

Informing Cancer Equity with Globally Diverse Data

ICAP-HICCC Cancer Initiative Webinar Series

July 5, 2023



HERBERT IRVING COMPREHENSIVE
CANCER CENTER

 COLUMBIA  NewYork-Presbyterian

Agenda

Welcome and Introduction

Wafaa El-Sadr, MD, MPH, MPA

Founder and Global Director
ICAP at Columbia University

Informing Cancer Equity with Globally Diverse Data

Timothy R. Rebbeck, PhD

Vincent L. Gregory Professor of Cancer Prevention
Harvard TH Chan School of Public Health and the Dana-Farber Cancer Institute

Q&A and Discussion

Reminders:

For questions to the speakers, please **use the Q&A box**

Please use **chat box** to indicate your name and organization

The webinar recording and slides will be posted on **www.icap.columbia.edu**

ICAP at Columbia University and the Herbert Irving Comprehensive Cancer Center (HICCC)

A major global health organization that has been improving public health in countries around the world for nearly two decades, **ICAP at Columbia University** works to transform the health of populations through innovation, science, and global collaboration.

The Herbert Irving Comprehensive Cancer Center (HICCC) is the home for cancer research and patient care at Columbia University and NewYork-Presbyterian/Columbia University Irving Medical Center.

Launched in January 2021, **The ICAP-HICCC Cancer Initiative (IHCI)** aims to advance training, research, education, and programs focused on cancer diagnosis prevention and management in low and middle-income countries.

Timothy R. Rebbeck, PhD

Professor Rebbeck studies the etiology and prevention of cancer, with an emphasis on cancer disparities and global health. He has directed large, multicenter studies and international consortia that have identified genetic, molecular, and epidemiological factors associated with cancer risk, outcomes, and disparities.

He leads the international Men of African Descent and Carcinoma of the Prostate (MADCaP) network and has led several consortia studying hereditary cancer risk and prevention. Dr. Rebbeck has received continuous federal research funding since 1994.

In addition to his research activities, Professor Rebbeck leads a number of initiatives on the Harvard Campus. He serves as Associate Director for Cancer Equity and Engagement in the Dana-Farber / Harvard Cancer Center. He is the founding director of the Zhu Family Center for Cancer Prevention at the Harvard TH Chan School of Public Health and Director for the Center for Global Health at Dana-Farber Cancer Institute.

In these roles, he fosters a variety of cancer research and educational activities to ensure that Harvard research engages with and positively impacts communities with the greatest disease burden worldwide.





Dana-Farber
Cancer Institute

Informing Cancer Equity with Globally Diverse Data

Timothy Rebbeck, PhD



HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH



ZHU FAMILY
CENTER FOR GLOBAL
CANCER PREVENTION



BROAD
INSTITUTE

Why Focus on Cancer in Africa?

“Creation of knowledge has been central to advancement of health in the 20th century and is critical for improved global health” (Julio Frenk)

Knowledge:

- Gets translated into appropriate technology (drugs, diagnosis, prevention, etc.).
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- Is the basis for health policy: Can guide decision makers, who can be convinced of what can and should be done when good data exist.



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 - Can be social and economic drivers (and disruptors):
 - Health status of a population relates to security, economic development, social development, etc.
 - Democratizing Expertise
 - Leapfrogging Technology
 - Fosters innovation and investment
 - Can stem brain drain
 - Becoming increasingly feasible due to lower costs and accessibility



Why Focus on Cancer in Africa?

Semper aliquid novi Africam adferre.

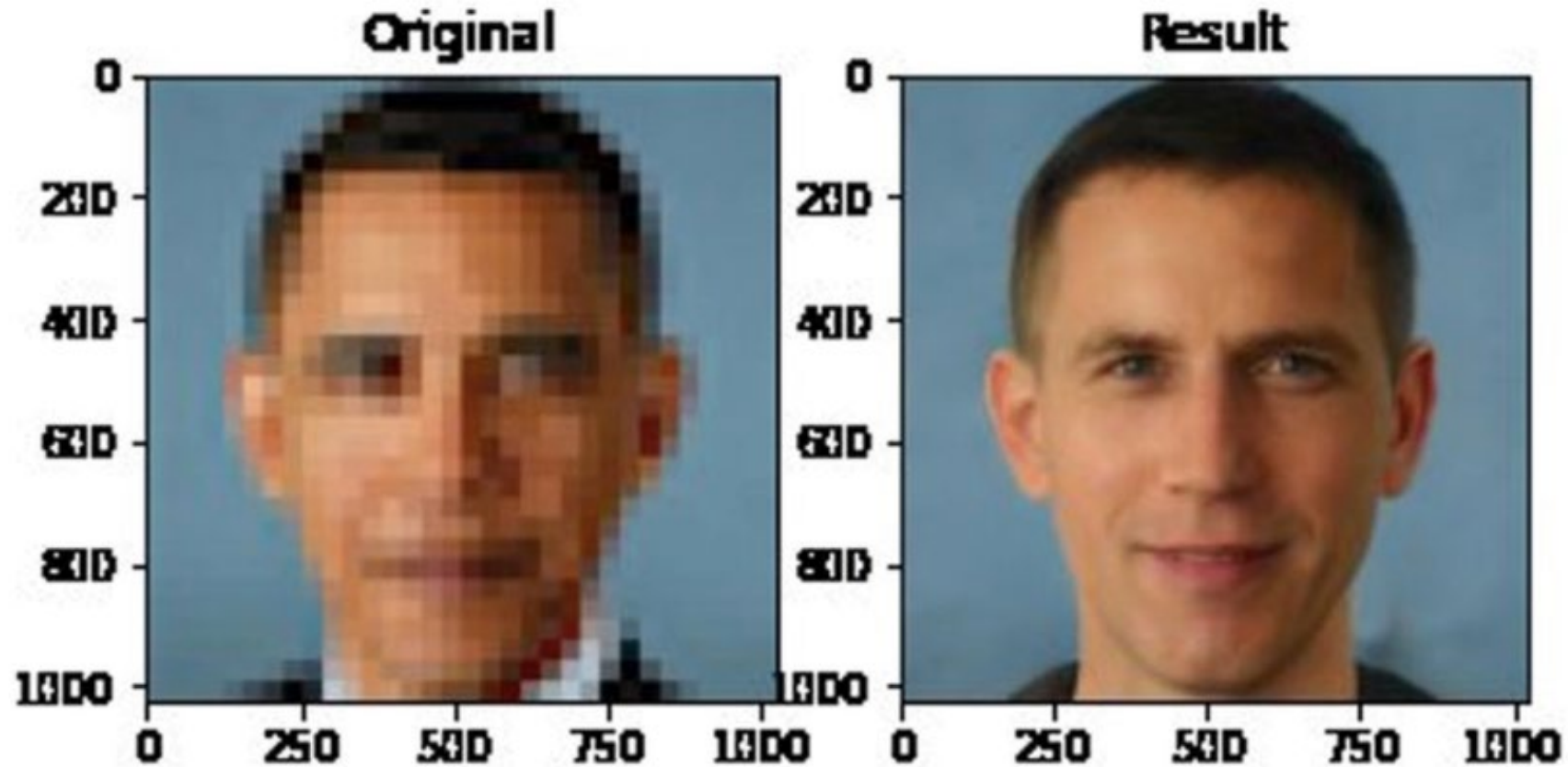
(Africa always brings [us] something new.)

Pliny the Elder, *Historia Naturalis*, Book 8, sect. 42

- We can learn from Africa:
 - Unique variation in risk and phenotype
 - Unique disease etiology and natural history
 - Ability to understand disease across the African diaspora
 - Diverse data informs disease globally



Why Do We Need Data Diversity?



The *PULSE* algorithm. <https://github.com/tg-bomze/Face-Depixelizer>



Diverse Research Data Improves Disease Management for All Populations

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Genetic Misdiagnoses and the Potential for Health Disparities

Arjun K. Manrai, Ph.D., Birgit H. Funke, Ph.D., Heidi L. Rehm, Ph.D., Morten S. Olesen, Ph.D., Bradley A. Maron, M.D., Peter Szolovits, Ph.D., David M. Margulies, M.D., Joseph Loscalzo, M.D., Ph.D., and Isaac S. Kohane, M.D., Ph.D.

N Engl J Med 2016; 375:655-665

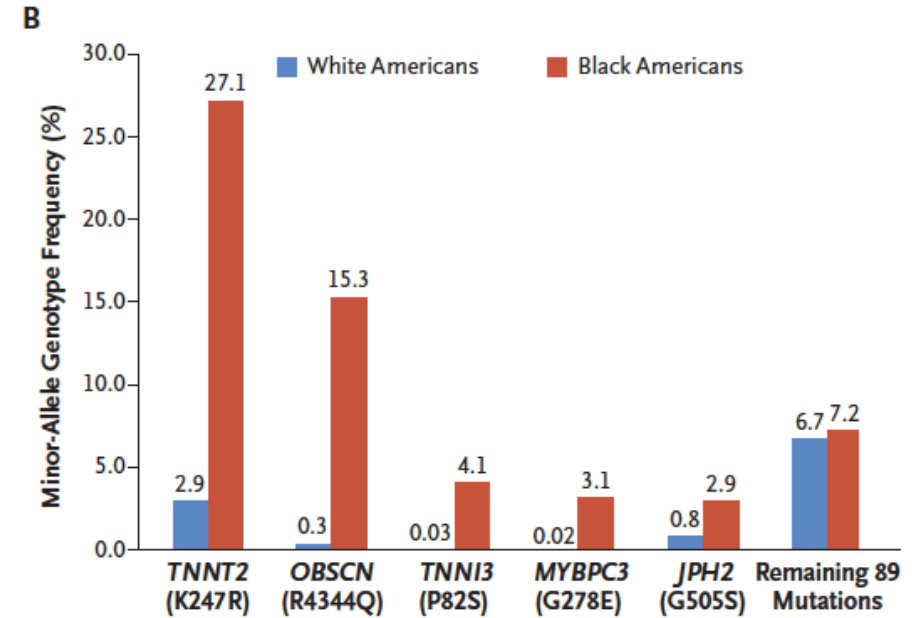
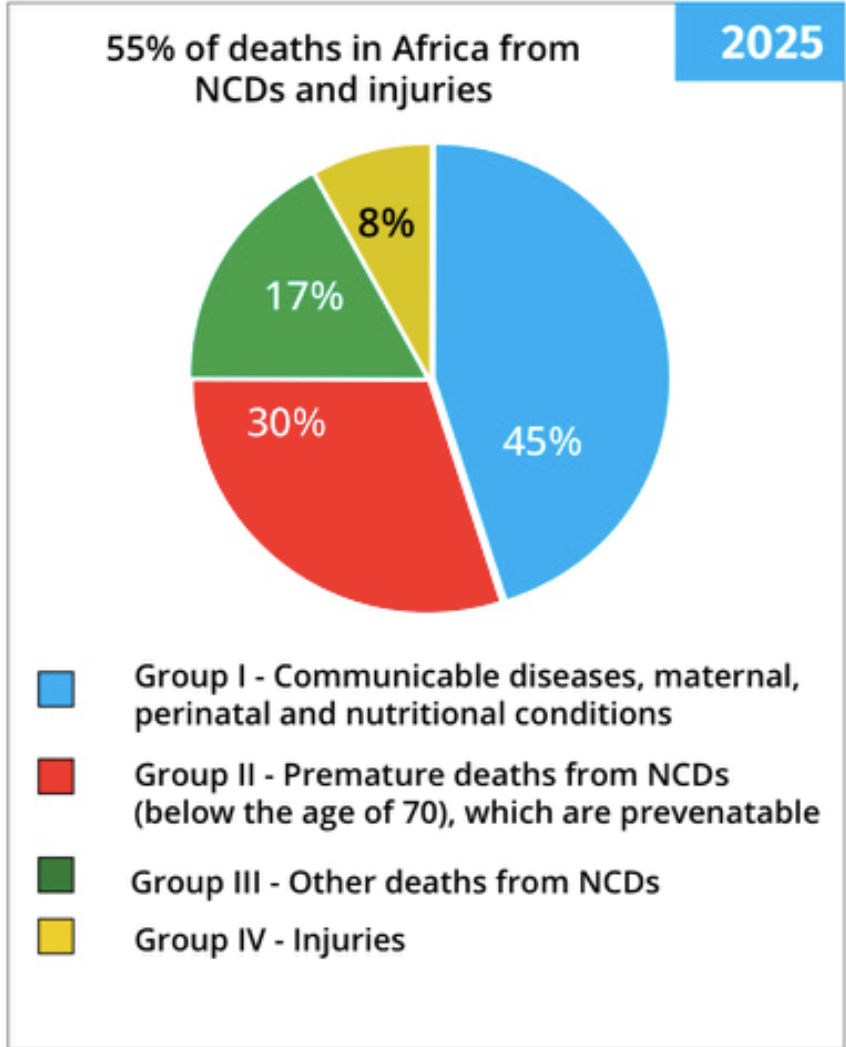
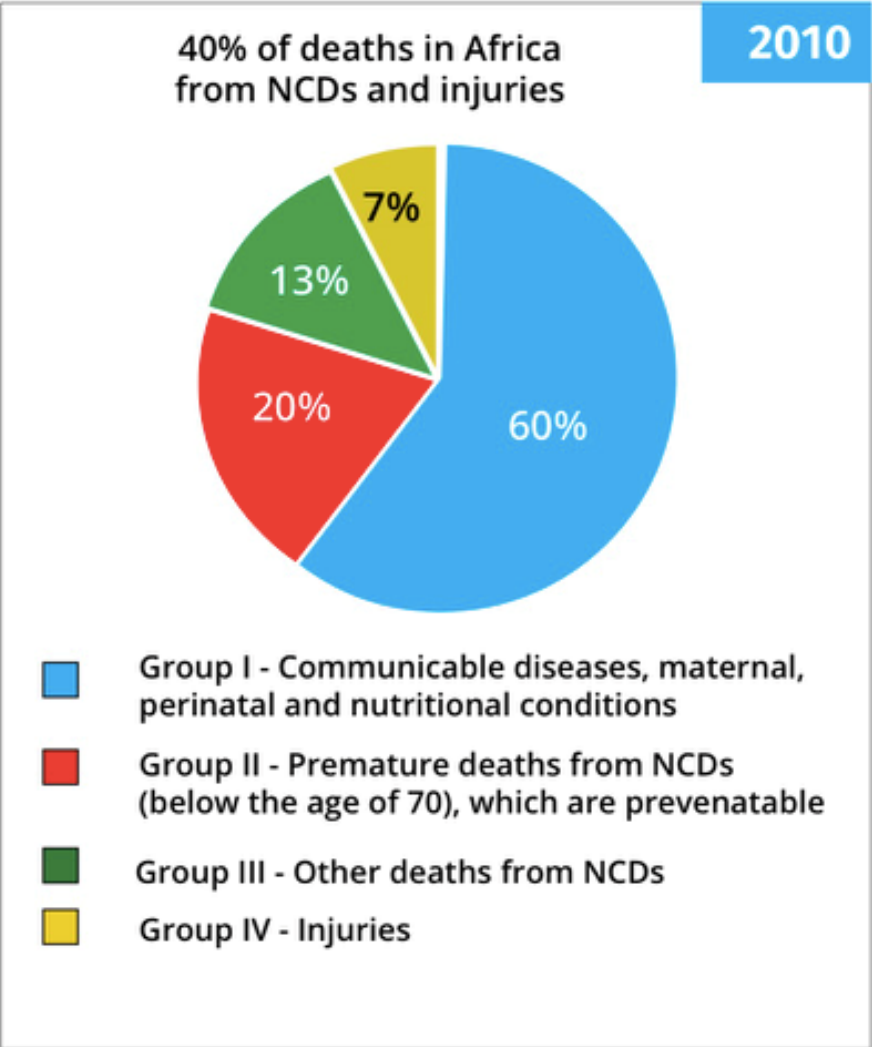


Figure 1. Genetic Variants Associated with Hypertrophic Cardiomyopathy.

Avoid misdiagnoses in all populations



Dual Burden of Disease: Communicable and Non-Communicable

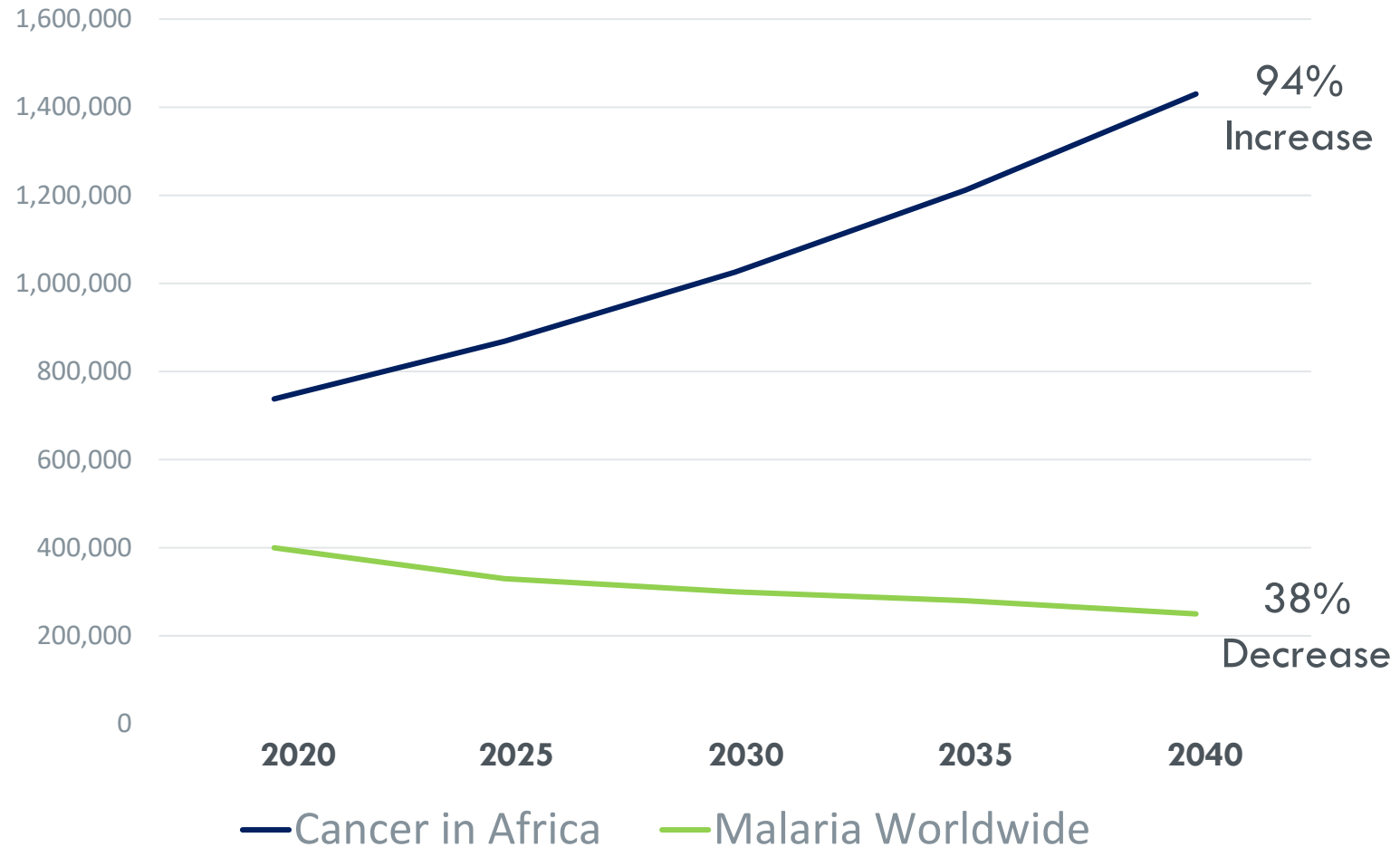


Africa's Future Cancer Burden

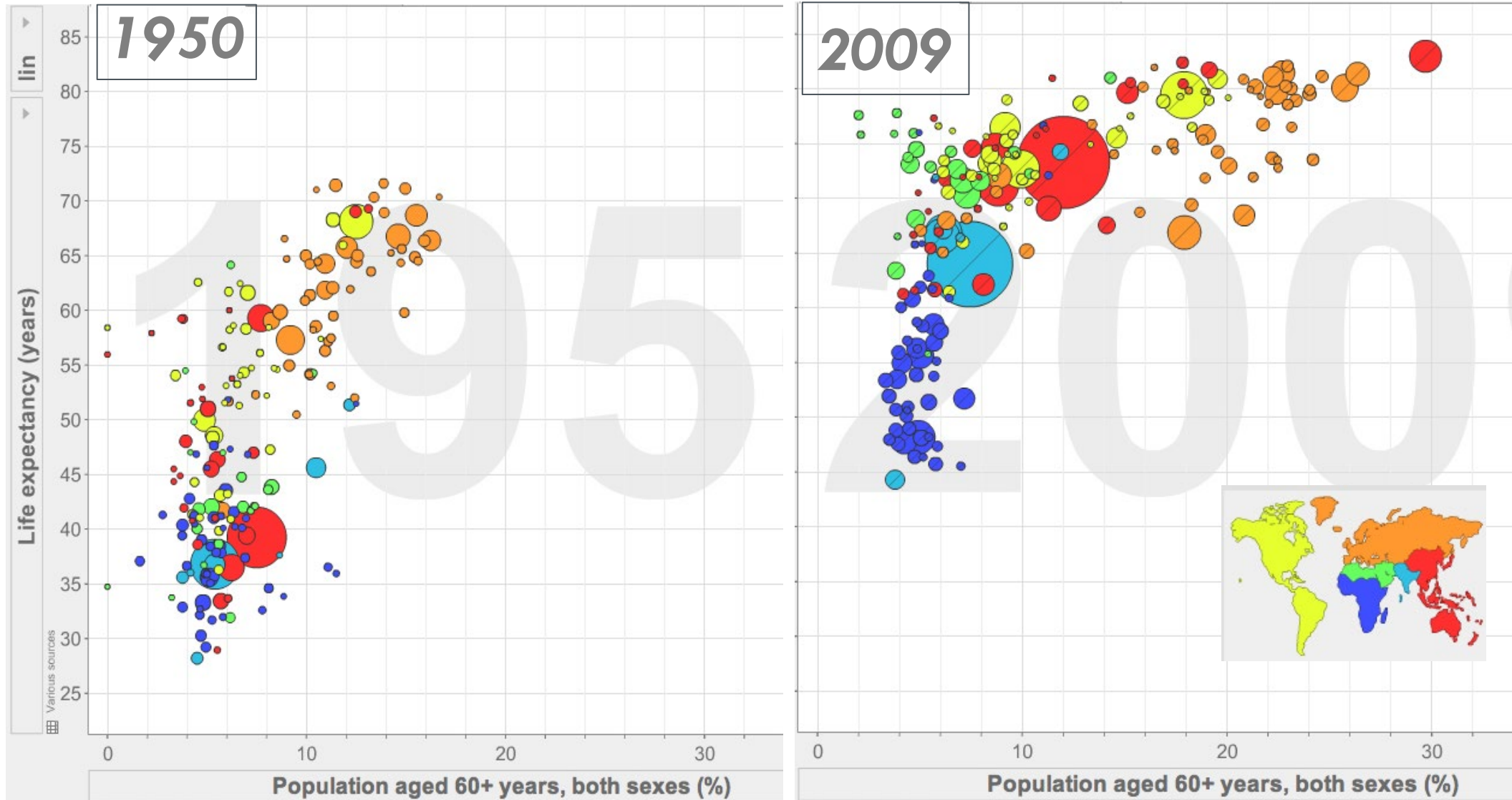
In the next two decades, cancer deaths in Africa will nearly double.

Approximately 1.4 million Africans will die of cancer in 2040.

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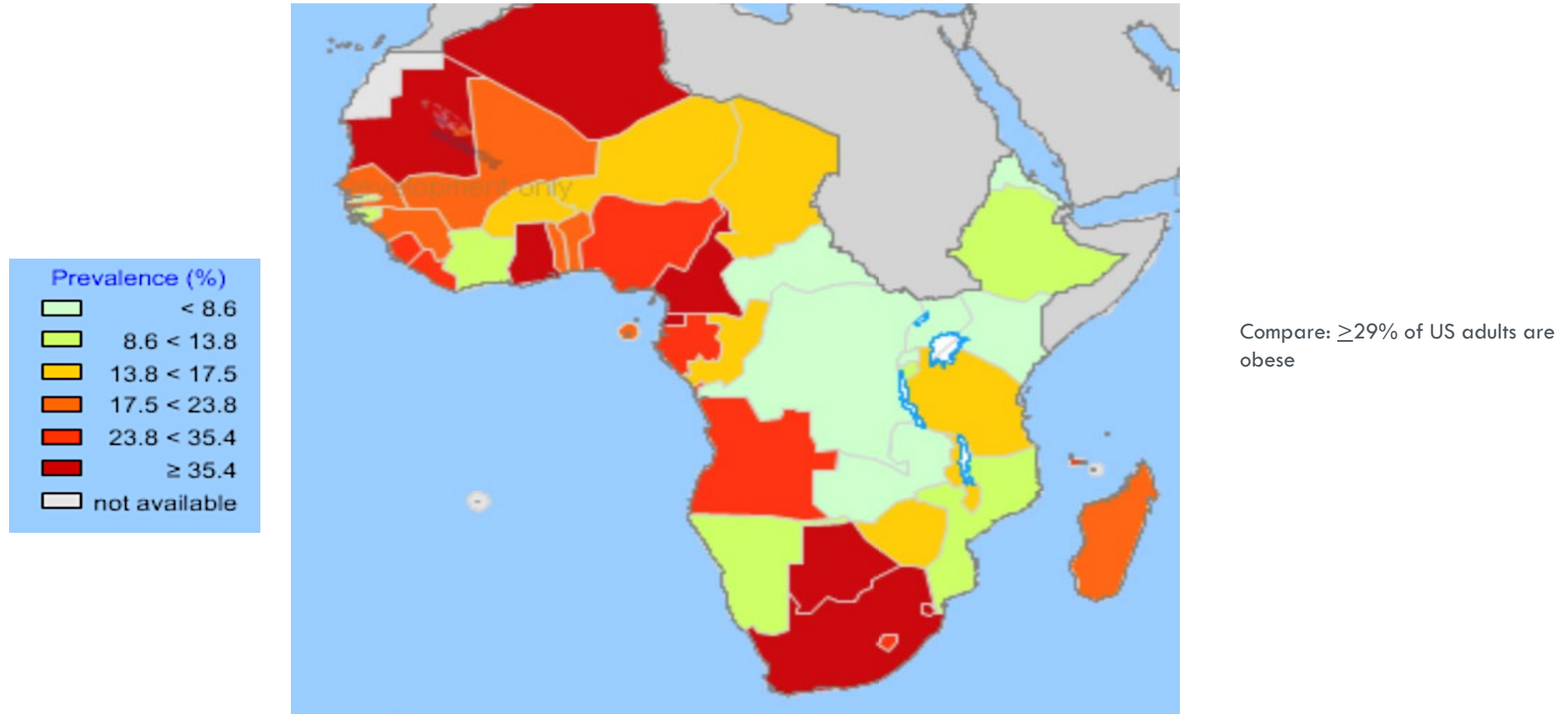


Increasingly Elderly Population in Africa



Africa's Cancer Burden

Exposure to factors associated with cancer risk is common and increasing

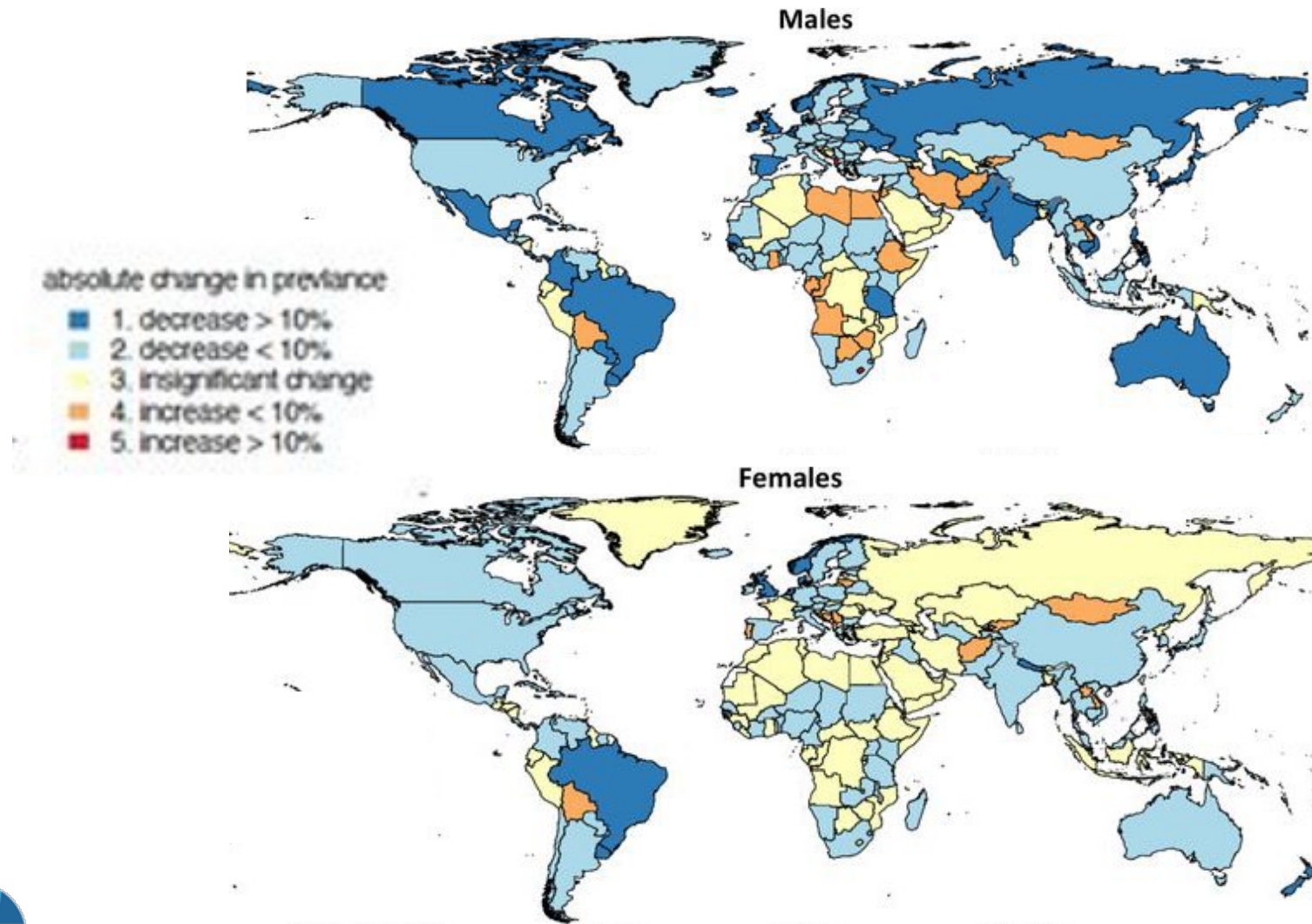


A large and increasing number of Africans are obese. (Data Shown: Men over age 30 with BMI ≥ 30 , 2010)



Percent Change in Prevalence of Current Smoking

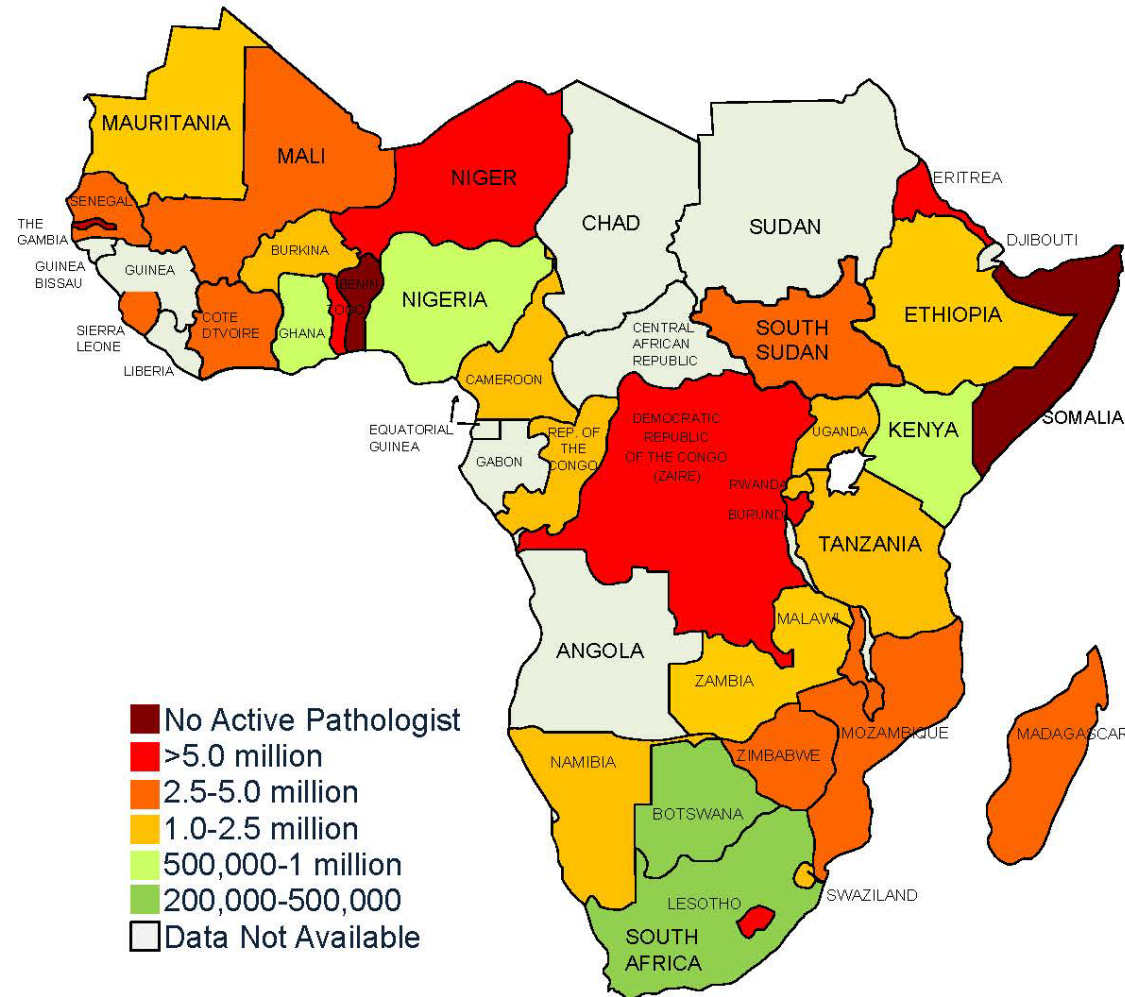
Age-standardized for men and women aged 15 years and above, 2000-2020



Percent of Population Covered by Cancer Registries (Number of Registries / Number of Countries Reporting)



Number of People Served By Each Pathologist in Sub-Saharan Africa

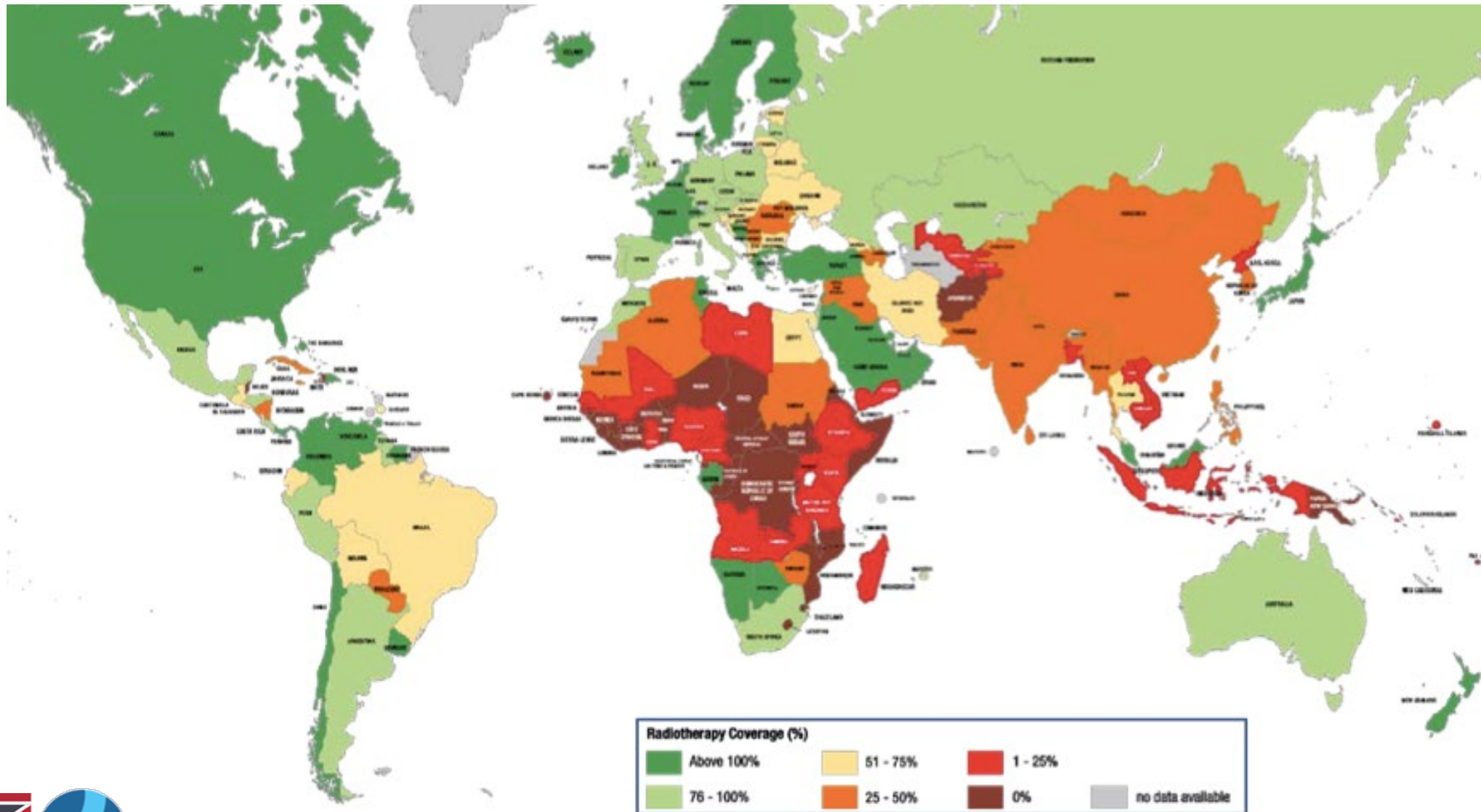


Number of People
Per Pathologist:
US*: 19,232

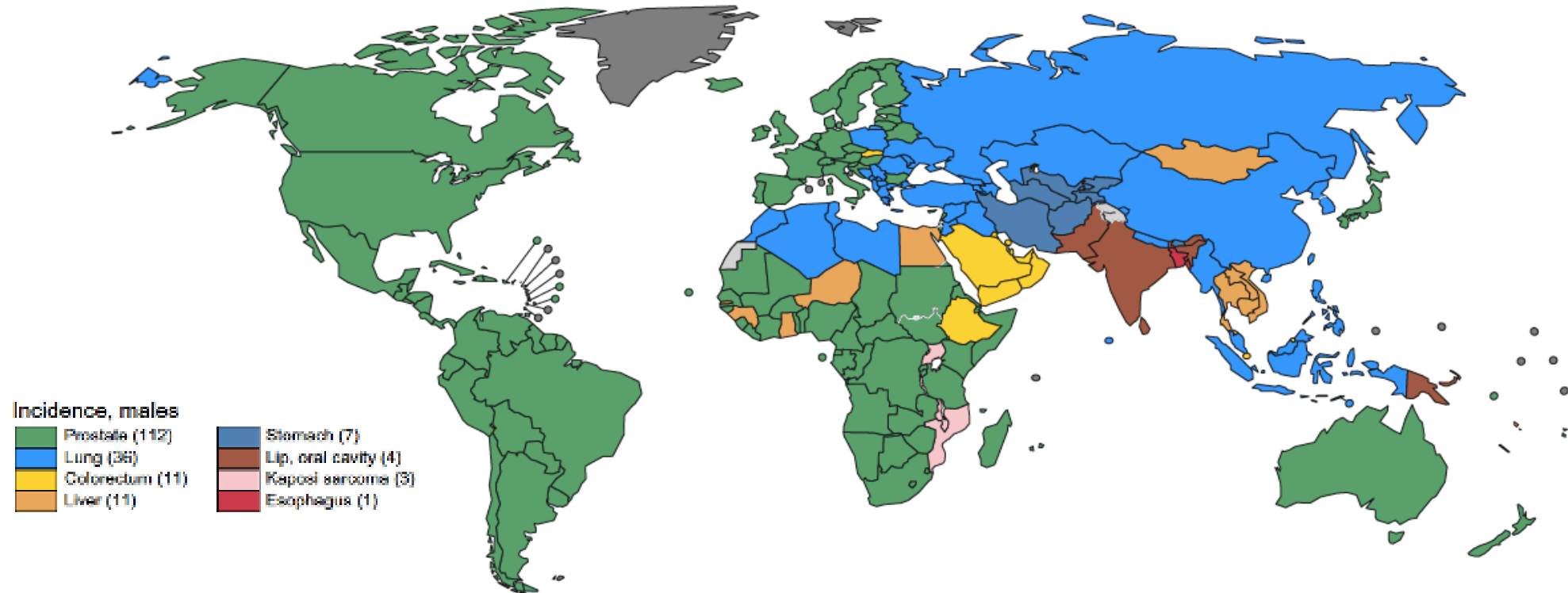
*Anatomic and Clinical Pathologists,
AAMC



Radiotherapy Coverage (% of Population)



Prostate Cancer



Known Risk Factors:

Age, Family History, Race, Obesity (Aggressive Disease).

Percent Variability Due to Genetic Factors: 57%

Most Recent Multiethnic Prostate GWAS: 451 Loci

MADCaP: Men of African Descent and Carcinoma of the Prostate

Supported by AACR Landon Foundation, Fulbright Program, R01-CA085074, P50-CA105641, P60-MD006900, U01-CA184374, P20-CA233255



Genetics: A Core Element of Cancer Risk Assessment, Prevention, Therapy, and Disease Monitoring



NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Genetic/Familial High-Risk Assessment: Breast and Ovarian

Version 3.2019 — January 18, 2019

special articles

Implementation of Germline Testing for Prostate Cancer: Philadelphia Prostate Cancer Consensus Conference 2019

Veda N. Giri, MD^{1,2,3}; Karen E. Knudsen, MBA, PhD³; William K. Kelly, DO¹; Heather H. Cheng, MD, PhD⁴; Kathleen A. Cooney, MD⁵; Michael S. Cookson, MD⁶; William Dahut, MD⁷; Scott Weissman, MS⁸; Howard R. Soule, PhD⁹; Daniel P. Petrylak, MD¹⁰; Adam P. Dicker, MD, PhD¹¹; Saud H. AlDubayan, MD¹²; Amanda E. Toland, PhD¹³; Colin C. Pritchard, MD, PhD¹⁴; Curtis A. Pettaway, MD¹⁵; Mary B. Daly, MD, PhD¹⁶; James L. Mohler, MD¹⁷; J. Kellogg Parsons, MD¹⁸; Peter R. Carroll, MD, MPH¹⁹; Robert Pilarski, MS, MSW²⁰; Amie Blanco, MS²¹; Ashley Woodson, MS²²; Alanna Rahm, PhD²³; Mary-Ellen Taplin, MD²⁴; Thomas J. Polascik, MD²⁵; Brian T. Helfand, MD, PhD²⁶; Colette Hyatt, MS²⁵; Alicia K. Morgans, MD, MPH²⁶; Felix Feng, MD²⁷; Michael Mullane, MD²⁸; Jacqueline Powers, MS²⁹; Raoul Concepcion, MD³⁰; Daniel W. Lin, MD³¹; Richard Wender, MD³²; James Ryan Mark, MD²; Anthony Costello, MBBS³³; Arthur L. Burnett, MD, MBA³⁴; Oliver Sartor, MD³⁵; William B. Isaacs, PhD³⁶; Jianfeng Xu, MD, DrPH²⁴; Jeffrey Weitzel, MD³⁷; Gerald L. Andriole, MD³⁸; Himisha Beltran, MD³⁹; Alberto Briganti, MD, PhD⁴⁰; Lindsey Byrne, MS⁴¹; Anne Calvaresi, DNP²; Thenappan Chandrasekar, MD²; David Y. T. Chen, MD¹⁶; Robert B. Den, MD¹¹; Albert Dobi, PhD⁴²; E. David Crawford, MD⁴³; James Eastham, MD⁴⁴; Scott Eggener, MD⁴⁵; Matthew L. Freedman, MD³⁹; Marc Garnick, MD⁴⁶; Patrick T. Gomella, MD, MPH⁴⁷; Nathan Handley, MD, MBA¹; Mark D. Hurwitz, MD¹¹; Joseph Izes, MD, MS²; R. Jeffrey Karnes, MD⁴⁸; Costas Lallas, MD²; Lucia Languino, PhD²; Stacy Loeb, MD, MSc⁴⁹; Ana Maria Lopez, MD, MPH¹; Kevin R. Loughlin, MD, MBA⁵⁰; Grace Lu-Yao, PhD, MPH¹; S. Bruce Malkowicz, MD⁵¹; Mark Mann, MD²; Patrick Mille, MD¹; Martin M. Miner, MD⁵²; Todd Morgan, MD⁵³; Jose Moreno, MD⁵⁴; Lorelei Mucci, ScD, MPH⁵⁵; Ronald E. Myers, DSW, PhD¹; Sarah M. Nielsen, MS⁴⁵; Brock O'Neil, MD⁵⁶; Wayne Pinover, DO⁵⁷; Peter Pinto, MD⁴⁷; Wendy Poage, MHA⁵⁸; Ganesh V. Raj, MD, PhD⁵⁹; Timothy R. Rebbeck, PhD⁵⁵; Charles Ryan, MD⁶⁰; Howard Sandler, MD, MS⁶¹; Matthew Schiewer, PhD¹; E. Michael D. Scott, BSc⁶²; Brittany Szymaniak, PhD, MS⁶³; William Tester, MD¹; Edouard J. Trabulsi, MD²; Neha Vapiwala, MD⁶¹; Evan Y. Yu, MD⁶⁴; Charnita Zeigler-Johnson, PhD, MPH¹; and Leonard G. Gomella, MD²

JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA-Related Cancer in Women

Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

Heidi D. Nelson, MD, MPH, MACP, FRCP; Miranda Pappas, MA; Amy Cantor, MD, MPH; Elizabeth Haney, MD; Rebecca Holmes, MD



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2020

Genetic/Familial High-Risk Assessment: Colorectal

[NCCN Guidelines Index](#)
[Table of Contents](#)
[Discussion](#)

MULTI-GENE TESTING

Table 1: Multi-Gene Testing Definitions

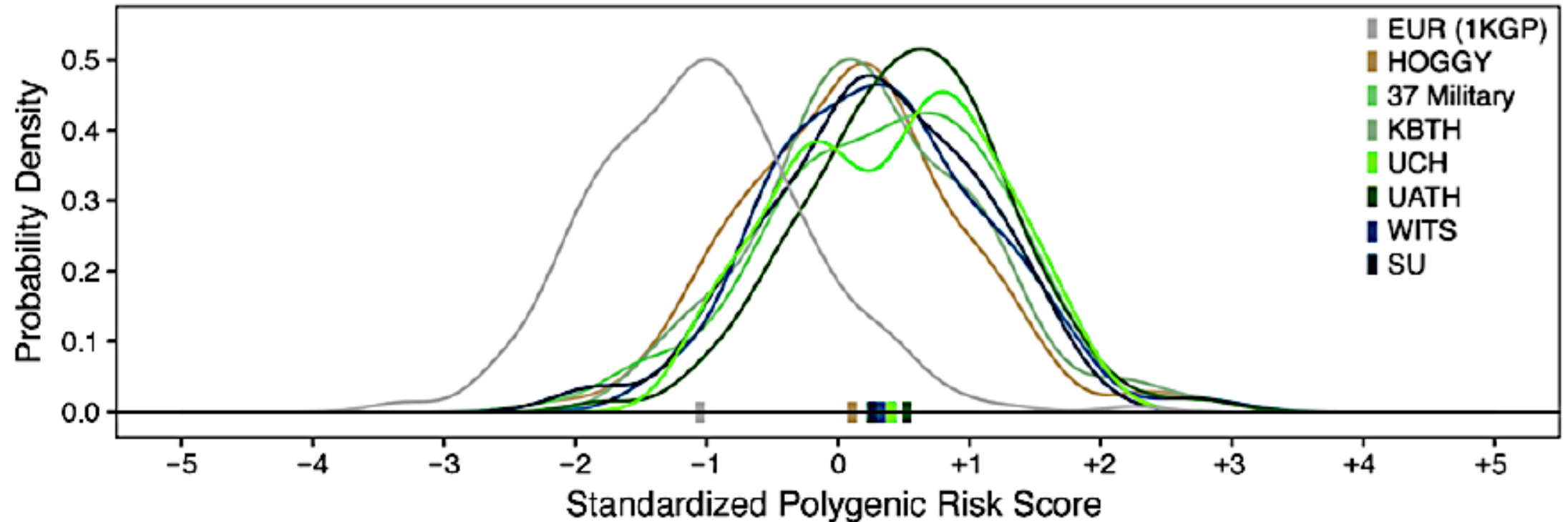
TERM	DEFINITION
Multi-gene panel	Laboratory test that includes testing for pathogenic variants of more than one gene.
Syndrome-specific panel	Panel that only tests for one syndrome (eg, LS, adenomatous polyposis).
Cancer-specific panel	Panel that tests for more than one gene associated with a specific type of cancer.
"Comprehensive" cancer panel	Panel that tests for more than one gene associated with multiple cancers or multiple cancer syndromes.
Actionable pathogenic variant	Pathogenic variant that results in a recommendation for a change in clinical management.
Variant of uncertain significance	Genetic test result indicating a sequence variant in a gene that is of uncertain significance. Variants are generally not clinically actionable, and most (but not all) are ultimately re-classified as benign. ^{1,2}

Table 2: Pros and Cons of Multi-Gene Testing for Hereditary Colorectal Syndromes*

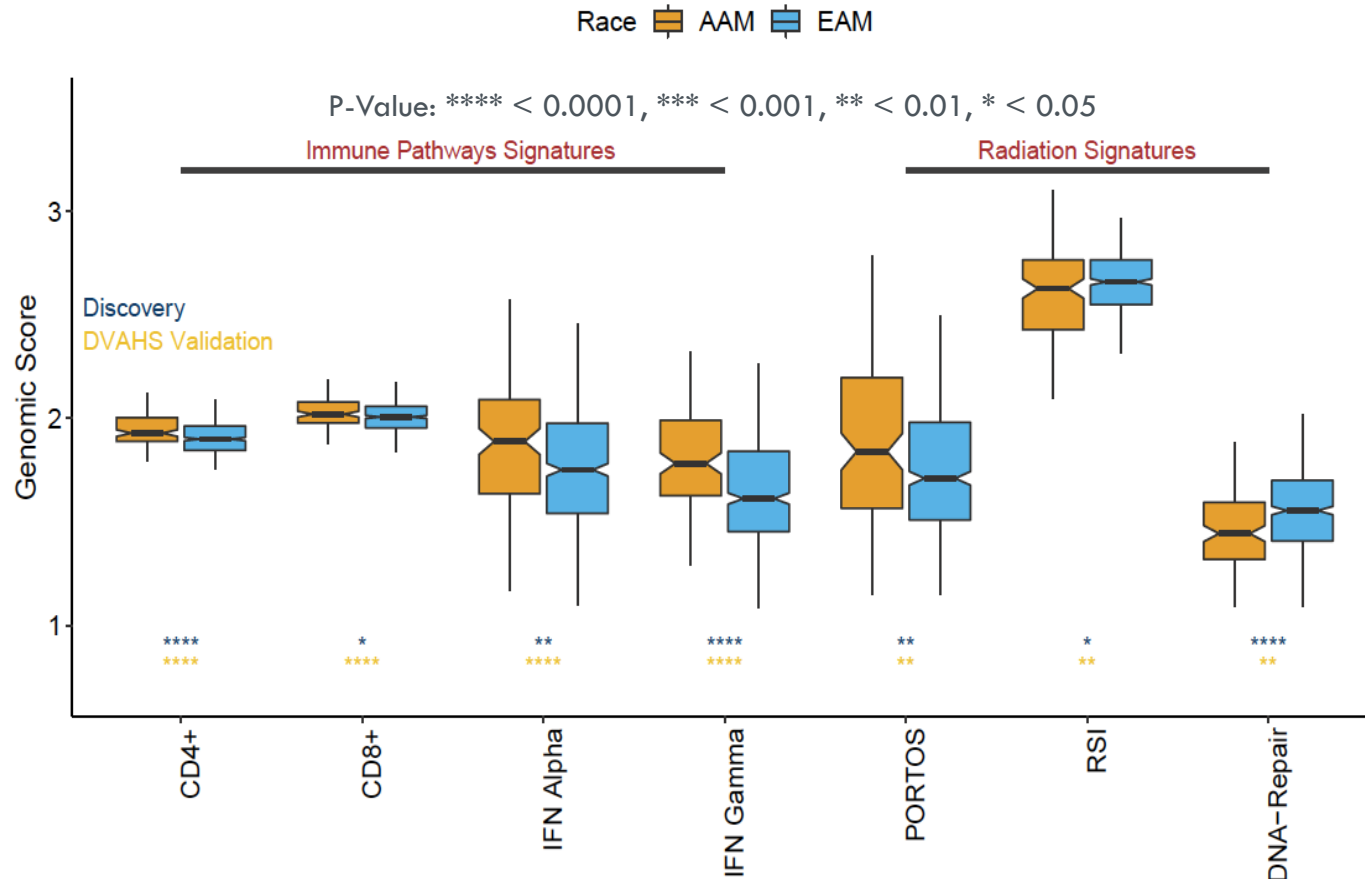
PROS	CONS
<ul style="list-style-type: none"> • More efficient testing when more than one gene may explain presentation and family history. • Higher chance of providing proband with possible explanation for cause of cancer. • Competitive cost relative to sequentially testing single genes. • Chance of identifying pathogenic variants in multiple actionable genes that could impact screening and management for the individual and family members that may be missed using cancer syndrome-specific panels. 	<ul style="list-style-type: none"> • Higher chance of identifying pathogenic variants for which clinical management is uncertain. Estimates suggest that 3%–4% (Gastroenterology 2015;149:604-13.e20; Clin Genet 2014;86:510-520) of pathogenic variants identified are not clearly clinically actionable, such as finding a pathogenic variant in a moderate-risk gene for which management is unclear. • Higher chance of identifying variants of uncertain significance that are not actionable; reported rates of finding variants of uncertain significance range from 17%–38%. • Higher chance that patient will mistakenly receive overtreatment and overscreening if variants of uncertain significance or pathogenic variants for which clinical management is uncertain are incorrectly interpreted.



Divergence in Polygenic Risk Scores Between European and African Populations

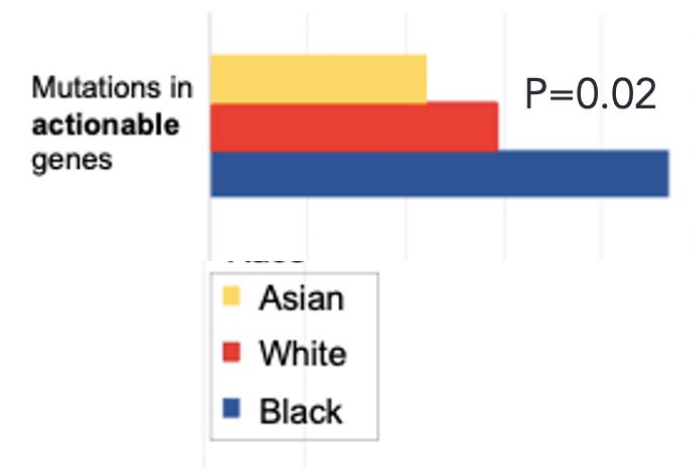


Enrichment of Immune-Oncologic Pathways, Lower DNA Damage Repair, Elevated Radiosensitivity, and Actionable Mutations in Black vs. White



- Decipher transcriptome data
- 1,173 radiation naive radical prostatectomy samples.

Awasthi et al., *Clin Cancer Res* 2020,
Mahal et al., *NEJM* 2020



- Project GENIE
- 2393 patients: 2109 White, 204 Black, and 80 Asian

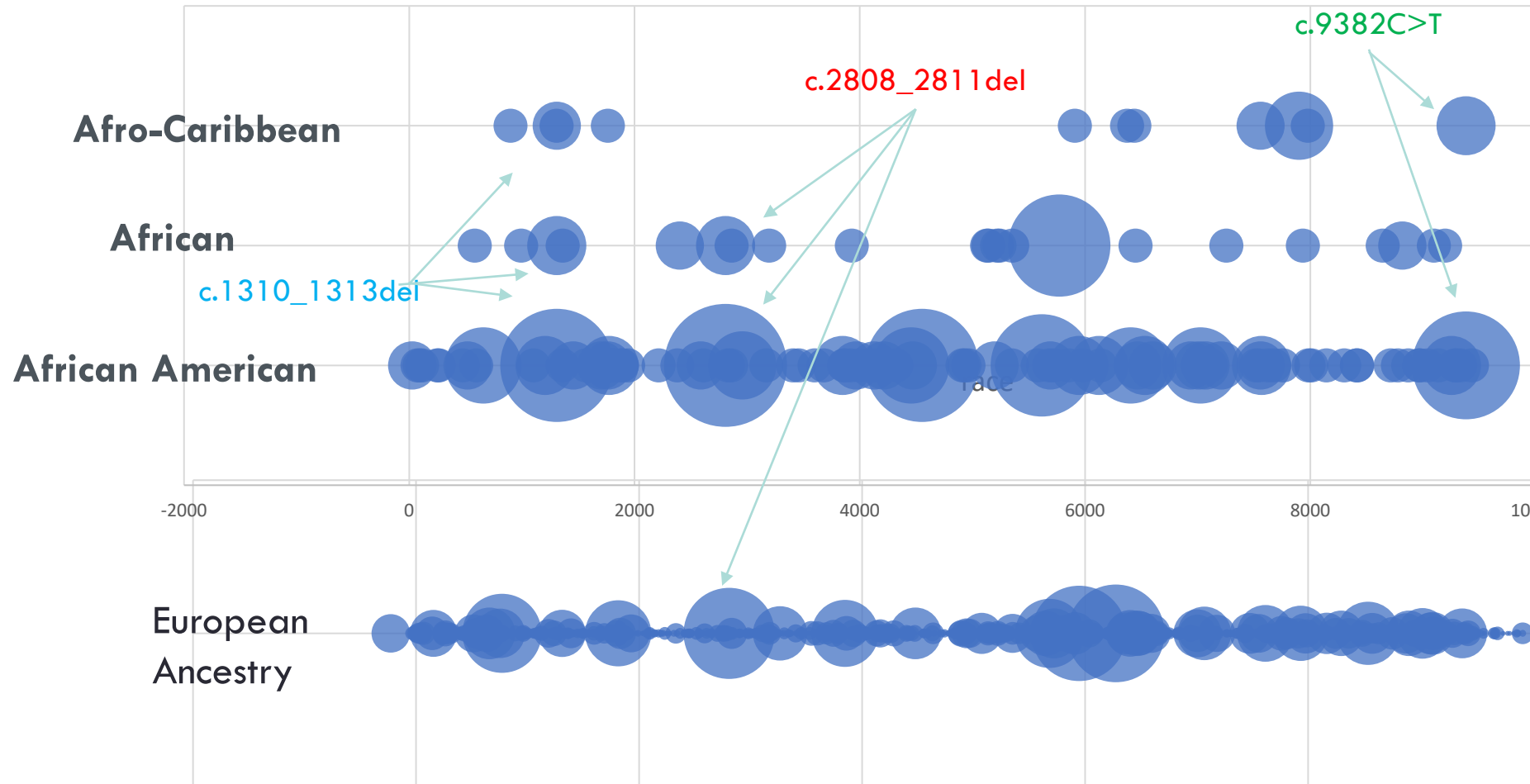


Pathogenic Sequence Variants by Inferred Continent of Origin

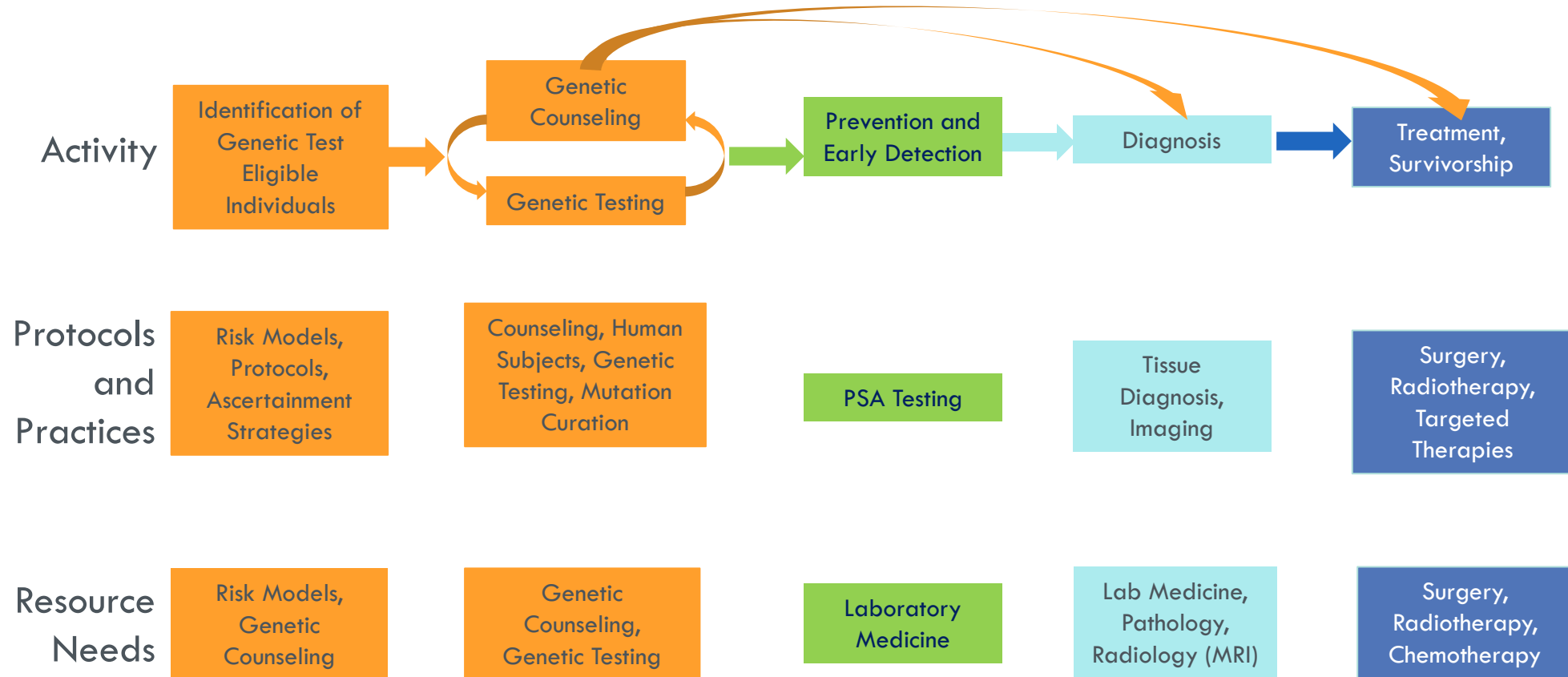
Designation	<i>BRCA1</i>		<i>BRCA2</i>	
	Count	%	Count	%
Likely African	35	34%	49	33%
Likely Non-African	18	17%	44	29%
Probably Not African	11	11%	2	1%
Cannot Determine	39	38%	53	36%
Total	103	100%	148	100



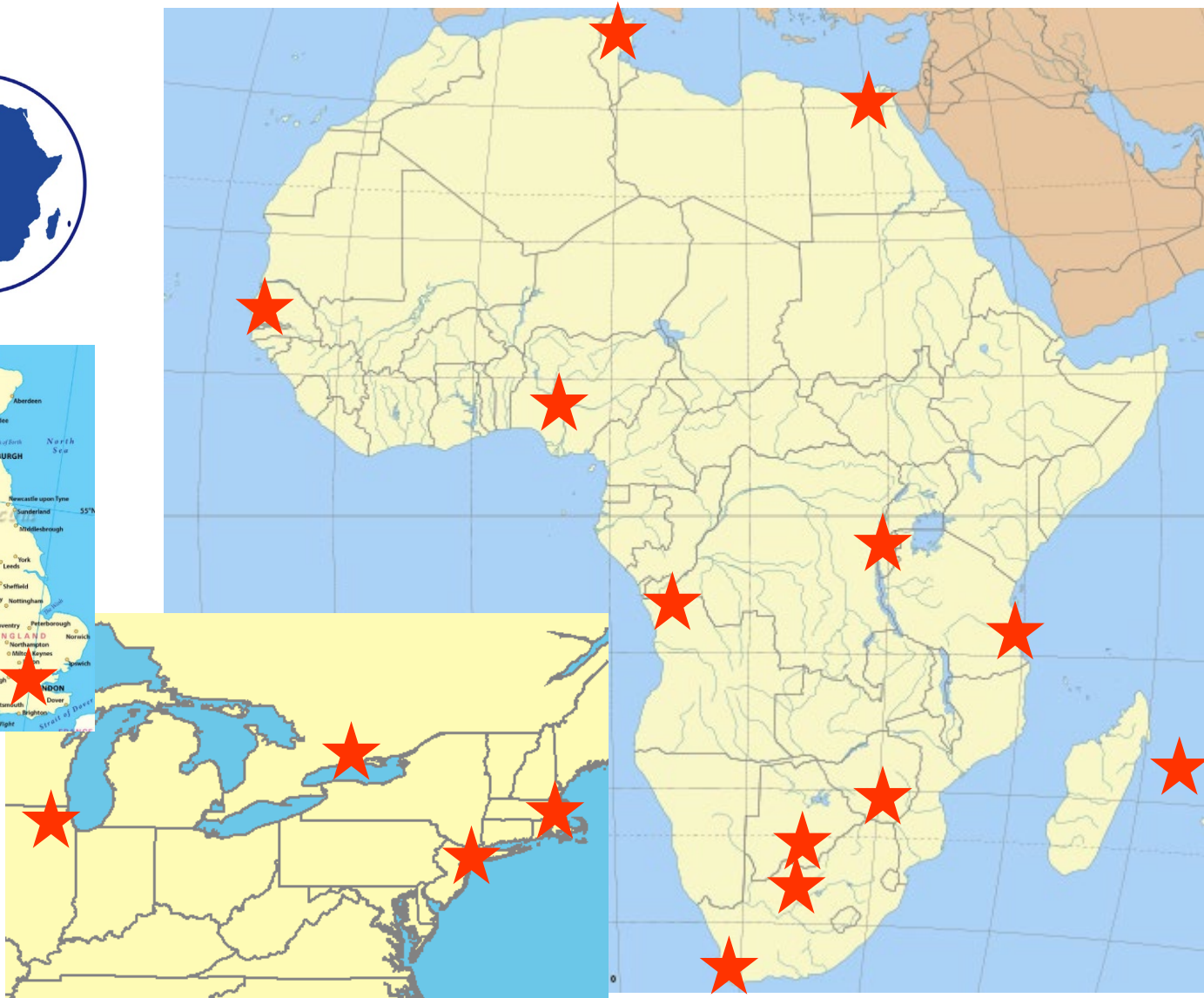
BRCA2 Mutations by Race/Ethnicity



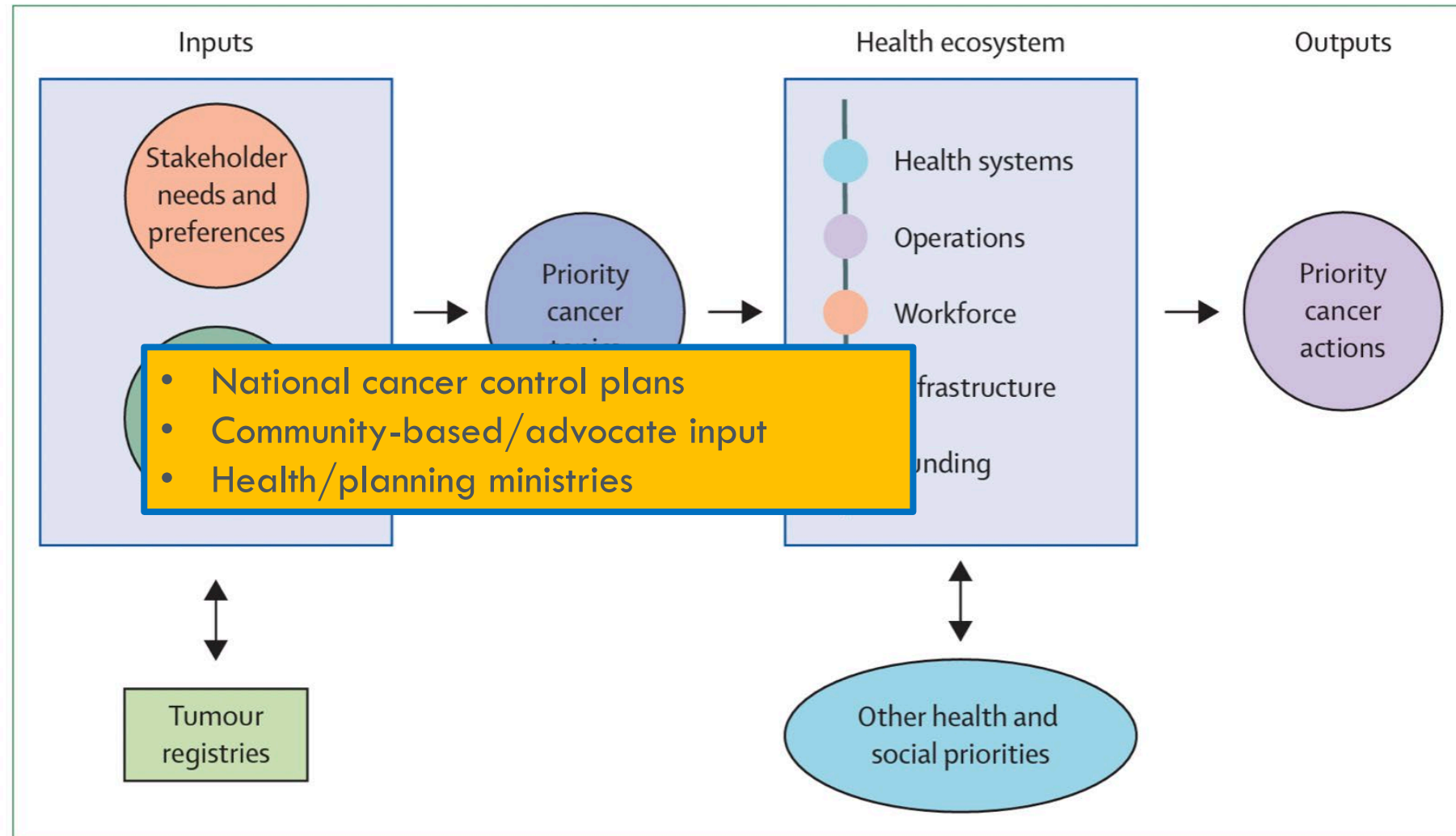
Leapfrogging Management of Prostate Cancer in 21st Century Africa



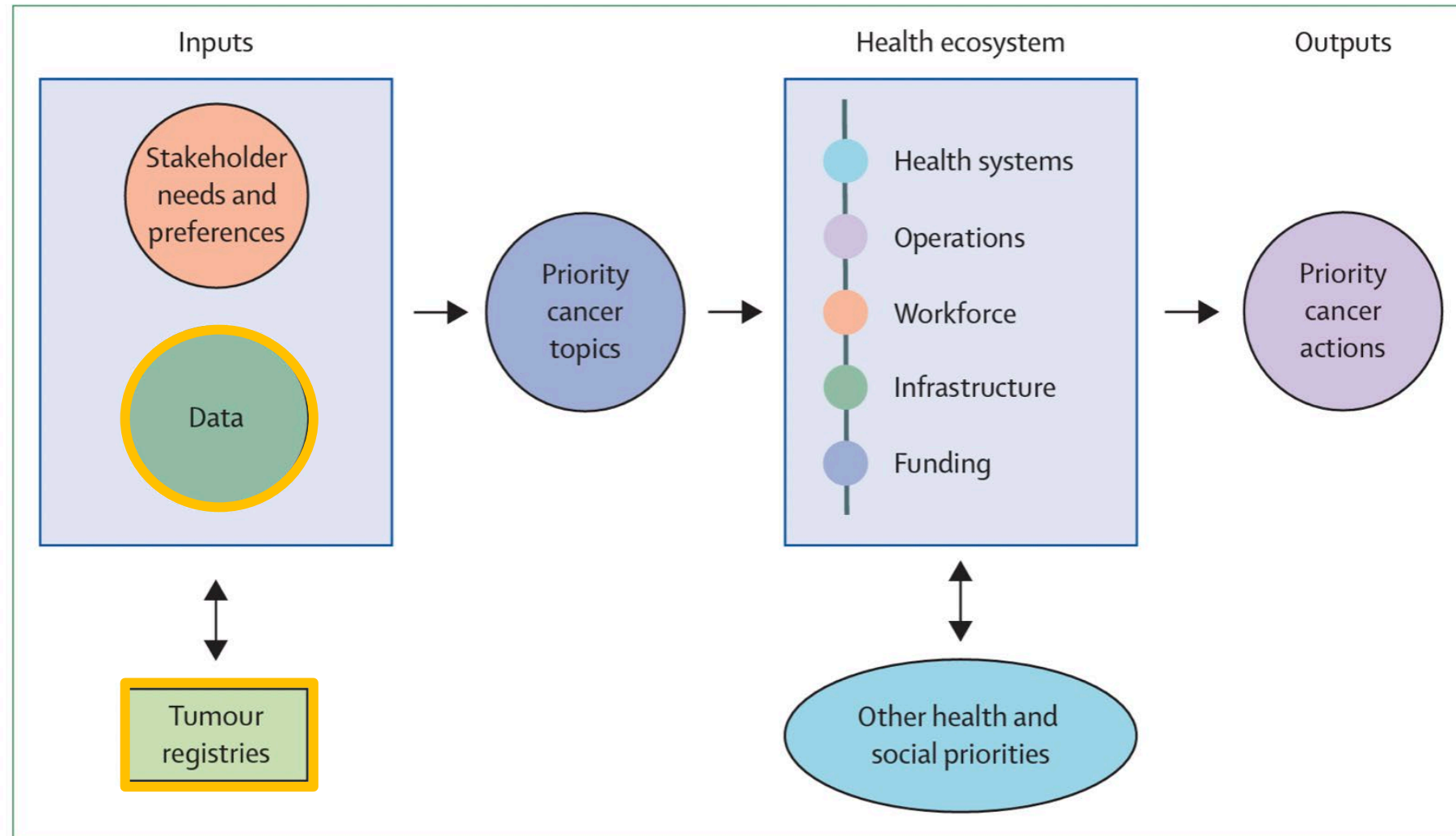
African Oncogenetics Network - Réseau Africain d'Oncogénétique



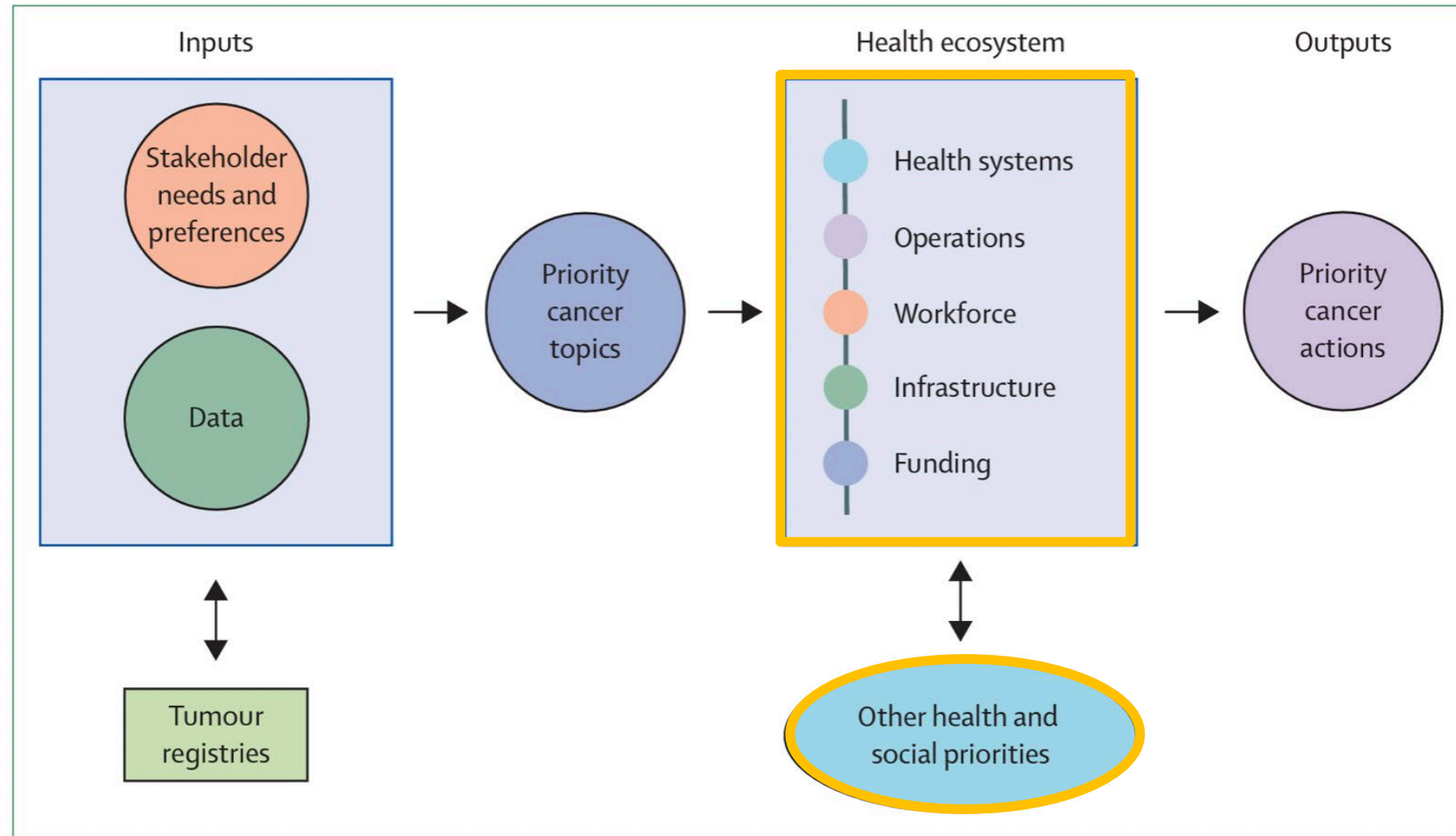
Pathways to Enhanced Cancer Capacity and Impact in Africa



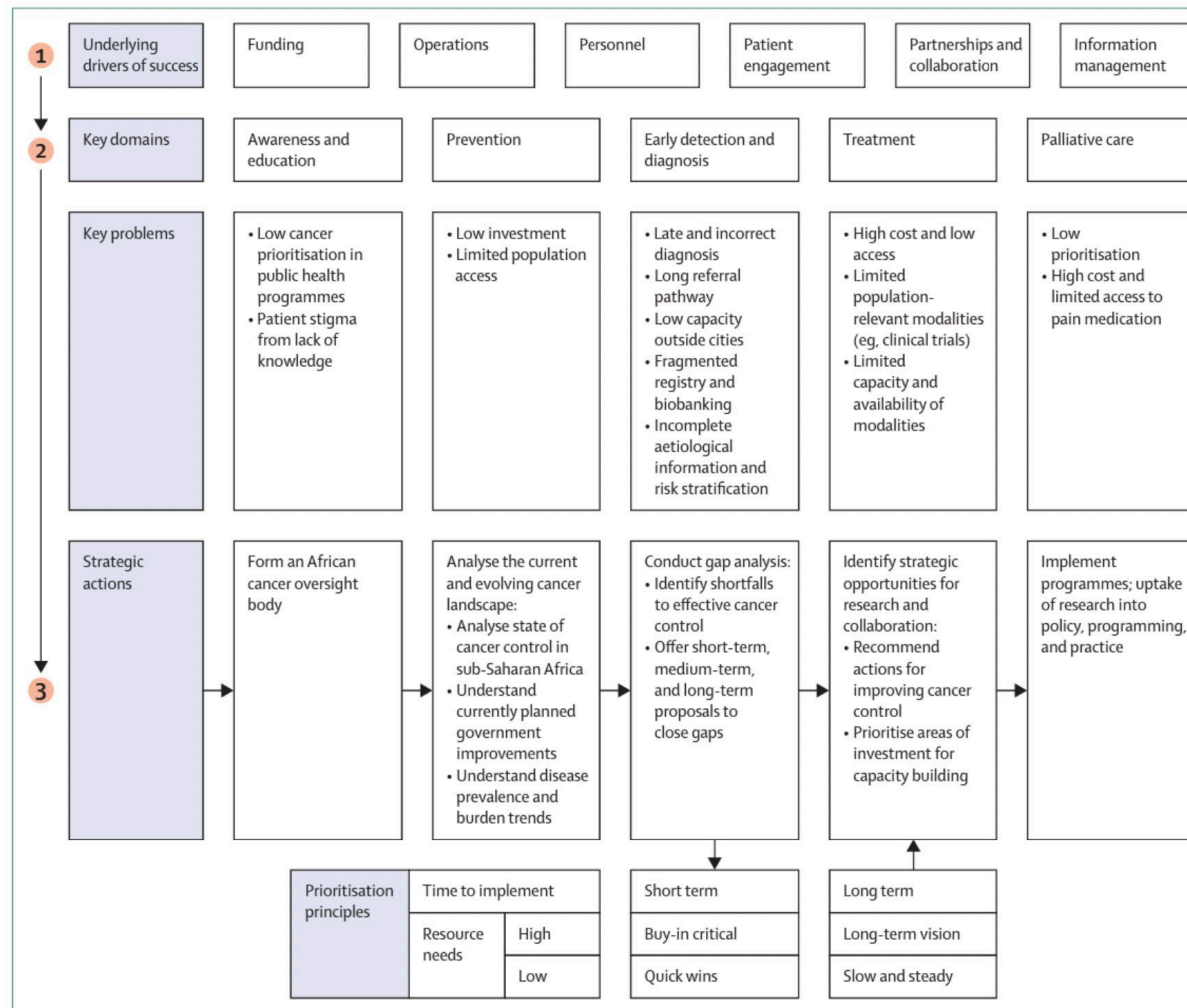
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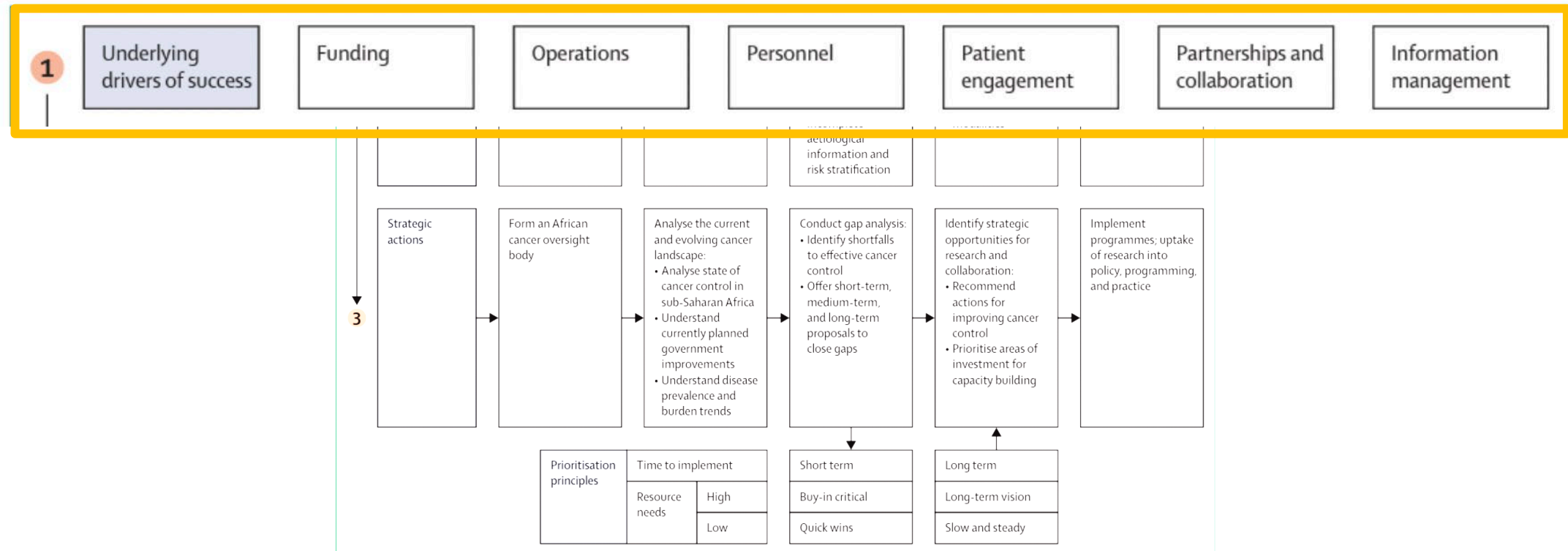
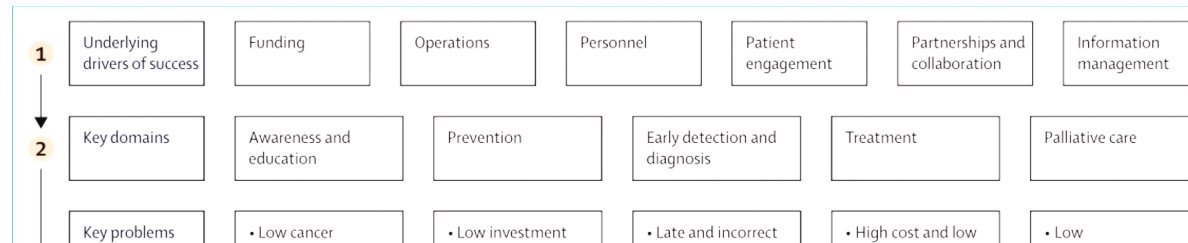
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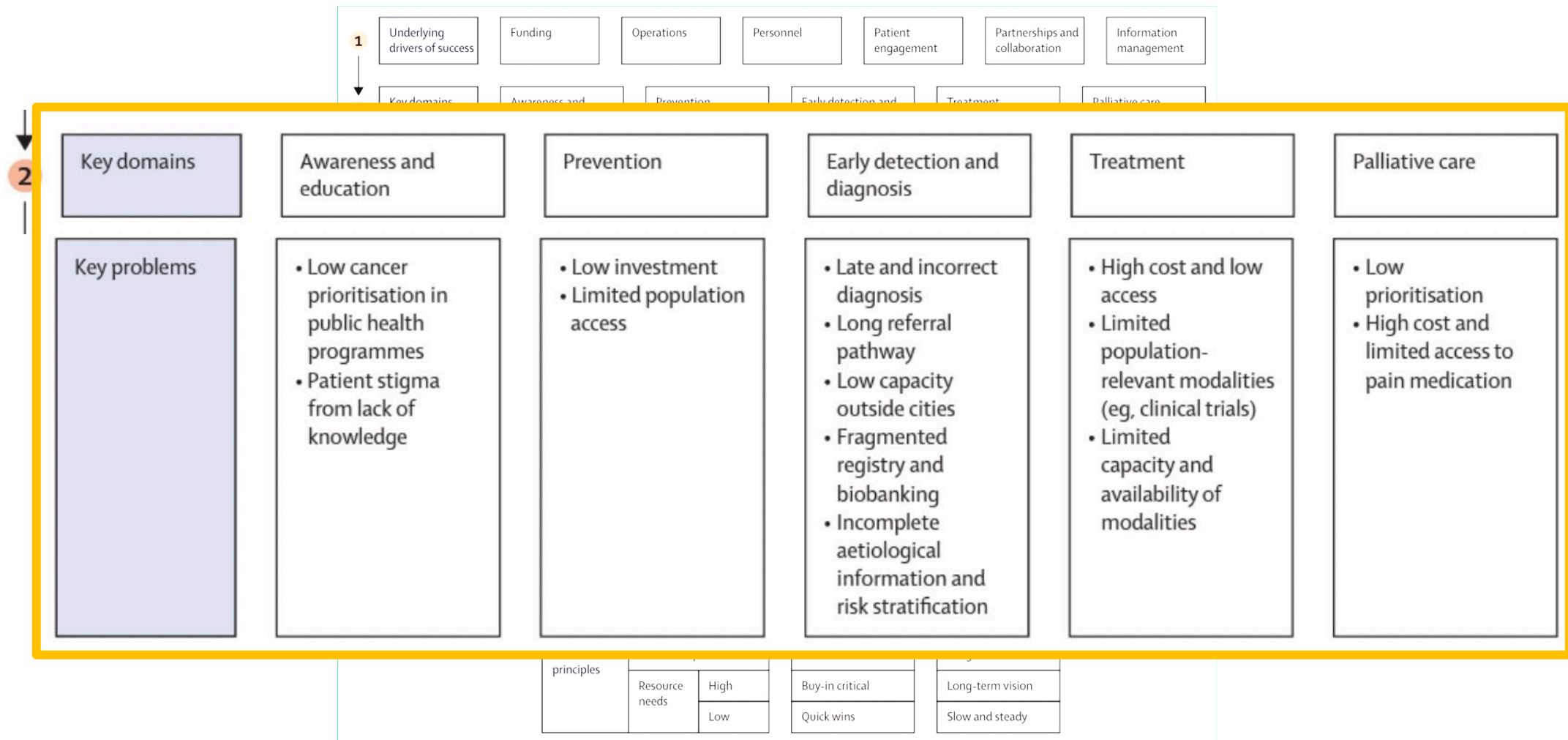
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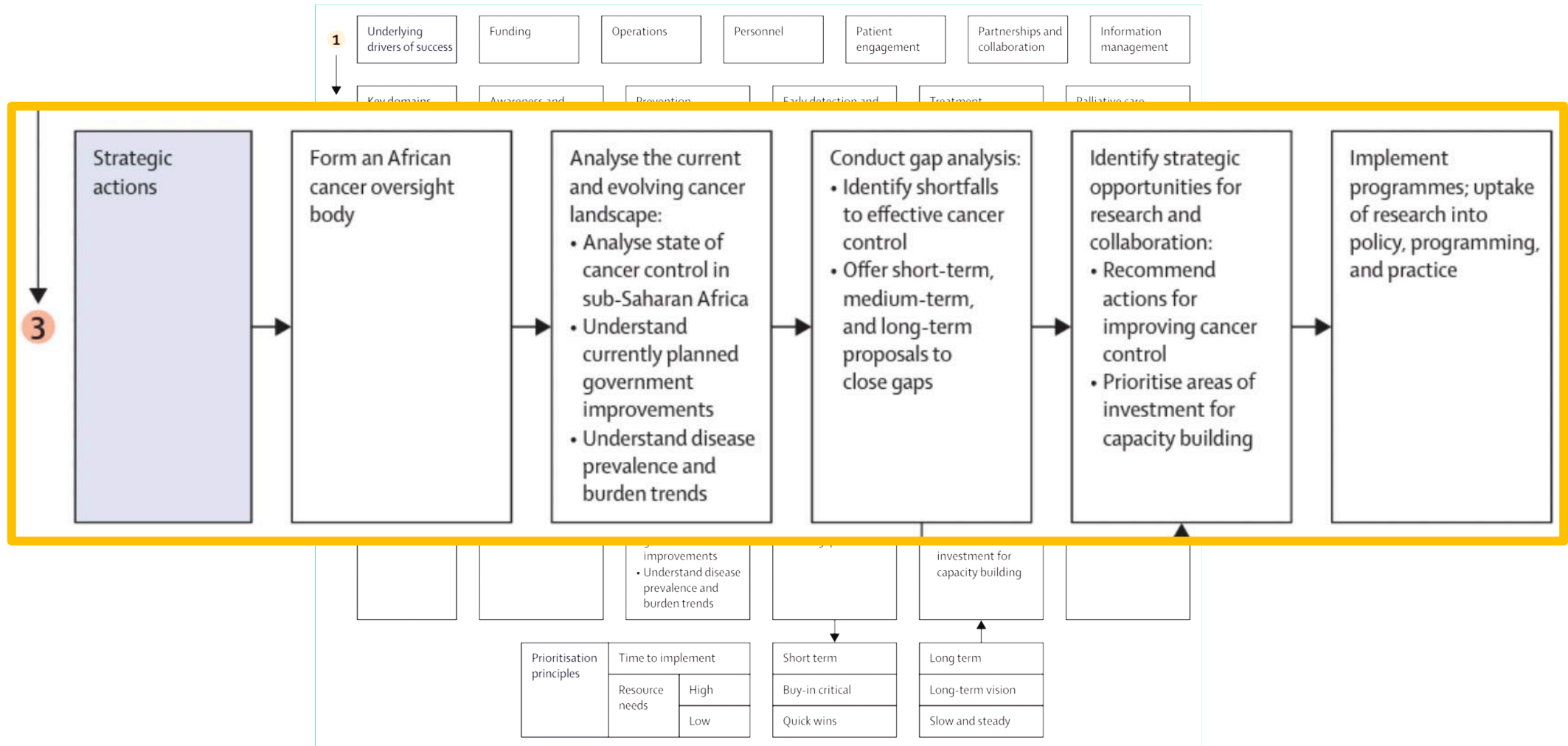
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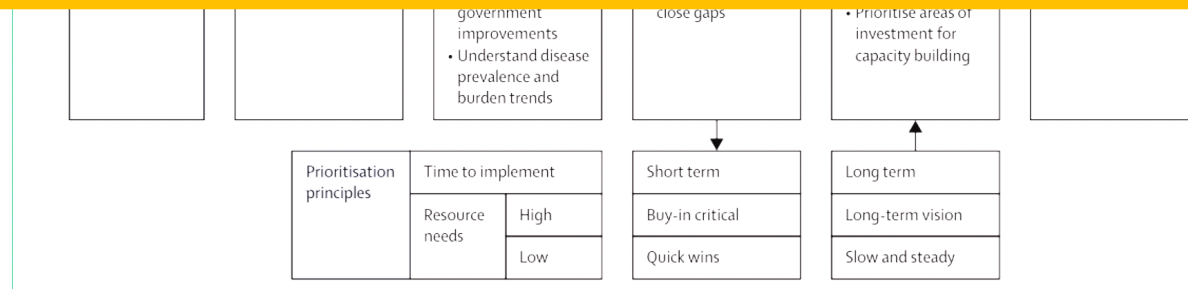
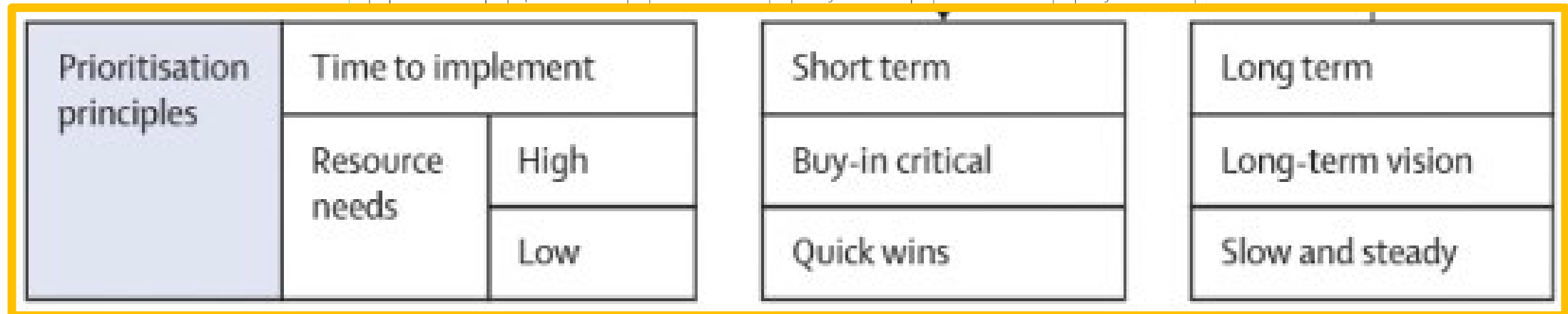
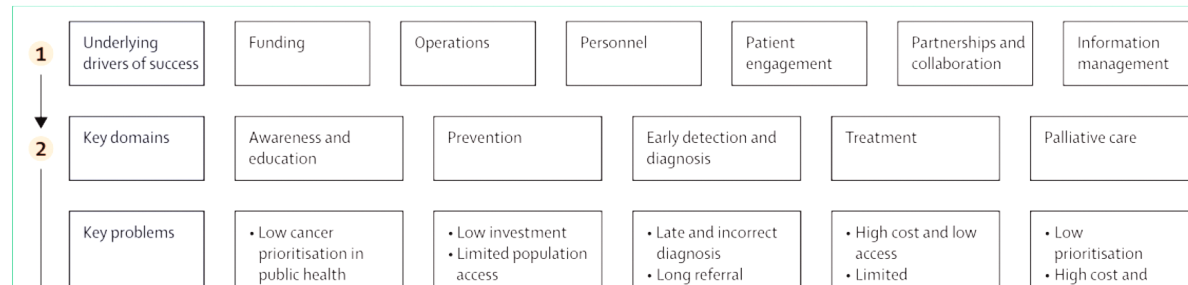
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Pathways to Enhanced Cancer Capacity and Impact in Africa



Pathways to Enhanced Cancer Capacity and Impact in Africa



Why Focus on Cancer in Africa?

- Foster social and economic progress:
 - Enhance health care capacity and systems
 - Impact education, training, and workforce
 - Ensure optimal health of Africans
- Inform cancer knowledge and practice worldwide
- Is not a luxury but a critical need



AACR

American Association
for Cancer Research

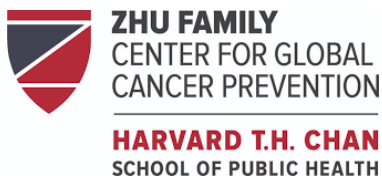
FINDING CURES TOGETHER™

AACR CANCER PREVENTION SUMMIT: SHAPING THE FUTURE

Thanks to:

OF CANCER PREVENTION

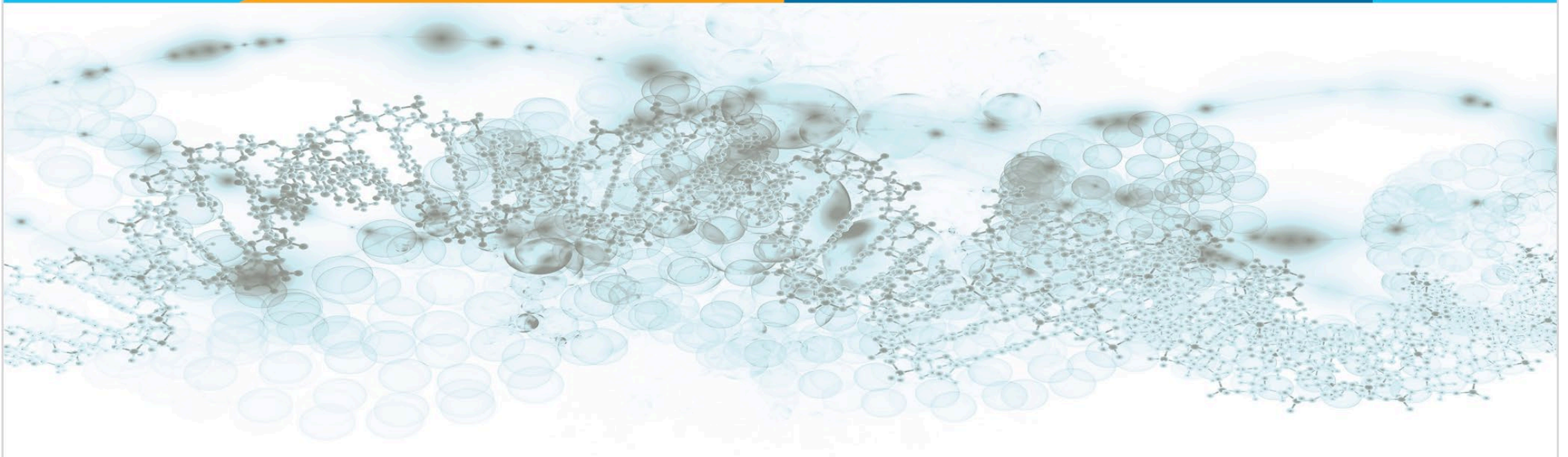
R01-CA259200, U2C-CA252974, R01-CA102776, R01-CA083855,
A Roadmap for Integrative Cancer Science and Public Health
R01-CA U2CCA252974, U01-CA184734, P20-CA233255.



February 3-5, 2016 | Lansdowne Resort, Leesburg, VA



Dana-Farber
Cancer Institute



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Timothy Rebbeck, PhD



HARVARD T.H. CHAN
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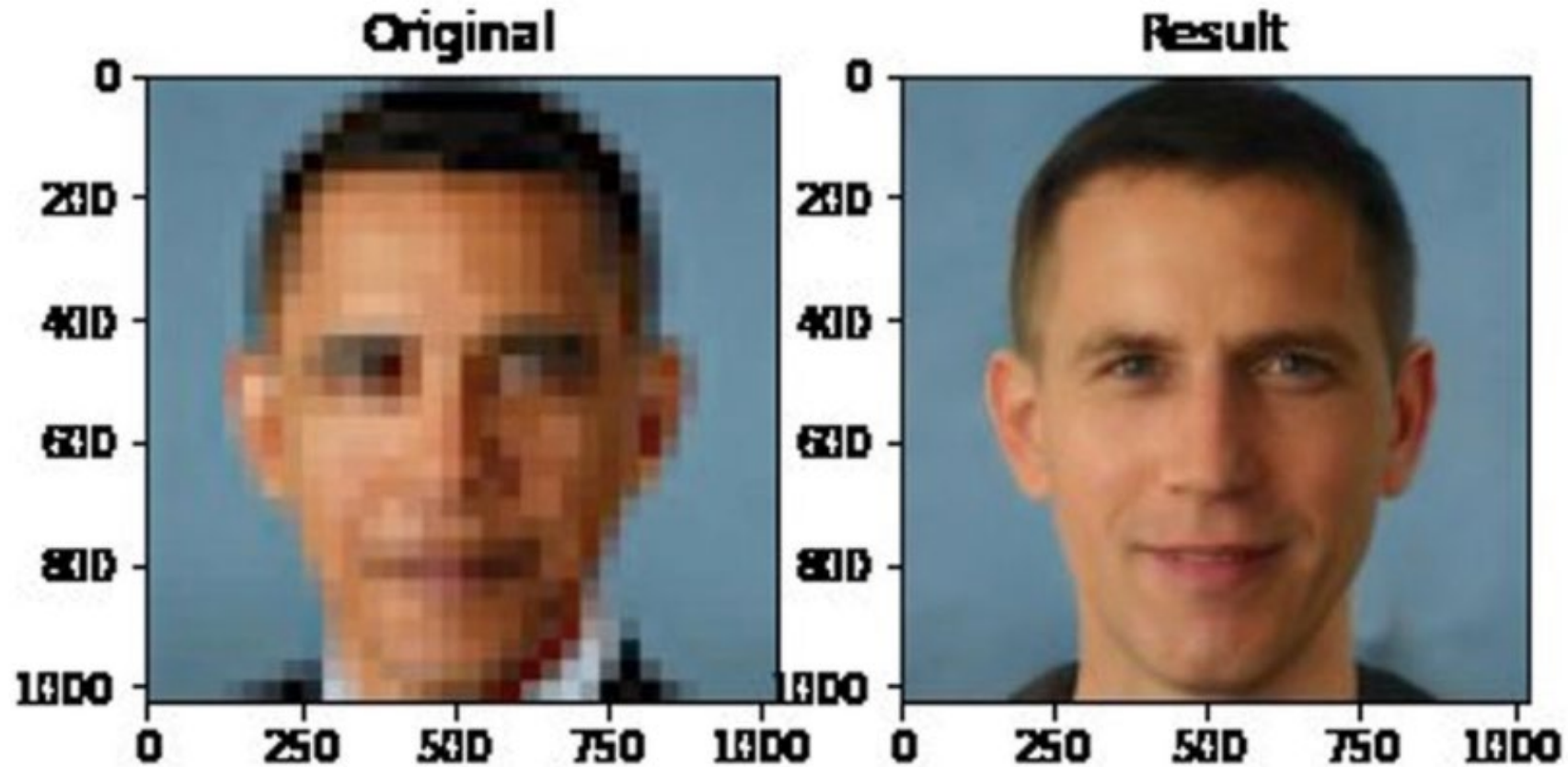
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Pliny the Elder, *Historia Naturalis*, Book 8, sect. 42

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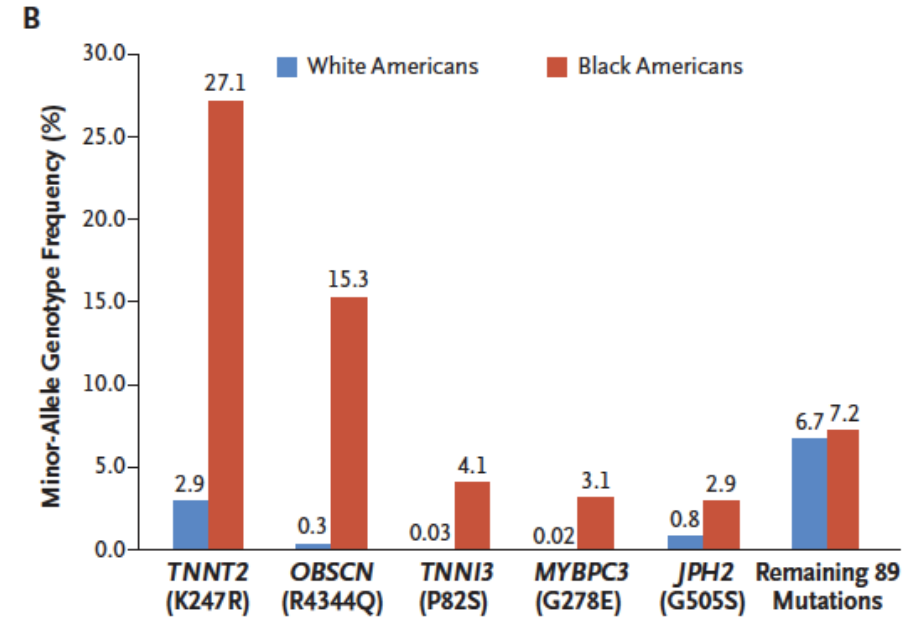
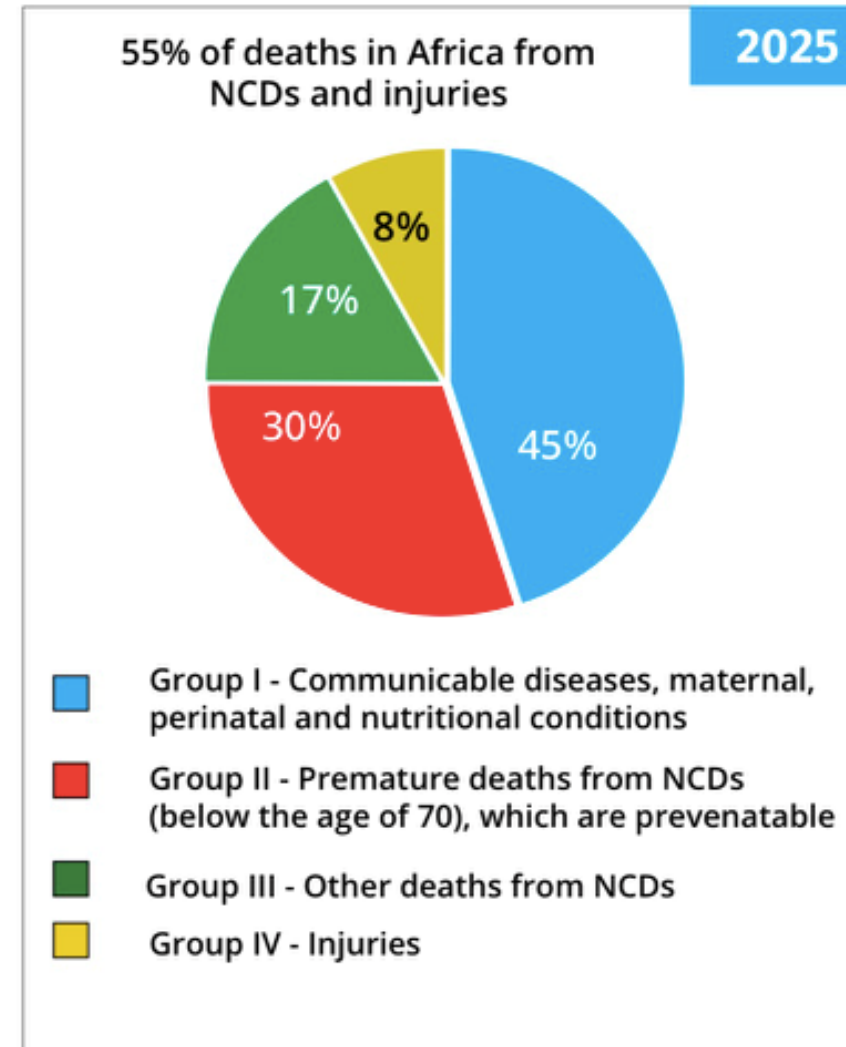
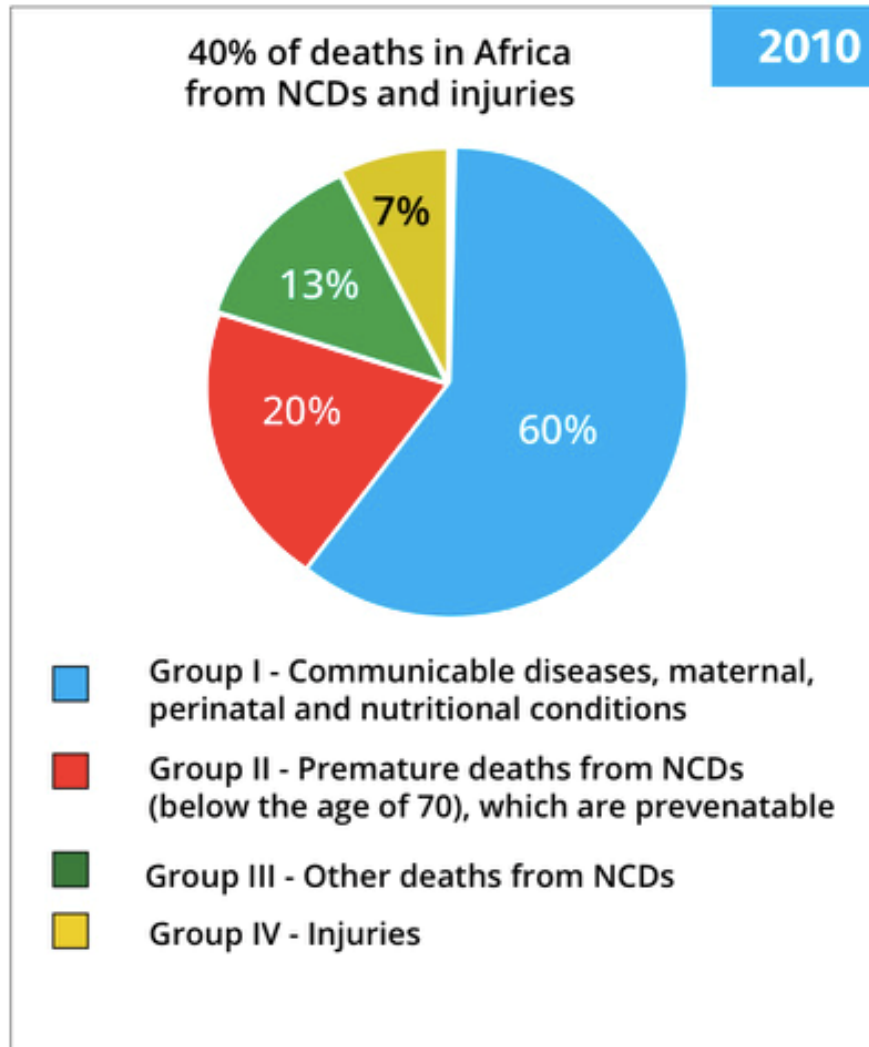


Figure 1. Genetic Variants Associated with Hypertrophic Cardiomyopathy.

Avoid misdiagnoses in all populations



Dual Burden of Disease: Communicable and Non-Communicable

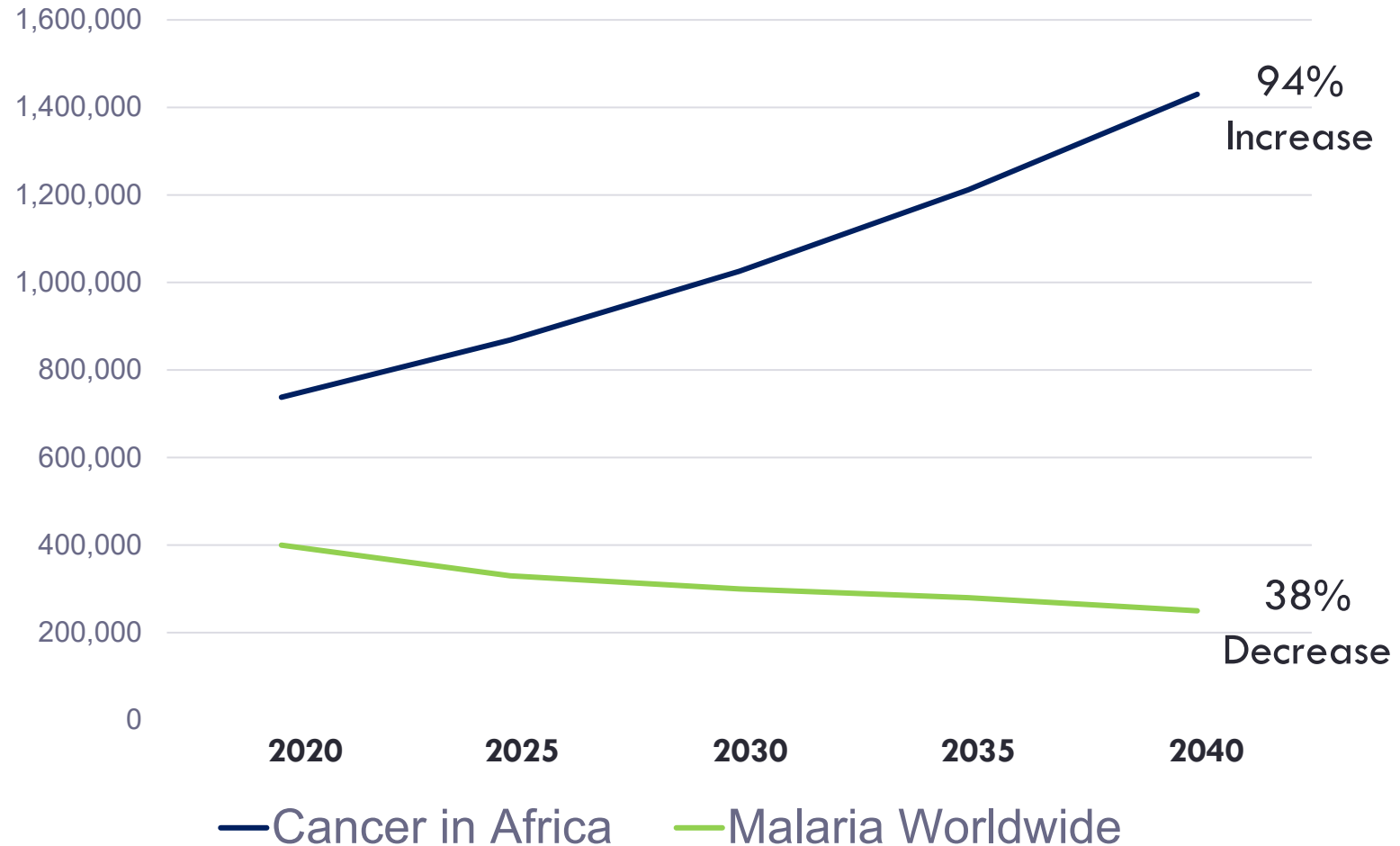


Africa's Future Cancer Burden

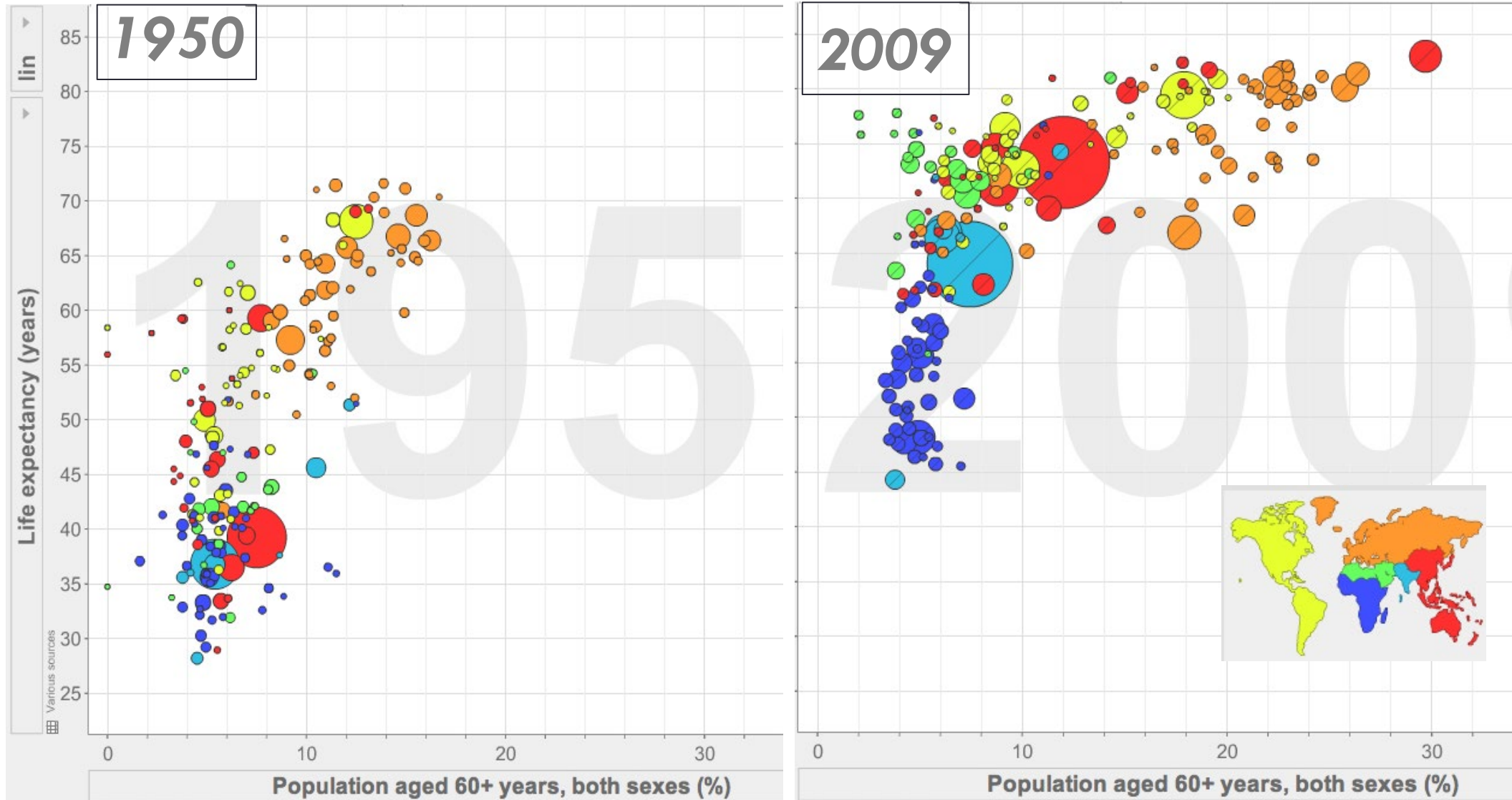
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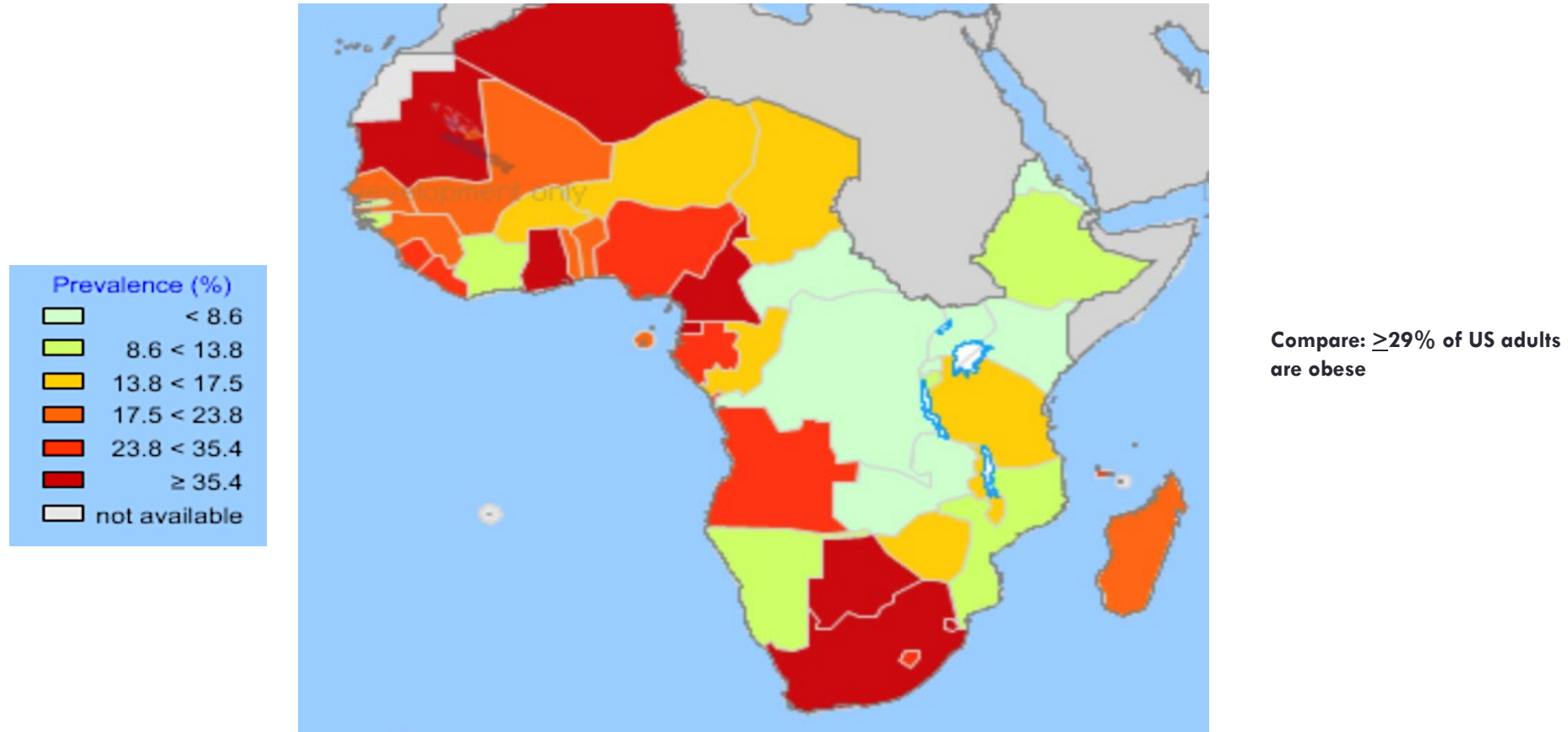


Increasingly Elderly Population in Africa



Africa's Cancer Burden

Exposure to factors associated with cancer risk is common and increasing

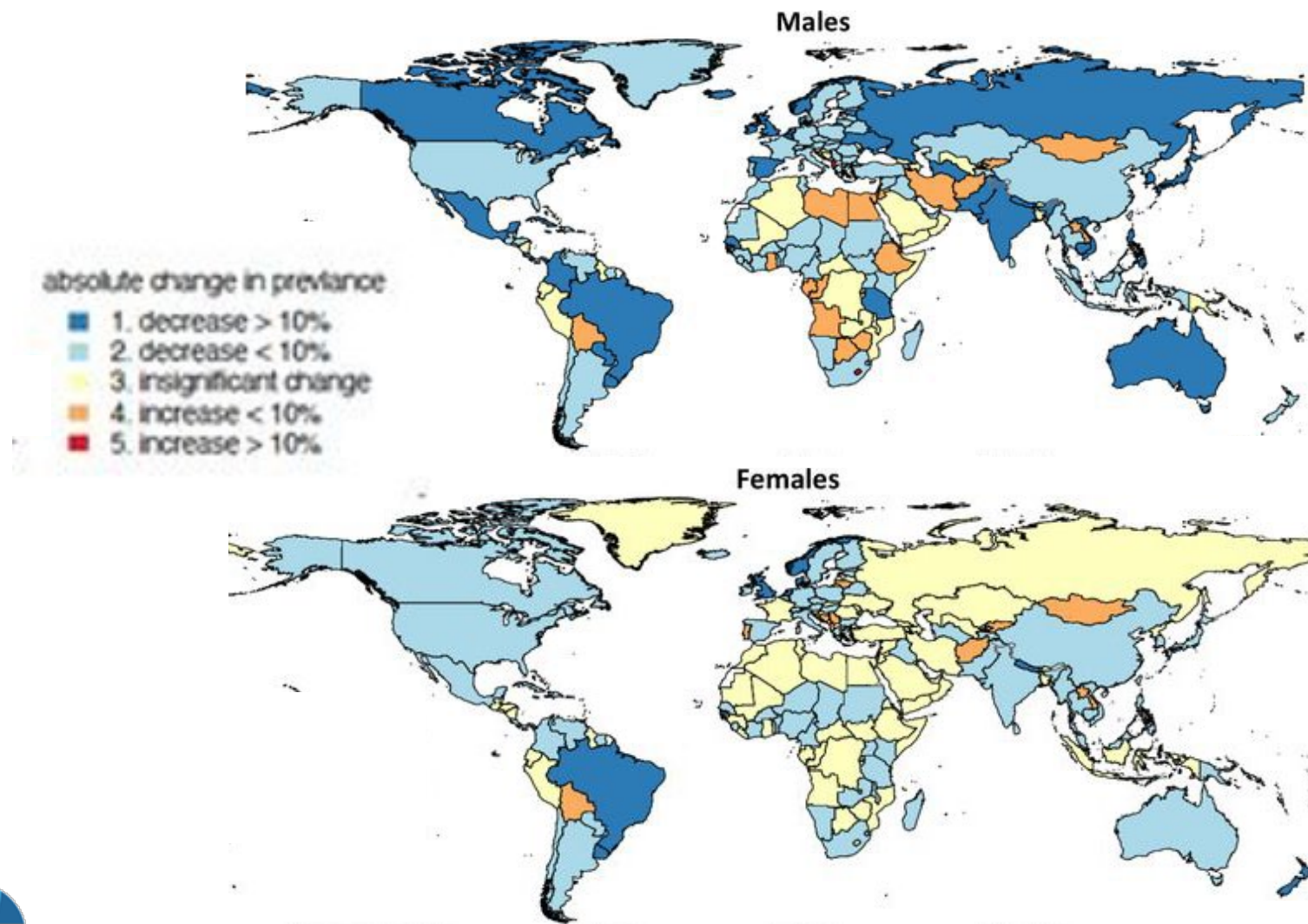


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Percent Change in Prevalence of Current Smoking

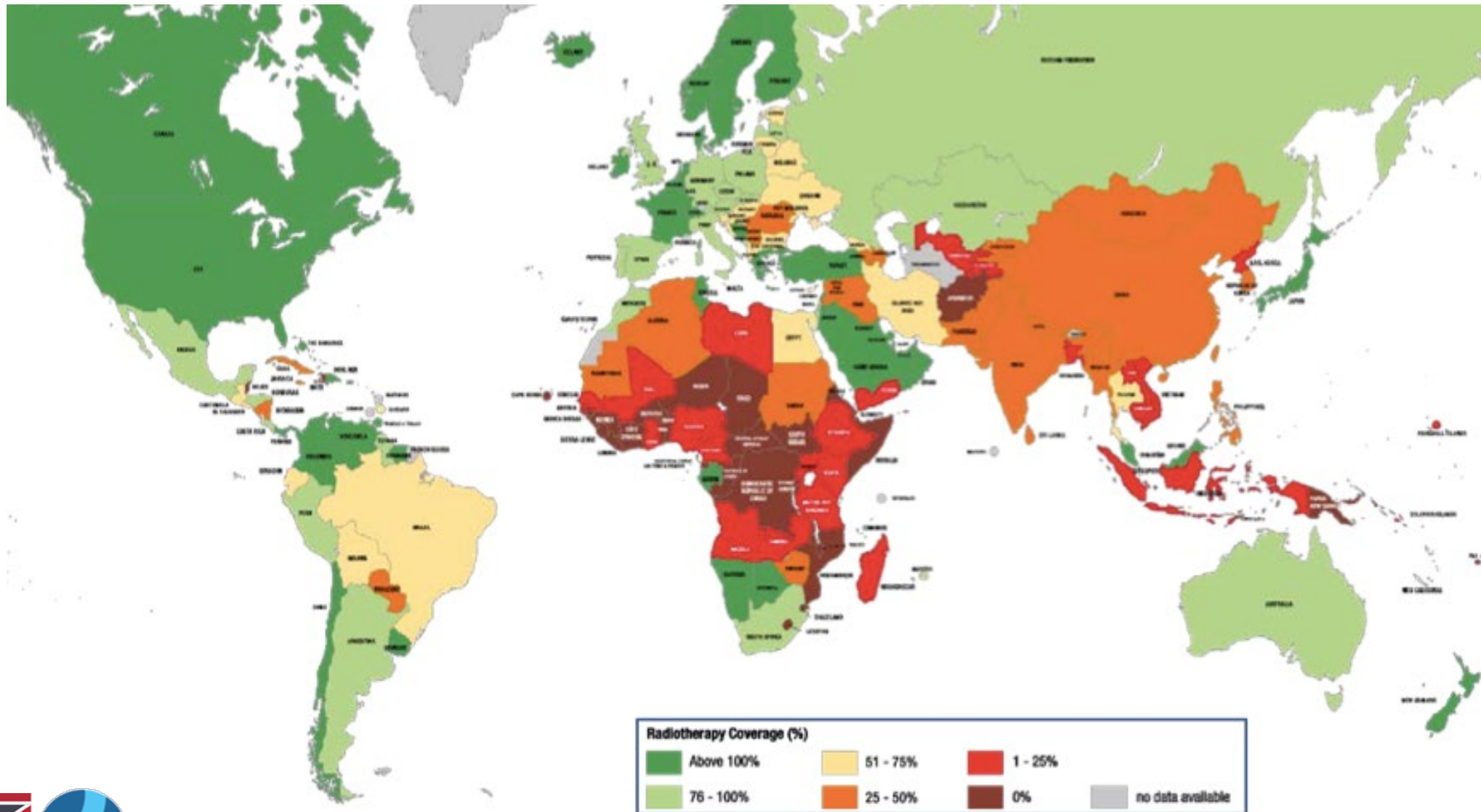
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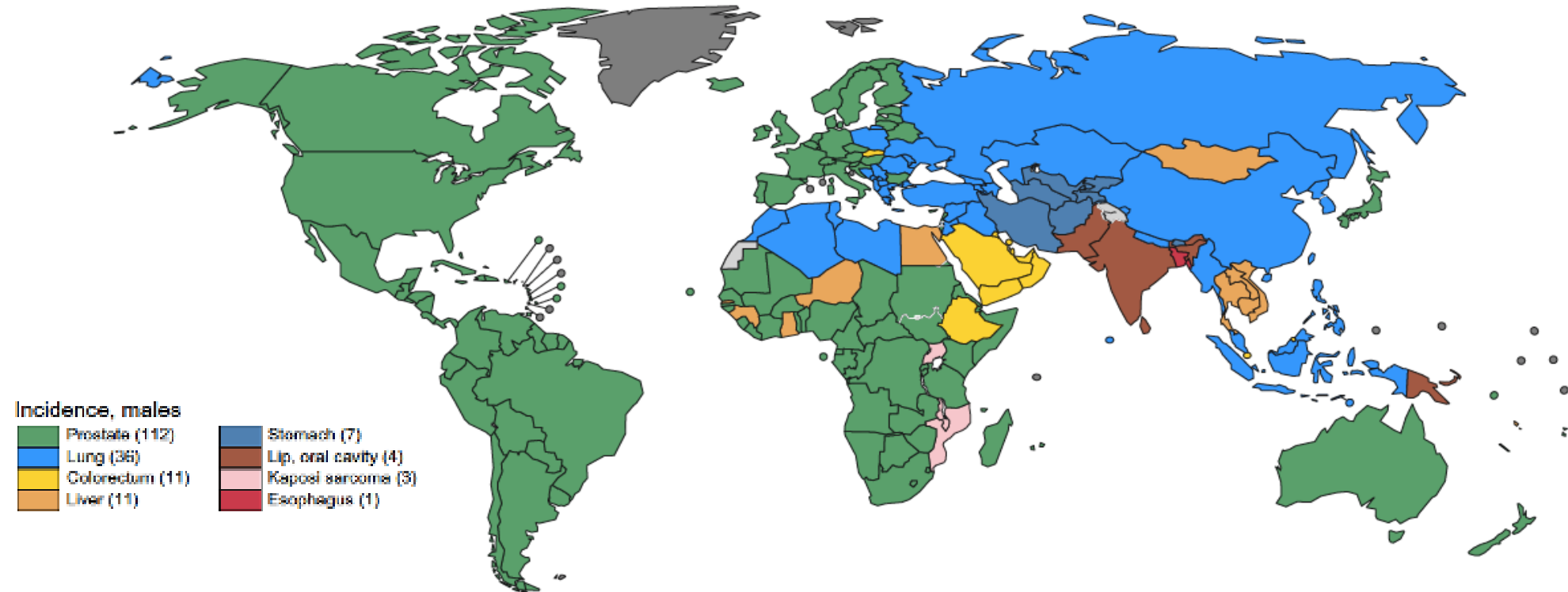
Percent of Population Covered by Cancer Registries (Number of Registries / Number of Countries Reporting)



Radiotherapy Coverage (% of Population)



Prostate Cancer



Known Risk Factors:

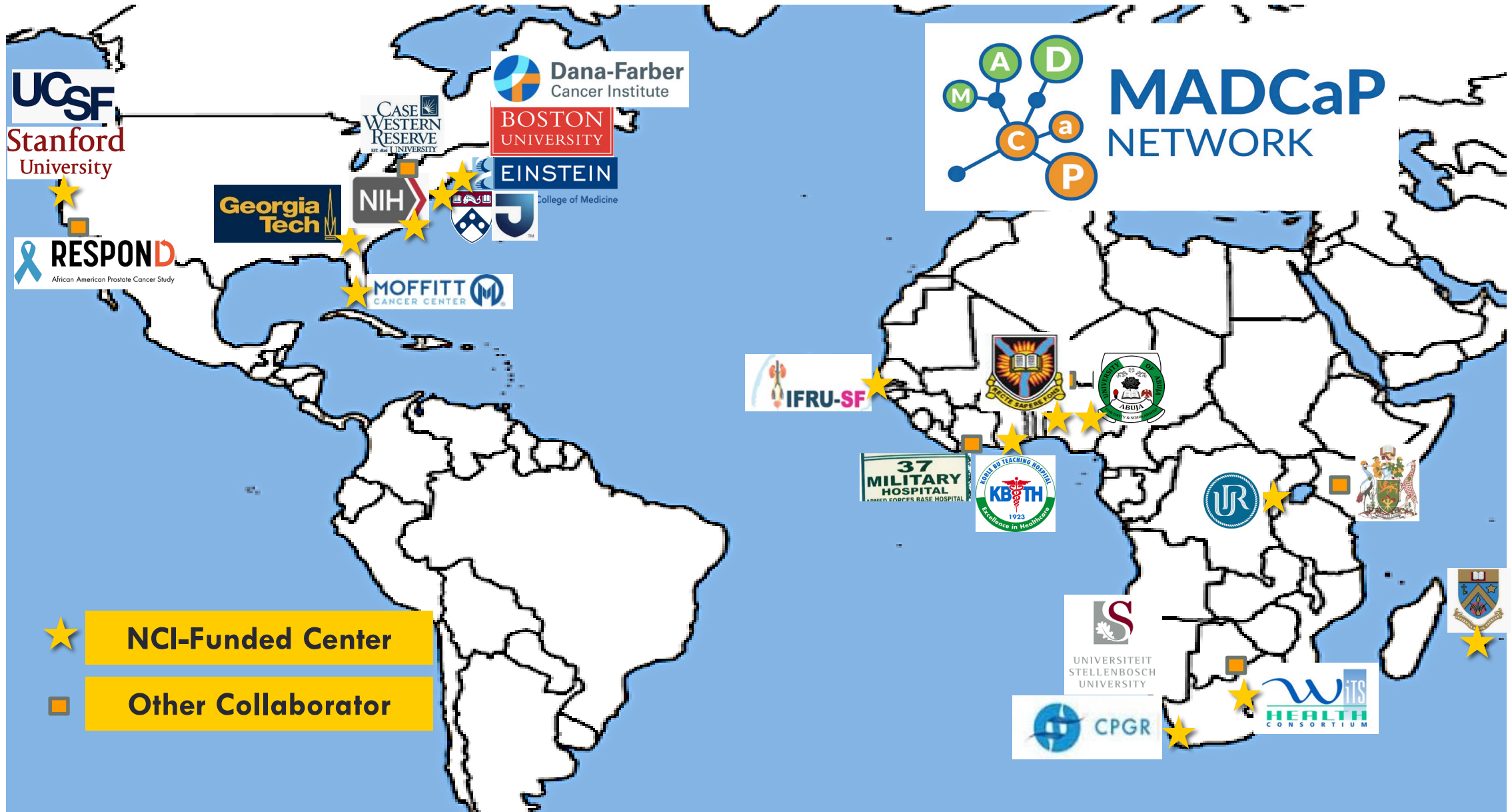
Age, Family History, Race, Obesity (Aggressive Disease).

Percent Variability Due to Genetic Factors: 57%

Most Recent Multiethnic Prostate GWAS: 451 Loci

MADCaP: Men of African Descent and Carcinoma of the Prostate

Supported by AACR Landon Foundation, Fulbright Program, R01-CA085074, P50-CA105641, P60-MD006900, U01-CA184374, P20-CA233255



Genetics: A Core Element of Cancer Risk Assessment, Prevention, Therapy, and Disease Monitoring



NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Genetic/Familial High-Risk Assessment: Breast and Ovarian

Version 3.2019 — January 18, 2019

special articles

Implementation of Germline Testing for Prostate Cancer: Philadelphia Prostate Cancer Consensus Conference 2019

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JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA-Related Cancer in Women

Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

Heidi D. Nelson, MD, MPH, MACP, FRCP; Miranda Pappas, MA; Amy Cantor, MD, MPH; Elizabeth Haney, MD; Rebecca Holmes, MD



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2020

Genetic/Familial High-Risk Assessment: Colorectal

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Table 1: Multi-Gene Testing Definitions

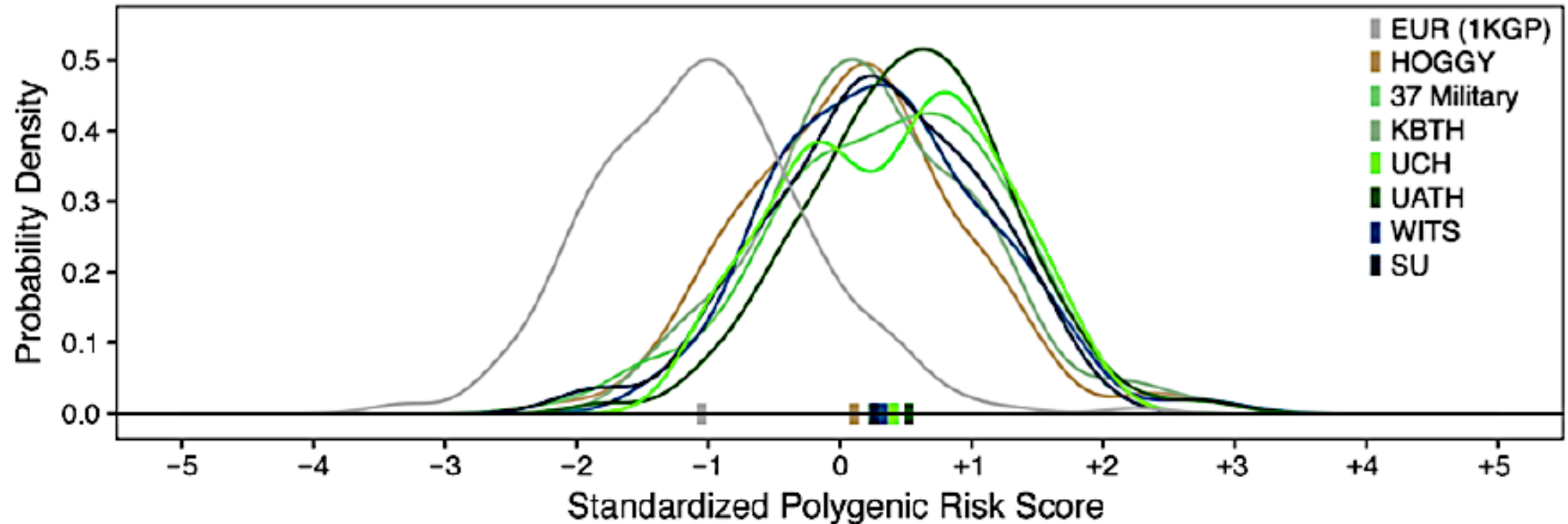
TERM	DEFINITION
Multi-gene panel	Laboratory test that includes testing for pathogenic variants of more than one gene.
Syndrome-specific panel	Panel that only tests for one syndrome (eg, LS, adenomatous polyposis).
Cancer-specific panel	Panel that tests for more than one gene associated with a specific type of cancer.
"Comprehensive" cancer panel	Panel that tests for more than one gene associated with multiple cancers or multiple cancer syndromes.
Actionable pathogenic variant	Pathogenic variant that results in a recommendation for a change in clinical management.
Variant of uncertain significance	Genetic test result indicating a sequence variant in a gene that is of uncertain significance. Variants are generally not clinically actionable, and most (but not all) are ultimately re-classified as benign. ^{a,b}

Table 2: Pros and Cons of Multi-Gene Testing for Hereditary Colorectal Syndromes^a

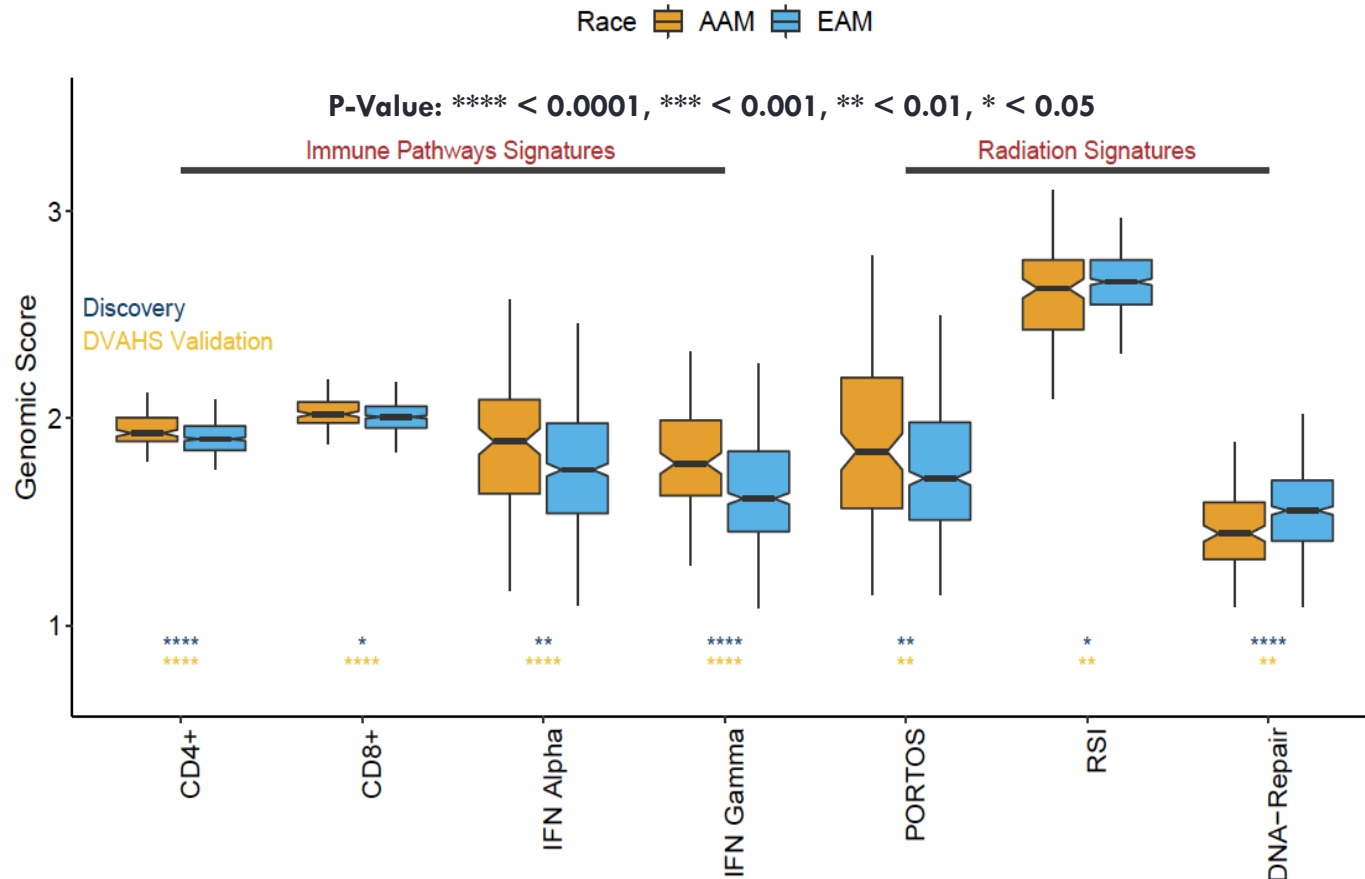
PROS	CONS
<ul style="list-style-type: none"> • More efficient testing when more than one gene may explain presentation and family history. • Higher chance of providing proband with possible explanation for cause of cancer. • Competitive cost relative to sequentially testing single genes. • Chance of identifying pathogenic variants in multiple actionable genes that could impact screening and management for the individual and family members that may be missed using cancer syndrome-specific panels. 	<ul style="list-style-type: none"> • Higher chance of identifying pathogenic variants for which clinical management is uncertain. Estimates suggest that 3%–4% (Gastroenterology 2015;149:604-13.e20; Clin Genet 2014;86:510-520) of pathogenic variants identified are not clearly clinically actionable, such as finding a pathogenic variant in a moderate-risk gene for which management is unclear. • Higher chance of identifying variants of uncertain significance that are not actionable; reported rates of finding variants of uncertain significance range from 17%–38%. • Higher chance that patient will mistakenly receive overtreatment and overscreening if variants of uncertain significance or pathogenic variants for which clinical management is uncertain are incorrectly interpreted.



Divergence in Polygenic Risk Scores Between European and African Populations

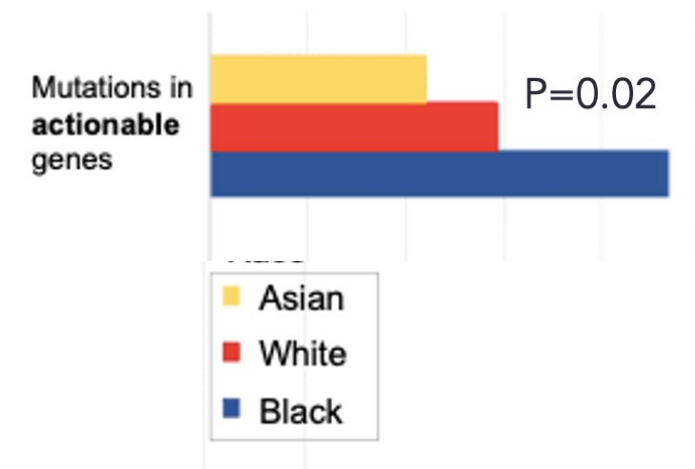


Enrichment of Immune-Oncologic Pathways, Lower DNA Damage Repair, Elevated Radiosensitivity, and Actionable Mutations in Black vs. White



- Decipher transcriptome data
- 1,173 radiation naive radical prostatectomy samples.

Awasthi et al., *Clin Cancer Res* 2020,
Mahal et al., *NEJM* 2020



- Project GENIE
- 2393 patients: 2109 White, 204 Black, and 80 Asian

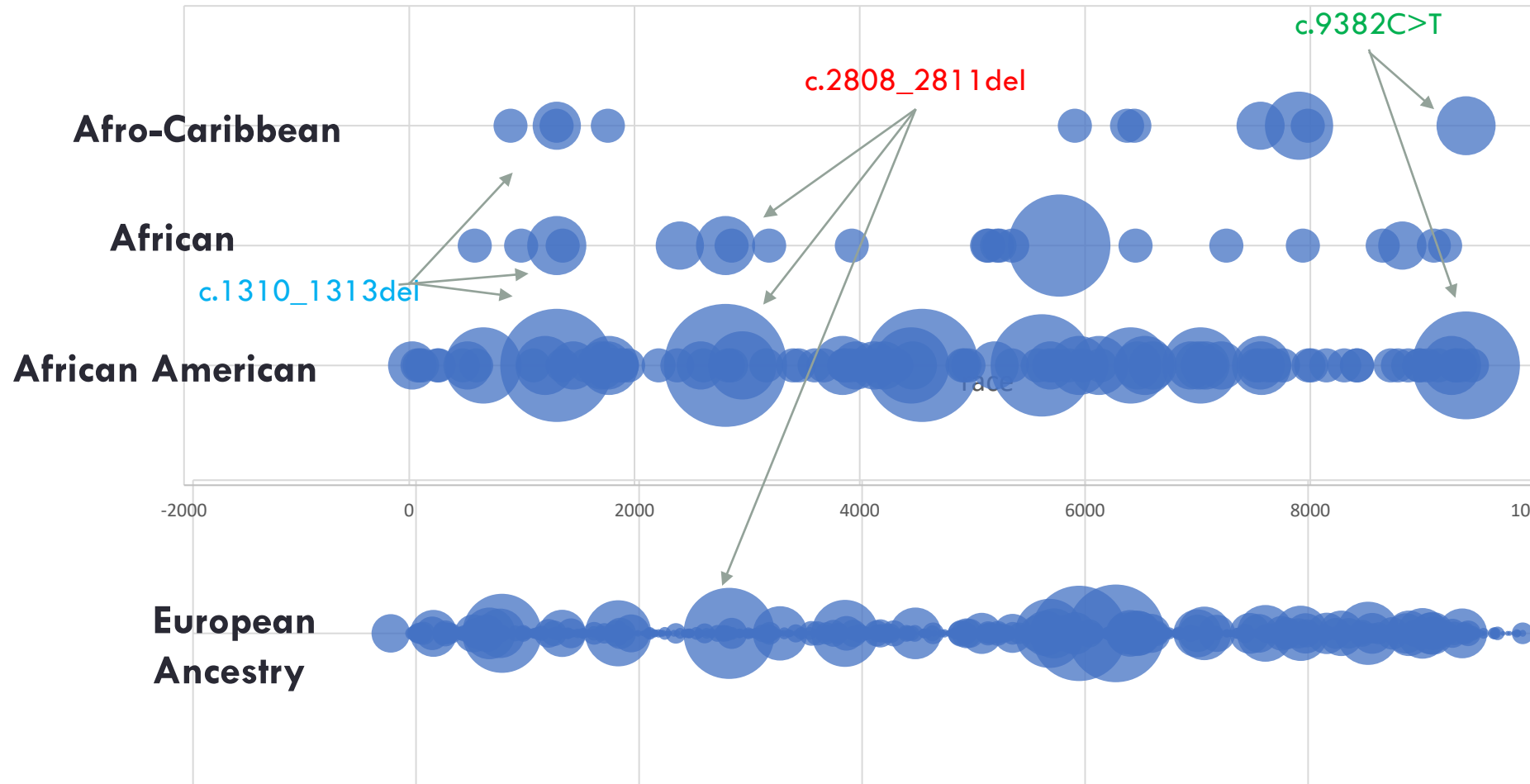


Pathogenic Sequence Variants by Inferred Continent of Origin

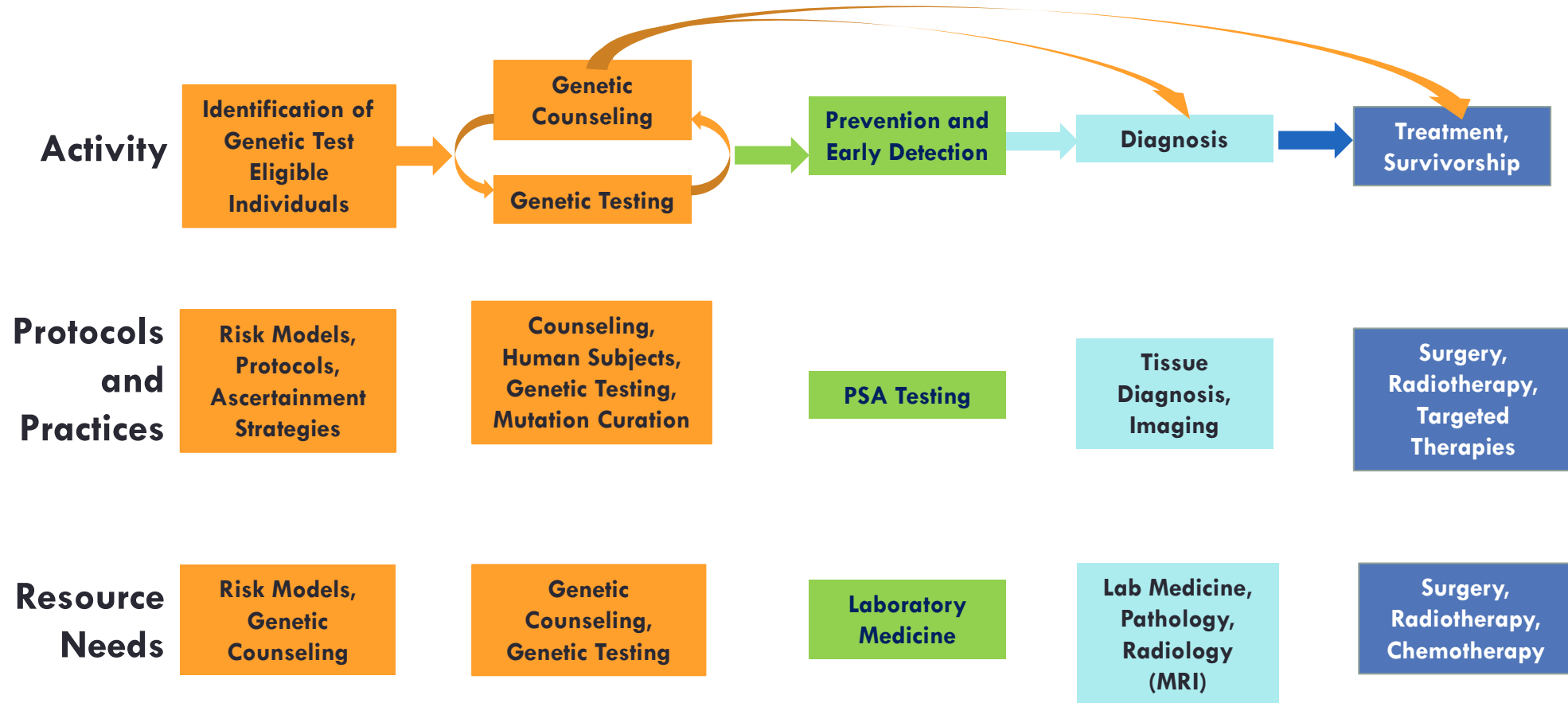
Designation	<i>BRCA1</i>		<i>BRCA2</i>	
	Count	%	Count	%
Likely African	35	34%	49	33%
Likely Non-African	18	17%	44	29%
Probably Not African	11	11%	2	1%
Cannot Determine	39	38%	53	36%
Total	103	100%	148	100



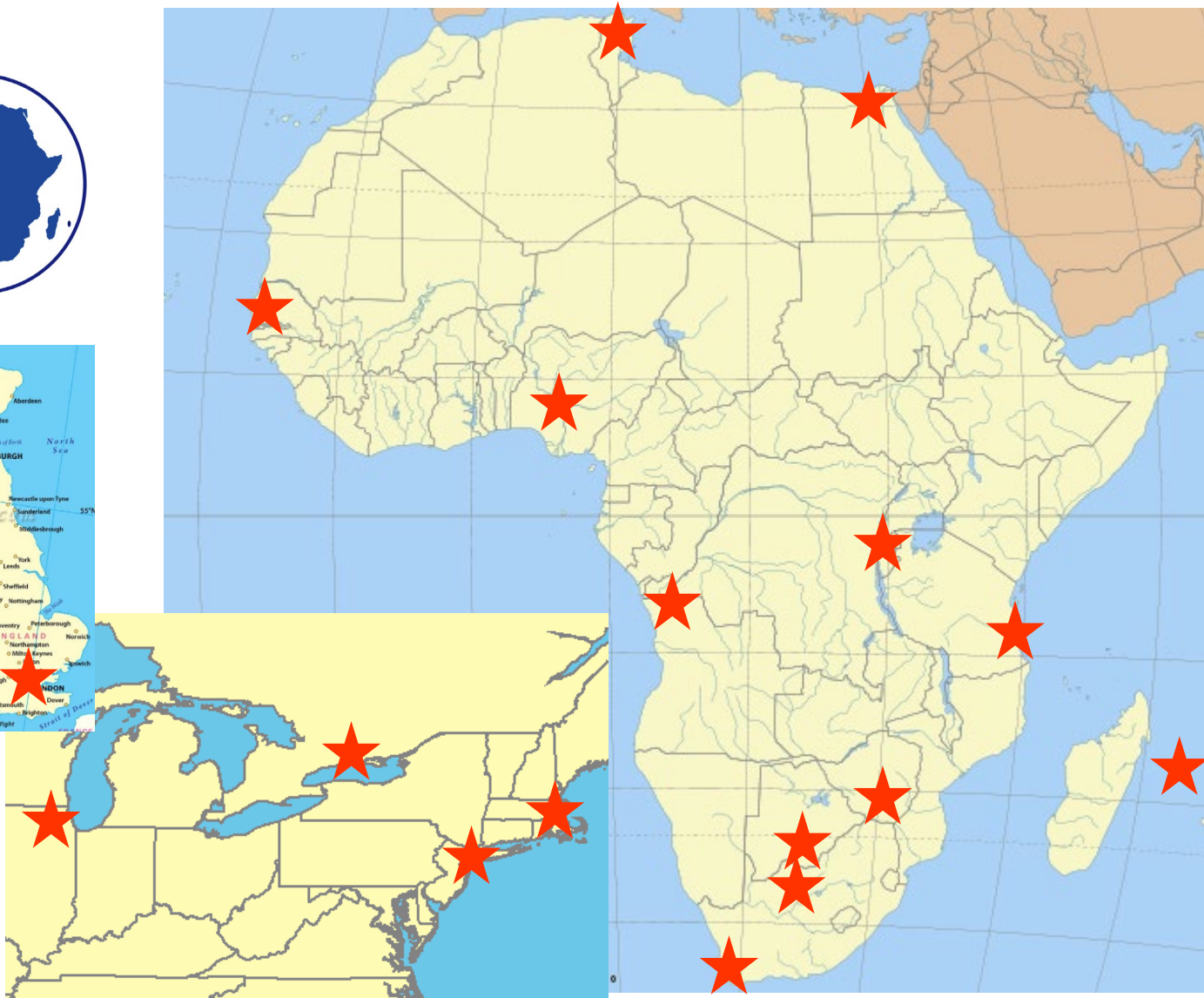
BRCA2 Mutations by Race/Ethnicity



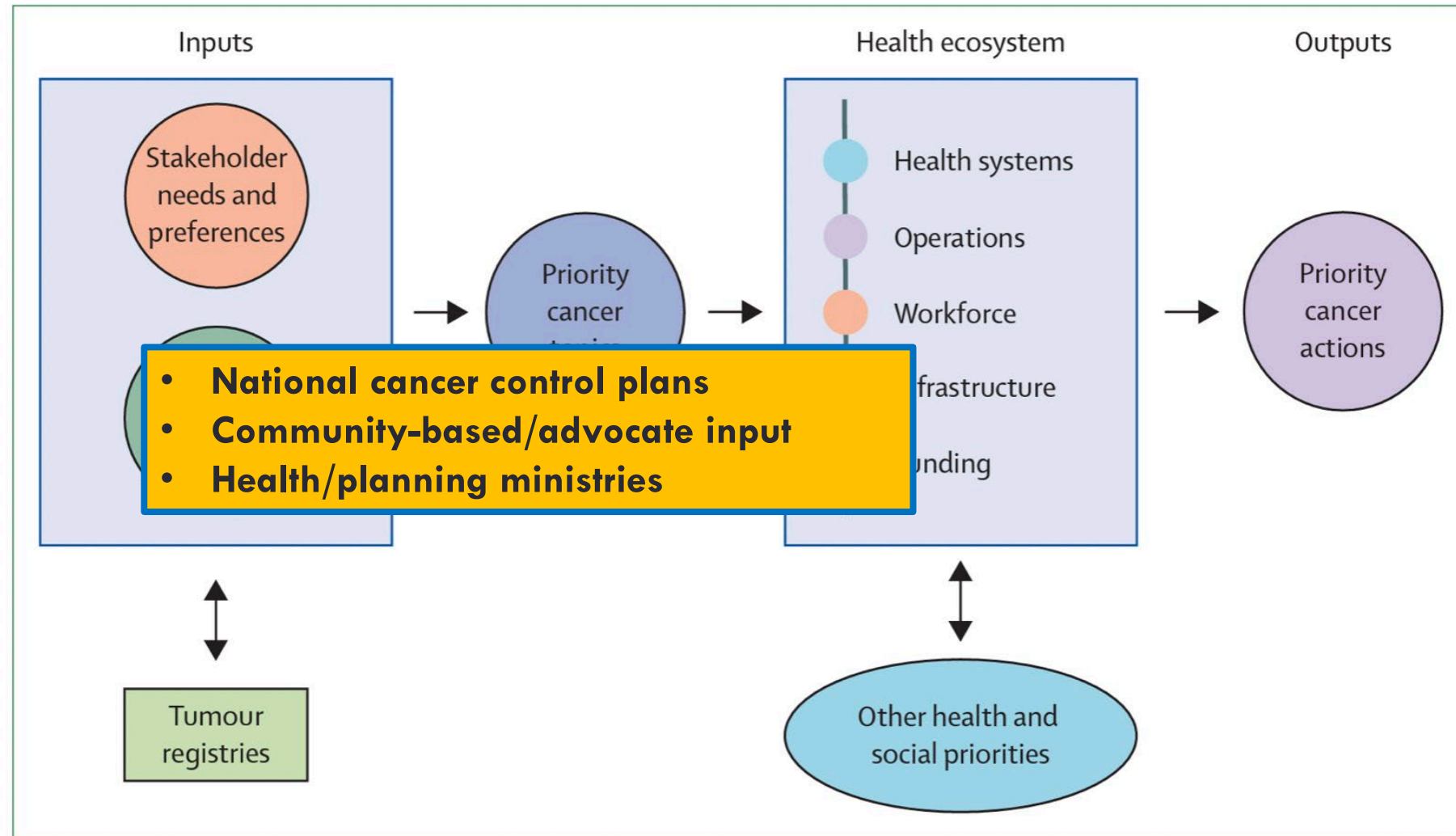
Leapfrogging Management of Prostate Cancer in 21st Century Africa



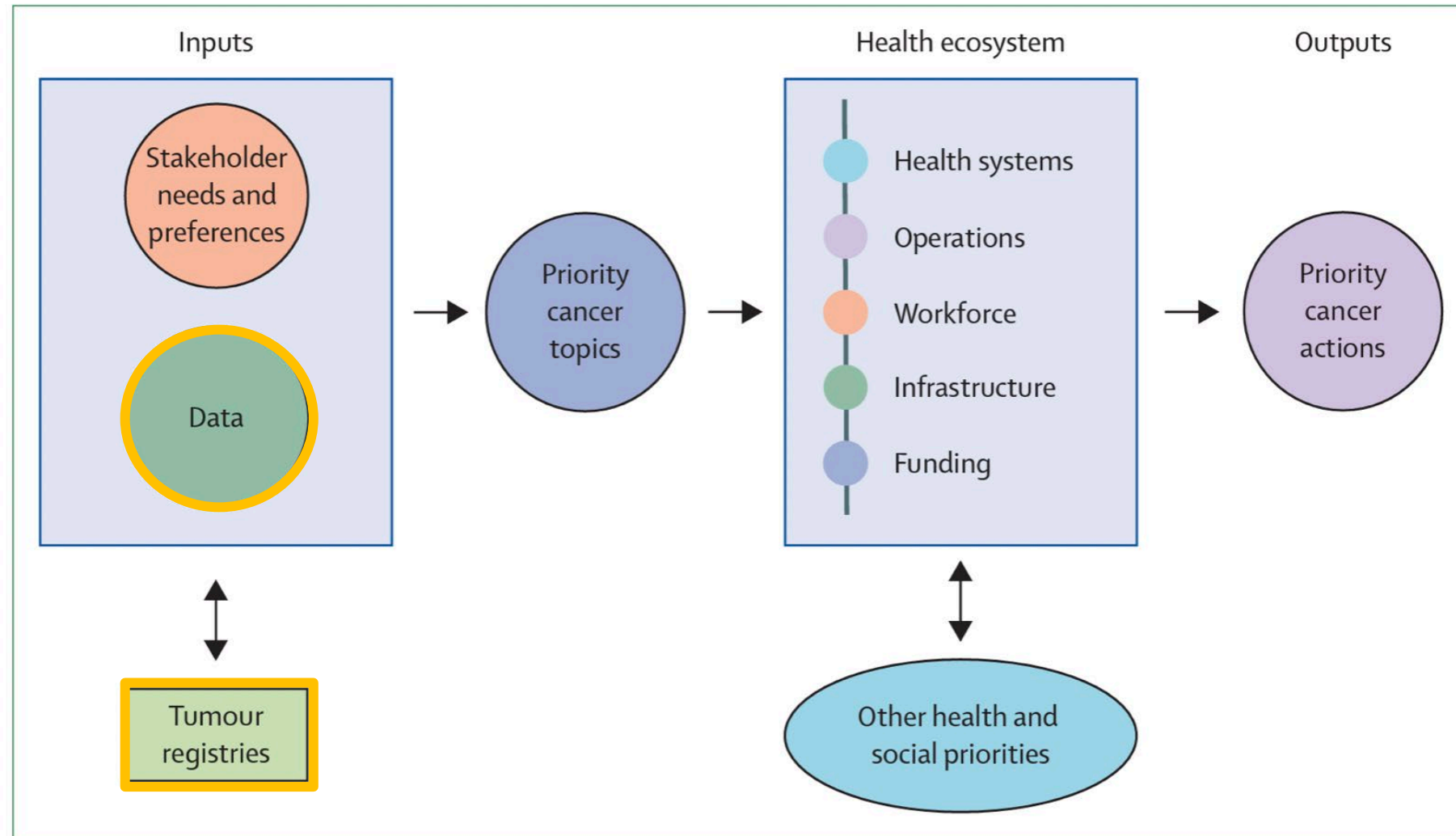
African Oncogenetics Network - Réseau Africain d'Oncogénétique



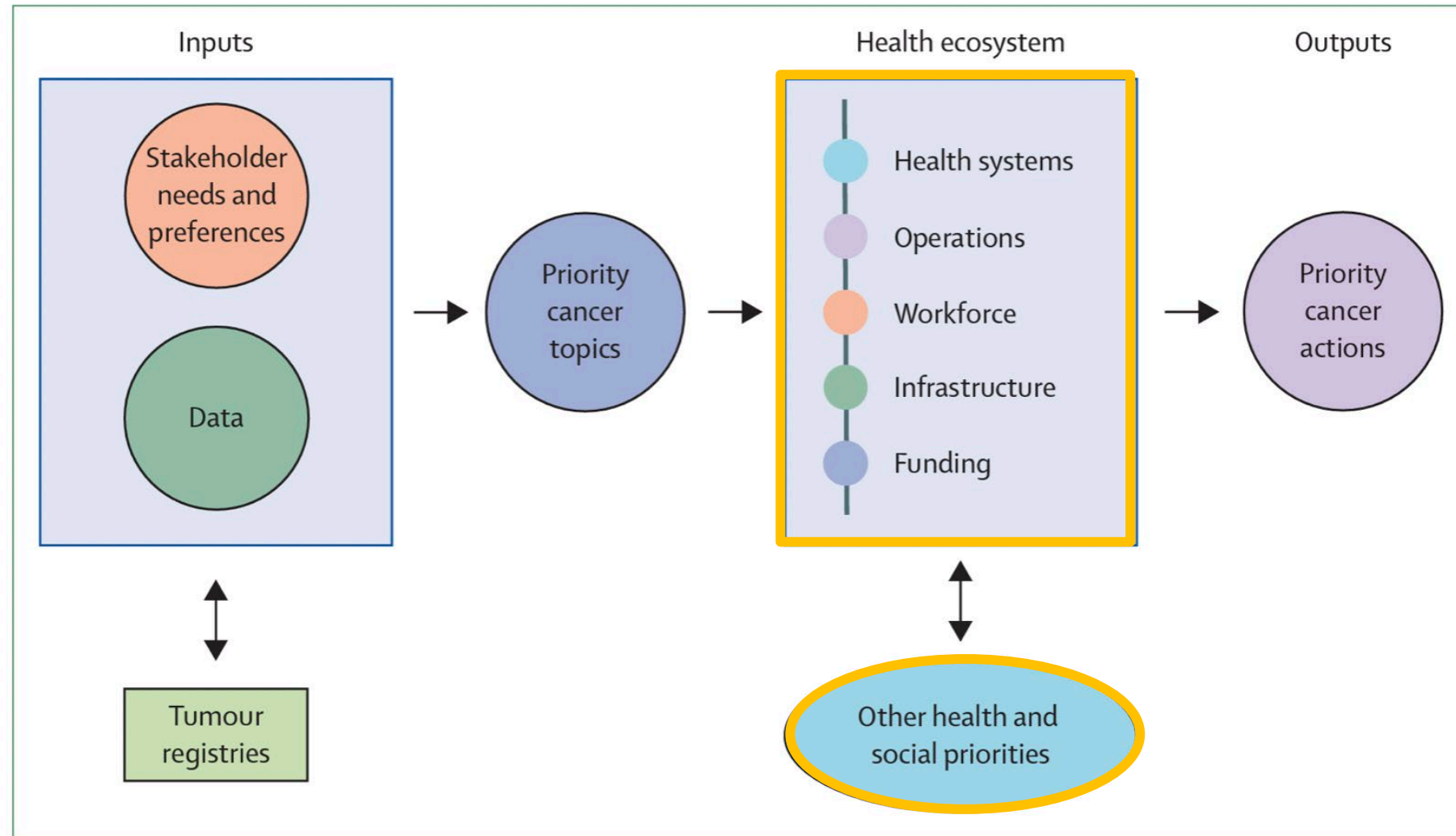
Pathways to Enhanced Cancer Capacity and Impact in Africa



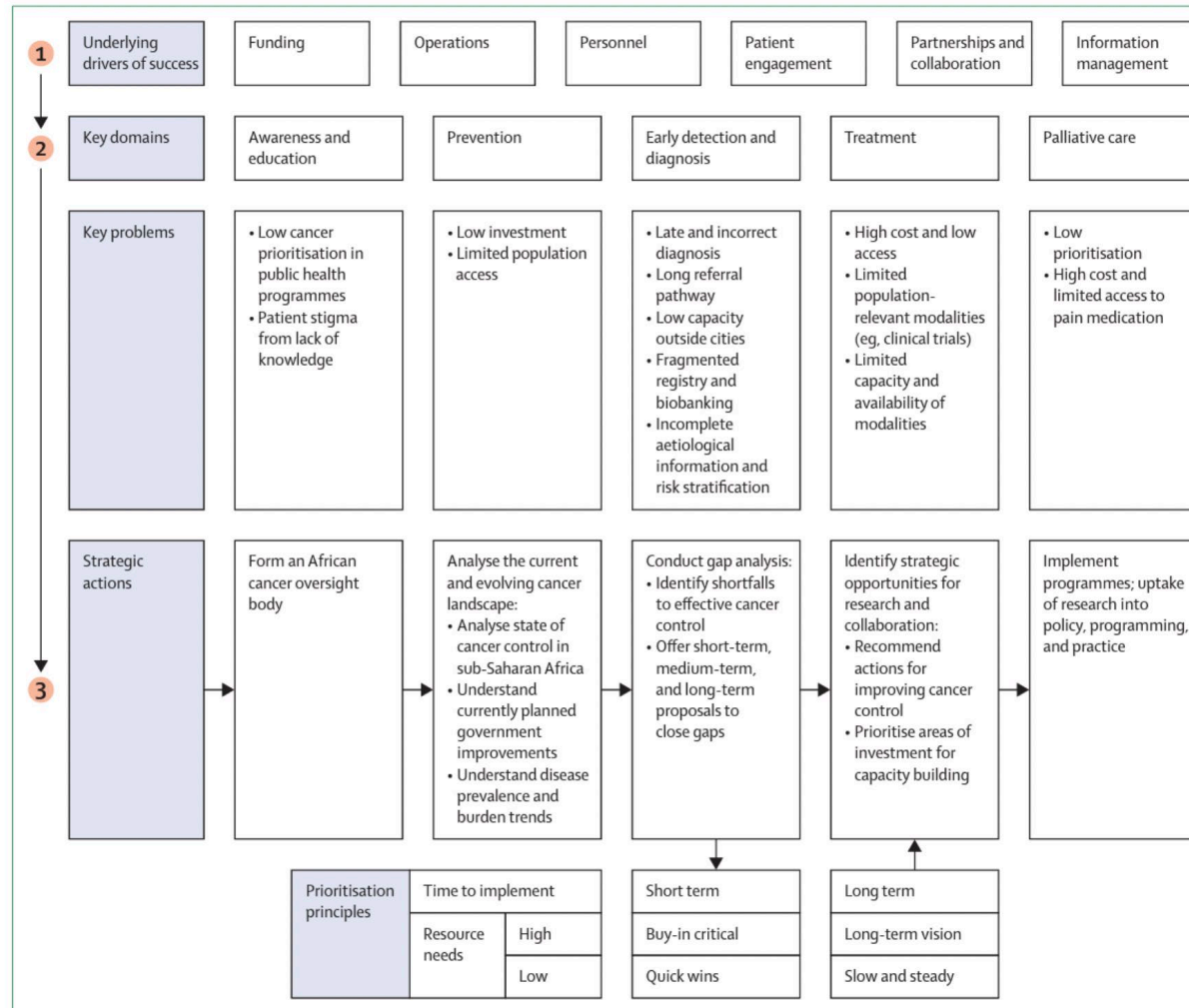
Pathways to Enhanced Cancer Capacity and Impact in Africa



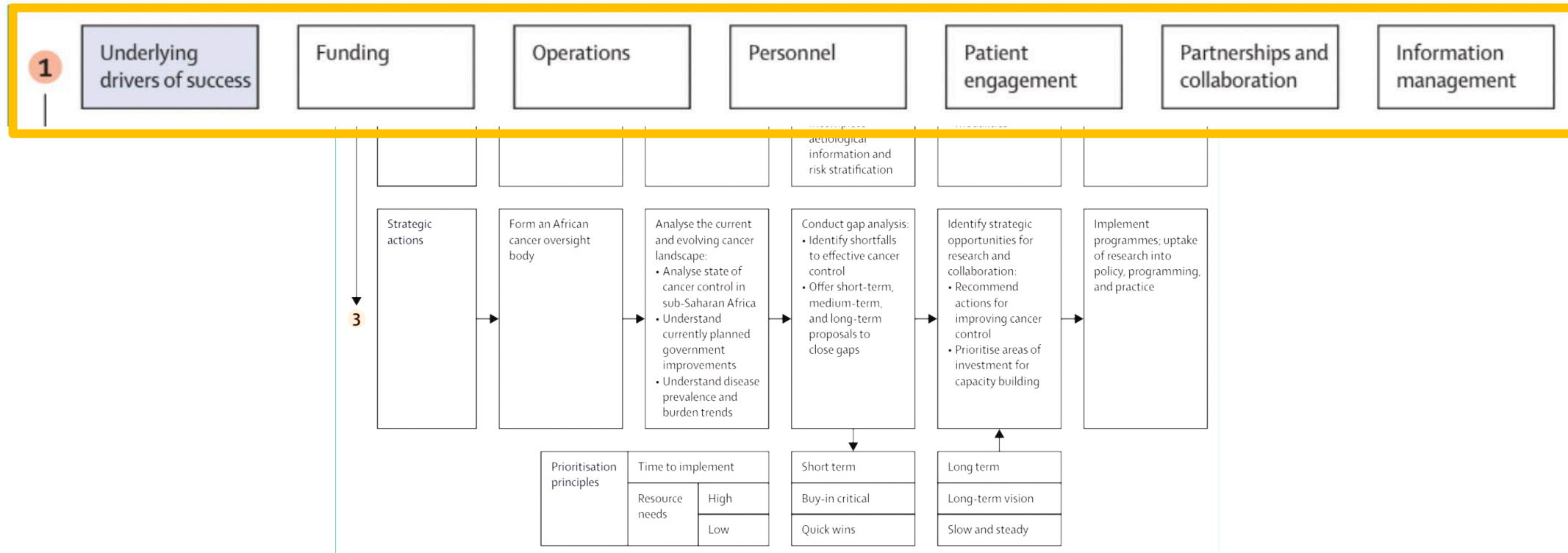
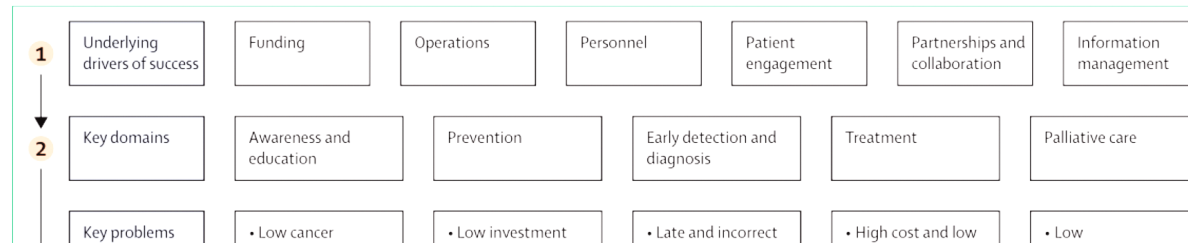
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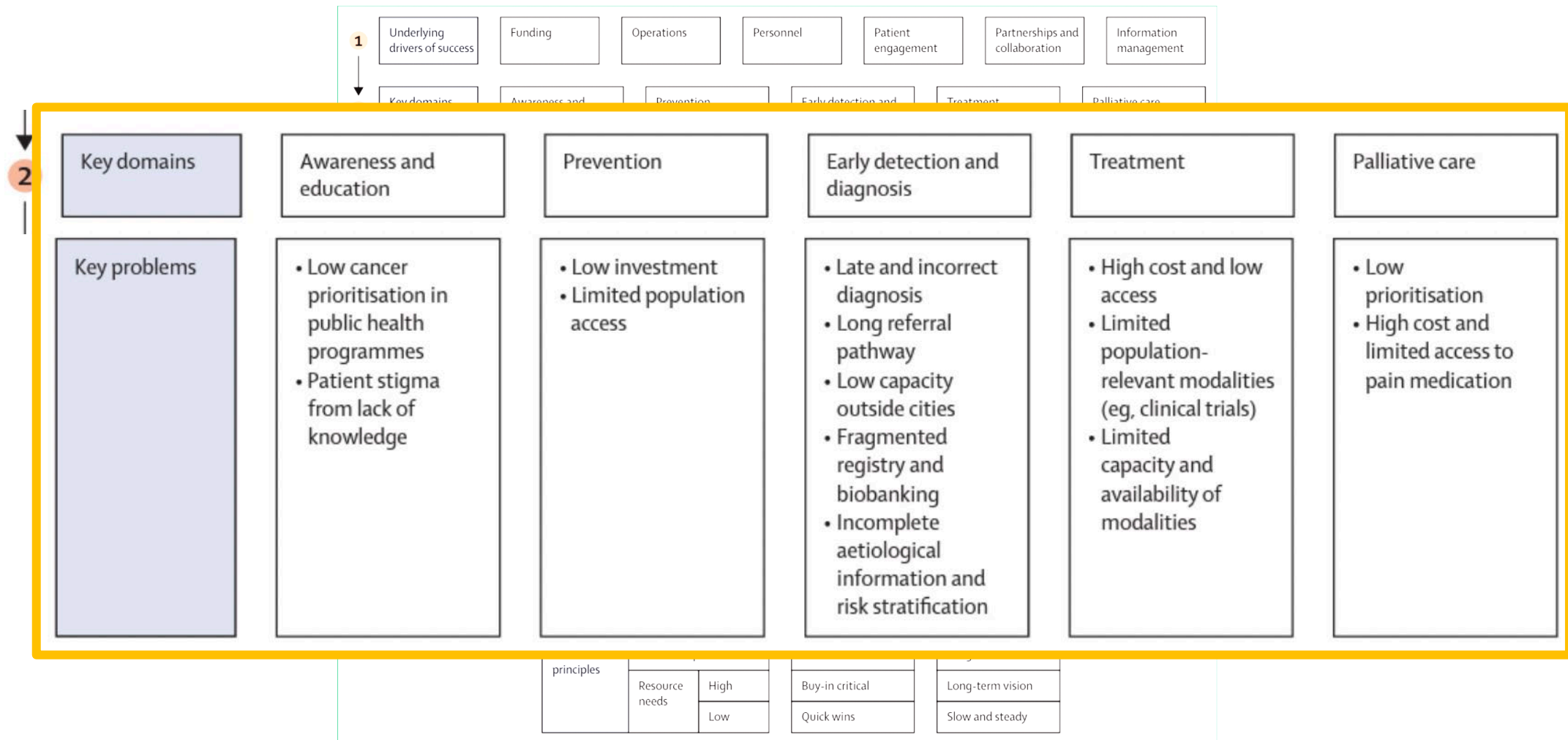
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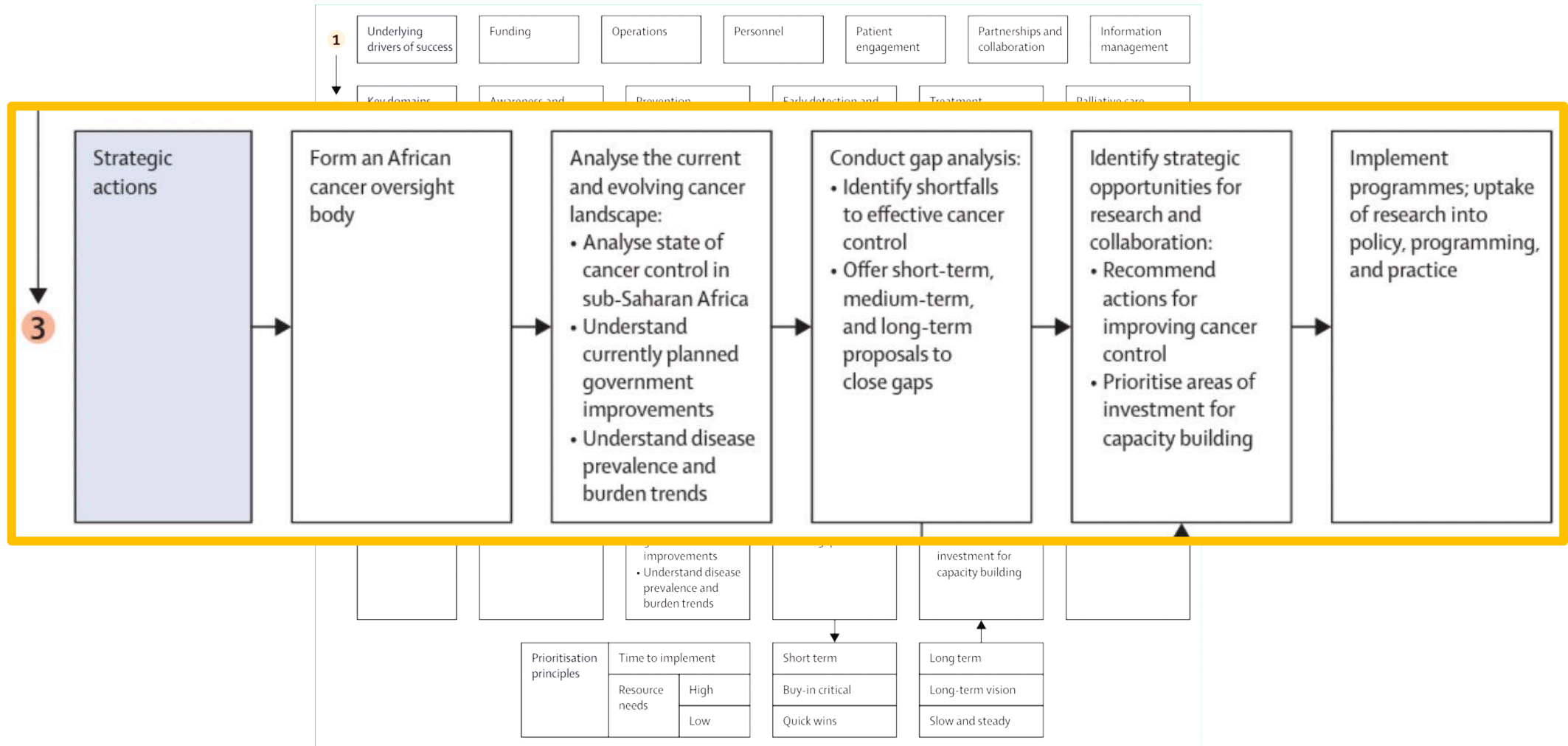
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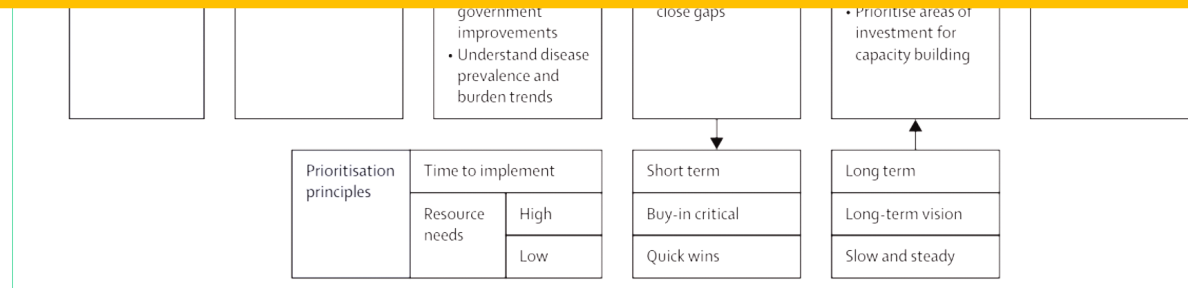
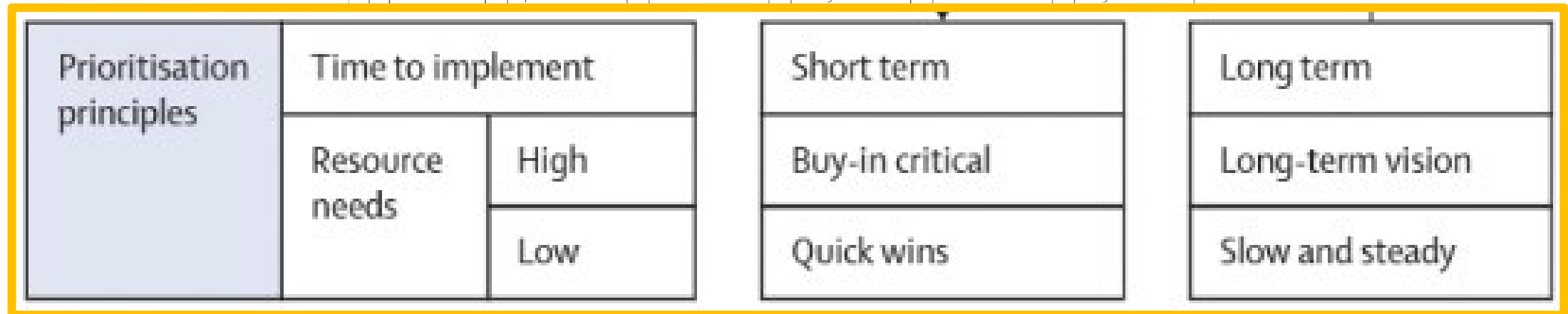
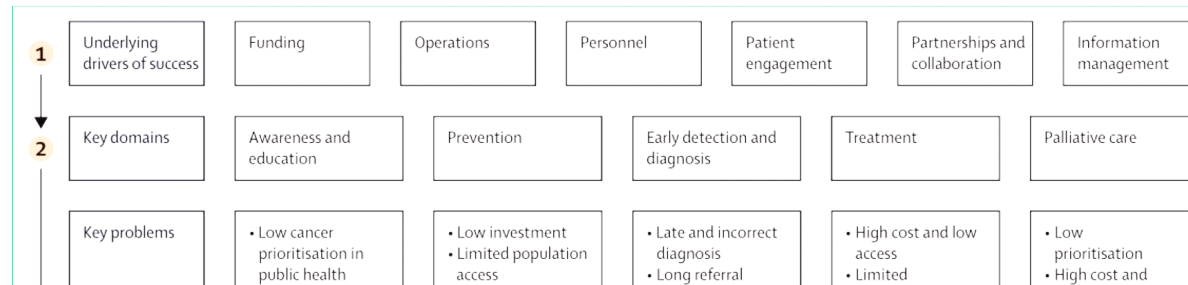
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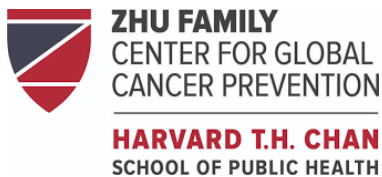
Why Focus on Cancer in Africa?

- Foster social and economic progress:
 - Enhance health care capacity and systems
 - Impact education, training, and workforce
 - Ensure optimal health of Africans
- Inform cancer knowledge and practice worldwide
- Is not a luxury but a critical need



Thanks to:

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R01-CA U2CCA252974, U01-CA184734, P20-CA233255.**



Q&A and Discussion



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Grand Rounds Webinar Improving Epidemic Readiness

July 18, 2023

At this July Grand Rounds, experts from Resolve to Save Lives will discuss two of the organization's flagship initiatives to strengthen epidemic readiness globally: the 7-1-7 framework and Epidemic Ready Primary Health Care.



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Thank You



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