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Ellen T. Chang,<sup>1</sup> Anuraag R. Kansal,<sup>1</sup> Earl Hubbell,<sup>1</sup> Graham A. Colditz,<sup>2</sup> Allison W. Kurian,<sup>3</sup> Christina A. Clarke<sup>1</sup>  
<sup>1</sup>GRAIL, LLC, Menlo Park, California; <sup>2</sup>Washington University School of Medicine, St. Louis, Missouri; <sup>3</sup>Stanford University, Stanford, California.

## INTRODUCTION

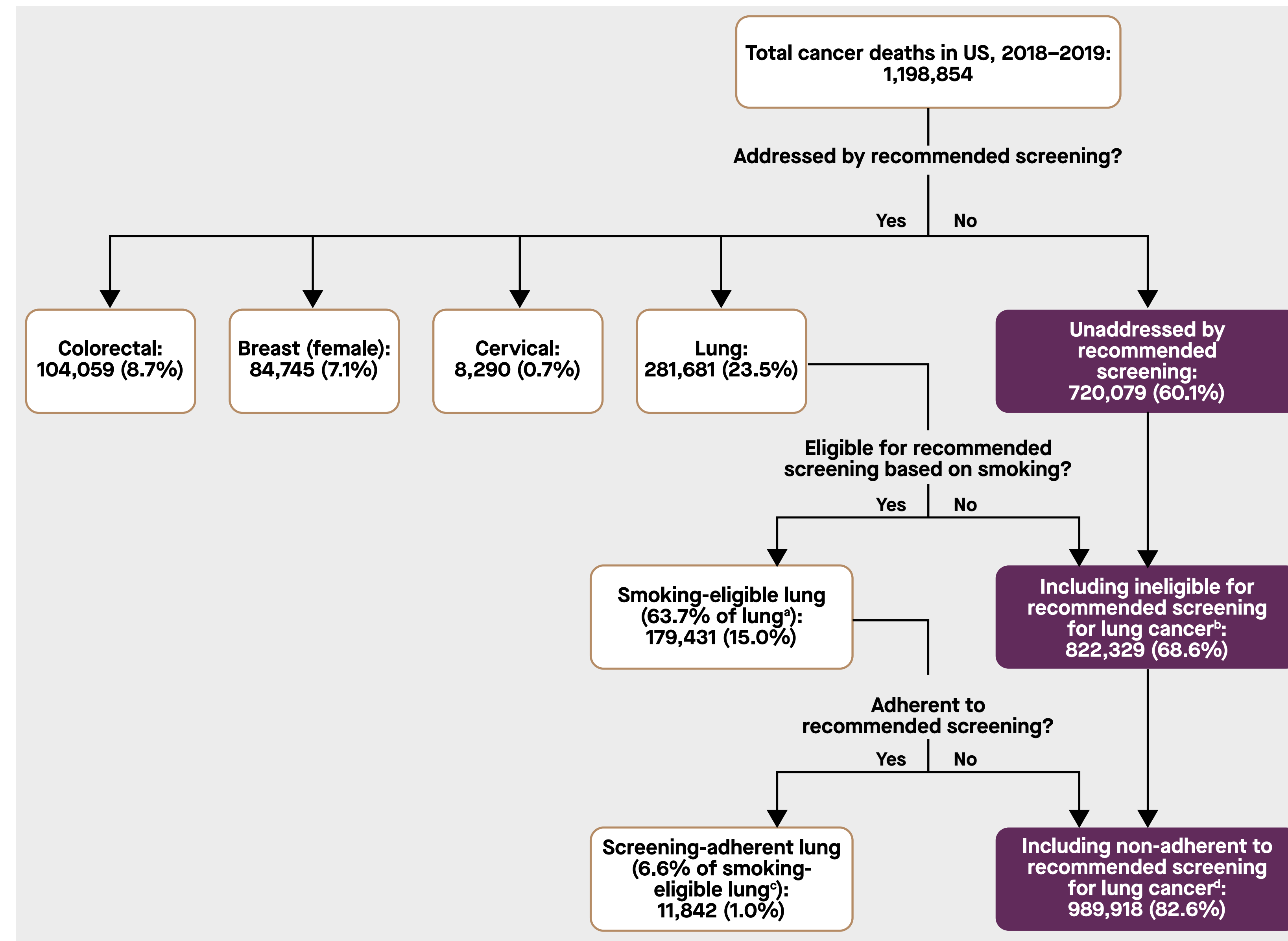
- In the United States (US), cancer is the leading cause of death among adults  $\leq 80$  years<sup>1</sup>
- Guideline-based screening programs (based on US Preventive Services Task Force [USPSTF] A & B recommendations) for colorectal, female breast, cervical, and lung cancers have contributed to sustained declines in cancer mortality rates<sup>2</sup>
- These four cancer types, however, account for less than half of the  $\sim 600,000$  cancer deaths per year in the US<sup>2</sup>
- Screening eligibility for colorectal, female breast, and cervical cancers is based on age, while eligibility for lung cancer screening is additionally based on smoking history;<sup>3</sup> this reduces the percentage of cancer deaths addressed by recommended screening guidelines

## OBJECTIVE

- To understand the burden of cancer death potentially addressable by new or improved screening approaches, we estimated the proportion of US cancer deaths unaddressed by current implementation of USPSTF screening recommendations, especially after accounting for lung cancer screening eligibility and adherence

## KEY RESULTS: WE ESTIMATED THAT AT LEAST 82% OF CANCER DEATHS ARE NOT ADDRESSSED BY CURRENT IMPLEMENTATION OF SCREENING RECOMMENDATIONS

**Figure 1. Deaths From Cancer in the US by Primary Type in 2018-2019, US National Center for Health Statistics,<sup>4</sup> with Eligibility for and Adherence to Guideline-Based Low-dose Computed Tomography Screening for Lung Cancer**



\*Modeled estimate of proportion of lung cancer patients eligible for screening.<sup>5</sup>  
<sup>†</sup>Does not account for age eligibility for recommended screening for colorectal, breast, and cervical cancers.  
<sup>‡</sup>Lung cancer screening receipt from 2019 American College of Radiology Lung Cancer Screening Registry.<sup>6</sup>  
<sup>§</sup>Does not account for adherence to recommended screening for colorectal, breast, and cervical cancers.  
 US, United States.

- We estimated that 31.4% of approximately 600,000 annual cancer deaths in the US were from colorectal, female breast, cervical, and smoking-eligible lung cancers (**Figure 1**)
- Further accounting for adherence to lung cancer screening guidelines reduced the estimated proportion of cancer deaths addressed by screening to 17.4% (**Figure 1**)
- Thus, at least 82.6% of cancer deaths (approximately 500,000 per year) may not be addressed by current implementation of recommended screening guidelines
- Individually uncommon cancer types (affecting  $<40,000$  people per year in the US,<sup>7</sup> excluding cervix), which are unaddressed by guideline-based screening, collectively comprised 30.4% of cancer deaths
  - These cancer types, which include brain cancer (2.9% of cancer deaths), esophageal cancer (2.6%), ovarian cancer (2.3%), myeloma (2.1%), stomach (1.9%), and other types that individually account for  $<2\%$  of cancer deaths, but together sum to 30.4%, are unlikely to be targeted by single-cancer screening strategies due to their rarity in the US population

**Table 1. Deaths From Cancer in 17 US Geographic Regions by Stage at Diagnosis in 2018-2019, Surveillance, Epidemiology, and End Results (SEER) Registries Incidence-Based Mortality Data<sup>8</sup>**

	Stage at Diagnosis			
	Localized (Column %)	Regional (Column %)	Distant (Column %)	Missing/Unstaged (Column %)
All cancer deaths, n	134,670	85,890	146,702	81,728
Lung cancer deaths, n	10,987	13,722	36,868	6,560
Colorectal, female breast, and cervical cancer deaths, n	33,700	27,942	19,164	17,682
Other cancer deaths, n	89,983 (66.8%)	44,226 (51.5%)	90,670 (61.8%)	57,486 (70.3%)

- According to incidence-based mortality data from 17 US Surveillance, Epidemiology, and End Results (SEER) cancer registries,<sup>8</sup> 24.7% of 367,262 stageable cancer deaths (61.8% of 146,702 distant-stage deaths) were from distant-stage cancer types that lack current guideline-based screening (i.e., types other than lung, colorectal, female breast, and cervical; **Table 1**)

## METHODS

- We used two years of mortality data from January 2018 through December 2019 (pre-COVID-19 pandemic) from the National Center for Health Statistics and published estimates of the proportion of screening-eligible lung cancer patients, accessed via the National Cancer Institute's SEER program<sup>4</sup>
- For further stratification of cancer deaths by stage at diagnosis, we used two years of incidence-based mortality data from January 2018 through December 2019 from 17 SEER geographic regions, with stage classified according to SEER Summary Stage<sup>8</sup>
- We accessed the most recent SEER data using SEER\*Stat software version 8.4.1 (Surveillance Research Program, National Cancer Institute, 2023)

- As an estimate of the proportion of lung cancer cases meeting the current US Preventive Services Task Force eligibility criteria for lung cancer screening (i.e., ages 50–80 years with 20+ pack-years of smoking and either currently smoking or having quit within the past 15 years), we used a recently published estimate (63.7%) based on modeling of Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial and National Lung Screening Trial data, as well as National Health Interview Survey data<sup>5</sup>
  - This estimate is consistent with other published estimates that we identified from a literature search of the PubMed database
- As an estimate of the proportion of screening-eligible adults who adhere to recommended lung cancer screening with low-dose computed tomography, we used a recently published estimate (6.6%) based on 2019 nationwide reports from the American College of Radiology's Lung Cancer Screening Registry<sup>6</sup>

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## Disclosures

This work was funded by GRAIL, LLC. ETC, ARK, EH, and CAC are employees of GRAIL, LLC, hold stock in or receive other support from Illumina, and report other support from GRAIL, LLC. EH also has multiple patents in the field of cancer detection pending to GRAIL, LLC. GAC reports other support from the National Institutes of Health outside of the submitted work. AWK reports a past grant from Myriad Genetics outside of the submitted work.

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## CONCLUSIONS

- In conclusion, we estimated that 68.6% of cancer deaths in the US are from cancer types that are not eligible for USPSTF-recommended screening, and 82.6% of cancer deaths are not addressed after additionally accounting for adherence to lung cancer screening
- We did not further account for non-adherence to recommended screening for breast, cervical, and colorectal cancers, or for eligibility restrictions by age
  - Even among cancer types with recommended screening, especially lung cancer, a sizable proportion of deaths after late-stage diagnosis indicates potential for improved screening implementation to reduce mortality
  - The proportion of unaddressed cancer deaths is expected to increase over time due to the rising percentage of lung cancer among never smokers, especially in non-White populations<sup>9</sup>
  - Effective implementation of preventive measures, such as smoking cessation and preventive cancer screening (for colorectal and cervical cancers), reduces both incidence and mortality from targeted cancers
- The large proportion of cancer deaths unaddressed by existing implementation of recommended screening represents a vast opportunity for new cancer screening technologies that are safe, effective, accessible, and affordable to enable earlier detection, which in turn enables a greater number of treatment options for the full spectrum of cancer types that contribute to the overall cancer burden