

Are We Underestimating Efficacy and Cost-Efficacy of Population Lung Cancer Computed Tomography Screening?



Frederic W. Grannis Jr., MD

Department of Surgery, City of Hope National Medical Center, Duarte, California

In a perfect world, governments would allocate sufficient funds to provide optimal care for every patient with cancer. Sadly, this is not now the case. Legislators worldwide are parsimonious in funding for medical care, concerned that their constituents are loathe to pay more taxes. Accordingly, it is important for medical researchers to provide accurate information on cost and cost-effectiveness of new medical interventions, so that politicians and public health officials have accurate information to guide just and efficient allocation of funding to optimize medical care.

Unfortunately, cost-effectiveness research has intrinsic problems. The methodology required to conduct such research is complex. Clinicians are well suited to provide input data on effectiveness of treatments, that is, duration of survival and quality of life, but are not typically skilled in evidence collection, economics, mathematical modeling, and biostatistics. Close collaboration between clinicians and methodologists is accordingly essential, if accurate information is to be published.

Major variance in cost-effectiveness data has important public health implications. Facing a decision on what to spend, from a tight budget, legislators might be more generous if data inform that many more lives could be saved at substantially lower cost.

The authors of “Expected Cost Savings From Low-Dose Computed Tomography Scan Screening for Lung Cancer in Alberta, Canada” have done a workman-like job of analyzing input data provided by clinicians and methodologists and have gotten the correct answer—computed tomography (CT) lung cancer screening is cost-effective.¹ So far, so good, but although the authors recommend CT screening for lung cancer as cost-effective, their estimate of the amount of the public health dollars saved in treating screen-detected, early stage lung cancer is probably far too small.

Input data they use in their calculations do not reflect current clinical practice. It is important for readers to

understand that effectiveness data often vary widely between studies. In the very specific case of lung cancer screening, there has been contentious disputation of risks, benefits, and costs for more than 20 years. For example, Bach and Gould² estimated that only one in five (21%) diagnosed by CT screening would achieve long-term survival. The corresponding figure in IELCAP research is greater than four in five (80%).³ In a 2015 update, long-term survival was substantially higher in IELCAP compared with National Lung Screening Trial (NLST) study subjects.⁴ The range of published results for the cost of a quality-adjusted life-year varies nearly a thousand-fold, between \$2500 (Wisnivesky)⁵ and \$2 million (Bach)!

What then is a cost-effectiveness researcher to do? What effectiveness data does he accept as valid to enter into his model? This question has plagued all past efforts at measuring cost-effectiveness of CT lung cancer screening.

If a researcher chooses input effectiveness data derived from the IELCAP study, the cost of a quality-adjusted life-year derived from CT screening will be substantially lower than cost output from a researcher who selects NLST data. In this study, the investigators specifically incorporate NLST entry criteria and limit analysis to only three annual screens. This design will

Disclosure: Dr. Grannis declares no conflict of interest.

Address for correspondence: Frederic W. Grannis, Jr., MD, City of Hope National Medical Center, 1500 East Duarte Road, Duarte, 90803 California. E-mail: fgrannis@coh.or

Cite this article as: Grannis FW, Jr. Are we underestimating efficacy and cost-efficacy of population lung cancer computed tomography screening? *JTO Clin Res Rep.* 2022;3:100383.

© 2022 The Author. Published by Elsevier Inc. on behalf of the International Association for the Study of Lung Cancer. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

ISSN: 2666-3643

<https://doi.org/10.1016/j.jtocrr.2022.100383>

predictably yield poorer cost-effectiveness in comparison to an IELCAP design that prescribes annual CT screening in a longer duration.

In NLST, as many as 2000 individuals died of lung cancer after CT screening had ceased, that is, after only three rounds of screening.⁶ As we have argued elsewhere, data extrapolated from NLST grossly underestimate long-term survival and overestimate putative harms of lung cancer screening, including downstream costs associated with false-positive test results, overdiagnosis, unnecessary biopsies, and surgical operations.⁷ Because NLST did not incorporate a diagnostic or treatment algorithm, it had higher false-positives and higher rates of unnecessary biopsy and surgical operation for benign nodules.

The Alberta investigators have correctly rejected the inaccurate (21%) estimate of long-term survival benefit from NLST, instead estimating that more than 70% will be diagnosed in stage 1 with high-commensurate long-term survival.

How Might Researchers Surmount the Problem of Selection of Input Data Into Cost-Effectiveness Models?

A number of years ago, I had the great privilege of working with a brilliant young premedical student, who designed a modeling spreadsheet that calculated 1500 different sets of cost-effectiveness output measures, on the basis of input of three sets of, respectively, high, median, and low estimates derived from review of multiple publications on lung cancer screening.^{8,9} Anthony Castleberry's method allows individual readers to reference cost-effectiveness using input data they deem appropriate and provides compelling data that—even using pessimistic assumptions—lung cancer screening outperforms treatment of symptomatic lung cancer, by a wide margin and has potential to prevent tens of thousands of lung cancer deaths and billions in health care expenditures. If our study were updated today, factoring in the far higher current costs of immunotherapy and other systemic therapies, relative cost-effectiveness of CT screening should prove substantially greater.

One last consideration: unrealistic expectations and magical thinking about discovering a “Holy Grail” in molecular cancer screening may be contributing to delay in acceptance and implementation of—highly effective and relatively inexpensive—CT screening, in many nations. Costs of molecular cancer tests vary widely. Food and Drug Administration–approved FoundationOne CDx is priced at \$5800.¹⁰ Guardant Health 360 is approximately a thousand dollars more expensive. Grail's Galleri test, sold under a “Clia waiver,” is considerably less

expensive, at \$949.¹¹ Prescreening millions of individuals at elevated risk, at any comparable cost, is clearly impossible.

It is imperative that we save lives (and dollars) by implementation of population CT screening—now.

CRedit Authorship Contribution Statement

Frederic W. Grannis, Jr. MD: It is the sole author.

References

1. Thanh NX, Pham TM, Wayne A, et al. Expected cost savings from low-dose computed tomography scan screening for lung cancer in Alberta, Canada. *JTO Clin Res Rep*. 2022;3:100350.
2. Bach PB, Gould MK. When the average applies to no one: personalized decision making about potential benefits of lung cancer screening. *Ann Intern Med*. 2012;157:571-573.
3. Henschke CI, Yankelevitz DF, Libby DM, Pasmantier MW, Smith JP, Miettinen OS. International Early Lung Cancer Early Action Program Investigators. Survival of patients with stage I lung cancer detected on CT screening. *N Engl J Med*. 2006;355:1763-1771.
4. Yip R, Henschke CI, Yankelevitz DF, Boffetta P, Smith JP. International Early Lung Cancer Investigators. The impact of the regimen of screening on lung cancer cure: a comparison of I-ELCAP and NLST. *Eur J Cancer Prev*. 2015;24:201-208.
5. Wisnivesky JP, Mushlin AI, Sicherman N, Henschke C. The cost-effectiveness of low-dose CT screening for lung cancer: preliminary results of baseline screening. *Chest*. 2003;124:614-621.
6. National Lung Screening Trial Research Team. Lung cancer incidence and mortality with extended follow-up in the National Lung Screening Trial. *J Thorac Oncol*. 2019;14:1732-1742.
7. Sands J, Tammemägi MC, Couraud S, et al. Lung screening benefits and challenges: a review of the data and outline for implementation. *J Thorac Oncol*. 2021;16:37-53.
8. Castleberry AW, Smith D, Anderson C, Rotter AJ, Grannis FW Jr. Cost of a 5-year lung cancer survivor: symptomatic tumour identification vs proactive computed tomography screening. *Br J Cancer*. 2009;101:882-896.
9. Castleberry AW, Grannis FW Jr. What is a reasonable cost to refute a preposterous hypothesis? *Br J Cancer*. 2010;102:627-628.
10. Philippidis A. Breaking NGS ground. *Gen: Genetic Engineering and Biotechnology News*. May 22, 2018. <https://www.genengnews.com/insights/breaking-ngs-ground/>. Accessed September 22, 2021.
11. Cairnes E. Grail launches pan-cancer screen—for those who can pay out of pocket. *Evaluate Vantage*; June 4, 2021. <https://www.evaluate.com/vantage/articles/news/snippets/grail-launches-pan-cancer-screen-those-who-can-pay-out-pocket>. Accessed September 30, 2021.