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Cite this as: *BMJ* 2022;376:o666
http://dx.doi.org/10.1136/bmj.o666
Published: 30 March 2022

Screening high risk populations for lung cancer

Early evidence of a stage shift suggests real world benefits

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Randomized trials show that screening of high risk populations for lung cancer with annual low dose computed tomography reduces lung cancer and all cause mortality through the earlier detection of non-small cell lung cancer (NSCLC).[1,2] Lung cancer remains the world's leading cause of death due to cancer, largely because most cases are diagnosed at an advanced and incurable stage. The goal of screening populations at high risk is to detect cancers at earlier, curable stages, ultimately preventing deaths from lung cancer.

Despite substantial evidence for benefits in idealized trial settings and near universal guideline recommendations supporting screening in high risk populations,[3] early evidence from the US suggests poor implementation of screening along the care continuum. This includes low uptake among eligible adults (approximately 5-15%)[4,5] and poor adherence to follow-up rounds of screening at less than 50% compared with 90% in trial settings.[6,7] Whether a substantial mortality benefit from screening can be achieved in real world settings without vastly improved implementation has remained uncertain.

In this context, the linked study by Potter and colleagues (doi:10.1136/bmj-2021-069008) provides key evidence supporting the beneficial effect for lung cancer screening in people at high risk in the US despite the poor state of implementation.[8] Using a quasi-experimental observational design, Potter and colleagues analyzed data from two large comprehensive US cancer registries—the National Cancer Database and the Surveillance Epidemiology End Results (SEER) program database. They identified a sample of patients diagnosed as having NSCLC between 2010 and 2018 who would have been eligible for screening by age criteria (age 55-79 years) and a comparator cohort, also with NSCLC, who would have been ineligible for screening (age 45-55),[9] together totaling 763 474 participants. Screening was first endorsed by guidelines in December 2013. The authors compared the rate of change in the percentage of patients with stage I cancer at diagnosis between 2010 and 2018. They used joinpoint modeling to identify an inflection point that would indicate a stage shift after the guidelines were published in the group eligible for screening.

Among the screen eligible cohort, the percentage of patients with stage I disease at diagnosis increased by 3.9% each year from 2014, following a minimal change from 2010 to 2013. No such finding was seen in the younger cohort. Several sensitivity analyses were done, including comparing findings between high and low screening states; rate of increase in stage I diagnoses was more rapid in high screening states. Results were consistent across multiple analyses.

Although the stage shift is compelling, Potter and colleagues also report an 11.9% increase (from 19.7 to 28.2 months) in median all cause survival in the screen eligible cohort between 2014 and 2018, compared with no change between 2010 and 2013. This mortality benefit, however, likely reflects advances in cancer treatment coinciding with the introduction of screening: advances such as widespread use of mutational testing and targeted inhibitors (beginning in 2012) and immunotherapy (beginning in 2015).[10] Given the slow natural history of NSCLC, we would not expect the observed stage shift to result in such early mortality benefits.

These results suggest that even poorly implemented screening can result in a stage shift that will almost certainly lead to downstream decreases in lung cancer mortality over the longer term. The benefits of screening will likely increase with improved awareness, education, and implementation.

Unfortunately, Potter and colleagues also found further evidence of long standing and pervasive disparities in lung cancer outcomes.[11] In 2010, the predominant stage at diagnosis in all ethnicities was stage IV. By 2018, non-Hispanic white patients were more likely to have stage I than stage IV at diagnosis (36.9% *v* 36.2%), and stage I predominated among patients with NSCLC living in areas with the highest median income and education. This is an impressive stage shift, but the benefits did not extend to patients living in economically deprived areas or to racial or ethnic minority groups. As currently implemented, screening will only exaggerate healthcare disparities still further, which is contrary to the goals of any population health intervention. This fresh evidence should be a call to arms for all stakeholders, to ensure more equitable screening and outcomes.

Equitable access to screening that reduces health disparities requires targeted multilevel intervention. Interventions must move beyond policies and guidelines aimed at payers, health systems, and clinicians to involve patients, families, communities, and the wider public.[12,13] Researchers and policy makers must analyze not just how many people are being screened but also the "mismatch" between who is screened and who bears the greatest burden of disease related to lung cancer. Through such targeted interventions, screening can realize its full potential for everyone at high risk for lung cancer.

Competing interests: The BMJ has judged that there are no disqualifying financial ties to commercial companies. The authors declare the following other interests: ACM has grant funding from the Department of Veterans Affairs and has reviewed grants for the LUNGevity non-profit organization; MT has grants from the LUNGevity Foundation, American Lung Association, and National Cancer Institute

and has received fees for medicolegal consulting from Quane McColl, PLLC. Further details of The BMJ policy on financial interests is here: https://www.bmj.com/sites/default/files/attachments/resources/2016/03/16-current-bmj-education-coi-form.pdf.

Provenance and peer review: Commissioned; not peer reviewed.

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