MCD Technology: Will it close or widen the gap?

Philip E. Castle, PhD, MPH
Director, Division of Cancer Prevention
Senior Investigator, Division of Cancer Epidemiology and Genetics,
NCI/NIH/DHHS

NIH NATIONAL CANCER INSTITUTE

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1. *Overview of the NCI's Plans to Evaluate MCDs*
2. *Cervical Cancer and Health Disparities*
3. *Implementation Challenges for MCD*

Personal Genome Diagnostics
Foundation Medicine
Burning Rock
Biological Dynamics
20/20 GeneSystems
Precision Epigenomics
EarlyDiagnostics
Epic Sciences
Singlera Genomics
Biocept
QIAGEN
Exact Sciences
Guardant Health
GRAIL
Natera
Bluestar Genomics
Oncocyte
Delfi Diagnostics
Freenome
StageZero
Cardiff Oncology
LungLife AI
Resolution Bioscience
Elypta
Exosome Diagnostics
Adela
Caris Life Sciences

I think I'd like to have an MCED test, Doc, but which one?

NCI Division of Cancer Prevention
https://prevention.cancer.gov/mced

My Views/Opinions of MCDs

- A very promising technology but there is no evidence to date that these tests provide any clinical benefit, even the low (and controversial (see Feng *et al*., JAMA, 2024) bar of reducing advanced stage cancer.
- Yet some of these tests are being offered to a public who are not being given enough information to and/or cannot make an informed decision.
- You cannot extrapolate from SEER data the potential benefits of MCD testing.
- I do believe that one (or more) of these tests will be demonstrated to provide a clinical benefit ("early detection"), but I don't know which one(s), for whom, for which cancers, and the magnitude of benefit.
- One size does not fit all.
- MCDs are definitely a disruptive technology. However, the healthcare guidelines and infrastructure are not there to support their use. Those marginalized individuals and communities will have significant challenges in accessing the test and the downstream care following a positive result.
- There is a great need to evaluate these technologies without bias and financial interest.

Examples of MCD Assays

Company	Assay	Technology	Targeted Cancers: Lung	CRC	Breast	Pancreas	Liver	Esophagus	Stomach	Ovary	Prostate	Bladder	Kidney	Uterus	H&N	Lymphoma	Leukemia	Plasma Cell
Adela Bio	adela™	cfMeDIP-seq; cfDNA fragmentomics	■	■	■	■						■	■				■	
Biological Dynamics	Tr(ACE)	EV proteins; AI				■				■		■						
Bluestar Genomics	BluestarMCED	cfDNA 5hmC-seq; fragmentomics	■	■	■	■	■	■	■	■								
Burning Rock	OverC™	ELSA-seq	■	■		■	■	■		■								
Caris Life Sci	MI GPSai™	cfDNA/cfRNA NGS; AI	■	■	■				■				■	■				
Delfi Dignostics	DELFI	cfDNA fragmentomics	■	■		■			■	■								
Early Diagnostics	cf Methyl-Seq	cfDNA mC-NGS	■	■			■		■									
Exact Sciences	CancerSEEK	cfDNA NGS; protein markers	■	■	■	■	■	■	■	■								
Freenome	FMBT	Multi-Omics/AI	■	■	■	■	■	■	■	■	■	■	■	■				
Grail	Galleri™	CpG-cfDNA NGS	■	■		■	■	■	■	■		■			■	■		■
LungLifeAI	LungLB	CTC FISH; Imaging AI	■		■		■						■					
Natera	Signatera™	cfDNA NGS; protein markers	■	■	■	■	■					■		■				
Precision Epigenomics	Sentinel-10™	CpG-cfDNA qPCR	■	■	■	■	■											
20/20 Gene Systems	oneTEST	circul. Cancer Ag's; AI	■	■	■	■	■				■							

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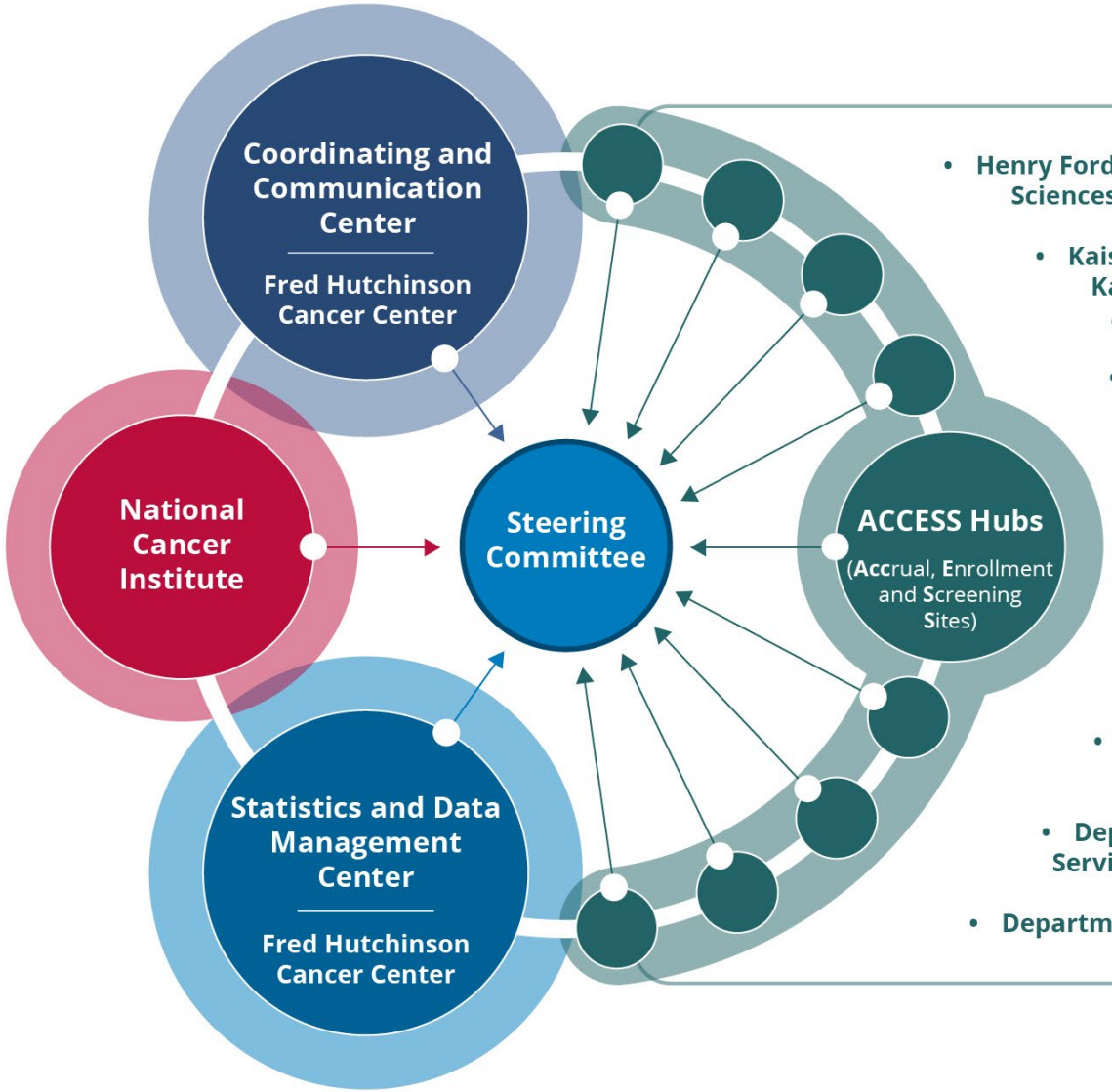
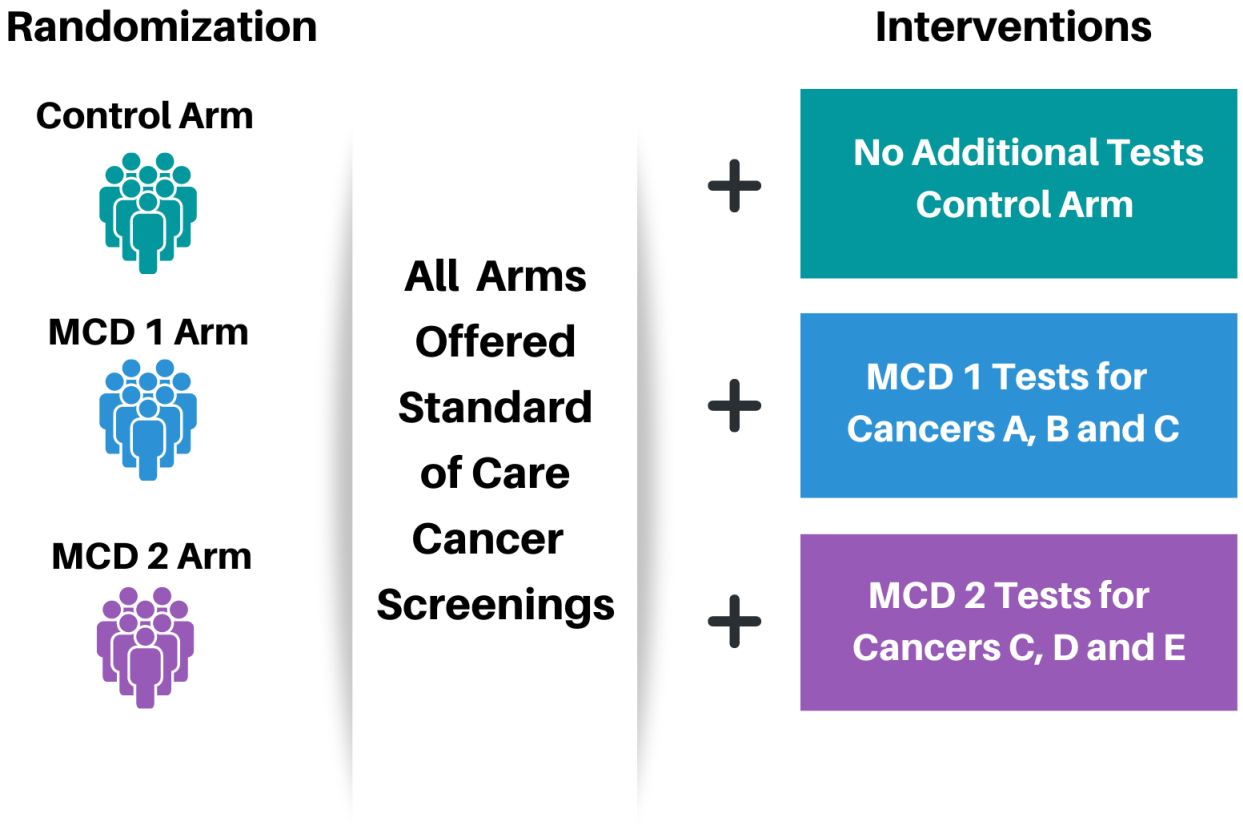
CANCER SCREENING RESEARCH NETWORK



- Henry Ford Health + Michigan State University Health Sciences
- Kaiser Permanente Northern California, Kaiser Permanente Southern California, and Kaiser Permanente School of Medicine
- OU Health Stephenson Cancer Center at the University of Oklahoma Health Sciences Center
- University of Colorado Cancer Center
- University of North Carolina Lineberger Comprehensive Cancer Center
- Virginia Commonwealth University, Inova, and Sentara Health
- Washington University School of Medicine in St. Louis
- Department of Defense Uniformed Services University
- Department of Veterans Affairs

The Vanguard Study



Objectives of Vanguard Study

- Assess participant willingness for randomization
- Determine adherence to testing and diagnostic follow-up
- Evaluate feasibility of protocol-defined diagnostic workflows
- Determine reliability and timeliness of blood specimen testing and return by MCD companies
- Identify facilitators and barriers to recruitment/retention/compliance of diverse participant groups

Estimated sample size for the Vanguard is 8,000 persons per arm

Possible Platform Randomized Control Trial Design

Randomization

Control Arm

MCD 1 Arm

MCD 2 Arm

MCD 3 Arm

All Arms Offered Standard of Care Cancer Screenings

Interventions

\+ No Additional Tests Control Arm

\+ MCD 1 Tests for Cancers A, B and C

\+ MCD 2 Tests for Cancers C, D and E

\+ MCD 3 Tests for Cancers E, F and A

All Cancer Cases and Cancer Deaths Captured (+ Other Data)

Primary Endpoints

All Cancer Deaths Measured

Deaths Rates from Cancers A , B and C Compared to Control Arm

Death Rates from Cancers C, D and E Compared to Control Arm

Death Rates from Cancers E, F and A Compared to Control Arm

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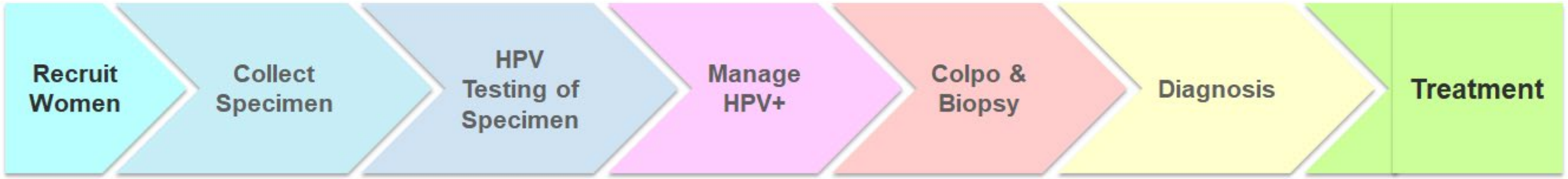
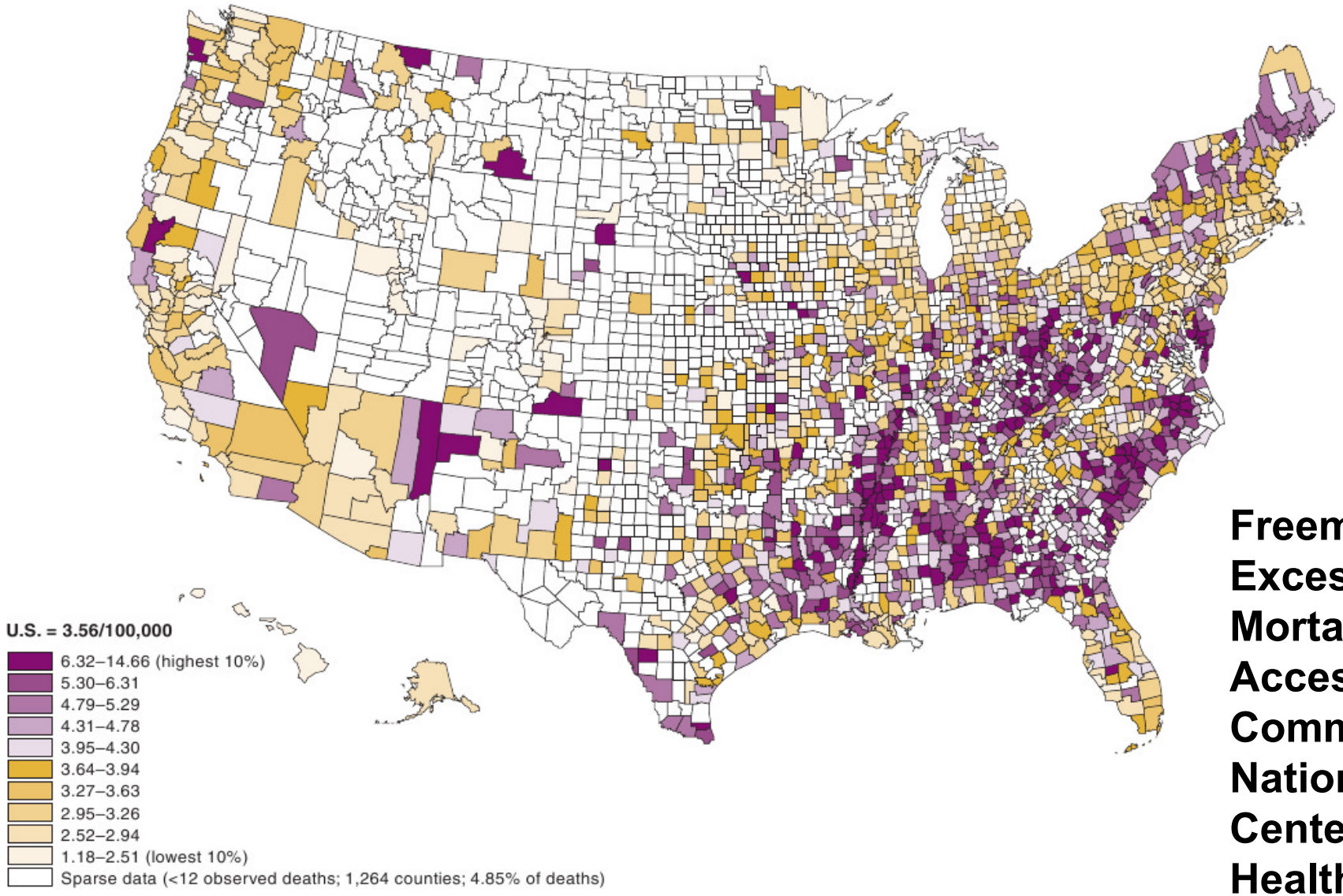
Cervical Cancer Screening Care Continuum: Screening is NOT just a Test

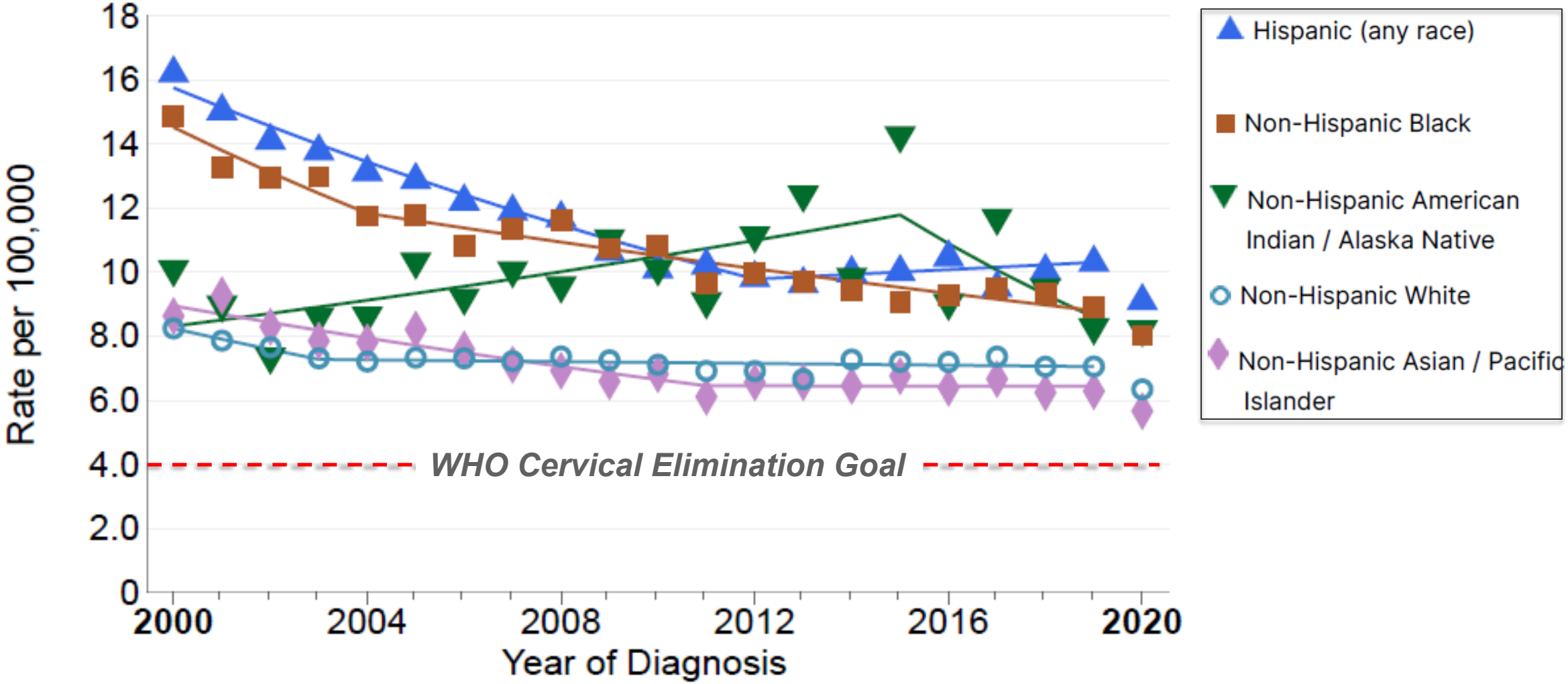


County-Level Cervical Cancer Mortality ~2005



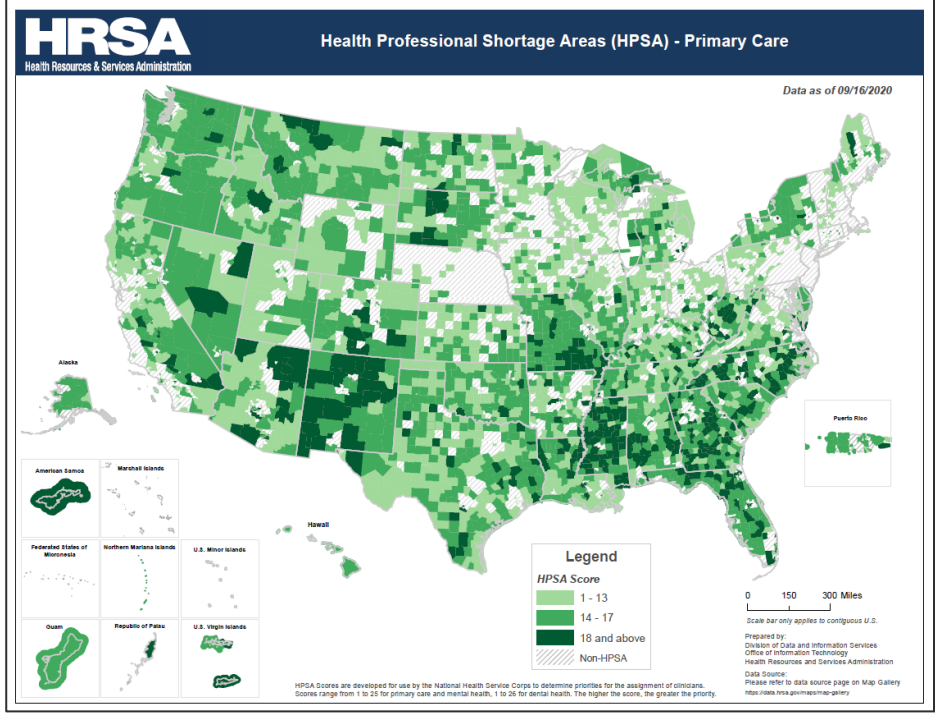
Freeman HP, Wingrove BK. Excess Cervical Cancer Mortality: A Marker for Low Access to Health Care in Poor Communities. Rockville, MD: National Cancer Institute, Center to Reduce Cancer Health Disparities, May 2005. NIH Pub. No. 05–5282.

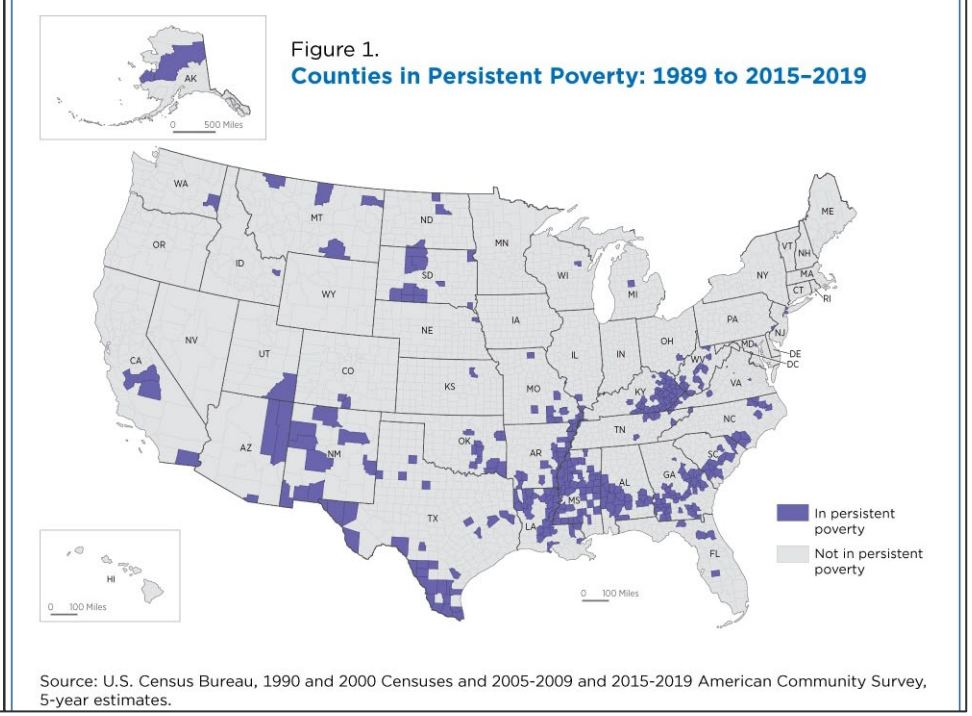
Cervical Cancer Incidence Rates by Race in the USA

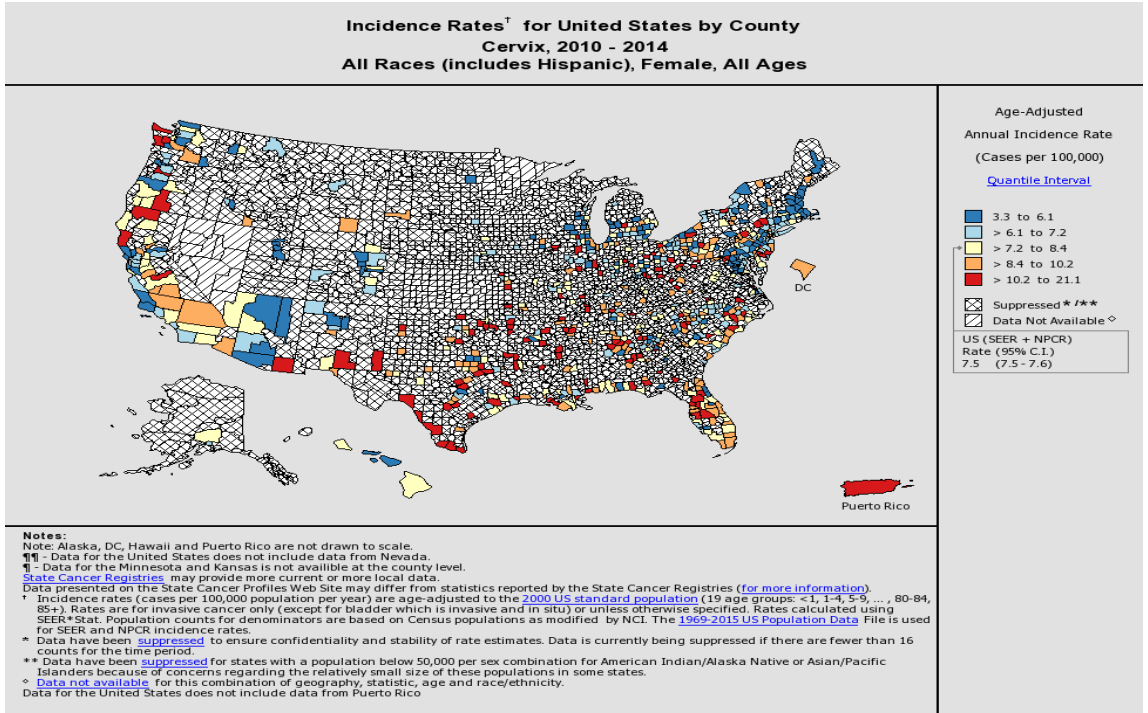


https://www.cdc.gov/cancer/cervical/statistics/index.htm

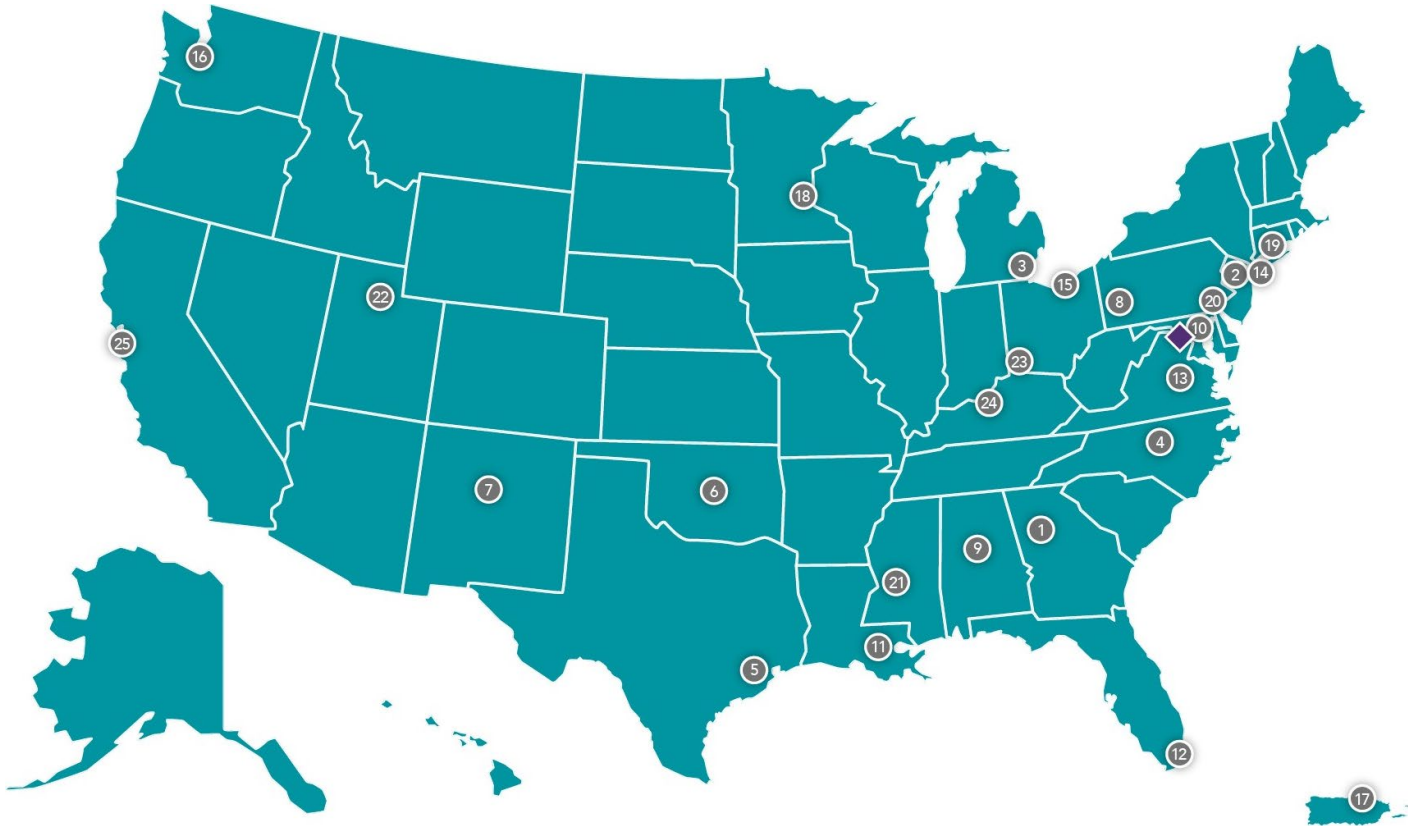
HPSAs, Poverty, and Cervical Cancer Incidence







NCI Cervical Cancer 'Last Mile' Initiative 'SHIP' Trial Network



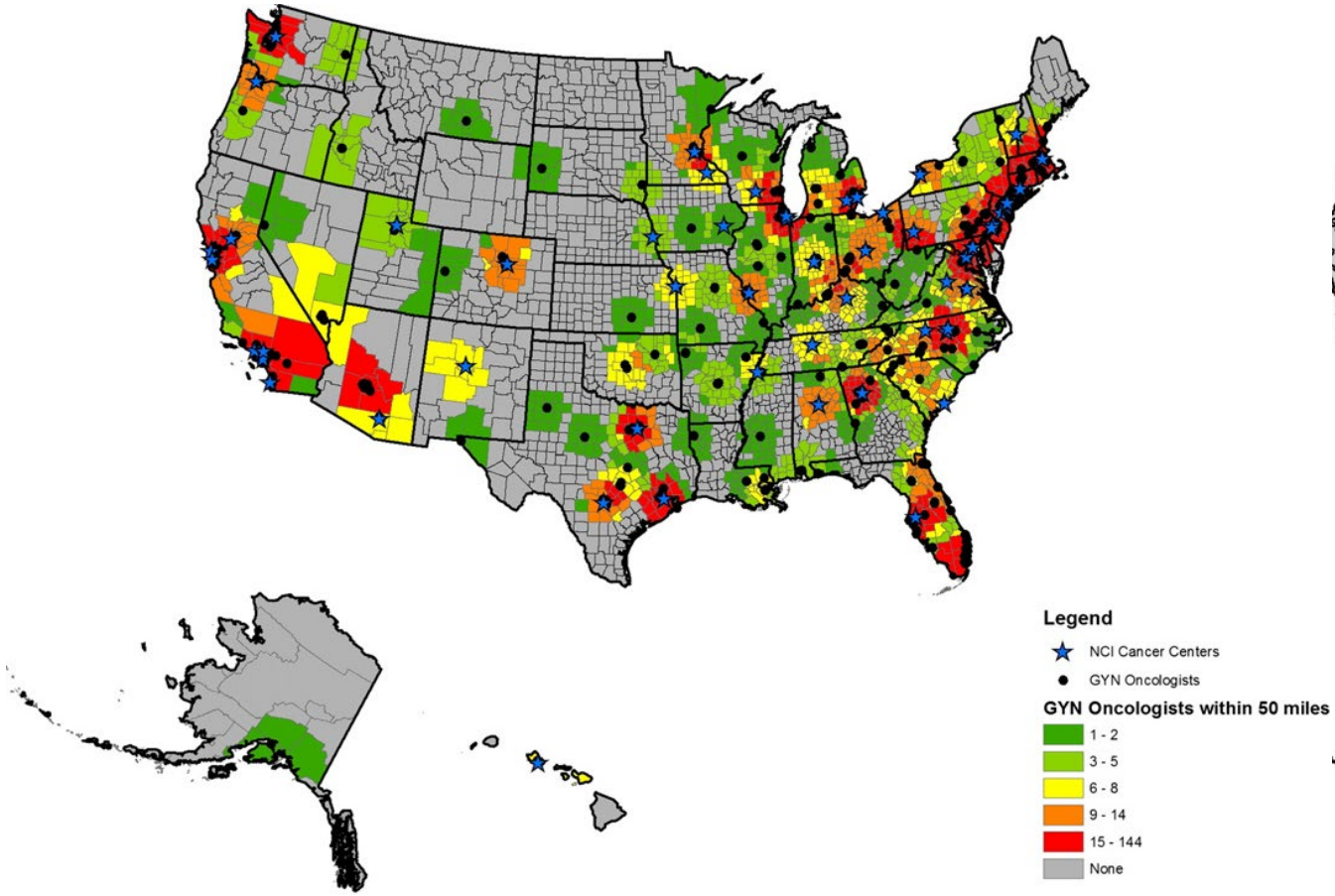
1. Emory University School of Medicine, Atlanta, GA
2. Rutgers New Jersey Medical School, Newark, NJ
3. University of Michigan Medical School, Ann Arbor, MI
4. University of North Carolina School of Medicine, Chapel Hill, NC
5. University of Texas MD Anderson Cancer Center, Houston, TX
6. University of Oklahoma Stephenson Cancer Center, Oklahoma City, OK
7. University of New Mexico Health Sciences Center, Albuquerque, NM
8. University of Pittsburgh Medical Center/Magee-Womens Hospital, Pittsburgh, PA
9. University of Alabama at Birmingham School of Medicine, AL
10. Johns Hopkins University School of Medicine, Baltimore, MD
11. Louisiana State University Health Sciences Center New Orleans, LA
12. University of Miami Sylvester Comprehensive Cancer Center, Miami, FL
13. Virginia Commonwealth University School of Medicine, Richmond, VA
14. Weill Cornell Medicine and New York Presbyterian Hospitals, New York, NY
15. Cleveland Clinic Ob/Gyn and Women's Health Institute, Cleveland, OH
16. University of Washington School of Public Health, Seattle, WA
17. University of Puerto Rico Comprehensive Cancer Center, San Juan, PR
18. Minneapolis VA Healthcare System, Minneapolis, MN
19. Yale New Haven Health, New Haven, CT
20. University of Pennsylvania Abramson Cancer Center, Philadelphia, PA
21. University of Mississippi Medical Center, Jackson, MS
22. University of Utah Huntsman Cancer Institute, Salt Lake City, UT
23. University of Cincinnati College of Medicine, Cincinnati, OH
24. University of Louisville School of Medicine, Louisville, KY
25. University of California, San Francisco School of Medicine, San Francisco, CA

Where are the Gynecologists?

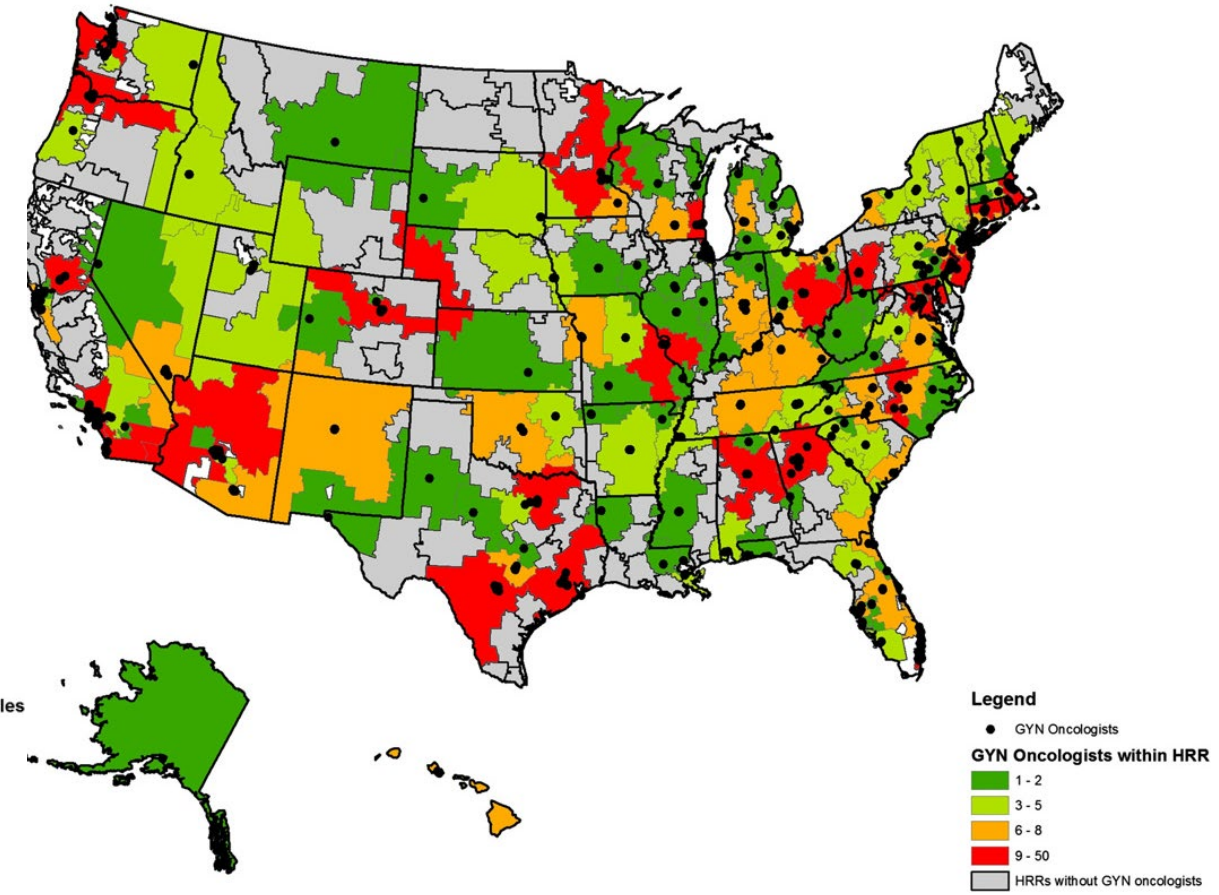
Distribution of American Congress of Obstetricians and Gynecologists fellows and junior fellows in practice in the United States (Rayburn *et al*., Obstet Gynecol, 2012):

- Approximately half (1,550, 49%) of the 3,143 U.S. counties lacked a single ob-gyn, and 10.1 million women (8.2% of all women) lived in those predominantly rural counties.
- Such counties, located especially in the central and mountain west regions, were commonly in designated Health Professional Shortage Areas.

Availability of Gynecologic Oncologists in the USA



Gynecologic Oncologists within 50 miles, by US County



Gynecologic Oncologists per Hospital Referral Region

Shalowitz *et al.*, Gynecol Oncol, 2015 [16]

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MCD Care Continuum

- Education
- Medical Mistrust

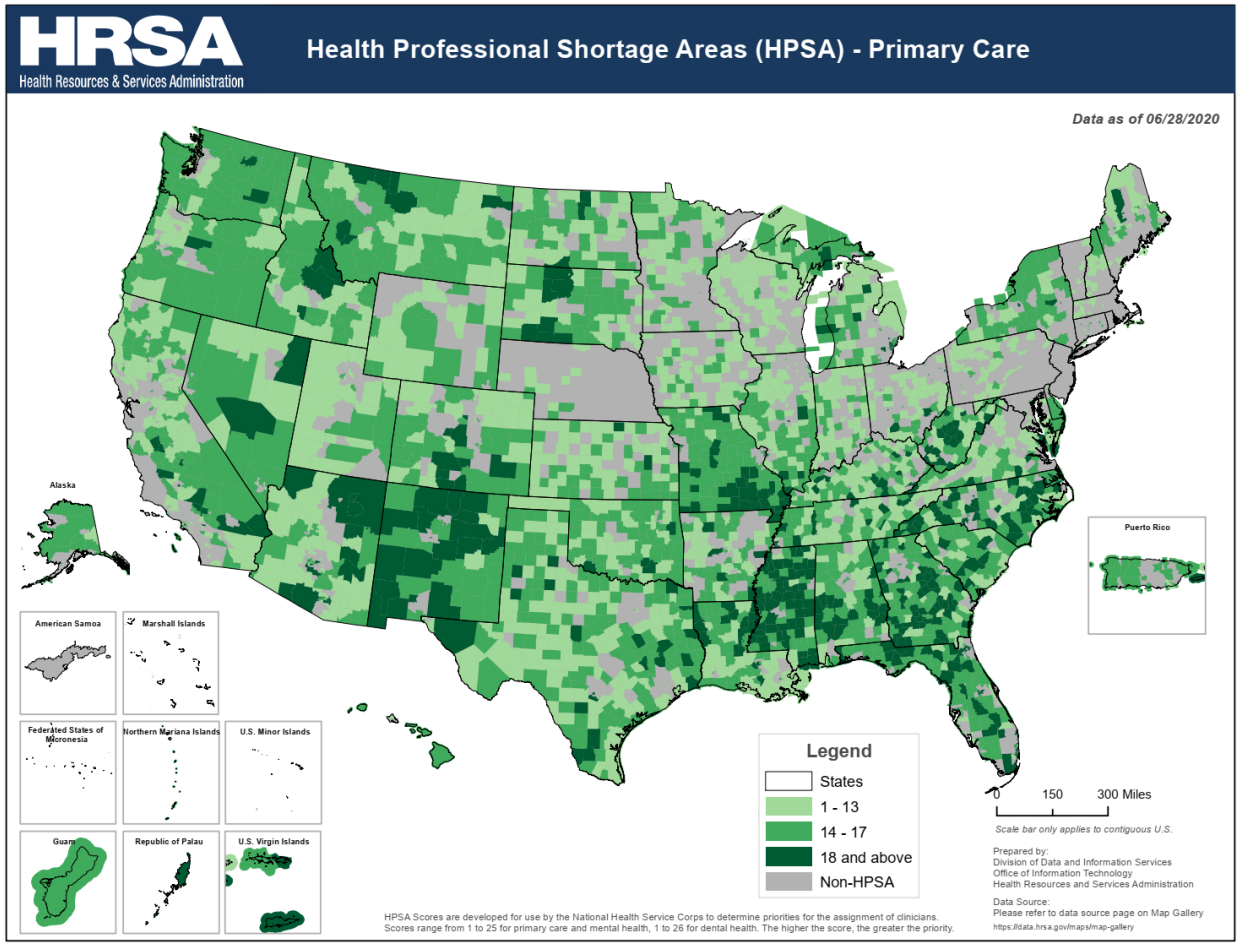
- Insurance/Ability to Pay
- Collection of Specimen (access to a phlebotomist)

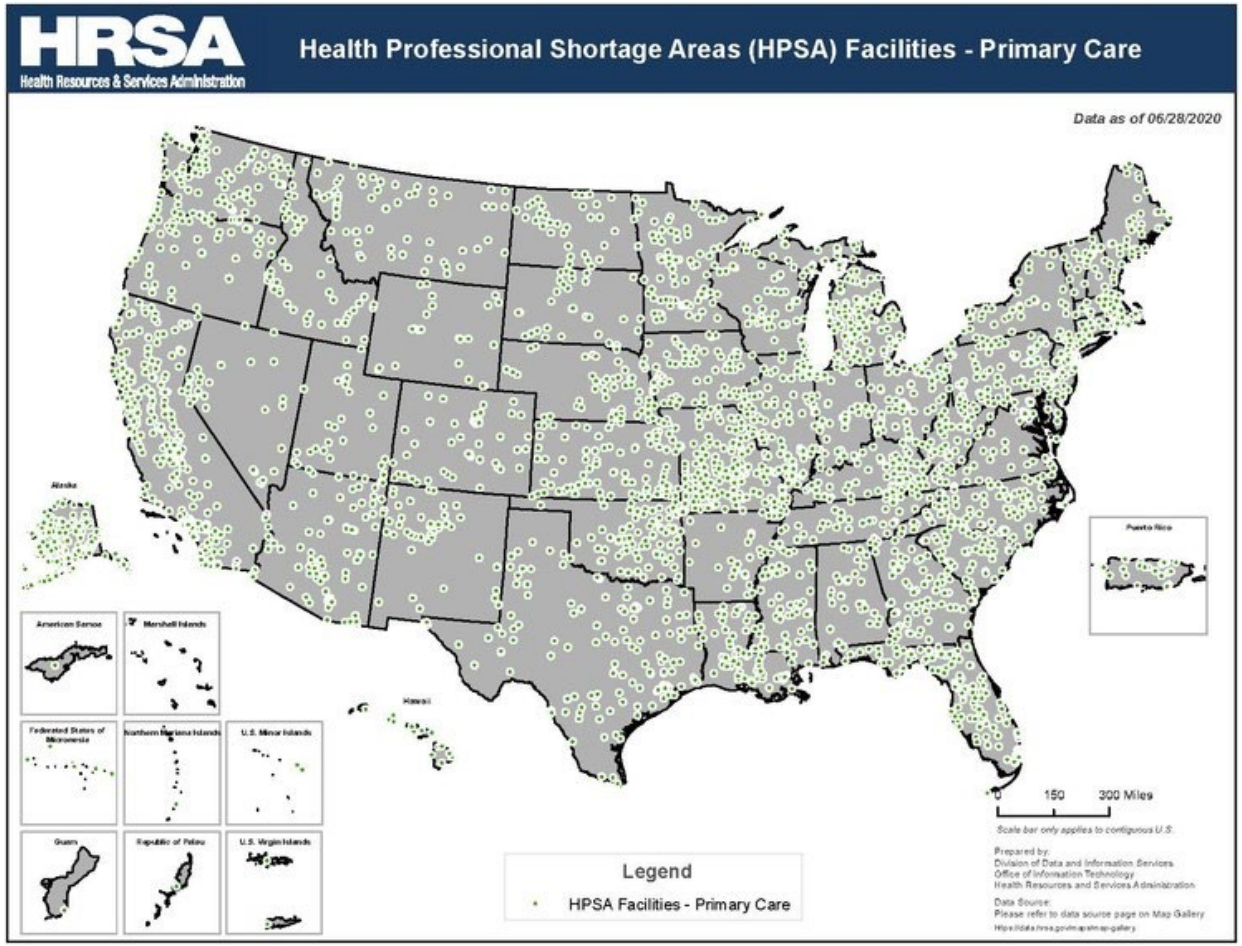
- Access to providers who know how to manage a + result
- Access to imaging
- Insurance/Ability to Pay
- Financial Toxicities

There are real financial and geographical barriers to accessing a site that can manage these results and provide care.

- Access to oncologists to treat the cancer

HPSA Areas and Facilities



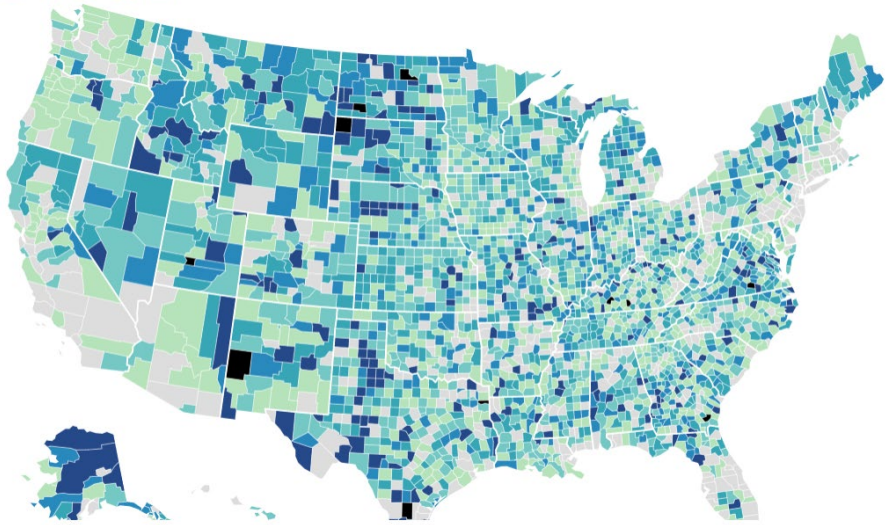


Healthcare Deserts, County by County

Counties where most people lack adequate access to pharmacies, primary care providers, hospitals, hospital beds, trauma centers, and/or low-cost health centers.

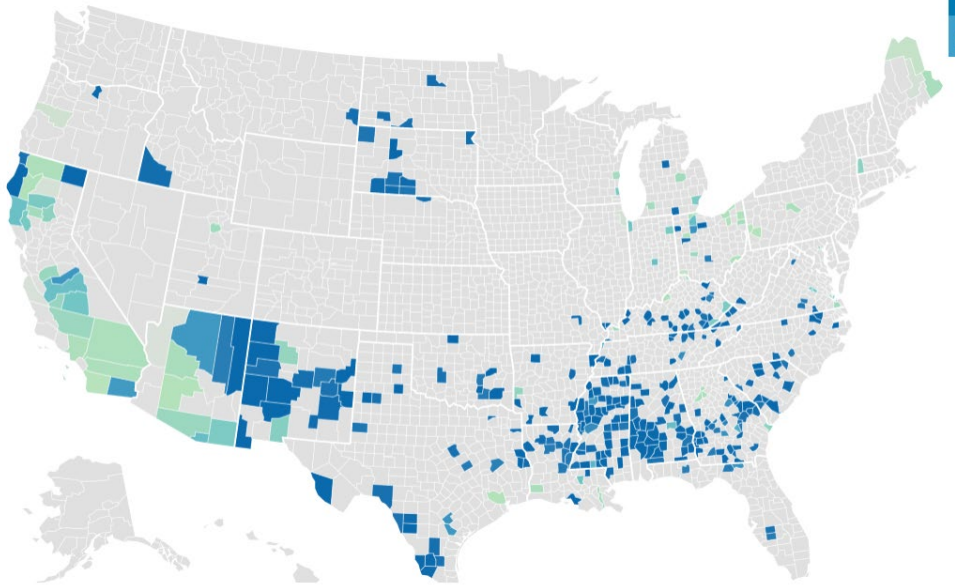
Number of healthcare deserts

1 2 3 4 5 6



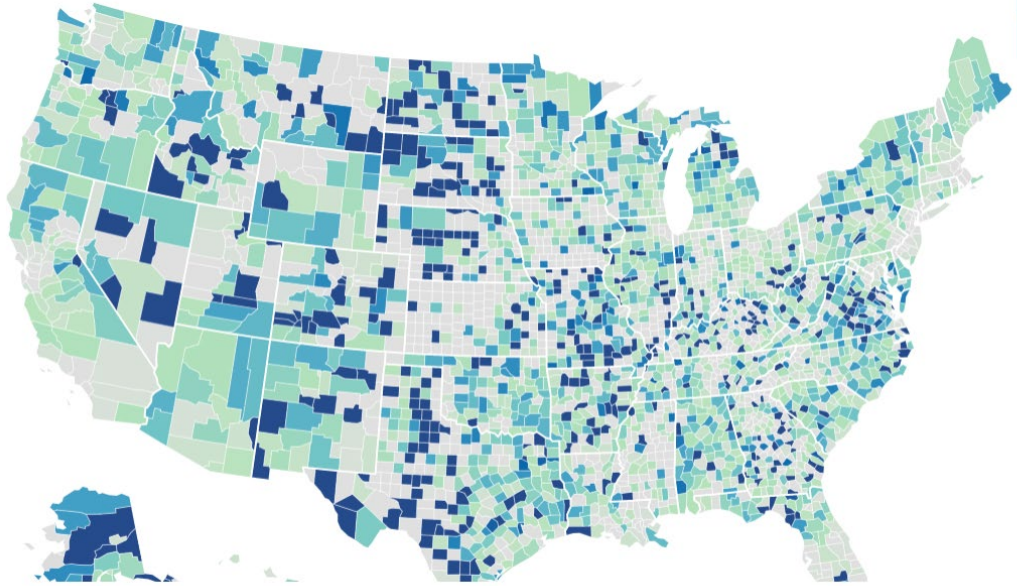
Population Living in a Primary Care Provider Desert

Percent of county's population living in a designated health professional shortage area (HPSA).



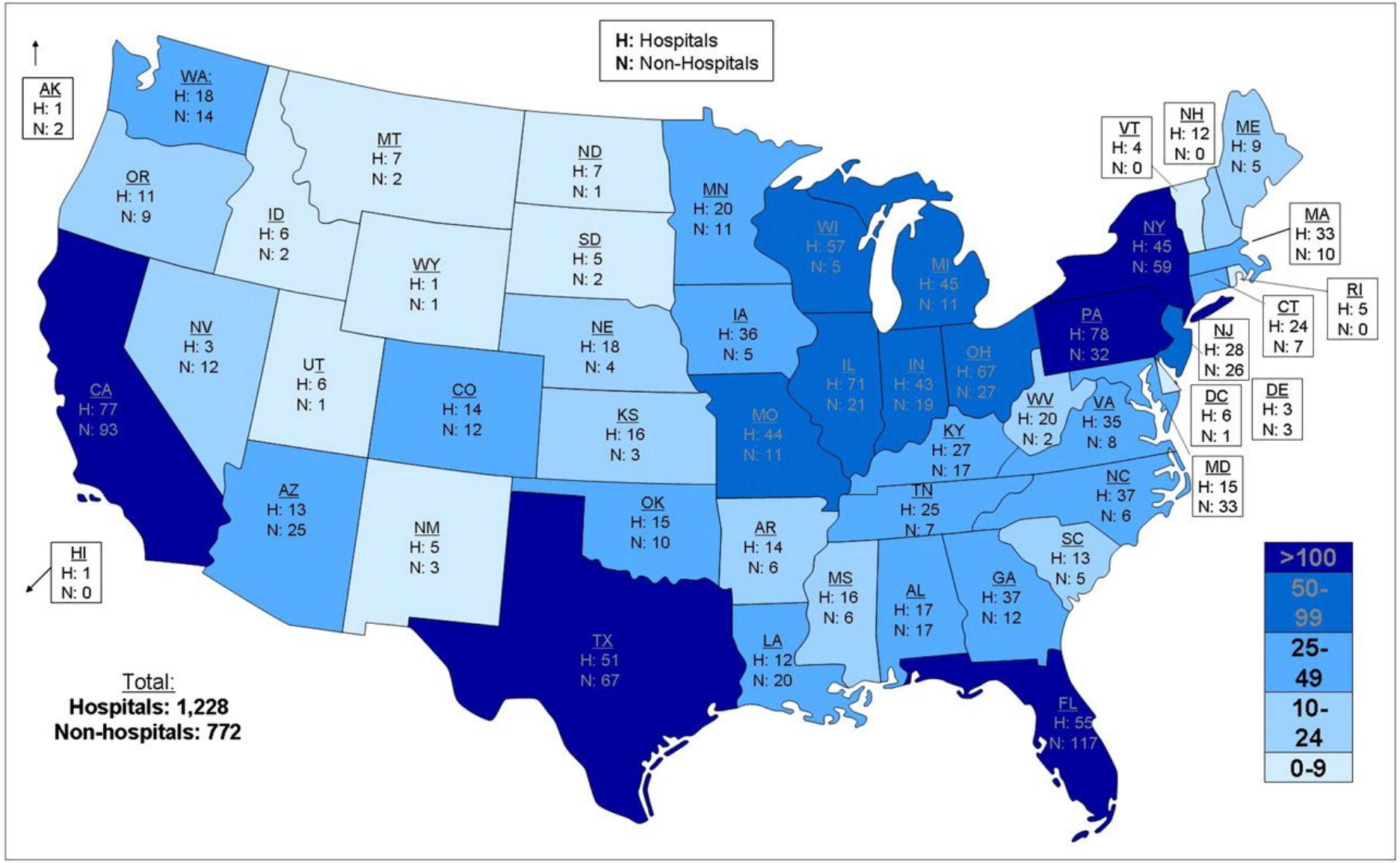
Population Living in a Hospital Desert

Percent of county's population living over 30 minutes from the closest hospital.



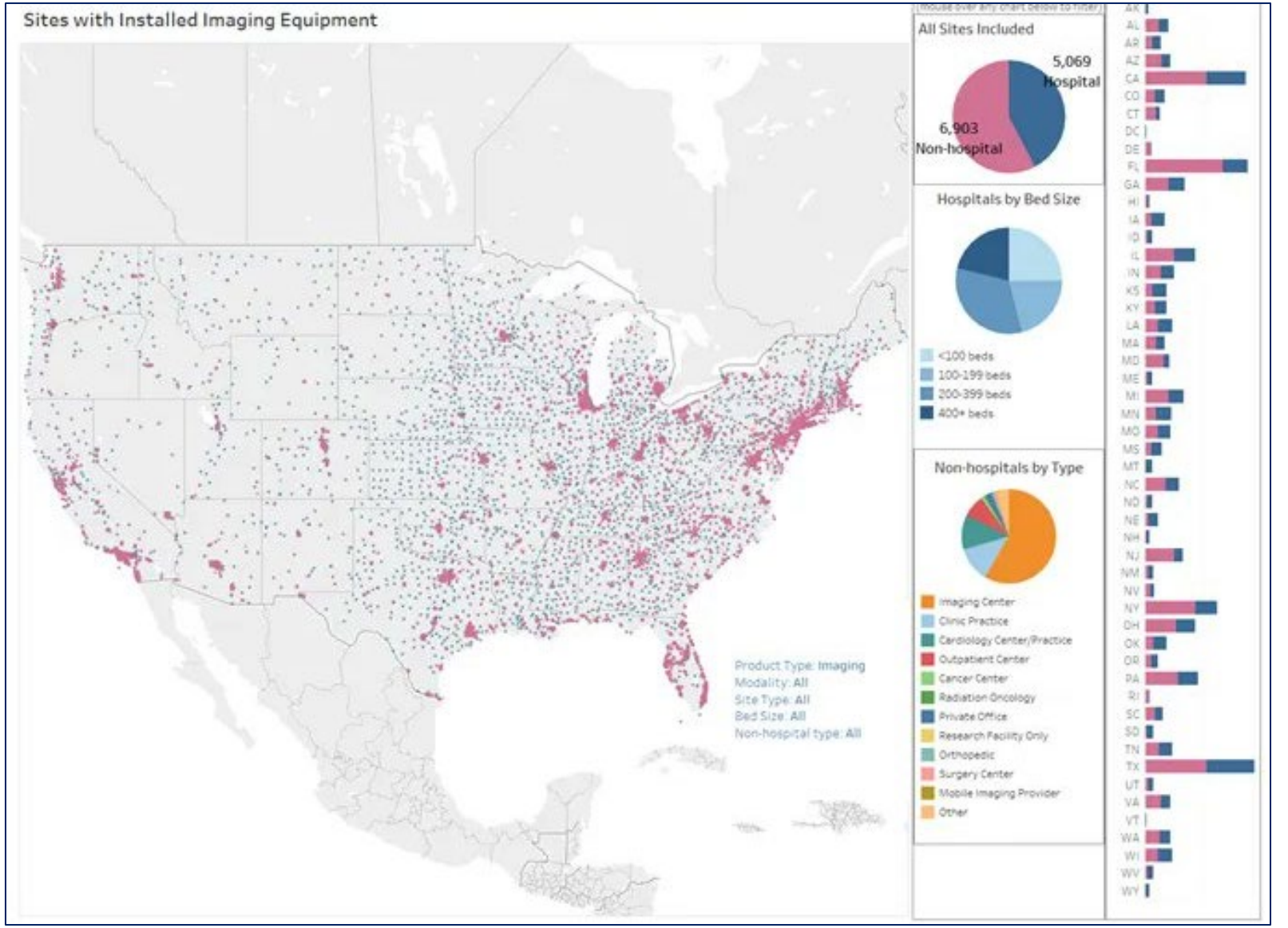
Deserts, Deserts, Deserts

State-Level Distribution of PET/CT



Buck *et al.*, J Nucl Med, 2010

Site-Specific Location of Imaging Equipment



SDoH & Imaging in Marginalized Communities

Table 1: Associations Between Social Determinants of Health and Access to Imaging Needs in Breast Cancer and Acute Stroke, With Proposed Strategies to Mitigate Such Disparities

Social Determinant of Health	Breast Cancer Screening	Acute Stroke Imaging	Strategies to Implement
Economic stability	Employment type affects prevalence of breast cancer screening utilization (22,26); cost is a barrier to screening (22)	Economic instability delays access to critical imaging resources for early diagnosis and management (29–31)	Cost-effective imaging (33,34); financial counseling (35); advocating for policy changes (33,36)
Education access and quality	Higher education is associated with increased participation in breast cancer screening (44,46,47)	Higher education is associated with timely diagnosis of stroke (49)	Interpreter services (50,52); health literacy assessment (8,43,44); health care navigation support (53); cultural competency training (8,36)
Neighborhood and built environment	Women in disadvantaged neighborhoods are less likely to undergo screening mammography (64,65)	The distance to a stroke center tends to be longer in rural regions (73); once patients secure access, disparities in the use of advanced imaging are reduced (75)	Design and accessibility of imaging centers (76); health-promoting infrastructure (36,77,78)
Social and community context	Women with higher social capital are more likely to undergo screening mammography (83–85); limited availability of accredited breast imaging facilities in these neighborhoods (66)	Limited evidence	Engaging patients and their support network (89); addressing structural racism (8); diversity in the radiology workforce (8); partnering with community-based organizations (8,36); community-based participatory research (33,90)
Health care access and quality	Uninsured women are less likely to undergo screening mammography (98,99)	Being uninsured is associated with lower odds of undergoing stroke imaging (23,108)	Mobile van approach (112,113); transportation assistance (115,116); teleradiology (117,118); structured imaging interpretation (119,120)

Elmohr *et al.*, Radiology, 2024

Final Comments

- MCDs are a promising technology but people are not experimental rats.
- Given the order-of-magnitude of greater complexity of MCD testing vs. single cancer screening, are we ready? (No!)
- There are significant education, financial, and geographical (to name a few) barriers to accessing MCD testing and the follow-up care. These will differentially and negative affect marginalized people, communities, and populations.
- Will those with these barriers chose MCD testing over proven, life saving cancer screenings, especially cervical and colorectal that actually prevent cancer?

THANK YOU!

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

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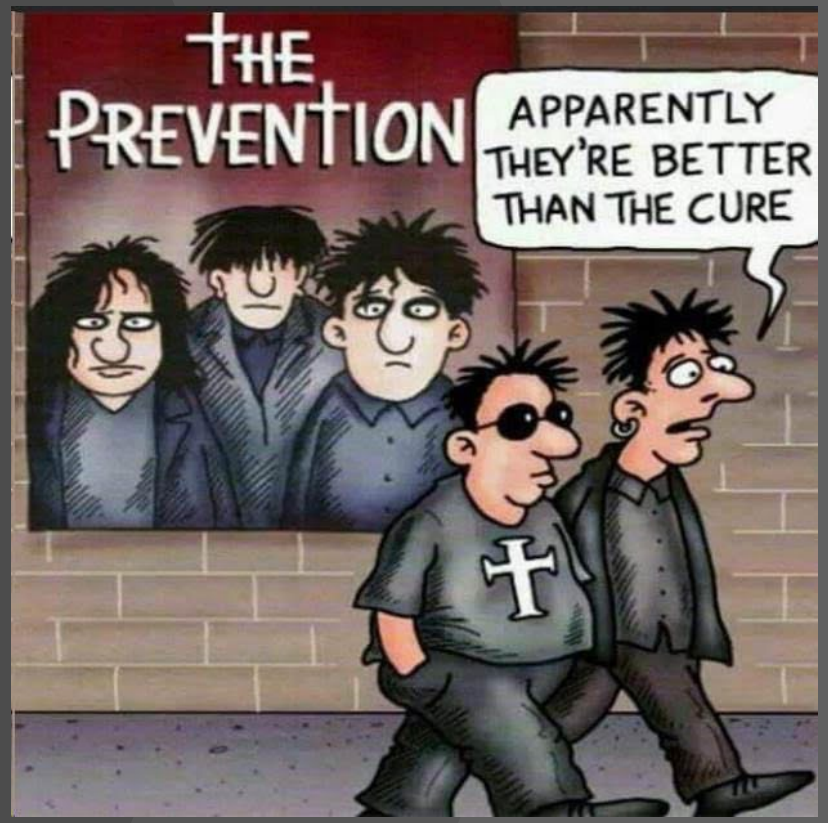

www.cancer.gov www.cancer.gov/espanol