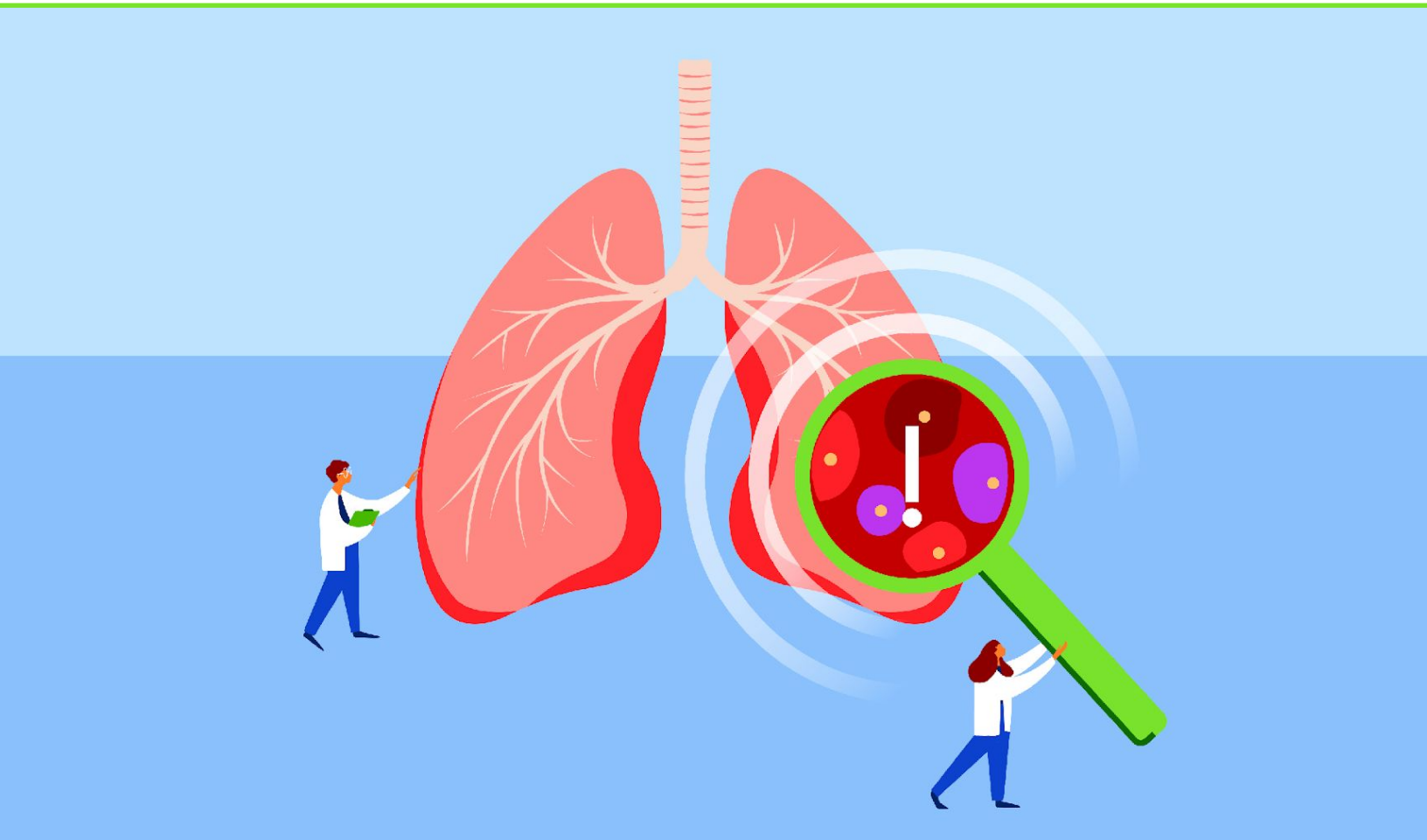
navify® Algorithms, LungFlag

Improve lung cancer screening programs

Discover a new possibility for personalized prescreening results with LungFlag



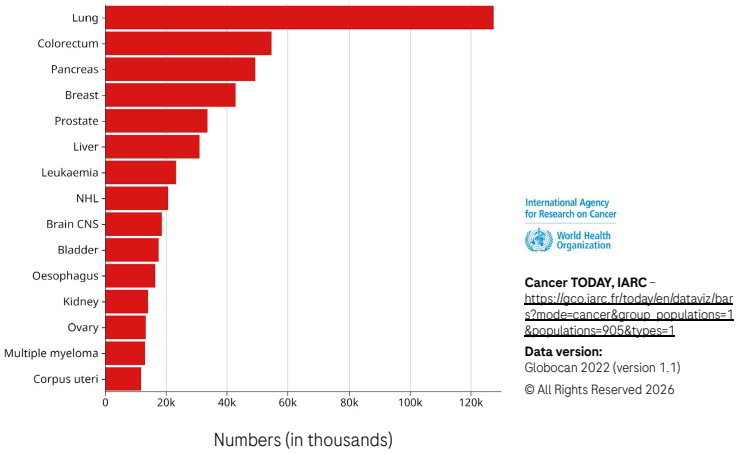
US epidemiology[1-3]

Lung cancer is a significant US health issue being the 2nd most frequently diagnosed cancer and the leading cause of cancer deaths. According to the American Cancer Society, the 2026 projections for lung cancer in the United States include:

~ 229,410 new cases of lung cancer
~ 124,990 deaths from lung cancer[1]

Lung cancer is classified into non-small cell lung cancer (NSCLC, 85% of cases) and small cell lung cancer (SCLC, 15% of cases).[2]

Absolute numbers, Mortality, Both sexes, in 2022
United States of America (Top 15 cancer sites)



Lung cancer screening[4-7]

Lung cancer screening (LCS) is a preventive health check, like a mammogram or a colonoscopy, helping to identify lung cancer early in people who are at high risk. Two large, independent, randomized controlled trials, NLST and NELSON, showed that lung cancer mortality was significantly lower among those who underwent LCS than among those who had no screening (NELSON) or were screened with a chest X-ray (NLST). Through these two studies, a clear disease-stage shift was demonstrated, with the majority of the cases being diagnosed and treated in early stages.

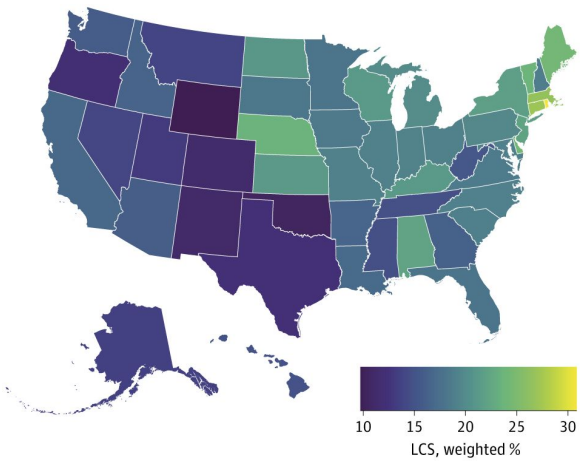
A low-dose computed tomography (LDCT) scan is the recommended method for LCS in high-risk patients. The screening rate for lung cancer in the high-risk population has shown limited improvement over time with only 20% of the high-risk population currently being screened. When compared with a screening rate of over 75% for breast cancer, it is clear more needs to be done to reduce the stigma and burden of LCS.

Guideline recommendations[6]

The USPSTF guidelines recommend annual Lung Cancer Screening (LCS) for adults:

- Aged 50-80 years old
- With a >=20 pack-year smoking history* and currently smoking or having quit within the past 15 years

LCS weighted rate, 2022[8]
State-Level Prevalence of Up-to-Date Lung Cancer Screening (LCS) in the US, 2022



USPSTF, U.S. Preventive Services Task Force; LCS, Lung Cancer Screening
* Cumulative assessment of smoking: packs per day x years of smoking

Risk stratification and population enrichment[9,10]

With the current screening guidelines, additional risk factors are largely excluded. This led to the development of a population-enrichment, or risk-stratification, algorithm.

The intent is to enrich the eligible population defined by the current guidelines in a way that will make screening more efficient.

Normally, a screening program would run on all eligible individuals (Figure 1). By instead applying population-enrichment algorithm, a high-incidence selection of individuals is obtained and screening can be immediately focused (Figure 2).

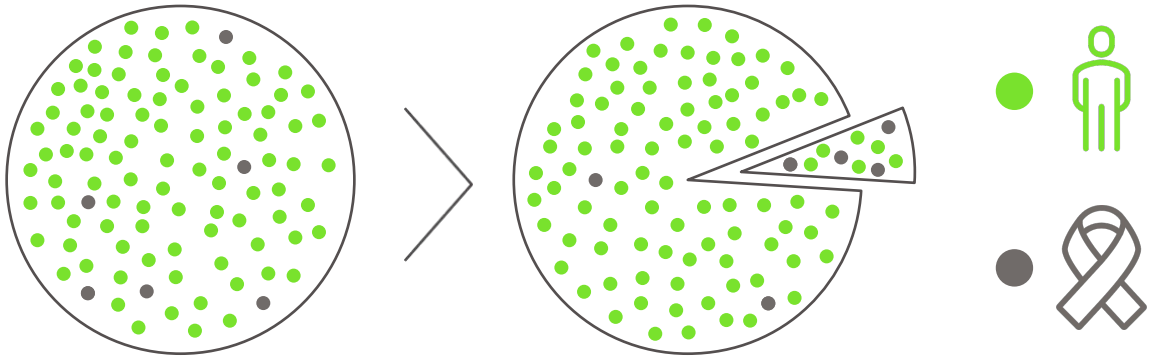


Figure 1 **Figure 2**

In a real-world study, LungFlag identified a high-risk population that was more likely to complete screening than those under standard care†. This targeted approach achieved 3x higher screening adherence‡ and a 4.8% cancer detection rate†‡, showing that LungFlag can identify the right patients for clinical intervention.

LungFlag software tool[11]

LungFlag is a computational software intended to aggregate, analyze, and organize health-related information from adults' electronic health records at a population level to identify individuals who may be at higher risk of developing certain respiratory illnesses, such as for example lung cancer.

LungFlag is intended to be used by healthcare systems and their affiliates within their IT environments to support population-level review and monitoring of respiratory-health-related information in their patient population.

LungFlag analyzes information documented in electronic health records or collected by health care professionals, including demographics, lifestyle factors (e.g., smoking status), weight, body mass index (BMI), spirometry results, blood test results (including white blood cells and platelets), and documented information related to respiratory health.

LungFlag provides informational outputs only and does not provide diagnoses, screening determinations, risk scores or probabilities, clinical interpretations, patient-specific alerts, or recommendations. All clinical decisions and actions remain entirely at the discretion and independent judgment of health care professionals.

†: WCLC 2025, ‡: Data on File 2026

LungFlag value proposition[9,10,12-18]

LungFlag is a machine learning based risk stratification algorithm to identify patients with higher relative risk of Lung Cancer and help HCPs increase screening effectiveness[9,10,12] and reduce costs.[16,17]

Improves LCS programs

By enriching the eligible population, **LungFlag helps make lung cancer screening initiatives more efficient.** Additionally, LungFlag may help encourage at-risk patients to get screened

Performance

LungFlag outperforms emrPLCOm2012,* the most studied prescreening algorithm LungFlag also shows meaningful improvement over traditional screening programs in flagging early stages of disease

Flexible cutoff

LungFlag offers providers the possibility to adjust the cutoff based on the capacity of the system to screen patients

Personalized results

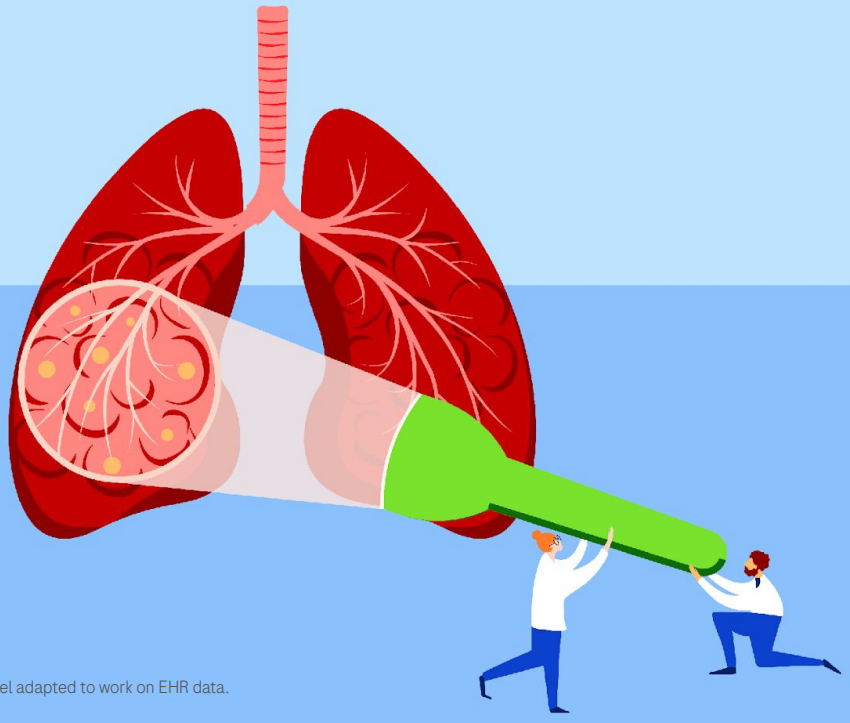
LungFlag provides **personalized risk** results that, when communicated to patients, may increase compliance with follow-up procedures

Limited set of parameters

With age, sex, smoking history, and white blood cell count, LungFlag requires a **limited set of parameters** to provide a personalized result

LungFlag demonstrated comparable performance with respect to sex and race in a large, community-based retrospective dataset.[9,18]

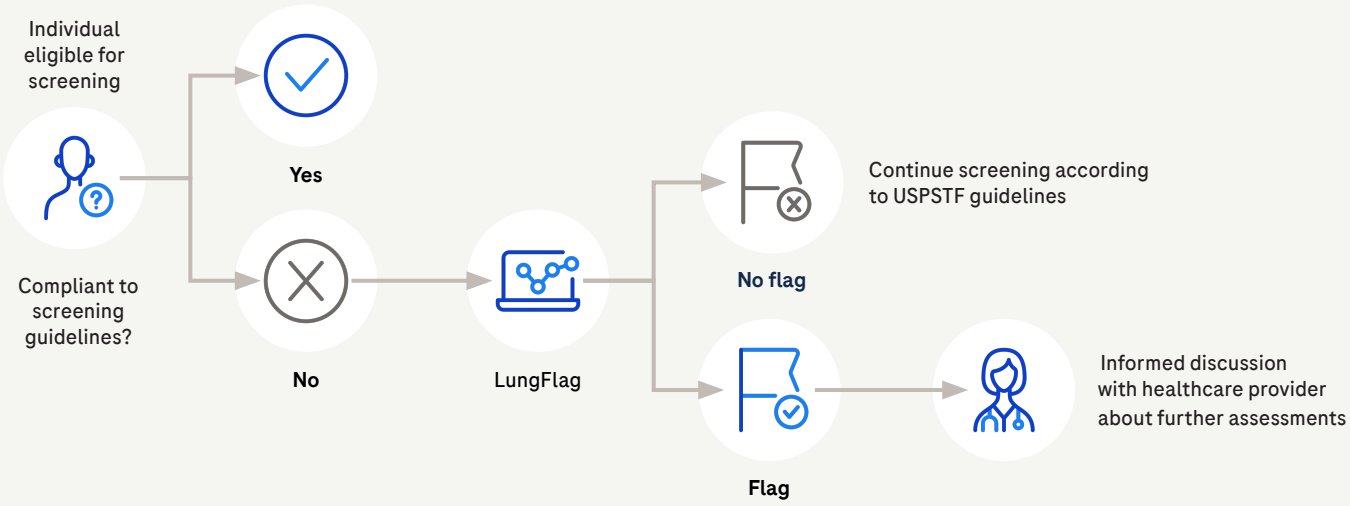
Using LungFlag to identify candidates for lung cancer screening was estimated to save **US$2.8 million over 5 years** from a US commercial health plan perspective, largely attributable to reduced costs of treating advanced NSCLC.[16]



*emrPLCOm2012: PLCOm2012 logistic regression model adapted to work on EHR data.

LungFlag workflow example[19,20]

For individuals eligible for and not compliant with recommended lung cancer screening, LungFlag can provide a signal that may encourage additional discussions with a healthcare provider about further medical assessments. LungFlag implementation can be tailored to the current existing screening program at any healthcare institution.



Example of LungFlag implementation in a screening program[21]

This simulation compares 2 strategies for selection of patients using US data, with scores run on patient data on a monthly basis for 2 years. The simulation estimates the impact of LungFlag in a hypothetical screening population using assumptions derived from real-world data.

In a normal screening program, of a general community population of 1,000,000 individuals, 45,000 were eligible to be screened and would need to undergo an LDCT. This way all the 1874 cases would be found with an NNS=24 (i.e. 45000/1874).

If we consider LungFlag, with a cutoff of roughly 3.3% it would determine 1500 LDCTs to be performed. In this cohort, based on LungFlag's performance, 100 cases would be found, with an NNS=15 (i.e. 1500/100).

To have similar terms of comparison, the very same 1500 LDCTs performed in the traditional screening program would detect 15 cases, with an NNS=100 (i.e. 1500/15).

Additionally, LungFlag shows good performance in early stages (0-II), giving patients a chance for treatment in a curative setting.[9,19,22]

Simulation comparing 2 strategies for selection of patients using US data, with scores run on patient data monthly for 2 years

based on epidemiological data

- 1,000,000 Individuals
- 45,000 eligible for screening according to USPSTF guidelines
- 1,500 LDCT scans in 2Y

	LungFlag	Random selection
Number needed to screen to find 1 case	**15**	**100**
Total cases	100	15
Stages 0-II, no. (%)	47 (47%)	5 (31%)
Stages III-IV, no. (%)	53 (53%)	10 (69%)

LDCT, low dose computed tomography; NNS, number needed to screen.

Key takeaways[9,10,12,13,18]

LungFlag is a computational software intended to aggregate, organize and analyze health-related information from adults' electronic health records at a population level to identify individuals at higher risk of developing certain respiratory illnesses, such as lung cancer.

- It uses easily accessible data
- Based on retrospective, real-world databases, LungFlag may help flag patients for screening 3-12 months before diagnosis
- LungFlag is HIPAA compliant
- LungFlag can help detect more patients at earlier stages[9]
- LungFlag can be implemented in EHR to automatically flag cases with existing data
- Developed and validated using control samples from over 5,000,000 individuals and more than 300,000 lung cancer cases in independent datasets

AI, artificial intelligence; HIPAA, Health Insurance Portability and Accountability Act; ML, machine learning.

Important Publications

1. **Machine Learning for Early Lung Cancer Identification Using Routine Clinical and Laboratory Data** by Michael K. Gould, Brian Z. Huang, Martin C. Tammemagi, Yaron Kinar, and Ron Shiff
2. **Flagging High-Risk Individuals With a ML Model Improves NSCLC Early Detection in a USPSTF-Eligible Population** by Eran N. Choman, Alon Lanyado, and Michael K. Gould
3. **Computer-Assisted Flagging of Never Smokers at High Risk of NSCLC in a Large US-Based HOM Using the LungFlag Model** by Eran N. Choman and Alon Lanyado
4. **LungFlag, a Machine-Learning (ML) Personalized Tool for Assessing Pulmonary Complications in a Community Setting Demonstrates Comparable Performance in Flagging NSCLC Regardless of Sex or Race** by David Morgenstern and Eran N. Choman
5. **Improved Efficiency with LungFlag vs. Opportunistic Selection in a Theoretical East Asian Lung Cancer Screening Program** by Eran N. Choman, Michael K. Gould, Pan-Chyr Yang, and David Morgenstern
6. **Maximizing Lung Cancer Screening in High-Risk Population Leveraging ML-Developed Risk-Prediction Algorithms: Danish Retrospective Validation of LungFlag** by Margarethe B. Henriksen et al.
7. **Budget Impact of the LungFlag™ Predictive Risk Model for Lung Cancer Screening** by Carolina Heuser, Michael K. Gould, Eran Choman, Nicolò Olghi, Sarika Ogale & Milan Obradovic

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14. Laisaar T, et al. 1561P Targeted screening methodologies to select high risk individuals: LungFlag performance in Estonia Lung Cancer Screening PilotAnn Oncol. 2024;35(2):S947-S948. LINK;
15. Atkar-Khattra S, et al. P1.04.36 LungFlagTM Risk Prediction Validation on Canadian Ever Smokers Pre-Classified as High Risk for Lung Cancer. J Thorac Oncol. 2025;20(10):S122-S123. LINK;
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