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EDITORIAL

The Future of Lung Cancer Screening

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The goal of cancer screening is to reduce the number of cancer deaths by identifying cancer early in its' course, before it has led to symptoms. For any cancer screening to be successful, the cancer must be potentially fatal and more likely to be cured when identified in a presymptomatic phase. The screening test must be able to identify the cancer when it is presymptomatic. Ideally, the test would lead to minimal downstream testing for benign findings, be affordable and available. A successful cancer screening program results in more benefit than harm on a population level. Lung cancer screening with a low radiation dose chest CT (LDCT) leads to fewer lung cancer deaths in an at-risk population, with harms that are felt to be outweighed by the mortality reduction. (1,2)

The implementation of research findings into standard practice frequently leads to the identification of care gaps. We also learn about deficiencies in what is considered standard of care. The future of lung cancer screening requires a thoughtful approach to applying measures that address these gaps and deficiencies.

Care gaps in the implementation of current standard of care

Implementation of current standard of care requires systems that enable most members of the screening target population to receive the LDCT, timely and accurate interpretation of the LDCT, efficient management of the LDCT findings, and adherence with test follow-up and annual screening. Gaps in care can occur at each of these steps. Structed approaches to the implementation of lung cancer screening result in better outcomes. The implementation of a structured approach to screening requires time and resources.

Many care gaps have been identified in the United States, where program structures vary considerably. In other countries, the desire to develop national or provincial structured screening programs has resulted in a slower roll-out of LDCT screening. Both scenarios have provided lessons to guide improvement. Possible future enhancements are described here.

Systems that enable screening uptake: Uptake of screening in the current target population has been slow in the US. (3) Uptake may be augmented by data management systems, capable of identifying individuals in the screening target population, and resources to help with patient communication and scheduling. These may function inside of, or parallel to, the electronic health record. Patient navigators may be assisted by AI agents capable of supporting communication and scheduling. Molecular biomarkers may encourage screening uptake in the target population. (4)

Timely and accurate interpretation the LDCT: Growth in the uptake of lung cancer screening may stress the capacity of available expert readers. Support for the radiology team may come from advances in the ability of AI tools to accurately identify abnormal imaging findings, making the reading and reporting of LDCT scans more efficient. (5)

Efficient management of LDCT findings: Optimal management of screen detected lung nodules has a major impact on the benefit to harm balance of LDCT screening. Lung nodule risk prediction may be augmented by AI imaging algorithms or blood molecular biomarkers. (6,7) Improvement in the accuracy of non-surgical biopsy tools could further decrease the percentage of surgical resections for benign disease. (8) Understanding the value of addressing non-lung nodule abnormal imaging findings could further improve outcomes.

Adherence with test follow-up and annual screening: Timely evaluation of screen detected lung nodules leads to lung cancer treatment at the earliest stage. (9) Navigation and communication tools, as discussed with screening uptake, may improve adherence with test follow-up and annual screening.

Opportunities to evolve the current standard of care

There are limitations to our current standard of care. Definitions of the screening target population, whether based on age and smoking history or on risk or benefit models,

lead to some people who develop lung cancer being excluded from LDCT screening. For a future lung cancer screening program to have as large a net benefit at the population level as possible, we must develop solutions that maximize the benefit and/or minimize the harm from lung cancer screening.

Maximize the benefit: Some individuals outside of the screening target population have a high enough risk of developing a potentially fatal lung cancer to have a net benefit from screening. These individuals may be identified with improvements in clinical risk prediction models (10), advances in our understanding of germline and genetic risks (11), multi-modal models that include diagnostic imaging features (12), or blood/breath/sputum molecular biomarkers. These tools may allow us to more accurately filter the population into those who will and those who will not develop a potentially fatal lung cancer, refining the screening target population to maximize the benefit at a population level.

Minimize the harm: The potential harm of lung cancer screening comes from the management of screen detected findings (mostly lung nodules) and the performance of the screening test. This harm can be minimized by removing those who are highly unlikely to benefit from lung cancer screening from the target population, by improving our management of lung nodules, by improving our understanding of which malignant lung nodule has the potential to be fatal, and by minimizing the cumulative radiation exposure from our imaging tests. Lung cancer prediction tools, as outlined above, may play a role in minimizing harm. Imaging AI tools and molecular biomarkers may augment our management of lung nodules, (6,7) decreasing avoidable invasive testing. Ultra-low radiation dose imaging techniques could further improve the safety of CT imaging.

The future of lung cancer screening

By addressing gaps with the implementation of current standard of care and by evolving standard of care to maximize the benefit and minimize the harm of lung cancer screening, we can envision a time when lung cancer screening is widely available on a global scale, the screening target population is enriched with individuals who develop potentially fatal lung cancer, members of the screening target population are up to date with screening, nearly all lung cancers are screen detected, and very few people are harmed from avoidable-testing or avoidable-treatment. This future requires a commitment to provide the resources necessary to develop structured screening programs and assess the utility of the tools capable of supporting all aspects of lung cancer screening.

It is interesting to consider whether we will always need lung cancer screening. If we can reduce exposure to lung cancer risk factors (eliminate cigarette smoking, reduce biomass fuel use, improve air quality), develop prevention strategies (supplements,

vaccination), or improve treatment to the point where all lung cancers are curable, lung cancer screening may not be necessary. Until that distant day, lung cancer screening will remain the best way to avert lung cancer deaths.

Ethics in publishing

1. Does your research involve experimentation on animals?:

No

2. Does your study include human subjects?:

No

3. Does your study include a clinical trial?:

No

4. Are all data shown in the figures and tables also shown in the text of the Results section and discussed in the Conclusions?:

Yes

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Implementation of standard of care and evolution of standard of care						
Target population	**Uptake**	**LDCT performance**	**LDCT interpretation**	**Nodule evaluation**	**Non-nodule findings**	**Adherence**
Clinical risk prediction	Data management	Ultra-low dose imaging	AI detection	Molecular biomarkers	Understanding of net benefit	Data management
Germline genetic	Communication tools		AI reporting	Imaging biomarkers		Communication tools
Molecular biomarkers	Scheduling tools			Non-surgical biopsy tools		Scheduling tools
Imaging biomarkers	Molecular biomarkers					Molecular biomarkers

Table: Tools and advances that may impact the future of lung cancer screening