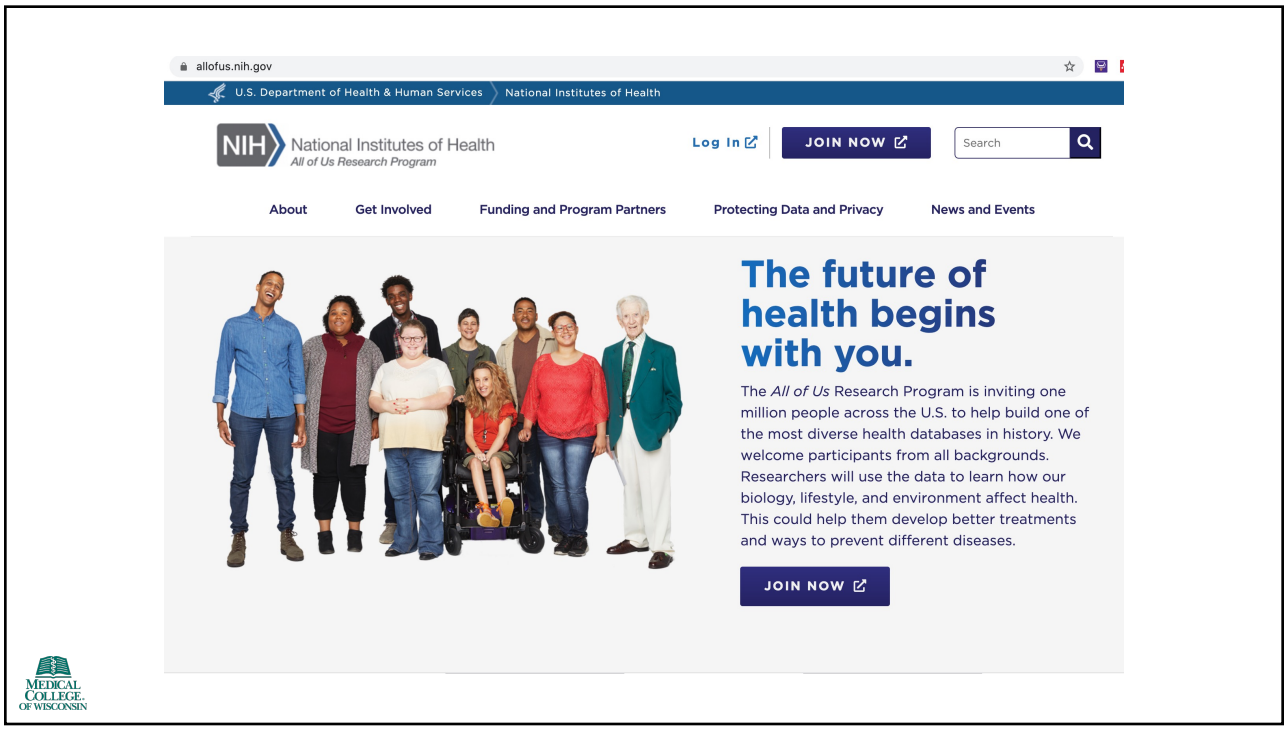

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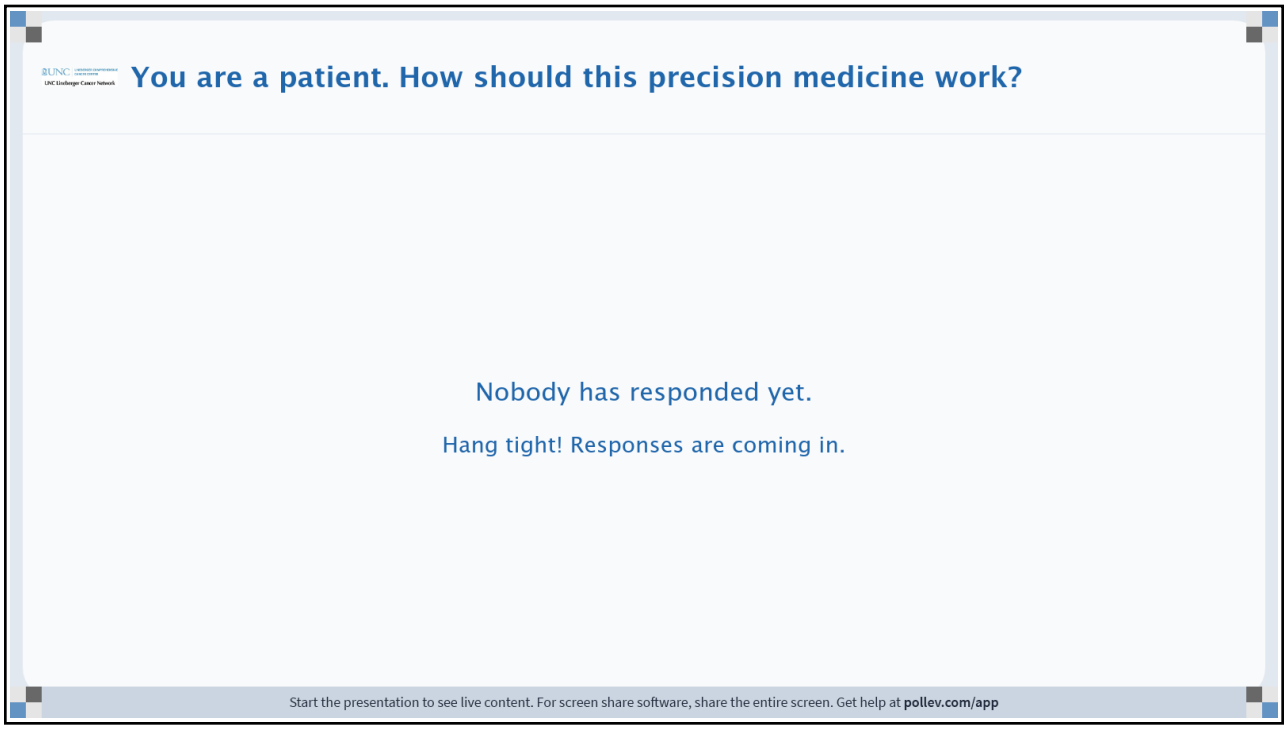

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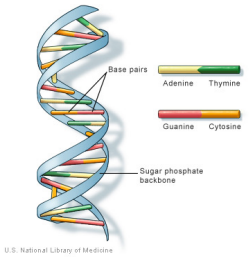
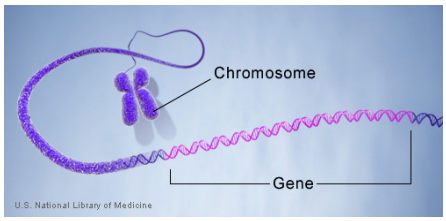
Glossary

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.nlm.nih.gov/primer/basics/gene
https://ghr.nlm.nih.gov/primer/genomicresearch/

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Video Example
Grey's Anatomy
S9:E15

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Precision Oncology Therapeutic Advances

Chronic Myeloid Leukemia

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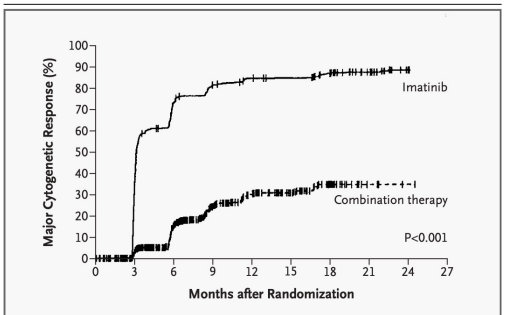

Figure 1. Kaplan–Meier Estimate of the Time to a Major Cytogenetic Response.

Data on patients who crossed over to the other treatment group or discontinued treatment for reasons other than progression were censored. At 12 months, the estimated rate of major cytogenetic response was 84.4 percent in the imatinib group and 30.3 percent in the group given interferon alfa plus low-dose cytarabine; the respective rates at 18 months were 87.1 percent and 34.7 percent.

Imatinib Compared with Interferon and Low-Dose Cytarabine for Newly Diagnosed Chronic-Phase Chronic Myeloid Leukemia

Stephen G. O'Brien, M.D., Ph.D., François Guilhot, M.D., Richard A. Larson, M.D., Insa Gathmann, M.Sc., Michele Baccarani, M.D., Francisco Cervantes, M.D., Jan J. Cornelissen, M.D., Thomas Fischer, M.D., Andreas Hochhaus, M.D., Timothy Hughes, M.D., Klaus Lechner, M.D., Johan L. Nielsen, M.D., Philippe Rousselot, M.D., Josy Reiffers, M.D., Giuseppe Saglio, M.D., John Shepherd, M.D., Bengt Simonsson, M.D., Alois Gratwohl, M.D., John M. Goldman, D.M., Hagop Kantarjian, M.D., Kerry Taylor, M.D., Gregor Verhoef, M.D., Ann E. Bolton, B.Sc.N., Renaud Capdeville, M.D., and Brian J. Druker, M.D., for the IRIS Investigators*

Random assignment
553 imatinib
553 interferon alfa plus low-dose cytarabine
to receive imatinib (553 patients) or interferon alfa plus low-dose cytarabine

After a median follow-up of 19 months, the estimated rate of a major cytogenetic response (0 to 35 percent of cells in metaphase positive for the Philadelphia chromosome) at 18 months was 87.1 percent (95 percent confidence interval, 84.1 to 90.0) in the imatinib group and 34.7 percent (95 percent confidence interval, 29.3 to 40.0) in the group given interferon alfa plus cytarabine (P<0.001).

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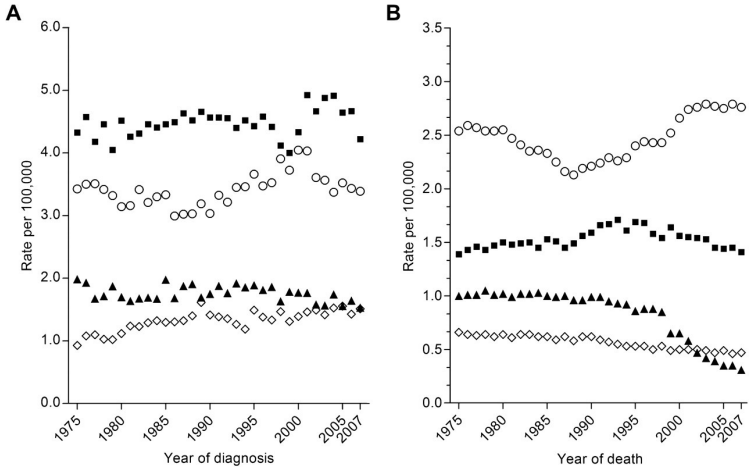
Precision Oncology Advances

Chronic Myeloid Leukemia



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.

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OXFORD UNIVERSITY PRESS

J Natl Cancer Inst, Volume 103, Issue 7, 6 April 2011, Pages 553–561, https://doi.org/10.1093/jnci/djr060

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Precision Oncology Therapeutic Advances

Breast Cancer

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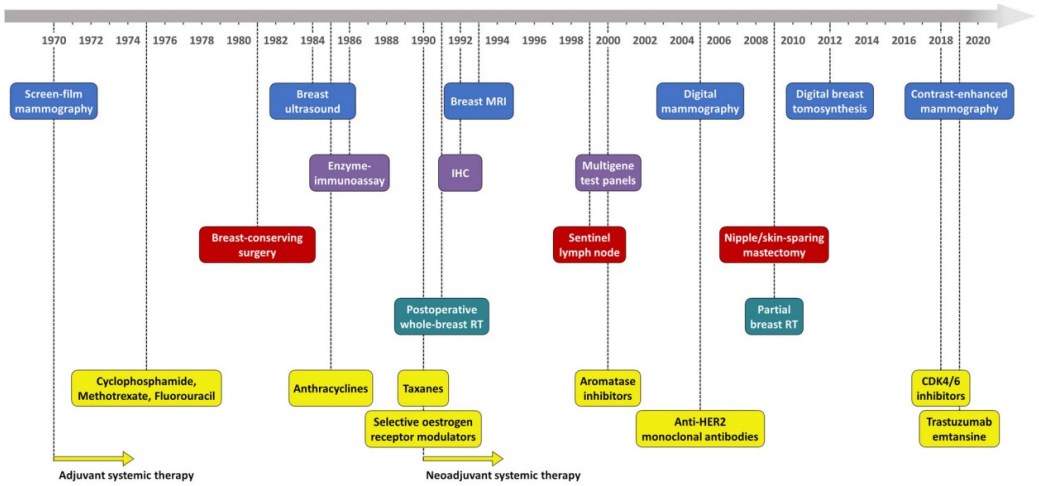

Fig. 1 Key advances in the recent history of breast cancer care (the date of introduction of each innovation was based on literature review with reference to first large studies confirming its clinical value). Specific evolutions or improvements are colour-coded. Imaging is in light blue, pathology in 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

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Trimboli RM, Giorgi Rossi P, Battisti NML, Cozzi A, Magni V, Zanardo M, Sardanelli 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.

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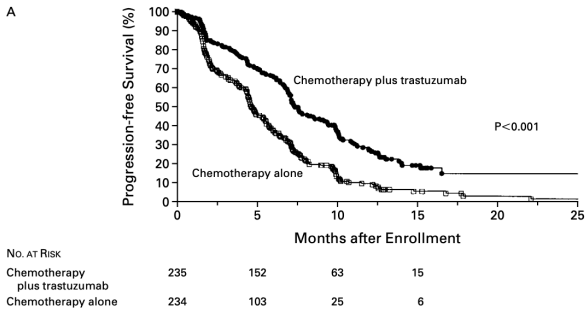
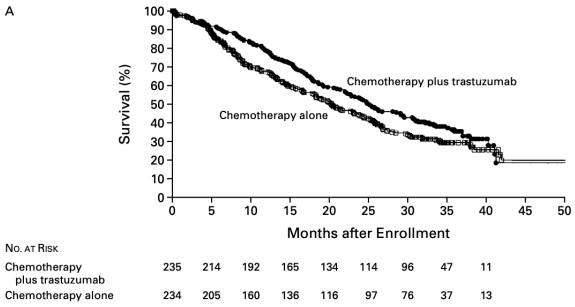
Precision oncology advances

Breast cancer



Progression free survival



Overall survival

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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Precision Oncology Therapeutic Advances

Melanoma

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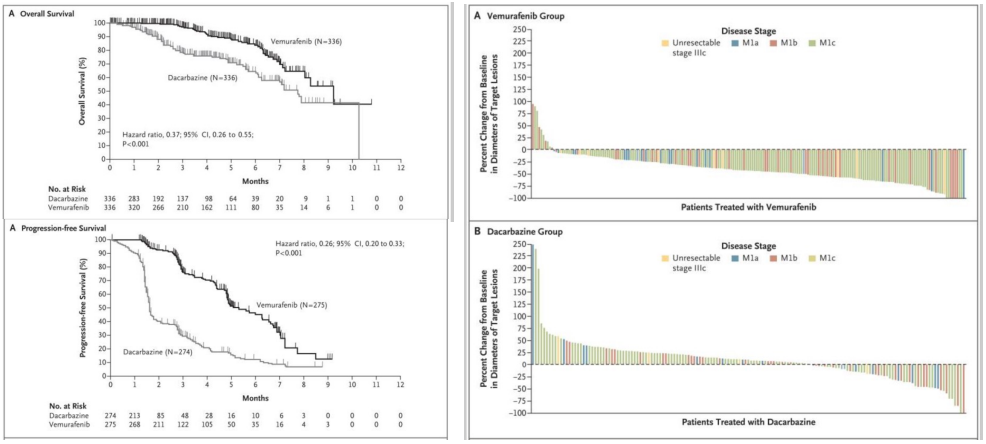
Precision Oncology Advances

Melanoma



Chapman PB, Hauschild A, Robert C, Haanen JB, Ascierto P, Larkin J, Dummer R, Garbe C, Testori A, Maio M, Hogg D, Lorigan P, Lebbe C, Jouary T, Schadendorf D, Ribas A, O'Day SJ, Sosman JA, Kirkwood JM, Eggermont AM, Dreno B, Nolop K, Li J, Nelson B, Hou J, Lee RJ, Flaherty KT, McArthur GA; BRIM-3 Study Group. Improved survival with vemurafenib in melanoma with BRAF V600E mutation. N Engl J Med. 2011 Jun 30;364(26):2507-16.

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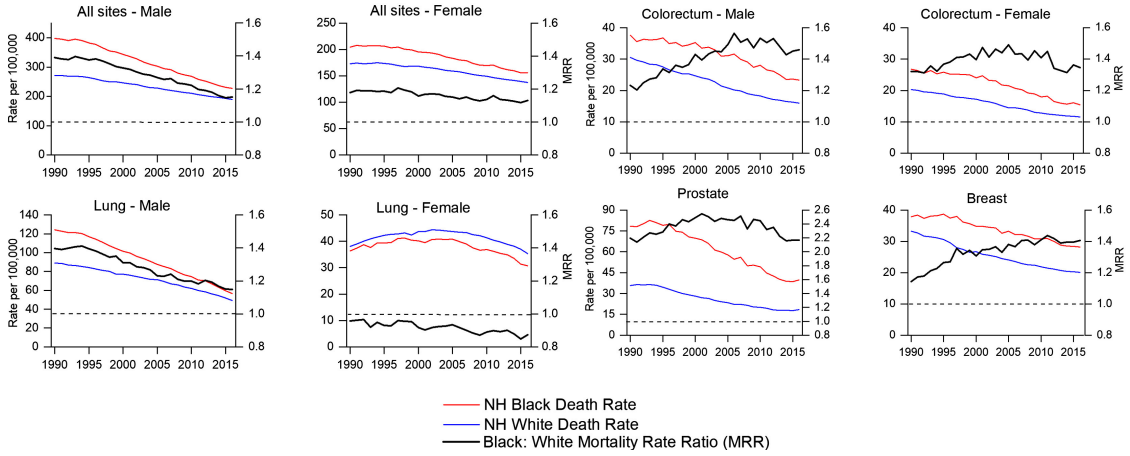
There is a persistent racial disparity in cancer mortality rate



Medical College of Wisconsin

Cancer statistics for African Americans, 2019
CA: A Cancer Journal for Clinicians, Volume: 69, Issue: 3, Pages: 211-233, First published: 14 February 2019,

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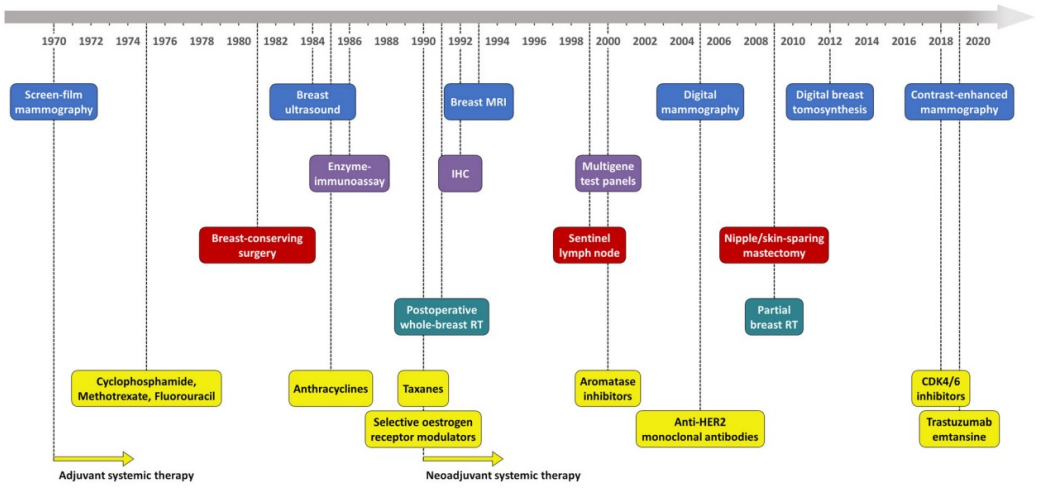

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Medical College of Wisconsin

Trimboli RM, Giorgi Rossi P, Battisti NML, Cozzi A, Magni V, Zanardo M, Sardanelli 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.

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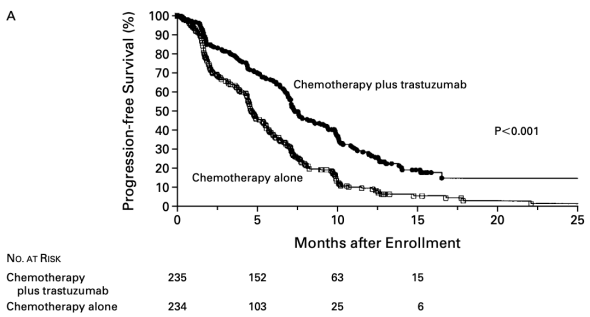
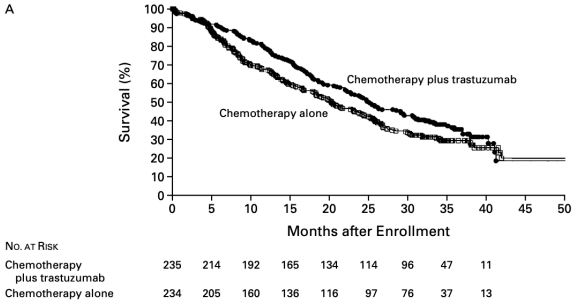
Precision oncology advances

Breast cancer



Progression free survival



Overall survival

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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Precision oncology advances

Differential burden of adverse effects of targeted therapy for breast cancer

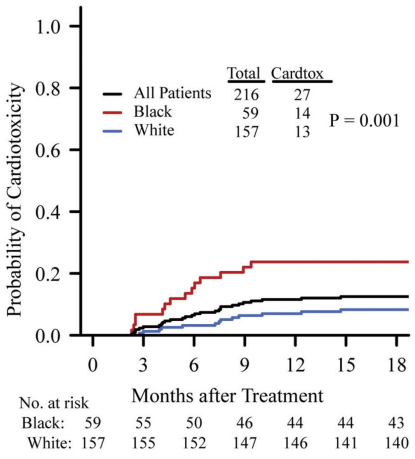

Figure 1.
Cumulative Incidence of Cardiotoxicity by Race. Curves were truncated at 18 months after treatment. P-value was based on log rank test

Litvak A, Batukbhai 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

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Equity

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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"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

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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.

Callier SL. The Use of Racial Categories in Precision Medicine Research. *Ethn Dis*. 2019;29(Suppl 3):651-658. Published 2019 Dec 12.

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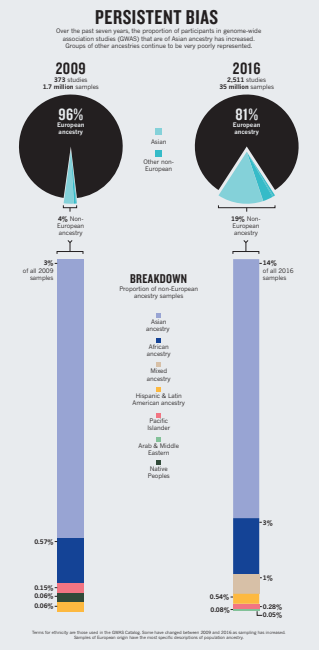

Over the past decade, GWAS have been the preferred tool for discovering the genetic factors involved in common diseases. Tens of thousands of significant associations between genetic variants and biological traits have

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

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.

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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 outcome

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

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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.

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Trust is an issue

From the Field: Community Perpspectives on Precision Medicine

Perspectives on Precision Health Among Racial/Ethnic Minority Communities and the Physicians That Serve Them

Lisa G. Rosas,PhD[1]; Catherine Nasrallah, MPH[2]; Van Ta Park, PhD, MPH[3]; Jan J. Vasquez, MPH[4]; Ysabel Duron, BA[5]; Owen Garrick, MD, MBA[6]; Riccesha Hattin, BA[6]; Mildred Cho, PhD[7]; Sean P. David, MD, SM, DPhil[8]; Jill Evans, MPH[9]; Rhonda McClinton-Brown, MPH[10]; Christopher Martin, MS[11]

100 community members who self-reported their race/ ethnicity as American Indian (n=17), African American (n=13), Chinese (n=17), Latino (n=27), and Viet-namese (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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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 VR, McLeod M, Carneiro F, Coit DG, D'Addario JL, van Dieren JM, Harris KL, Hoogerbrugge N, Oliveira C, van der Post RS, Arnold J, Benusiglio PR, Bisseling TM, Boussioutas A, Cats A, Charlton A, Schreiber KEC, Davis JL, Pietro MD, Fitzgerald RC, Ford JM, Gamet K, Gullo I, Hardwick RH, Huntsman DG, Kaurah P, Kupfer SS, Latchford A, Mansfield PF, Nakajima T, Parry S, Rossaak J, Sugimura H, Svrcek M, Tischkowitz M, Ushijima T, Yamada H, Yang HK, Claydon A, Figueiredo J, Paringatai K, Seruca R, Bougen-Zhukov N, Brew T, Busija S, Carneiro P, DeGregorio L, Fisher H, Gardner E, Godwin TD, Holm KN, Humar B, Lintott CJ, Monroe EC, Muller MD, Norero E, Nouri Y, Paredes J, Sanches JM, Schulpen E, Ribeiro AS, Sporle A, Whitworth J, Zhang L, Reeve AE, Guilford P. Hereditary diffuse gastric cancer: updated clinical practice guidelines. Lancet Oncol. 2020 Aug;21(8):e386-e397

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The New York Times May 15, 2013

Oli Scarff/Getty Images

Angelina Jolie underwent a preventive double mastectomy.

Close Window

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 24, 2015

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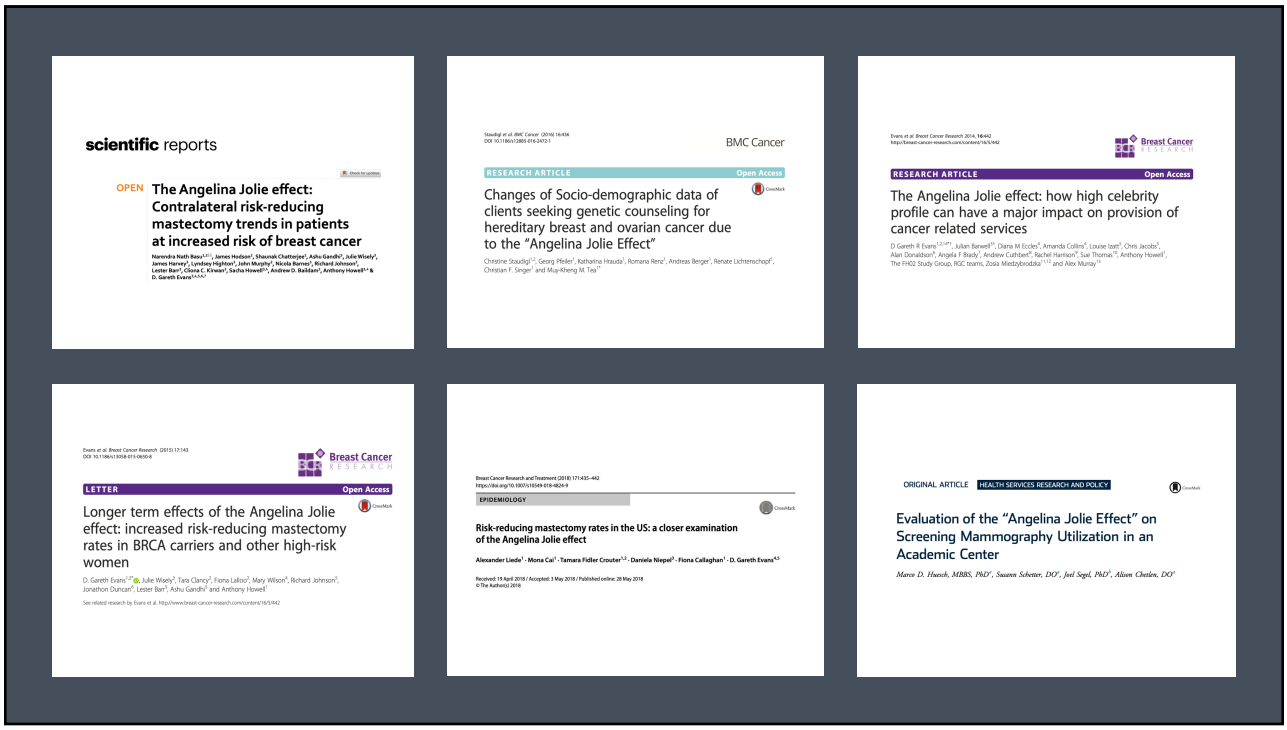

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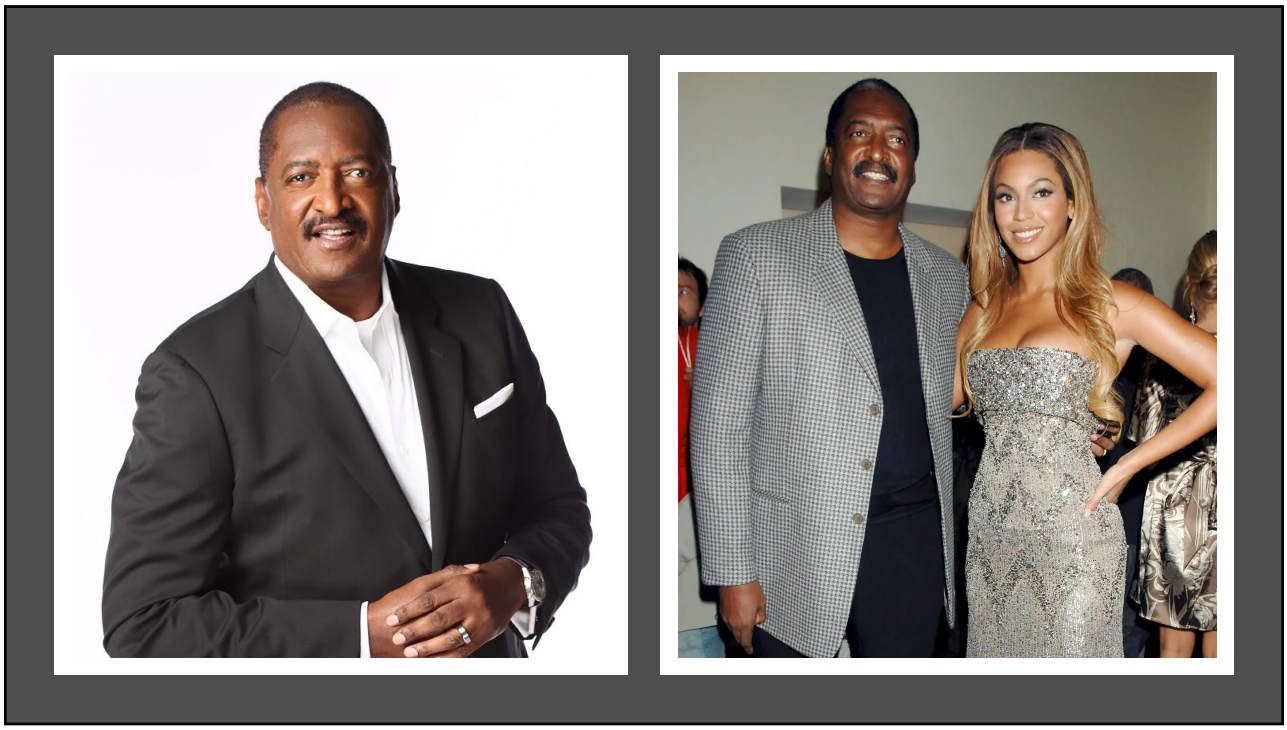

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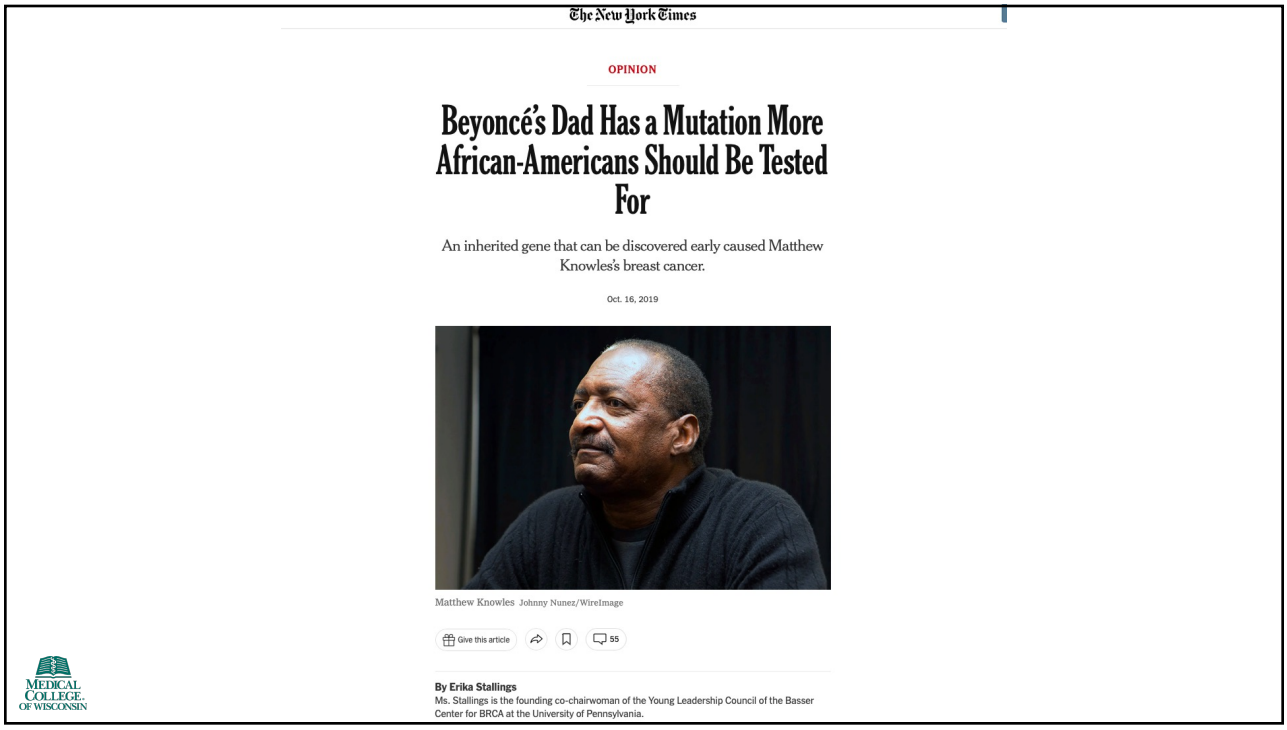

The New York Times

OPINION

Beyoncé's Dad Has a Mutation More African-Americans Should Be Tested For

An inherited gene that can be discovered early caused Matthew Knowles's breast cancer.

Oct. 16, 2019

Matthew Knowles Johnny Nunez/WireImage

Give this article 55

By Erika Stallings
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Risk reducing surgery should be considered for BRCA carriers

BRCA1

55% risk of ovarian cancer

BRCA2

16.5% risk ovarian cancer
Increased risk of pancreatic cancer
Increased risk of male breast cancer

60 – 80% lifetime risk of breast cancer

Mastectomy decreases breast cancer risk 95 - 99%

Oophorectomy decreases ovarian cancer risk 72 - 88%

Ludwig KK, Neuner J, Butler A, Geurts JL, Kong AL. Risk reduction and survival benefit of prophylactic surgery in BRCA mutation carriers, a systematic review. Am J Surg. 2016 Oct;212(4):660-669.

Nasim Mavaddat, Susan Peock, Debra Frost, Steve Ellis, Radka Platte, Elena Fineberg, D. Gareth Evans, Louise Izatt, Rosalind A. Eeles, Julian Adlard, Rosemarie Davidson, Diana Eccles, Trevor Cole, Jackie Cook, Carole Brewer, Marc Tischkowitz, Fiona Douglas, Shirley Hodgson, Lisa Walker, Mary E. Porteous, Patrick J. Morrison, Lucy E. Side, M. John Kennedy, Catherine Houghton, Alan Donaldson, Mark T. Rogers, Huw Dorkins, Zosia Miedzybrodzka, Helen Gregory, Jacqueline Eason, Julian Barwell, Emma McCann, Alex Murray, Antonis C. Antoniou, Douglas F. Easton, on behalf of EMBRACE, Cancer Risks for *BRCA1* and *BRCA2* Mutation Carriers: Results From Prospective Analysis of EMBRACE , *JNCI: Journal of the National Cancer Institute*, Volume 105, Issue 11, 5 June 2013, Pages 812–822

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

Table 3. Suggested Approaches to Care of Patients with Hereditary Breast and Ovarian Cancer Syndrome.*

Focus and Approach	*BRCA1* Carriers	*BRCA2* Carriers	No Mutation Detected in Known Predisposing Genes
Breast cancer in women			
Surveillance	NCCN[34] guidelines recommend breast "awareness" starting at age 18 yr; clinical breast examination, every 6–12 mo, starting at age 25 yr; ages 25–29 yr: annual MRI (preferred) or mammography if MRI unavailable; ages 30–75 yr: annual mammography and MRI; >75 yr: individualized care	NCCN[34]guidelines recommend breast "awareness" starting at age 18 yr; clinical breast examination, every 6–12 mo, starting at age 25 yr; ages 25–29 yr: annual MRI (preferred) or mammography if MRI unavailable; ages 30–75 yr: annual mammography and MRI; >75 yr: individualized care	Annual breast MRI with mammography recommended for lifetime risk >20–25%, starting 5–10 yr before youngest age of diagnosis of breast cancer in family
Risk-reducing medication†	Inadequate data to support its use	Option, given anticipated 50% risk reduction in ER-positive breast cancers[63]	Option, given anticipated 50% risk reduction in ER-positive breast cancers[35]
Risk-reducing mastectomy	Given the often aggressive high-grade, ER-negative nature of breast cancers and uncertain benefit of chemoprevention, surgical prevention may be given higher priority than surveillance	Option for women who prefer surgical risk reduction rather than surveillance and chemoprevention	Consider on a case-by-case basis, informed by risk estimates
Ovarian cancer			
Surveillance	NCCN guidelines do not endorse routine screening with transvaginal ultrasonography and measurement of serum CA-125 levels. Not to be considered a reasonable substitute for risk-reducing salpingo-oophorectomy in *BRCA1* and *BRCA2* carriers. In women who delay risk-reducing salpingo-oophorectomy, these approaches may be considered, starting at age 30–35 yr[34]	NCCN guidelines do not endorse routine screening with transvaginal ultrasonography and measurement of serum CA-125 levels. Not to be considered a reasonable substitute for risk-reducing salpingo-oophorectomy in *BRCA1* and *BRCA2* carriers. In women who delay risk-reducing salpingo-oophorectomy, these approaches may be considered, starting at age 30–35 yr[34]	Not indicated
Risk-reducing medication	No prospective trials; observational studies of oral contraceptives are consistent with 40–50% reduction in risk[64,65]	No prospective trials; observational studies of oral contraceptives are consistent with 40–50% reduction in risk[64,65]	Oral contraceptives may reduce risk; may be relevant in families with ovarian-cancer history
Risk-reducing salpingo-oophorectomy	Recommended by age 40 yr	Recommended by age 45–50 yr	Consider on a case-by-case basis, informed by risk estimates and new genetic information
Breast cancer in men			No evidence of increased risk
Surveillance	NCCN guidelines recommend training in breast self-examination and initiation of annual clinical breast examinations starting at age 35 yr[34]	NCCN guidelines recommend training in breast self-examination and initiation of annual clinical breast examinations starting at age 35 yr[34]	Not indicated
Risk-reducing mastectomy	Given that risk of male breast cancer among *BRCA1* carriers is lower than that among average-risk women, risk-reducing mastectomy is not recommended	Given that risk of male breast cancer among *BRCA2* carriers is lower than that among average-risk women, risk-reducing mastectomy is not recommended	Not indicated

* The suggested approaches are those of the authors unless otherwise indicated. ER denotes estrogen receptor, and MRI magnetic resonance imaging.
† Risk-reducing medications are tamoxifen for premenopausal women and tamoxifen or an aromatase inhibitor for postmenopausal women.

Hartmann LC, Lindor NM. N Engl J Med 2016;374:454-468.

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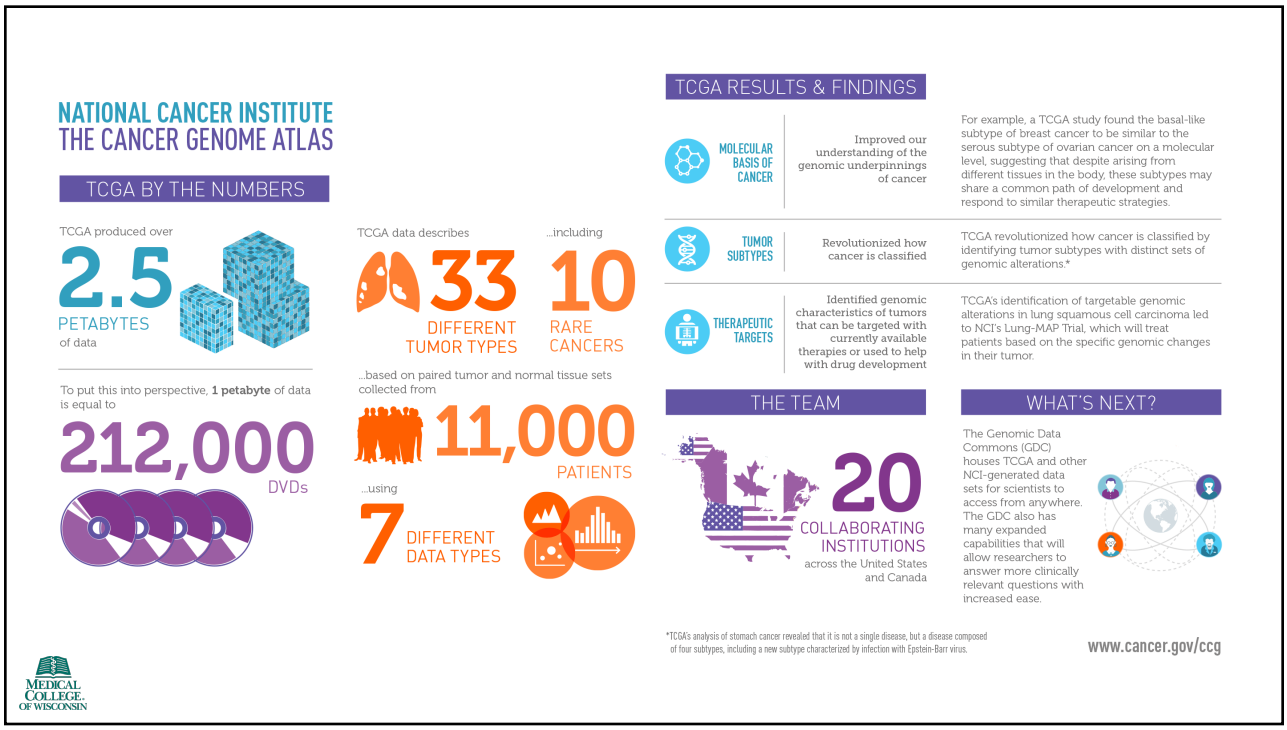

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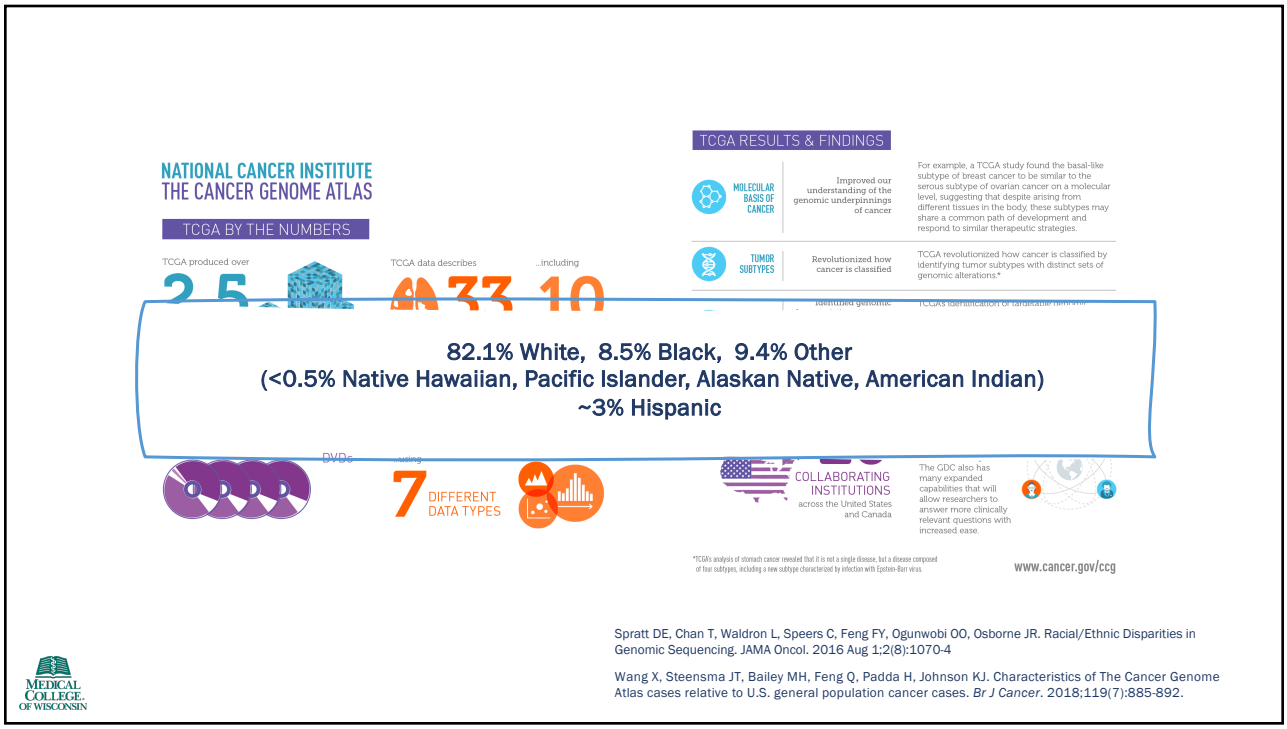

Spratt DE, Chan T, Waldron L, Speers C, Feng FY, Ogunwobi OO, Osborne JR. Racial/Ethnic Disparities in Genomic Sequencing. JAMA Oncol. 2016 Aug 1;2(8):1070-4

Wang X, Steensma JT, Bailey MH, Feng Q, Padda H, Johnson KJ. Characteristics of The Cancer Genome Atlas cases relative to U.S. general population cancer cases. *Br J Cancer*. 2018;119(7):885-892.

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PROCLAIM

PROmoting CLinicAl TrIal EngageMent for Pancreatic Cancer App Study

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PROCLAIM

01

DEVELOPMENT

What do our patients need?

02

TESTING

Does this help achieve the goal?

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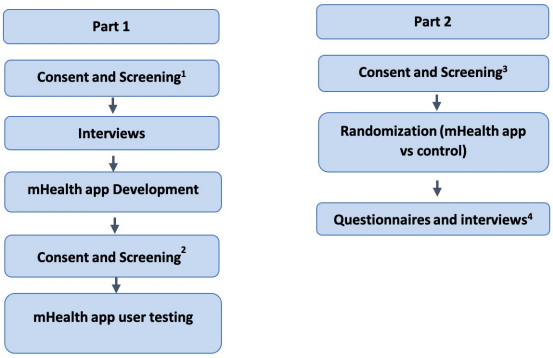
PROCLAIM: STUDY SCHEMA



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Benyam Muluneh,
PharmD., BCOP, CPP

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MSN, RN, OCN, CNL

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Exploring Cancer

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