Incidental Pulmonary Nodule (IPN) and Low-Dose CT Lung Cancer Screening Programs: How They Compare

Ray U. Osarogiagbon, MBBS FACP
Chief Scientist, Baptist Memorial Health Care Corporation
Director, Multidisciplinary Thoracic Oncology Program
Baptist Cancer Center, Memphis, TN.

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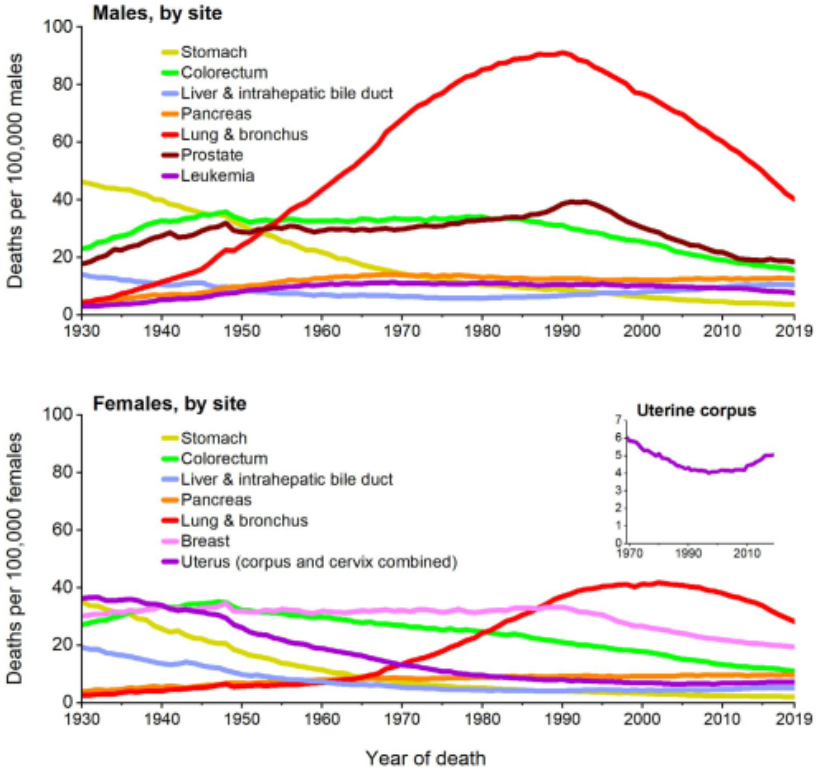
DECLARATIONS

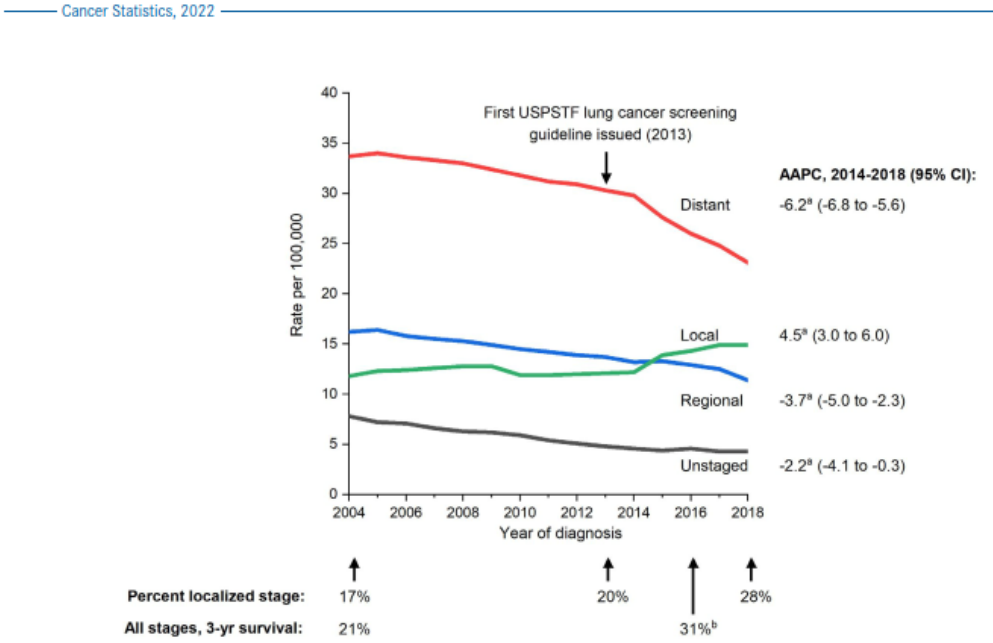
Chair:	Board of Directors, Hope Foundation for Cancer Research (SWOG)
Co-chair:	IASLC N-Staging Sub-Committee, IASLC Prognostic Factors Subcommittee; SWOG Early Lung Cancer Sub-Committee
Consultant:	American Cancer Society, AstraZeneca, Genentech/Roche, National Cancer Institute
Member:	Fleischner Society
Patents:	Lymph node specimen collection kit, Method for lymph node analysis
PI:	S1934 (NASSIST: NeoAdjuvant chemoradiation +/- immunotherapy before Surgery for SuperIor Sulcus Tumors)
Scientific Advisory Board:	Druckenmiller Center for Lung Cancer Research, MSKCC; GO2 Foundation; Lung Cancer Foundation of America; LUNGevity Foundation, NCI Board of Scientific Advisors
Speaker:	Biodesix, Genentech/Roche, Medscape, Tryptych Healthcare Partners
Steering Committee:	National Lung Cancer Round Table, NCI Cancer Prevention Steering Committee
Stock:	Eli Lilly, Gilead Sciences, Pfizer

Objectives

1. Overview US lung cancer population dynamics.
2. Review two approaches to early lung cancer detection.
3. Discuss challenges, opportunities in implementing early detection programs.
4. Describe early learnings from the **D**etecting **E**arly **Lu**n**g** Canc**e**r (**DELUGE**) in the Mississippi Delta project.
5. Outline future directions.

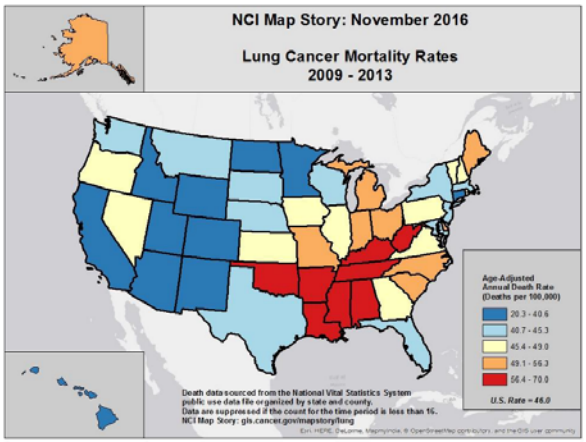
The Good News: Evolving US Lung Cancer Statistics

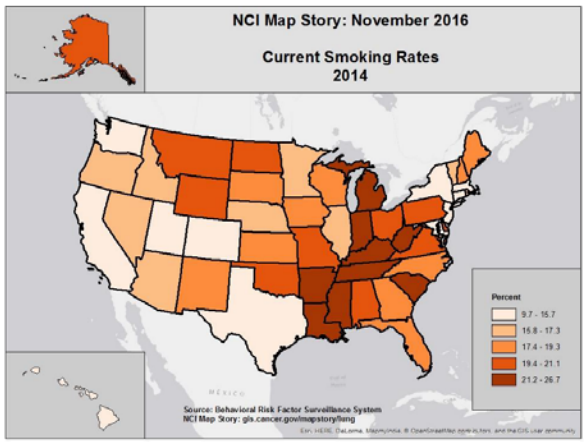


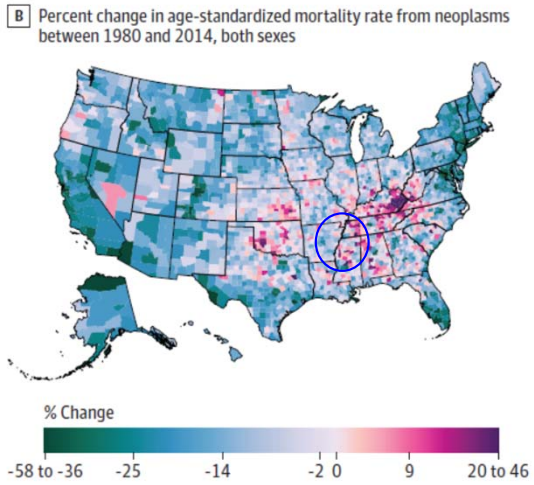


Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022 PMID: 35020204.

Epidemiology of Lung Cancer in the US:
A Tale of Geographic Disparity

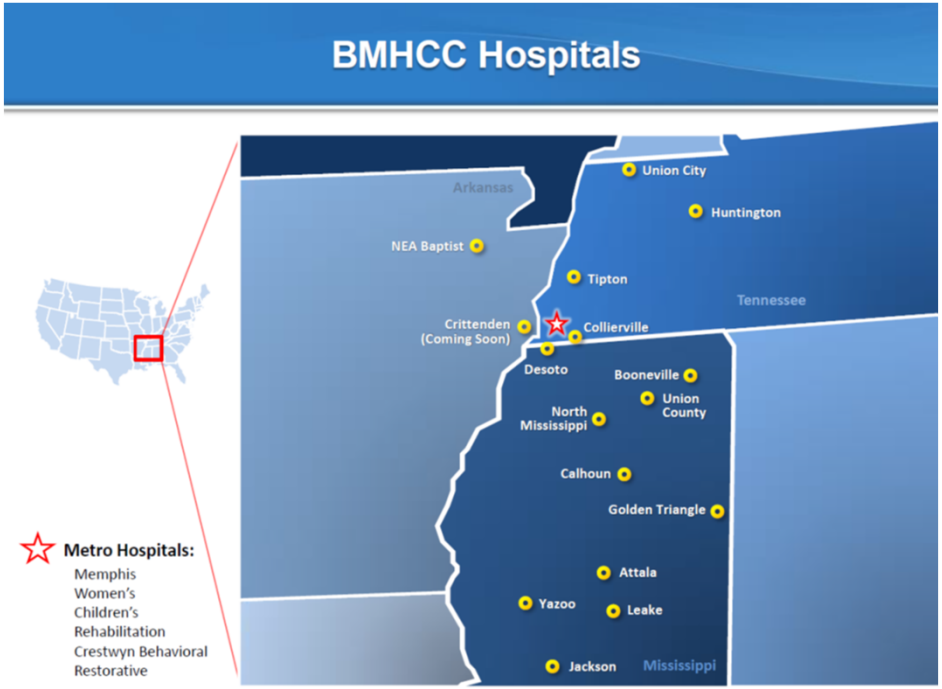






Trends and Patterns of Disparity in Cancer Mortality Among US Counties. Mokdad AH et al, JAMA.2017; 317(4):388-406.

If BMHCC was a state….



	State	Estimated new lung cancer cases, 2020[1]	NCI-Designated Cancer Center?
37	Nebraska	1270	1
38	New Hampshire	1220	1
	BMHCC	**1200 - 1300**	**0**
39	New Mexico	1040	1
40	Idaho	990	0
41	Rhode Island	920	0
42	Delaware	890	0
43	Hawaii	870	1
44	Montana	770	0
45	Utah	730	1
46	South Dakota	590	0
47	Vermont	570	0
48	North Dakota	460	0
49	Alaska	400	0
50	Wyoming	320	0
	DC	300	1

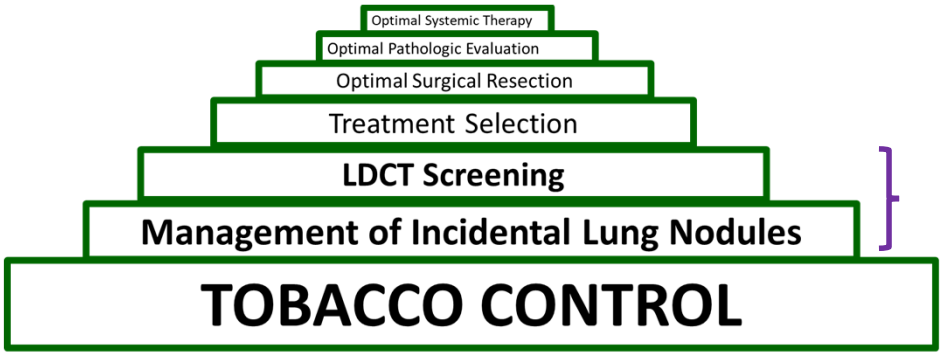
[1] Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2020. CA Cancer J Clin 2020;70:7-30.

Implementing The Mid-South Miracle:

Goal: Reduce Lung Cancer Mortality >25% Over 10 Years

Objectives: sustained, rigorous implementation of seven specific clinical programs

The Population Impact Pyramid



A Three-Tiered Approach

Approaches to Early Detection: LDCT Screening

- Pros:
  - Reduces lung cancer-specific and overall mortality
  - High level evidence: 3 large RCT + international meta-analysis[1-4]
- Cons:
  - Implementation barriers[5-7]
  - Low adoption rates (US);[8] no adoption (rest of the world)[7]
  - Eligibility criteria limitations[9,10]
  - Potential to exacerbate care and outcome disparities[8,10-15]

[1]Aberle et al. NEJM 2011 **PMID: 21714641**; [2]de Koning et al. NEJM 2020 **PMID: 31995683**; [3]Pastorino et al. Ann Oncol. 2019 **PMID: 31168572**; [4]Field et al Lancet Reg Health Eur. 2021. **PMID: 34806061**

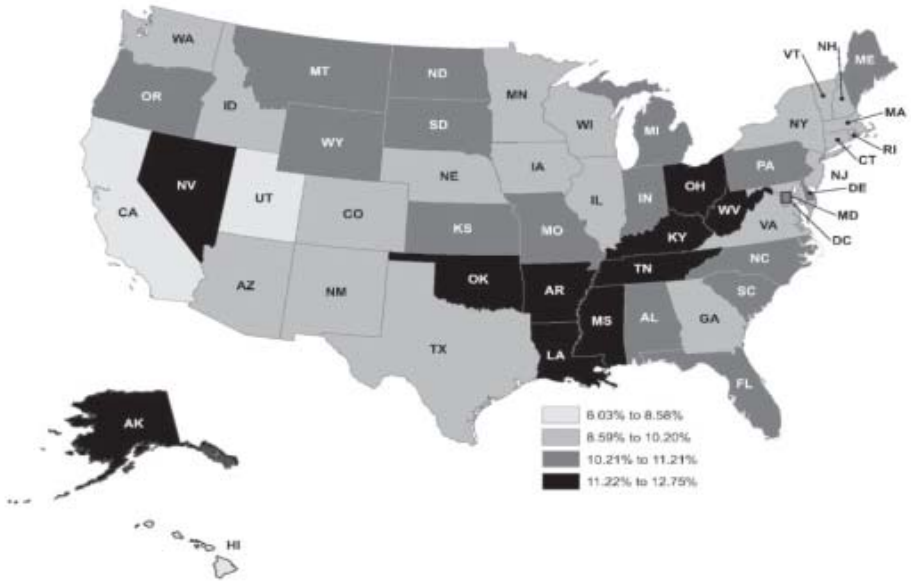
[5]Kinsinger et al. JAMA Intern Med. 2017 **PMID: 28135352**; [6]Field JK, et al. ESMO Open. 2019. **PMID: 31673428**; [7]Veronesi et al. Cancers (Basel). 2020 **PMID: 32599792**

[8]Fedewa et al. JNCI 2021 **PMID: 33176362**

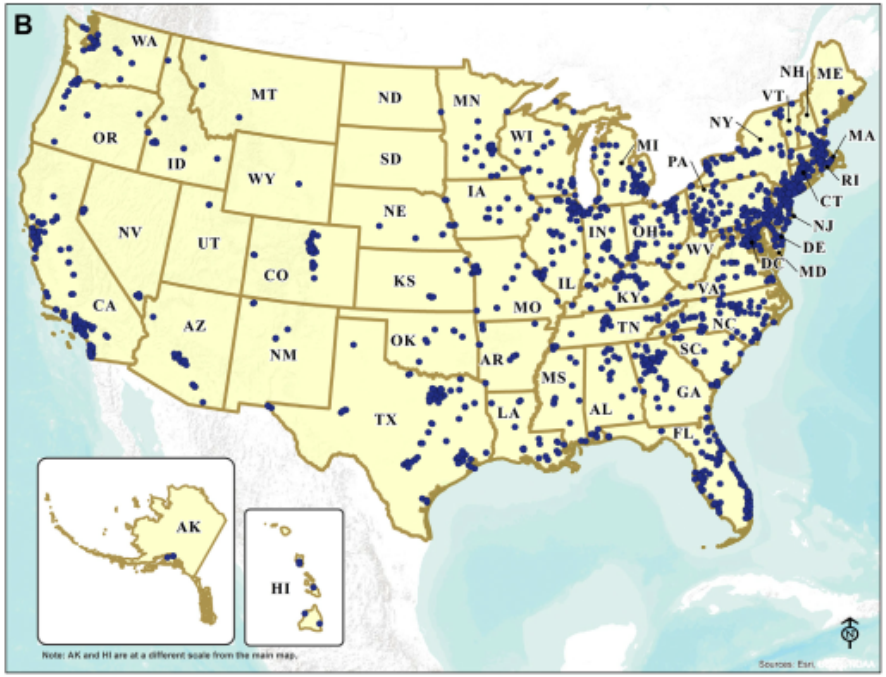
[9]Pinsky PF, Berg CD. J Med Screen 2012 **PMID: 23060474**; [10] Pinsky PF et al Chest. 2021 **PMID: 33545164**

[11] Aldrich et al. JAMA Oncol 2019 **PMID: 31246249**; [12]Han et al. JNCI 2020 **PMID: 32040195**; [13]Prosper et al. JAMA Netw Open. 2021 **PMID: 34427681**; [14]Tanner et al. Am J Respir Crit Care Med. 2015 **PMID: 25928649**; [15]Rivera et al. Am J Respir Crit Care Med. 2020 **PMID: 33000953**.

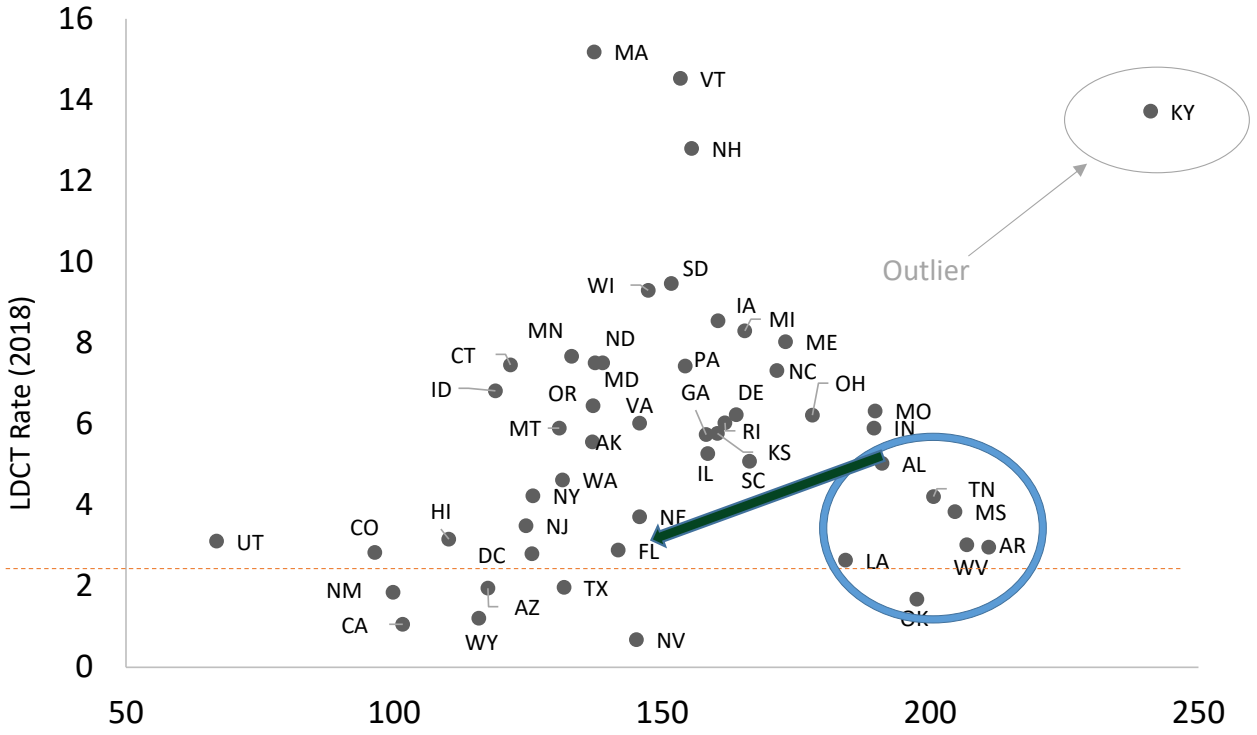
Lung Cancer Burden v Screening: State-Level



Fedewa SA, et al. J Natl Cancer Inst. 2020. PMID: 33176362.



Sahar L, et al. Chest. 2021. PMID: 32888933.



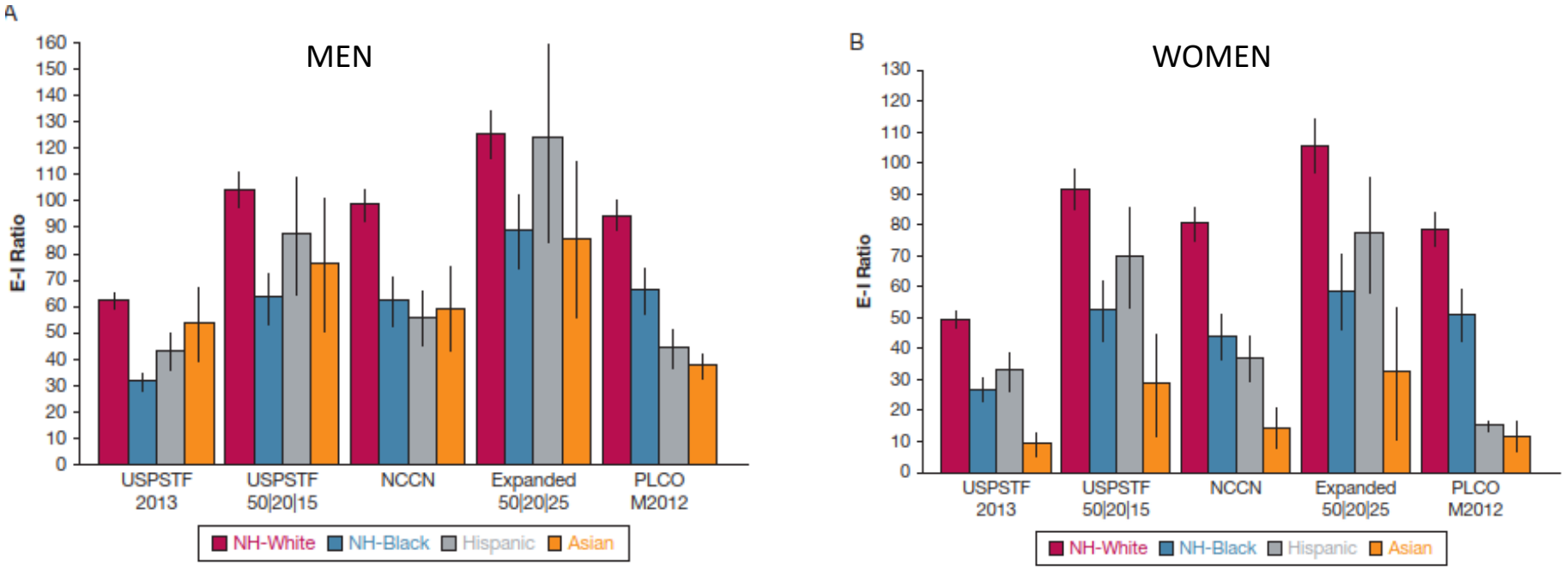
BURDEN

Lung Cancer Mortality Rate Per 100,000 Adults 55-80 years (2013-2017)

Fedewa SA, et al. J Natl Cancer Inst. 2020. PMID: 33176362.

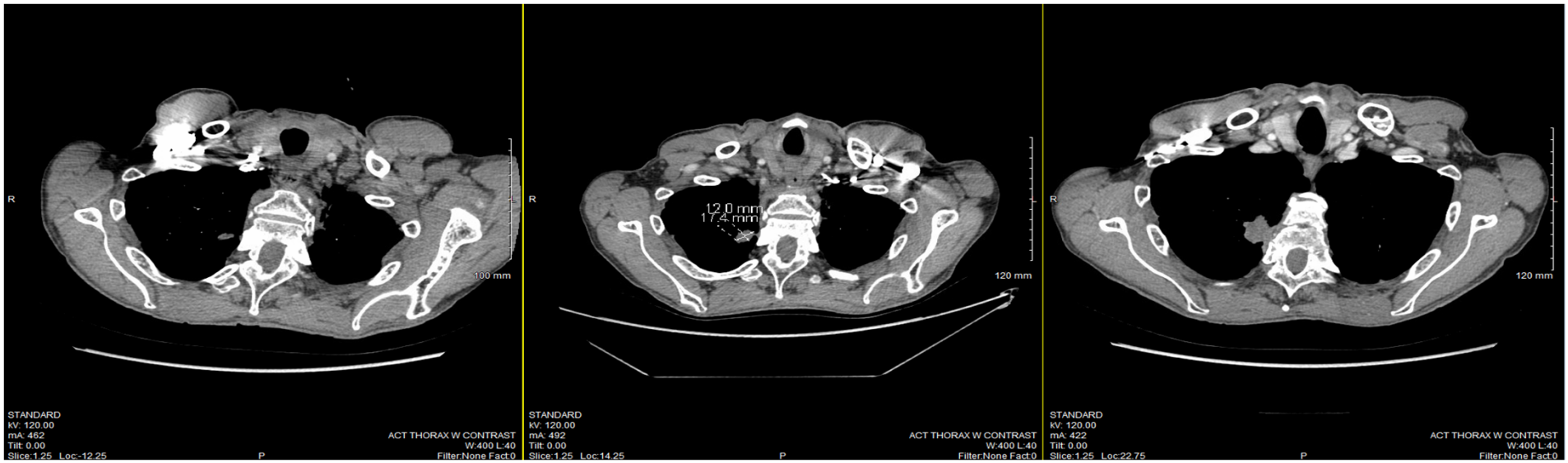
LDCT Screening Eligibility v Per-Capita Lung Cancer Incidence

How Selection Criteria (Policy-Level) Drive Sex, Race and Ethnic (Seemingly Person-Level) Disparities in Access to Lung Cancer Screening in the US



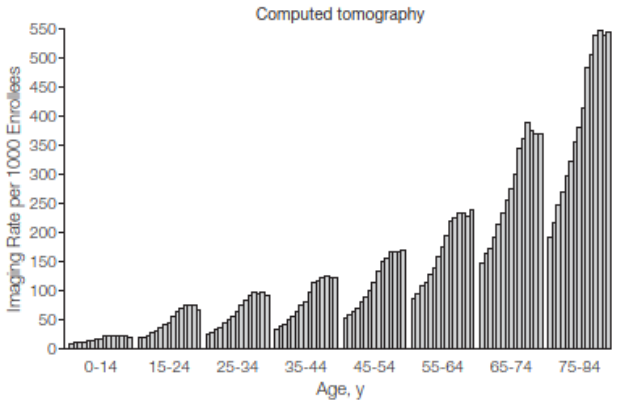
Pinsky PF, et al. Chest. 2021. PMID: 33545164.

Avoid this… save lives!

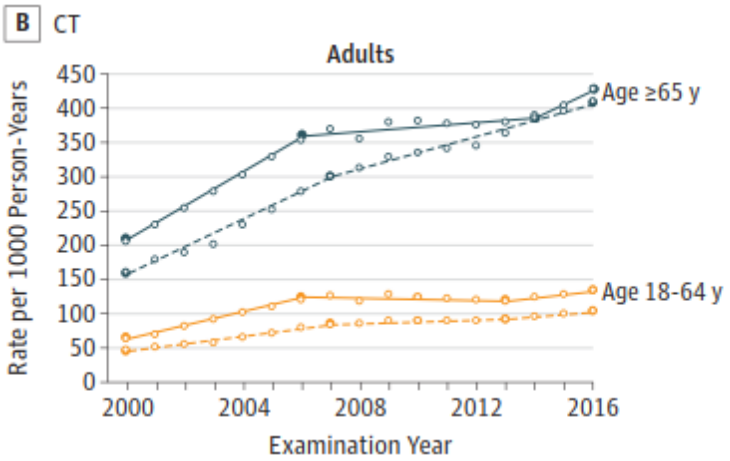


February, 2020 **June, 2020** **April, 2021**

Use of CT Imaging Keeps Rising…



Smith-Bindman R, et al. Use of diagnostic imaging studies…in large integrated health care systems, 1996-2010. JAMA. 2012 **PMID: 22692172**



Smith-Bindman R, et al. Trends in Use of Medical Imaging in US Health Care Systems and in Ontario, Canada, 2000-2016. JAMA. 2019. **PMID: 31479136**

Guideline-Concordant Management of Incidentally Detected Lung Nodules[1,2]

- Pros:
  - Starts from the point of detection of potentially malignant lung lesion
  - LDCT eligibility criteria less relevant
  - Bypasses LDCT implementation barriers
  - Leverages existing clinical material, infrastructure
  - Expands the reach of early detection to hard-to-reach populations
  - Alleviates a medico-legal quandry
- Cons:
  - Requires some infrastructure for identifying, tracking, oversight
  - Optimally requires transparent, interdisciplinary decision-making

[1]Gould MK, Donington J, Lynch WR, et al. ACCP evidence-based clinical practice guidelines. Chest. 2013 **PMID: 23649456,**
[2]MacMahon H, Naidich DP, Goo JM, et al. From the Fleischner Society 2017. Radiology. 2017 **PMID: 28240562.**

original reports

Lung Cancer Diagnosed Through Screening, Lung Nodule, and Neither Program: A Prospective Observational Study of the Detecting Early Lung Cancer (DELUGE) in the Mississippi Delta Cohort

Raymond U. Osarogiagbon, MBBS[1]; Wei Liao, PhD[1]; Nicholas R. Faris, MDiv[1]; Meghan Meadows-Taylor, PhD[1]; Carrie Fehnel, BBA[1]; Jordan Lane, MA[1]; Sara C. Williams, MFA[1]; Anita A. Patel, MBBS[1]; Olawale A. Akinbobola, MPH[1]; Alicia Pacheco, MHA[1]; Amanda Epperson, RN[1]; Joy Luttrell, RN[1]; Denise McCoy, BS[1]; Laura McHugh, RN[1]; Raymond Signore, RN[1]; Anna M. Bishop, MSN[1]; Keith Tonkin, MD[1,2]; Robert Optican, MD, MSHA[1,2]; Jeffrey Wright, MD, PhD[1,3]; Todd Robbins, MD[1]; Meredith A. Ray, PhD[4]; and Matthew P. Smeltzer, PhD[4]

PMID: 35258994 DOI: 10.1200/JCO.21.02496

DELUGE: Processes

1. Concurrent implementation projects_ 2015: LDCT and Incidental Lung Nodule Program

2. Prospective observational cohorts.

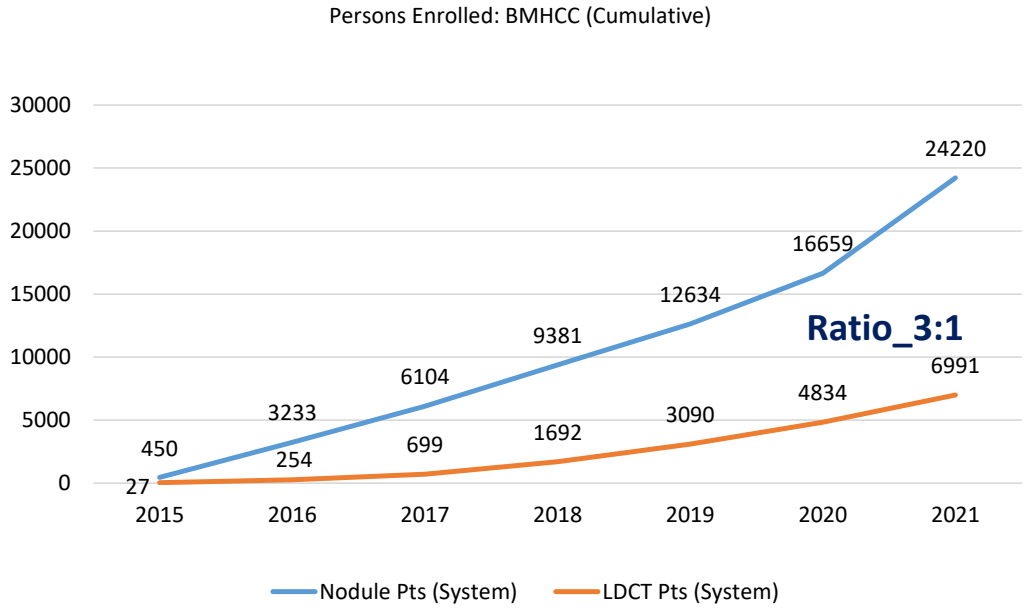
3. LDCT: consenting, apparently health eligible adults; Lung-RADS

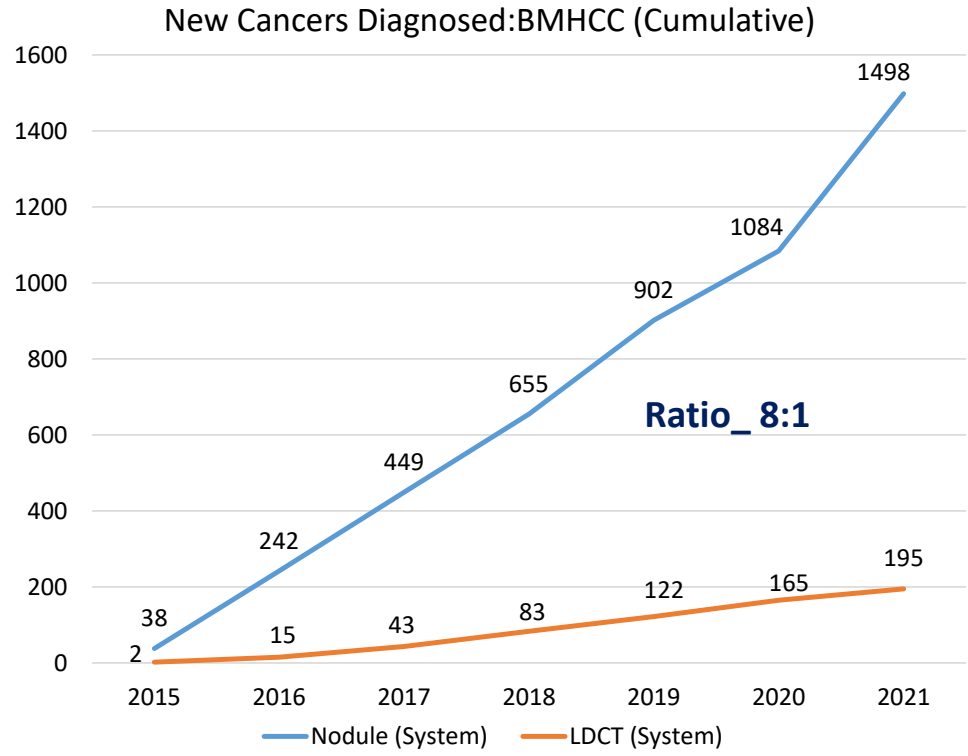
4. ILNP: automated report capture; physician (patient) notification; Fleischner Society guidelines

5. High-risk patients triaged into Multidisciplinary decision-making forum

Detecting Early Lung Cancer (DELUGE) in MS Delta

Program Volumes





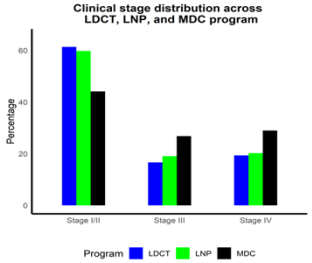
Annual Volumes	2015	2016	2017	2018	2019	2020	2021
Nodule	450	2783	2871	3277	3253	4025	7561
LDCT	27	277	445	993	1398	1744	2157

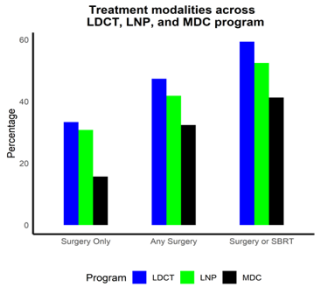
Rates of Lung Cancer Detection

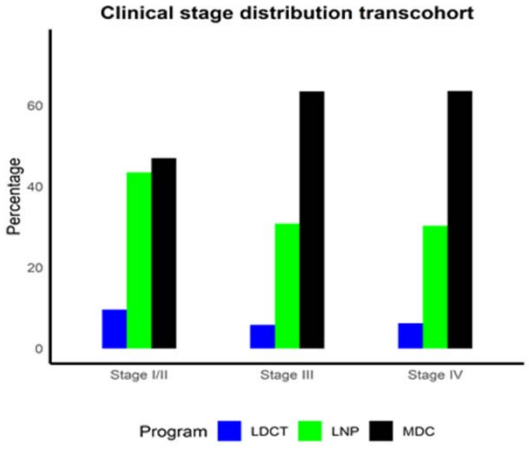
Nodule – 6.2% LDCT – 2.8%

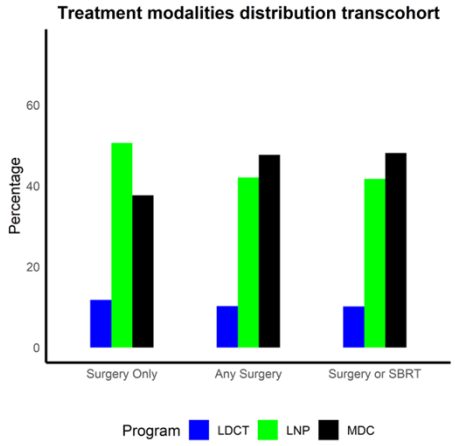
Stage Distribution, Curative-Intent Treatment, Survival

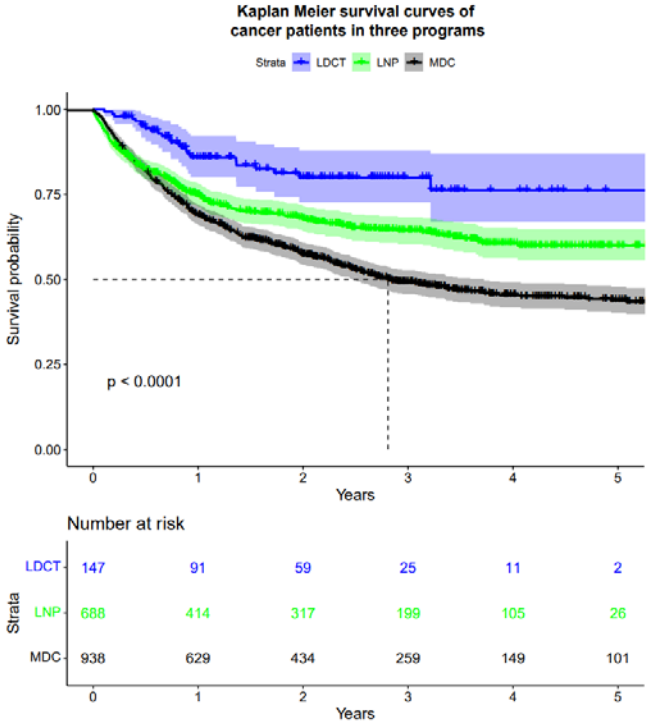
DELUGE in the Mississippi Delta: LDCT v LNP v MDC











Osarogiagbon, et al. Epub J Clin Oncol.
PMID: 35258994 **DOI: 10.1200/JCO.21.02496**

DELUGE in the Mississippi Delta: LDCT v LNP v BMHCC

	LDCT	LNP	BMHCC
Demographics	N = 156	N = 772	N = 1150
Age, median (Q1 - Q3)†	68 (64 - 72)	69 (63 -76)	68 (61-75)
Race			
White	84	71	69
Black	16	27	30
Other/Not Reported	0	2	1
Smoking Status			
Active	72	46	41
Former	28	40	45
Never	0	13	13
Pack years - Former Smoker			
Median (Q1-Q3)†	55 (40.75 - 72.5)	41 (24.25 - 60)	20.25 (21.5 - 60)
Quit Duration - Former Smoker			
Median (Q1-Q3)†	8 (2.75 - 11.25)	16 (7 - 28)	11 (4 - 24)

ILNP: Complementary Pathway to Early Lung Cancer Detection?

Patient Group	LDCT	LNP	MDC	*P*
Proportion eligible for LDCT by USPSTF 2013 Criteria, No. (%)				
All patients	4,513 (79.75)	1,756 (11.36)	570 (32.28)	< .0001
Patients with lung cancer	133 (88.67)	298 (42.69)	430 (42.57)	< .0001
Proportion eligible for LDCT by USPSTF 2021 Criteria, No. (%)				
All patients	4,720 (83.41)	2,280 (14.75)	718 (40.66)	< .0001
Patients with lung cancer	137 (91.33)	344 (49.28)	529 (52.38)	< .0001

Abbreviations: LDCT, Low-Dose Computed Tomography Lung Cancer Screening Program; LNP, Lung Nodule Program; MDC, Multidisciplinary Care Program; USPSTF, US Preventive Services Task Force.

Even if 100% of eligible persons by USPSTF 2021 criteria had been enrolled into LDCT screening, ILNP would have detected 20% of all stage I/II patients in the entire cohort.

Osarogiagbon, et al. Epub J Clin Oncol.
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Are The DELUGE in the Mississppi Delta Data Generalizable?

SEER-Medicare Cohort

1. 629,953 subjects from 2014 - 2019 in the 5% sample cohort: 26.3%, chest CTs; 12.0%, IPNs

2. Cumulative lung cancer rates at 6, 12, 18 and 24 months: 1.6%, 2.4%, 3.2% and 3.8%.

3. 44,194 lung cancer cohort cases: 26.9%, IPN-only; 2.9%, LDCT; 70.2%, Referent

4. Localized stage: IPN-only 52%; LDCT, 50.3%; Referent group, 21.5%.

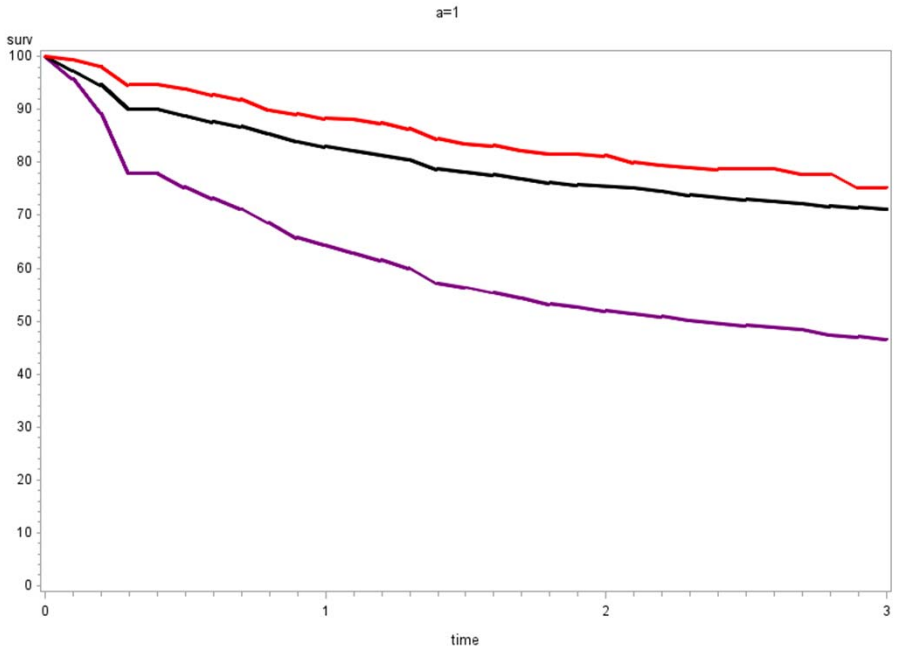
5. Among all localized cases: IPN-only, 45.4%; 4.9%, LDCT

Ratio 9:1

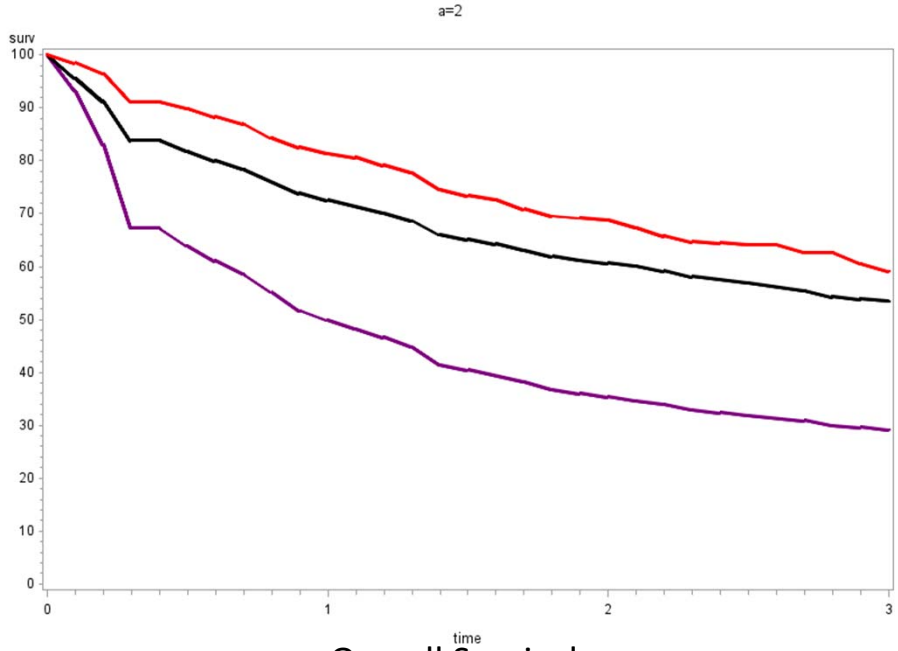
Pinsky, Miller, Faris, Osarogiagbon. Pulmonary Nodules, Lung Cancer Screening and Lung Cancer in the Medicare Population. Chest. 2022 Dec 15:S0012-3692(22)04230-1. doi: 10.1016/j.chest.2022.12.006. Epub ahead of print. PMID: 36529155.

Survival: LDCT v IPN v Referent

SEER-Medicare Population 2015 - 2017



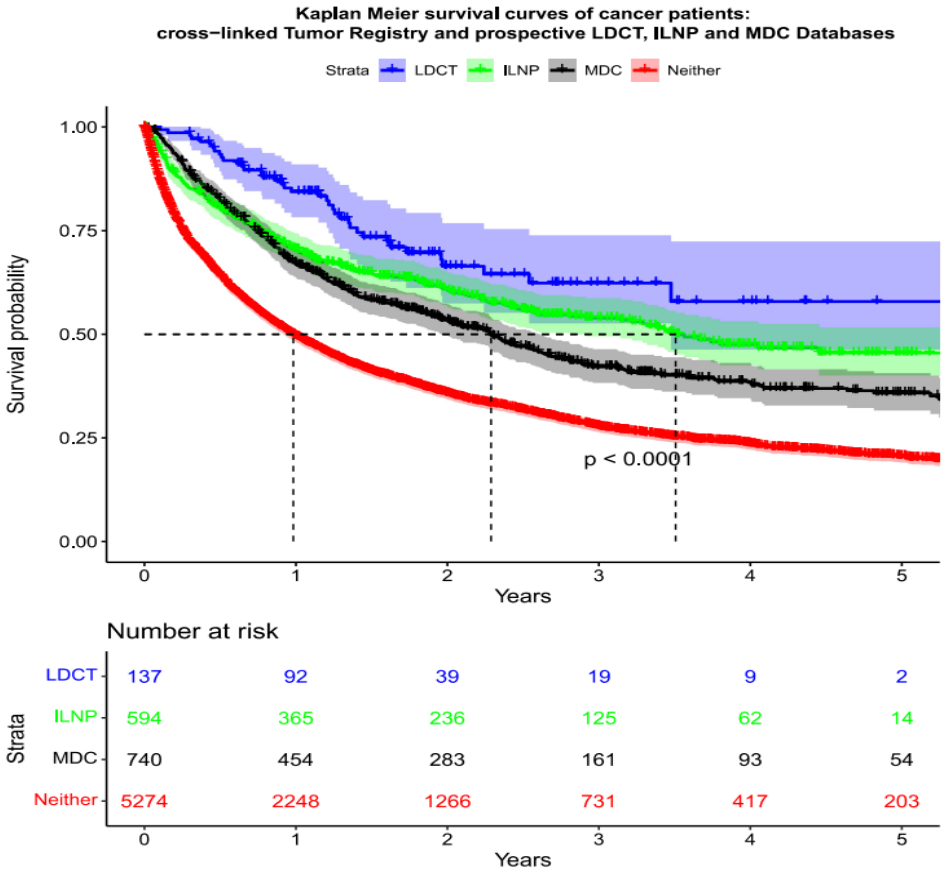
Lung Cancer Specific Survival

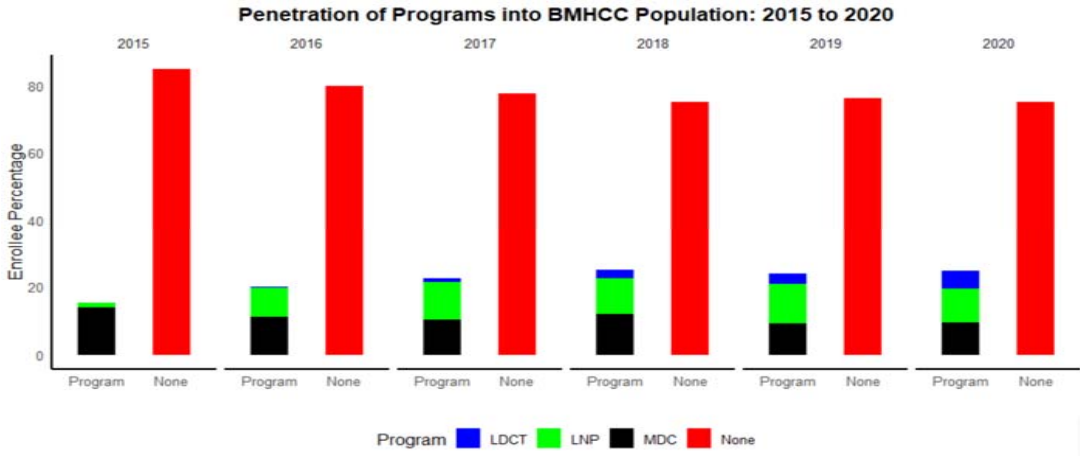


Overall Survival

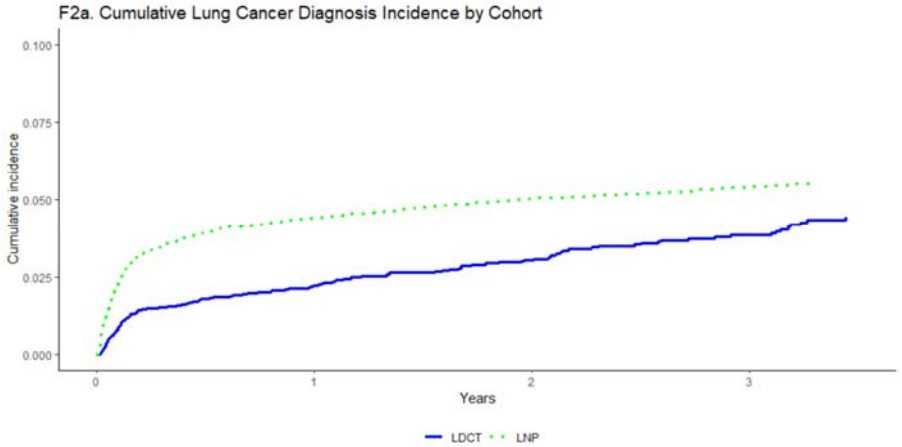
Pinsky, Miller, Faris, Osarogiagbon. Pulmonary Nodules, Lung Cancer Screening and Lung Cancer in the Medicare Population. Chest. 2022 Dec 15:S0012-3692(22)04230-1. doi: 10.1016/j.chest.2022.12.006. Epub ahead of print. PMID: 36529155.

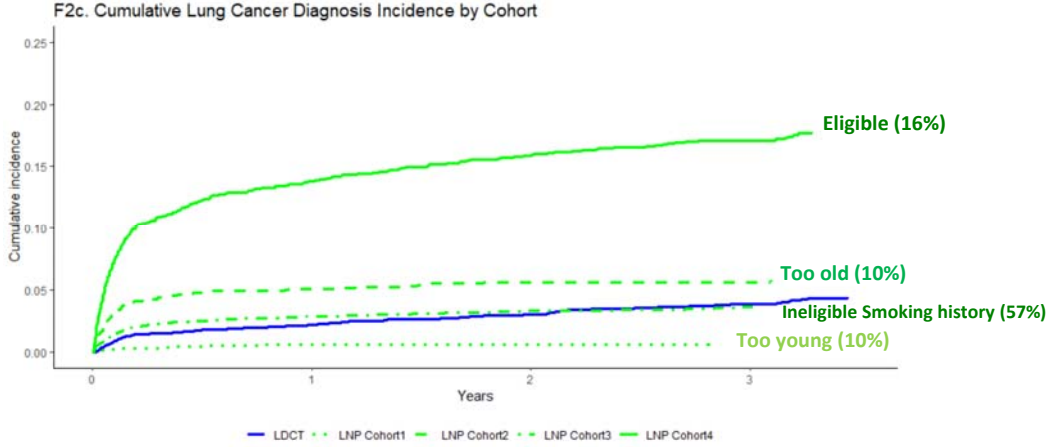
Lung Cancer Diagnosed Through Different Pathways: BMHCC 2015 - 2020

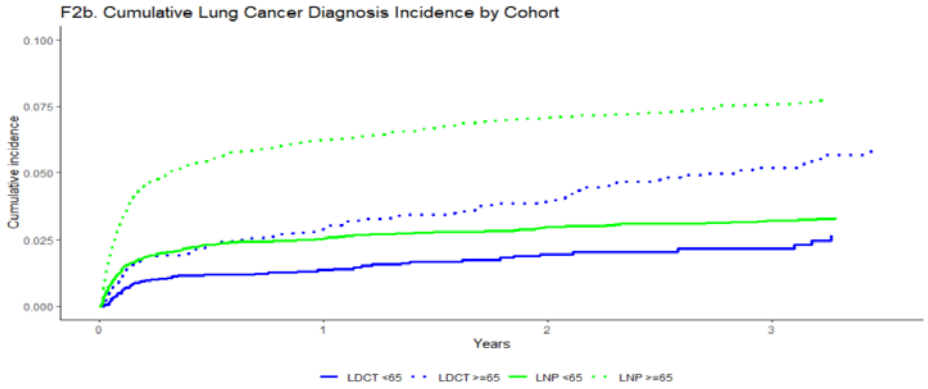


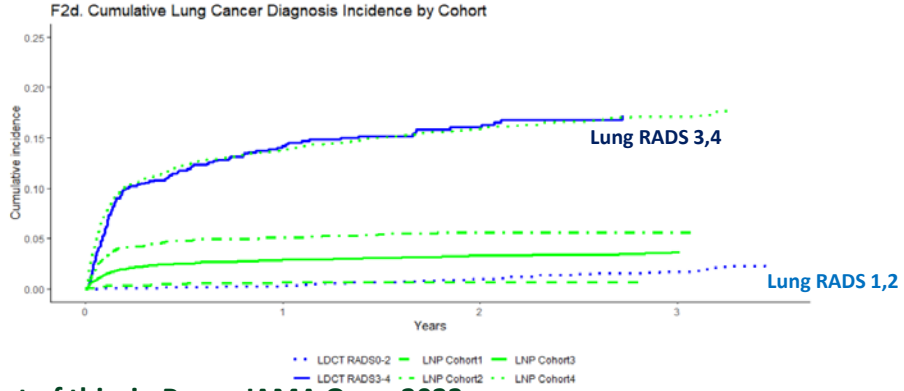


Cumulative Lung Cancer Risk: LDCT v ILNP





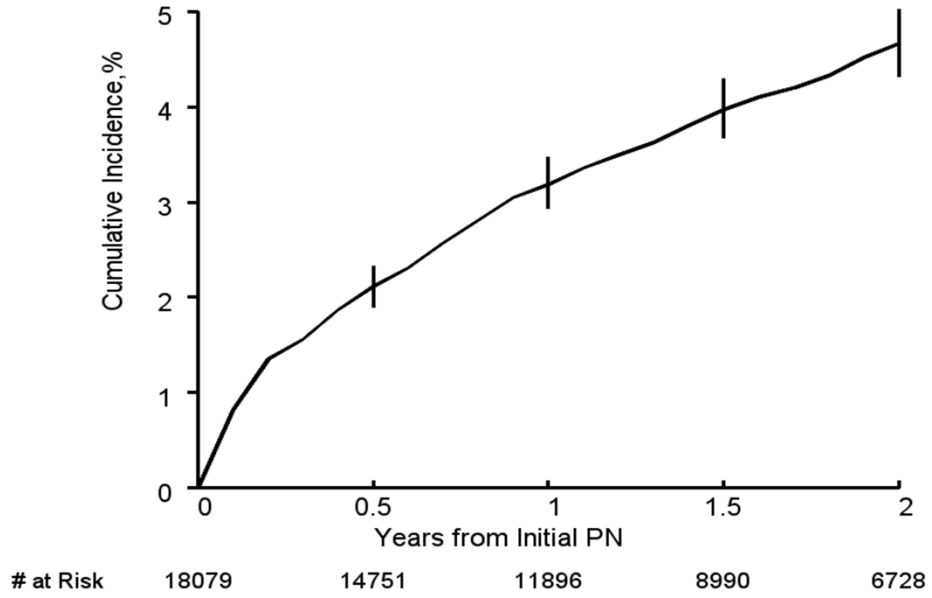




Osarogiagbon et al. Part of this, in Press, JAMA Open 2023

Cumulative Incidence of Lung Cancer after IPN Detection

SEER-Medicare Database 2015 - 2017



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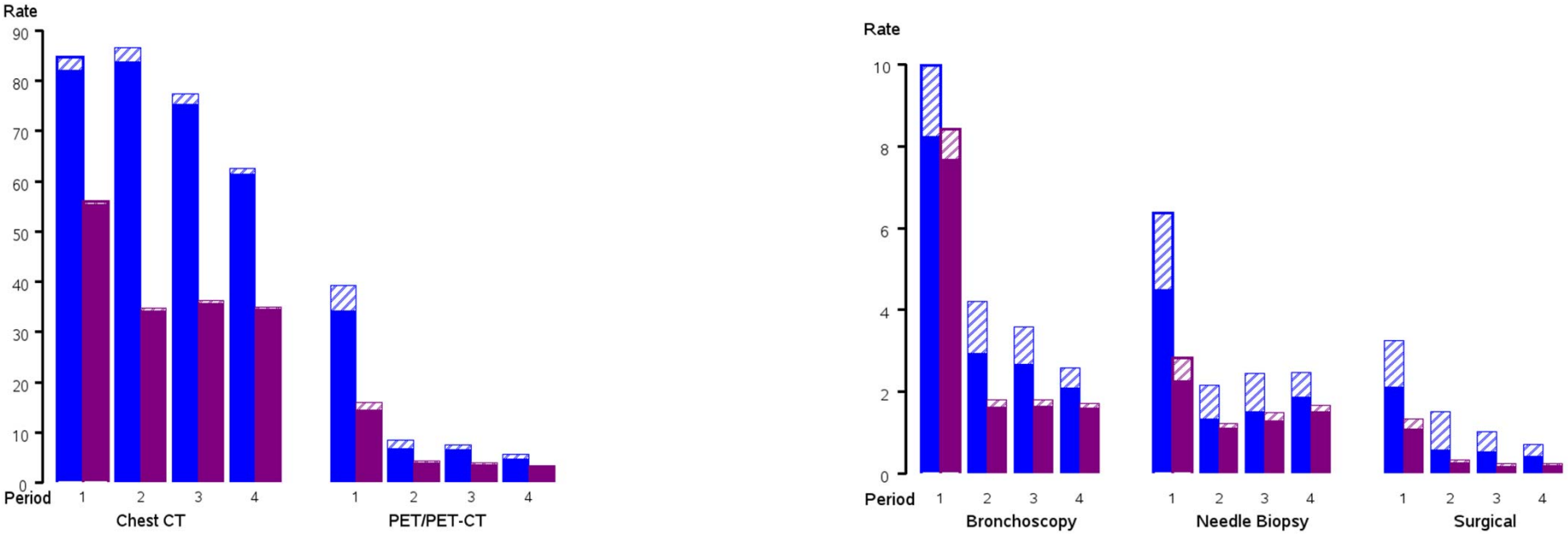
Rates of Diagnostic Follow up of IPNs

SEER-Medicare 2014 - 2015



Excess procedures per late-stage cancer prevented:

39 (chest CT), 4.8 (PET-CT), 0.5 (bronchoscopy), 0.8 (needle biopsy) and 0.6 (surgical procedure)

Pinsky, Osarogiagbon. Unpublished.

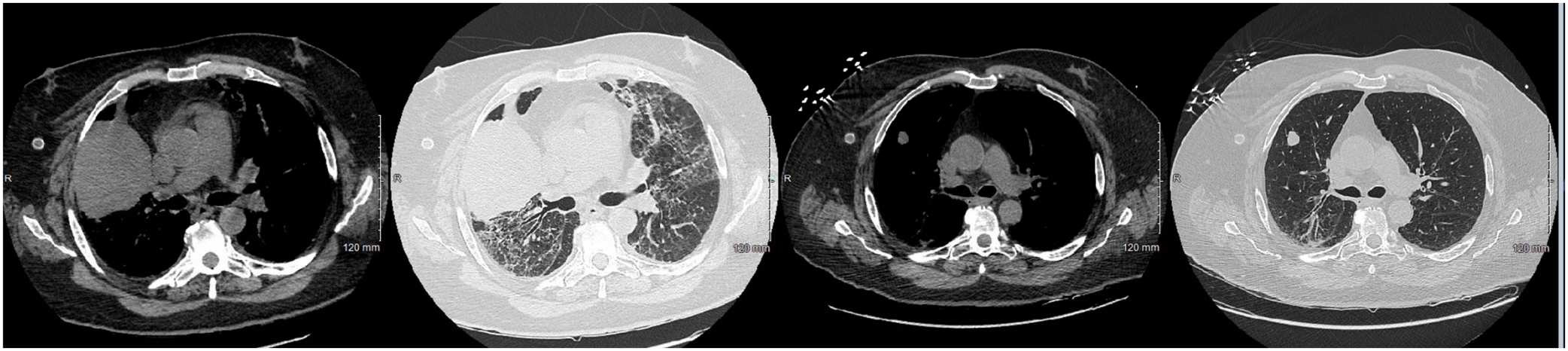
Next Steps

1. Program dissemination.
2. Evaluation of generalizability.
3. Quantifying population-level impact: county-level differences-in-difference analysis
4. Integrating a framework for optimization, discovery
    1. AI/radiomics approaches
    2. Biomarker validation

Take-Home Messages

- Incidental Lung Nodule Programs provide an alternative pathway to early detection of lung cancer.
- Epidemiologically powerful: may rescue more people than LDCT
- LDCT + ILNP: concurrent deployment may expand population-level impact, alleviate looming disparities inadvertently induced by LDCT.
- ILNP can be implemented even in places where LDCT is not available.

Avoid This…. Save Lives



02/14/22

10/24/20

MSM: Acknowledgements

DELUGE

Administrators
Parker Harris, MHA
Margaret DeBon, PhD
Nicholas Faris, M.Div. (Clinical Program)
Carrie Fehnel, BBA (Research Program)

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Angela Fox
Dustin Box
Robert Vest
Praveen Pola
Shirley Banks
Pam Beasley

Data managers
Jordan Lane, MA
Talat Qureshi, BS
Rudy Ramos, BA
Sara C. Williams MFA

Data scientists
Wei Liao, PhD
Matthew Smetlzer, PhD
Meredith Ray, PhD

Navigators
Amanda Epperson, RN
Joy Luttrell, RN
Denise McCoy, BA
Linda Ragon, RN

Audrey Rushing, RN
Beth Smith, AAS
Kim Adams

Clinicians
Greg Jenkins, MD

Pulmonologists:
Anurag Mehotra, MD
Muhammad Sheikh, MD
Jeffrey Wright, MD

Radiologists:
Shannon Gulla, MD
James Machin, MD
Robert Optican, MD
Keith Tonkin, MD

Thoracic Surgery:
Todd Robbins, MD
Sam Signore, RN

Past Support
Diane Richards

Funding Support
Baptist Memorial Health Care Foundation

MultiD Program

Administrators
Carrie Fehnel, BBA

Data managers
Anita Patel, MBBS

Navigators
Jasmine Banks
Christie Ellis, RN
Laura McHugh, RN
Samantha Parker, RN
Sam Signore, RN

Research Coordinators
Courtney Berryman
Sarah Lafferty
Erin Finley

Data scientists/Analysts
Meghan Taylor, PhD

Clinicians
Philip Lammers, MD
Thomas Ng, MD
Todd Robbins, MD
Shailesh Satpute, MD

Past Support:
Penny Kershner
Angela Fulford
Laurie Quick
Kristi Roark
Shirley Banks
Folabi Ariganjoye

Funding Support
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MS-QSR

Administrators
Carrie Fehnel, BBA

Data managers
Wale Akinbobola, MPH
Kourtney Dortch
Andrea Saulsberry

Data scientists/Analysts
Meredith Ray, PhD

Epidemiologists
Matthew Smeltzer, PhD

Past Support
Philip Ojeabulu, MD

Funding Support
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Tobacco Control

Clinical Support
John Powell, NP
Laura McHugh, RN
Joy Luttrell, RN

Pharmacy
Alexander Quesenberry
Hannah Alley
Glenn Roma

Data scientists/Analysts
Meredith Ray, PhD

Past Support
Laurie Quick
Rachel Hendrix

NCORP

System Support
Reyna Aza Salinas
Lucinda Boldien
Paige Gibbons
Mary Rehak
Lori Lynch
Tracy Stewart
Ann Bishop

Research Coordinators
Komal Lotay
Laurel Morgan
Mariesha Willliams
Elizabeth Mathews, RN
Rita Frank
Jodie Baker
Katie Baty, RN
Carol Ragon, RN
Lauren Wheeler, RN
Lauren Wooten, RN

Clinicians
Stephen Behrman, MD
Salil Goorah, MD
Donald Gravenor, MD
Philip Lammers, MD
Alyssa Throckmorton, MD

Pharmacy
Alexander Quesenberry
Hannah Alley
Glenn Roma

Past Support
Amber Sinquefield
Liset Taybo
Emma Draluck
Bianca Jackson
Toya Kimble
Manali Jaglekar
Cheryl Houston-Harris
Antoinette Stone
Dawn Smith
Linda Sullins
Samantha Potts
Shelia Carr
Tracy Camp

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