Opportunities to Spur Progress in Cancer Prevention and Risk Reduction: National Cancer Institute

Philip E. Castle, PhD, MPH

Director, Division of Cancer Prevention

Senior, Tenured Investigator, Division of Cancer Epidemiology and Genetics

NCI, NIH, DHHS

NIH NATIONAL CANCER INSTITUTE

June 28, 2022

Disclaimers and Disclosures

- Opinions expressed are mine alone and should **not** be interpreted as representing the official viewpoint of the U.S. Department of Health and Human Services, the National Institutes of Health, the National Cancer Institute, or the Division of Cancer Prevention.
- My comments are informal and should **not** be taken as a “signal” for funding priorities.
- If I mention specific products to illustrate my points, these comments should **not** be taken as an endorsement of said products.
- I have received HPV tests and assays for research at a reduced or no cost from Roche, Cepheid, Becton Dickinson, Arbor Vita Corporation, and Atila Biosystems.

Mr. Spock, Public Health Scientist

The needs of the many outweigh the needs of the few. And the one.”
[Provided that everyONE is counted equally…]

Translational Research at DCP

Tools of Prevention

	COVID-19	Cancer
Screen & Interception	DNA and Antigen Tests (followed by antivirals)	Breast, Cervix, Colon, Lung, Prostate*, and HCV (for liver)
Awareness	Masking & Physical Distancing	Smoking Prevention/Cessation; Weight control
Vaccination	mRNA Vaccines	HPV; HBV

The **S**creening, **A**wareness, & **V**accination for **E**veryone (***SAVE***) Campaign: Stopping Cancer Before It Starts

Castle PE. Applying a pandemic-like response to prevent cancer. STAT. August 9, 2021. Applying a pandemic-like response to cancer prevention - STAT (statnews.com)

Today's Agenda

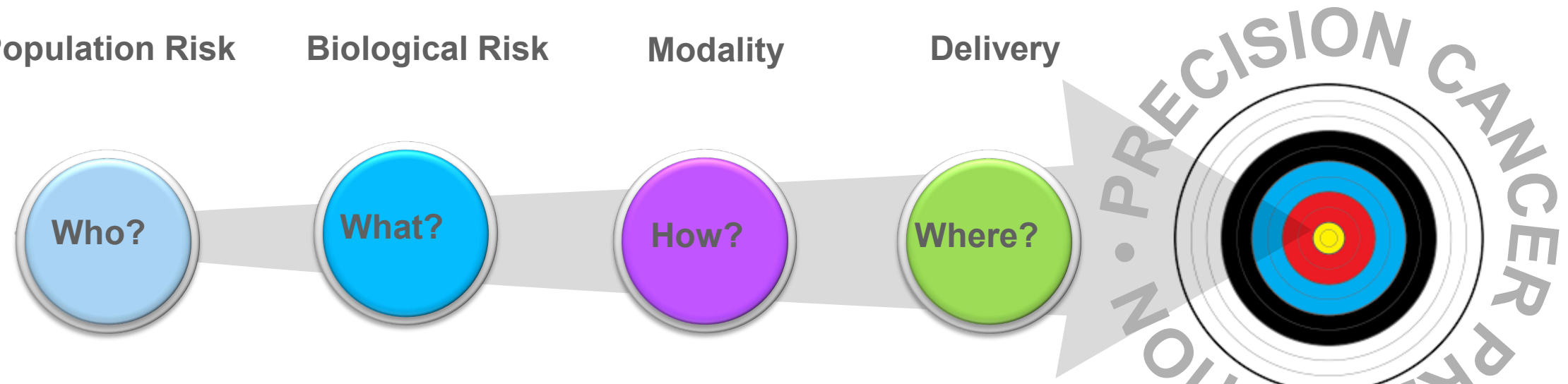
1. *An Inclusive Model for Precision Cancer Prevention*
2. *Riding on Coattails: Bundling of Interventions*

An Inclusive Model for Precision Cancer Prevention

- Rather than just focus on biological susceptibility to cancer, consider all determinants of health, including SDH, in the development and targeting of interventions to prevent cancer incidence and mortality.
- Consider that the basic science that has fueled our prevention and treatment interventions has been subject to biases. Several examples related to those of African descent: OncoType Dx; HPV35 not included in current prophylactic HPV vaccines; and TCGA was not representative of the population getting colorectal cancer.
- An inclusive model will not only improve health of all but improve the representativeness in research, thereby reducing aforementioned biases.
- Precision cancer prevention is not just what you deliver but to whom, how, and where you deliver it (next slide).

Butler…Castle, Trends Cancer, 2022 (PMID: 35181273)

Precision Cancer Screening and Prevention Strategies



Population Risk	Biological Risk	Modality	Delivery
Population Risk/Benefits: Harms	Biologic/ Targeted Intervention	Mode of Delivery e.g., topical, intermittent, or control release	Accessibility e.g., home-based sampling or testing or point-of-care testing
Biological and Non-Biological Risk Factors (Risk-Informed Interventions)	Vaccines vs. Neoantigens & Tumor-Associated Antigens	Topical vs. Oral (Systemic) Tamoxifen	Self-Collection: HPV; FIT Self-Testing: HCV?

Butler…Castle, Trends Cancer, 2022 (PMID: 35181273)

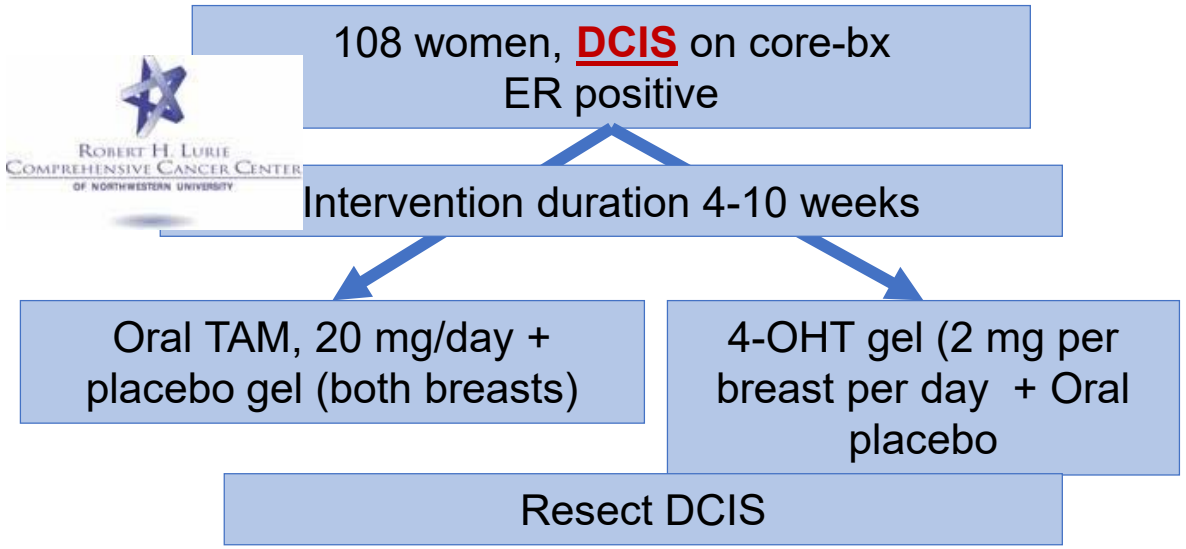
Examples of Cancer Preventive Vaccines (Preclinical)

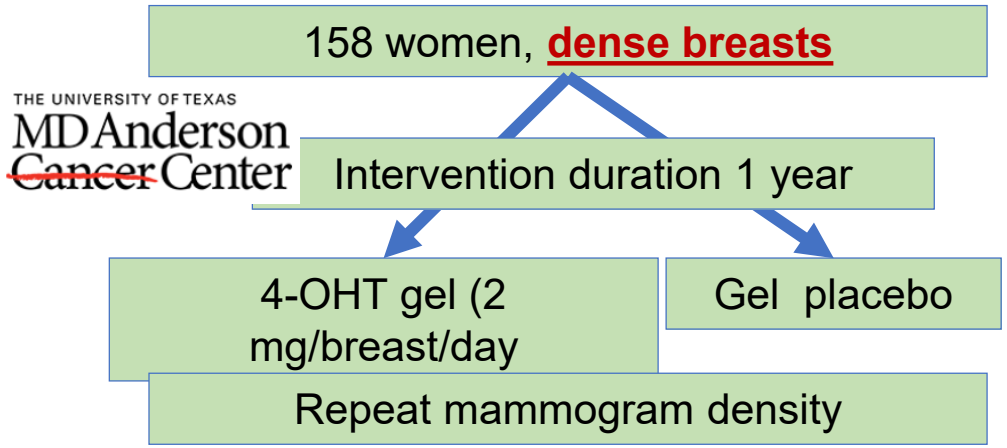
Vaccine/Agent	Target Organ	Target Population	Status
FSP Peptide Vaccine	Colon	Lynch Syndrome Carriers	CGMP
ATI-1013 Anti-nicotine Human mAb	Smoking-related Cancers	Smokers	CGMP
Artemis Vaccine	Breast	Women at High-Risk for Breast Cancer	pre-CGMP
ColoVac DNA Vaccine	Colon	Individuals at High-Risk for Colon Cancer (e.g., High-grade Dysplasia)	pre-CGMP
WOKVAC with 9cUAB30	Breast	DCIS	Secondary Testing
AMHR2-ED Vaccine	Ovary	Women with BRCA1/2 Mutations	Secondary Testing
Multi-peptide Vaccines	Bladder	Subjects Previously Treated for NMIBC	Proof-of-Concept
EGFR or KRAS Vaccines w/ Avasimibe	Lung	Patients with KRAS- or EGFR-mutant Lung Premalignant Lesions	Proof-of-Concept
Multi-peptide KRAS Vaccine	Pancreas	Individuals at High-Risk for Pancreatic Cancer or with Premalignant Precursors	Proof-of-Concept
Protein-ERG Fusion RNA Vaccine	Prostate	Low-grade Prostate Cancer Patients (Gleason score ≤ 6)	Proof-of-Concept

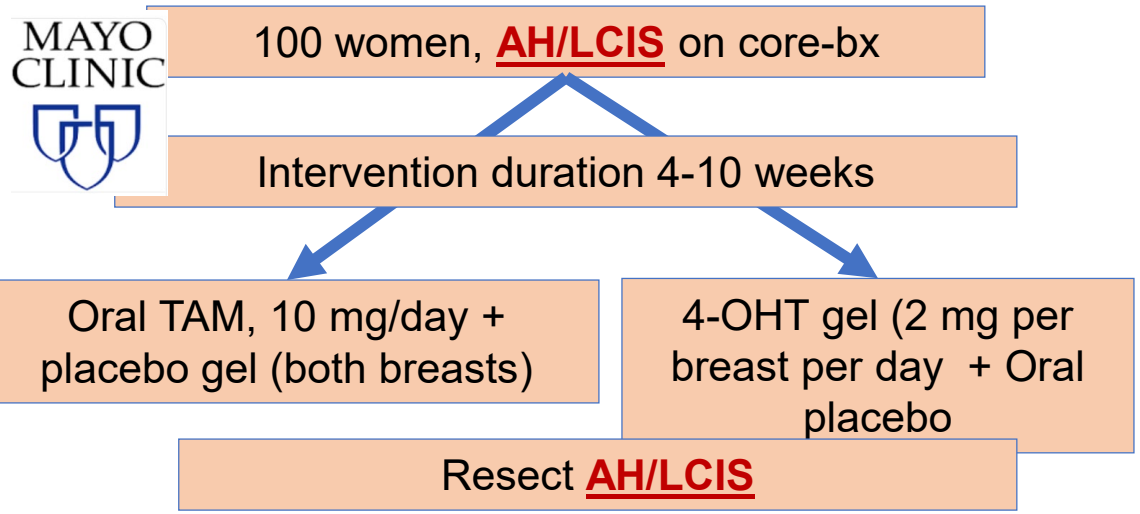
Examples of Cancer Preventive Vaccines (Clinical Trials)

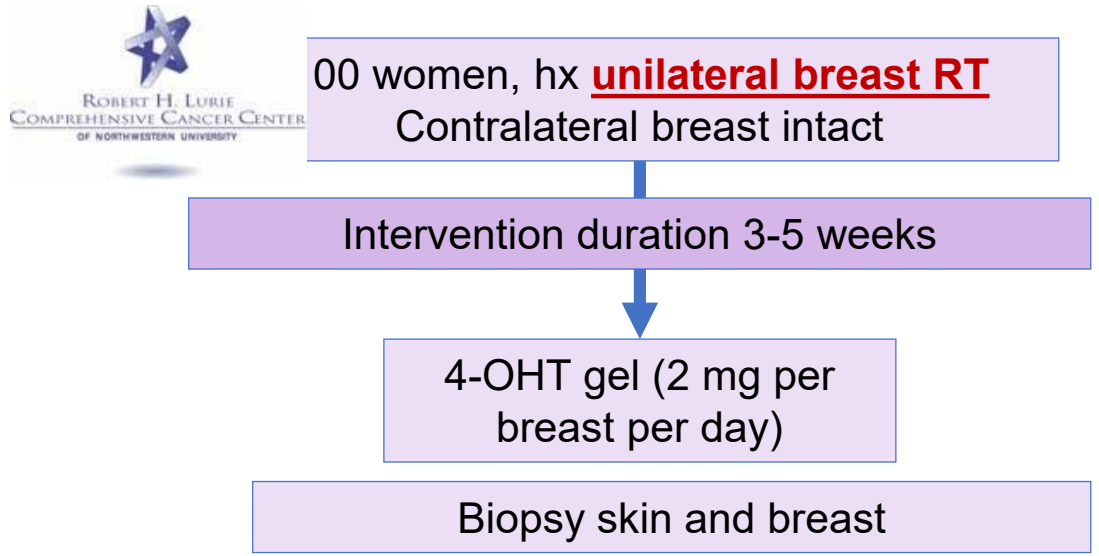
Vaccine/Agent	Target Organ	Target Population	Status
Nous-209 (frameshift peptide (FSP) neoantigens)	Colorectal	Lynch syndrome	Opening this summer/autumn
Tri-Ad5 Vaccines (adenoviral vaccine against CEA, MUC1, and brachyury) and N-803 (IL-15 superagonist) vs. placebo	Colorectal	Lynch syndrome	Opening this summer/autumn
MUC1 peptide	Colon and lung	1) Individuals with history of advanced colorectal adenomas 2) Heavy smokers undergoing CT screening	Finished, Analyses Underway
WOKVAC- Plasmid based vaccine targets Her-2, IGF-BP2, IGF-1R	Breast	DCIS	Phase I does escalation study complete and analysis underway.
STEMVAC- Plasmid based vaccine targeting MDM2, YB1, SOX2, CDH3, CD105	Breast	Triple negative breast cancer prevention	Phase II study starting

Ongoing Trials with 4-Hydroxytamoxifen (4-OHT) Gel









Self-Collection and HPV Testing Meta-Analysis

Method	Endpoint	N	Relative Sensitivity	Relative Specificity
Signal Amplification	CIN2+	23	0.85 (0.80-0.89)*	0.96 (0.93-0.98)*
	CIN3+	9	0.86 (0.76-0.98)*	0.97 (0.95-0.99)*
PCR	CIN2+	17	0.99 (0.97-1.02)	0.98 (0.97-0.99)*
	CIN3+	**8**	**0.99 (0.96-1.02)**	**0.98 (0.97-0.99)***

Scenario of invitation	# of Studies	Absolute Participation		Participation Difference % (95% CI)
		Self-Collection % (95% CI)	Control % (95% CI)	
Intention-to-Treat				
Mail-to-all	21	24.8 (21.6 to 28.1)	11.5 (8.3 to 15.1)	**12.8 (10.4 to 15.1)**
Opt-in	8	17.7 (12.3 to 23.9)	13.4 (10.2 to 16.9)	**3.3 (−0.7 to 7.3)**
Campaign	1	15.6 (12.4-19.5)	6.0 (4.2-8.7)	**9.5 (5.4-13.7)**
Door-to-door	4	94.6 (83.0-99.9)	53.3 (10.5-93.2)	**40.5 (3.0-78.0)**

Arbyn…Castle, BMJ, 2018 (PMID: 30518635)

Screening in the NW Mississippi (Mississippi Delta Region)

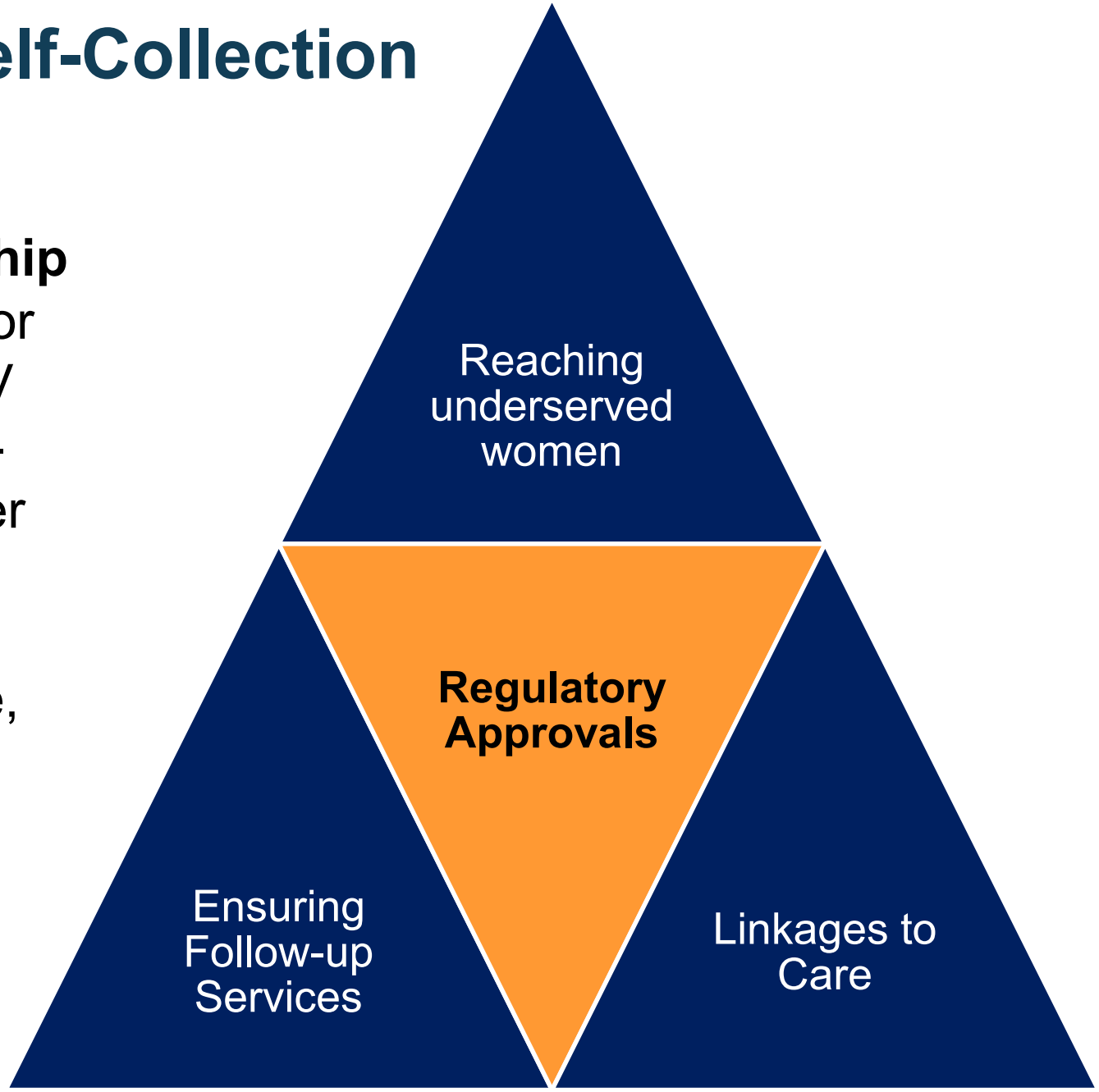
- **First Study (2009-10)**: Pilot Study of Choice of Self-Collection vs. Clinic-Based (n=119); Aged 26-65 years, No screening in the last 3 years
  - **65% Chose and 80% Adhered to Self-Collection vs. 35% Chose and 40% Adhered to Clinic-Based Screening (~4-fold effect)**
- **Second Study (2016-9)**: Cluster RCT of Choice vs. Clinic-Based Screening (n=335); Aged 25-65 years; No screening in the last 4 years
  - **Adherence: 38.2% for Choice vs. 9.4% for Clinic-Based; Adjusted OR=5.62**
  - **Among Choice: 76% Chose and 48% Adhered to Self-Collection vs. 24% Chose and 8% Adhered to Clinic-Based Screening (~20-fold effect)**

Castle *et al.*, Prev Med, 2011 (PMID: 21497619)
Scarinci…Castle, Prev Med, 2021 (PMID: 33338505)

NCI's Last Mile Initiative: Self-Collection & HPV Testing

- **NCI-led Public Private Partnership** to facilitate regulatory approvals for self-sampling approaches for HPV testing as alternatives to provider-based sampling for cervical cancer screening.

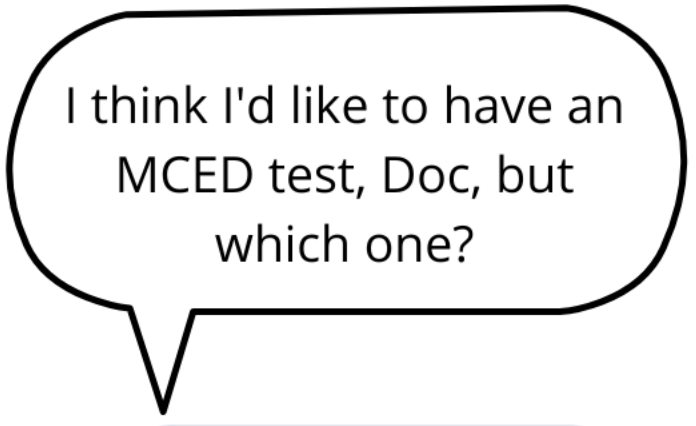
- Planning underway for nationwide, multicenter screening trial to examine self-sampling in diverse delivery settings



https://prevention.cancer.gov/lastmile

The Multi-Cancer Early Detection Tsunami: Hope or Hype?

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



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

Today's Agenda

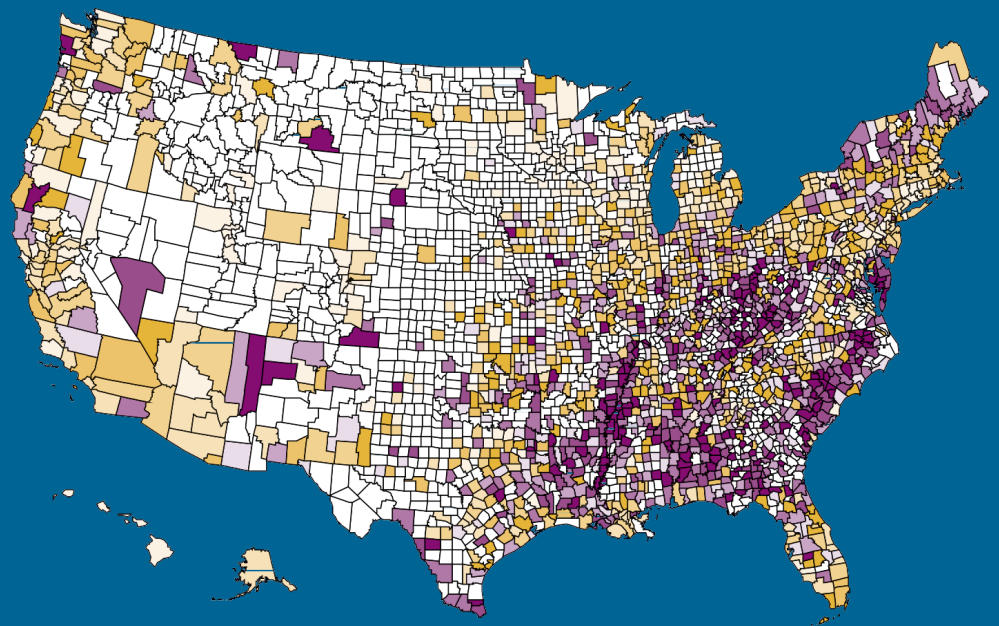
1. *An Inclusive Model for Precision Cancer Prevention*
2. *Riding on Coattails: Bundling of Interventions*

An Analysis

Excess Cervical Cancer Mortality

A Marker for Low Access to Health Care in Poor Communities

Center to Reduce Cancer Health Disparities



U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Cancer Institute

The WHOLE FAMILY Needs (Better Access to) Cancer (NCD) Prevention (not an exhaustive list….)

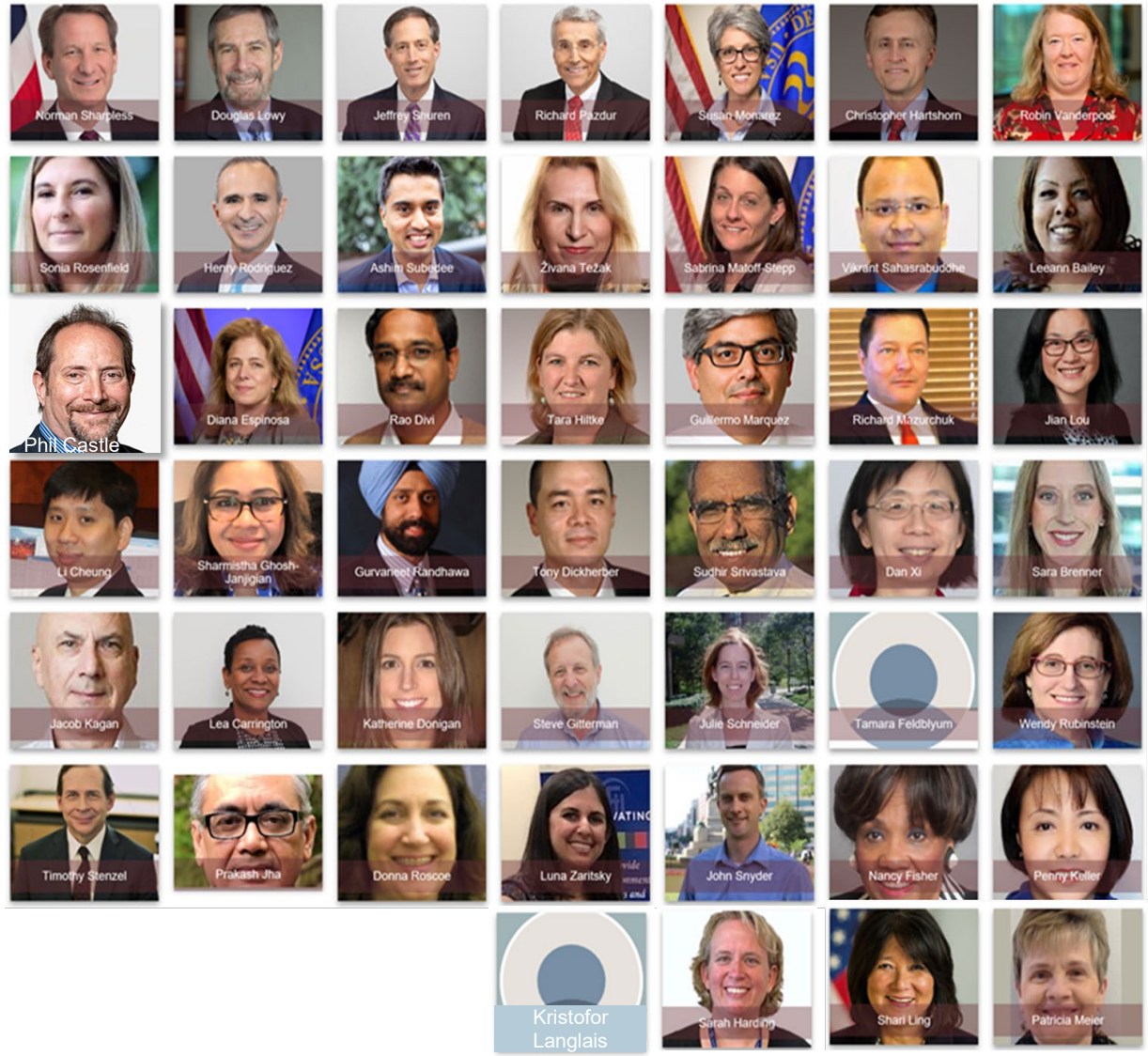
Intervention	Facilitated method at home/in the community	Mom	Dad	Kids
Cervical Screening	Self-Collection & HPV Testing	√		
Colorectal Screening	FIT (and *h. pylori*?)	√	√	
Breast Screening	CHW* Navigation/Mobile Van for Mammography	√		
Lung Screening	CHW* Navigation for LDCT	√	√	
HPV-Related Cancer Prevention	HPV Vaccination; Condom Use Promotion & Distribution	?	??	√
Multiple Cancers	Smoking Prevention/Cessation	√	√	√
Multiple Cancers	Healthier Lifestyle (e.g., energy balance) Promotion	√	√	√
Liver Prevention	HBV Vaccination Promotion/Distribution	√	√	√
Liver Screening (Future)	Oral HCV Antibody POCT for Referral; HCV mRNA blood test; Home Blood Collection for Lab Testing	√	√	
HPV-related Oropharyngeal Screening (Future)	POCT E6 Serology; Home Blood Collection for Lab Testing	√	√	
Prostate Cancer?	POCT PSA Serology; Home Blood Collection for Lab Testing		√	
Multiple Cancers?	Diabetes Screening (A1C); Home Blood Collection for Lab Testing	√	√	

*Community Health Workers (trained also to provide navigation) need to be a paid member of the Medical Home

CD2 Task Force

- New partnership among NCI/NIH, FDA, CMS, HRSA, CDC, AHRQ, and NIST

- **Mission:** *Bring more cancer diagnostic devices closer to patients, particularly patients who are members of medically underserved and geographically isolated communities*



POUND

"I'll have ~~an ounce~~ of prevention."

THANK YOU!

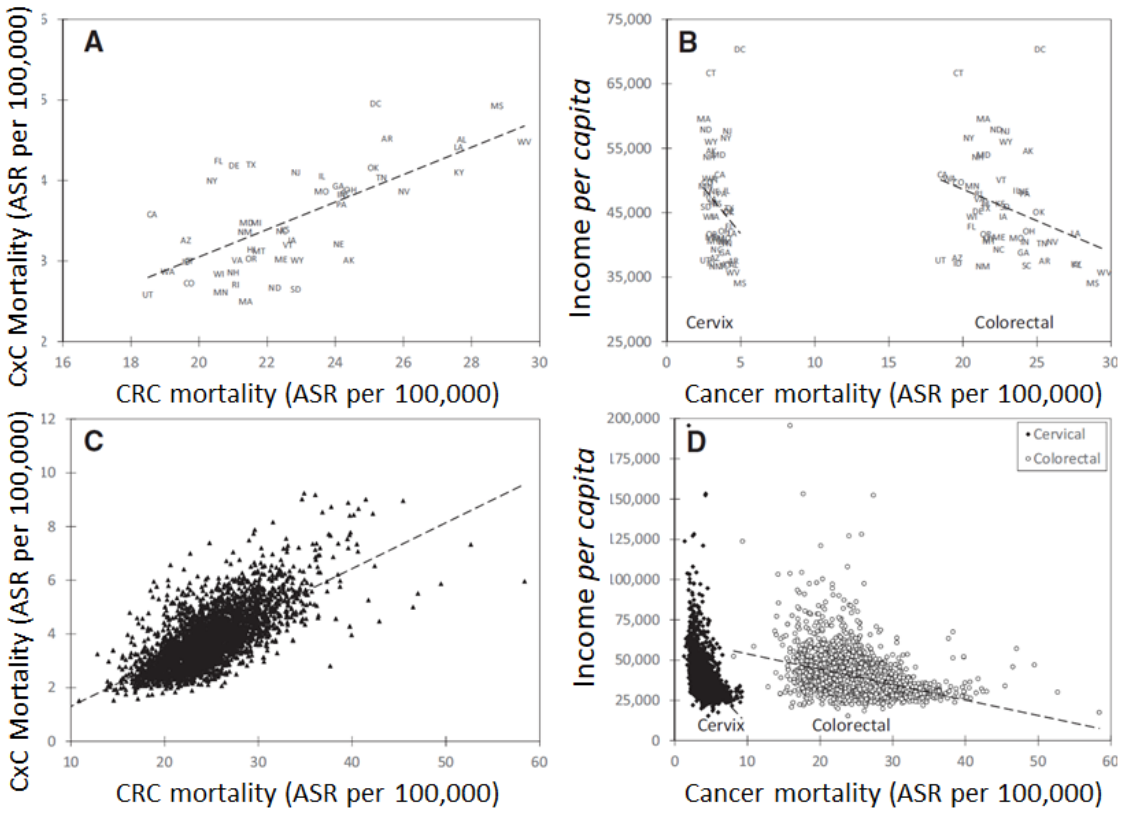
NATIONAL CANCER INSTITUTE

www.cancer.gov

www.cancer.gov/espanol

Cancer Mortality Correlations

	Esophageal	Colorectal	Liver	Pancreas	T, B, & L	Breast	Cervi
Esophageal	1.00						
Colorectal	0.43	1.00					
Liver	0.04	0.44	1.00				
Pancreas	0.50	0.65	0.49	1.00			
T, B, & L	0.40	0.76	0.49	0.67	1.00		
Breast	0.28	0.69	0.55	0.68	0.66	1.00	
Cervix	0.20	0.68	0.71	0.53	0.65	0.70	1.00
Uterine	0.48	0.20	−0.11	0.35	0.05	0.24	0.10
Ovary	0.36	0.27	0.09	0.40	0.31	0.44	0.22
Prostate	0.27	0.45	0.28	0.50	0.28	0.45	0.30
Bladder	0.57	0.25	0.00	0.42	0.44	0.26	0.10
B&N	0.22	0.33	0.04	0.25	0.44	0.21	0.10
NHL	0.47	0.42	−0.01	0.39	0.50	0.29	0.15
Leukemia	0.50	0.57	0.10	0.49	0.56	0.39	0.29
Income	−0.14	−0.42	−0.42	−0.31	−0.55	−0.40	−0.56



Castle, Cancer Res, 2018 (PMID: 29506973)

Possible Platform Randomized Control Trial Design

Randomization

Control Arm

MCED 1 Arm

MCED 2 Arm

MCED 3 Arm

All Arms Offered Standard of Care Cancer Screenings

Interventions

\+ No Additional Tests Control Arm

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

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

\+ MCED 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

Cancer Screening Research Network