Editorial

The impact of patients' preferences on the decision of low-dose computed tomography lung cancer screening

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Lung cancer is the 2nd most common cancer diagnosis by gender, behind prostate cancer for men and breast cancer for women in the US. At present, the general prognosis of lung cancer is poor, as close to 50–70% of lung cancers are diagnosed in advanced stages without screening (1,2). The National Lung Screening Trial (NLST) demonstrated that annual lung screening of high-risk population (smokers and ex-smokers) with low-dose computed tomography (LDCT) results in a 20% reduction in lung cancer-related mortality rate (3,4). In 2014, the U.S. Preventive Services Task Force (USPSTF) issued a grade B recommendation for LDCT lung cancer screening for individuals at high risk meeting eligibility criteria for the NLST. However, there is still some controversy regarding high false positive rate of LDCT, unnecessary further diagnostic testing and invasive procedure, patient anxiety and overdiagnosis (5). Shared decision making (SDM) for lung cancer screening is recommended for promoting patient-centered clinician communication due to the uncertainty regarding the risks and benefits of screening (6,7).

However, if we are unable to tailor personal risks and preference, we can only tell the patient whether they have met the criteria for inclusion based on evidence-based medicine or not. Often it is difficult for patients to make the most appropriate decision when there is no strong evidence for or against the screening, and patients usually prefer taking actions that physicians recommend. Therefore, it is important to figure out how clinicians can determine whether screening is highly preference-sensitive or not within limited time of the clinical visit.

In July 2018, the *Annals of Internal Medicine* published a microsimulation study to investigate the net benefits of LDCT lung cancer screening based on patient preference, life expectancy and lung cancer risk stratification (8). The authors' contention is that a personalized clinical decision making regarding the benefits and harms in LDCT lung cancer. Screening should be made based on patient preference and lung cancer risk. The model was developed based on the database of NLST, PLCO (The Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial) and SEER (the Surveillance, Epidemiology and End Results) to investigate the clinical outcome and health states from two cohorts (LDCT versus no screening) (9,10).

The rationale of this interesting study is to determine best candidate and preference-sensitive candidate for lung cancer screening in NLST cohort.

A microsimulation model study revealed that the benefits and harms of LDCT screening for lung cancer varied substantially across the eligible population, with three factors being particularly influential: lung cancer risk-prediction, life expectancy, and patient preferences. In this article, the authors suggest that the widely used rules of thumb developed for selecting the best candidates and preference-sensitive candidates for lung cancer

screening meet USPSTF eligible criteria. For selecting the best candidate, screening is likely to be high-benefit if the patient's annual lung cancer risk is greater than approximately 0.3% and less than approximately 1.3%. In addition, this study revealed that those with higher risk and longer life expectancy also had a robust net benefit even in clinical scenarios where false-positive rates were very high (i.e., a 60% rate of false-positive findings) in the calibration model. For selecting candidate which is likely to be highly preference-sensitive, those who have the following three conditions need to consider. (I) The patient's annual lung cancer risk is less than approximately 0.3%. (II) The patient's annual lung cancer risk is greater than approximately 1.3% (due to severe comorbidity and limited life expectancy in this group). (III) The patient has a limited life expectancy of <10.5 y. This report provides the evidence from a microsimulation model that is consistent with the notion that a more-detailed assessment of individual lung cancer risk with patient preference may be more effective than focusing only using NLST criteria. This study result demonstrate more detail individual-risk based detail shared decision plan for individualizing the benefit harm trade off depending on the patient's risk (11). The authors also develop a new online education tool designed to facilitate tailored SDM by helping patients and their physicians choose personal trade-offs between risks and benefits consciously in the implementation of personalized medicine in the clinical setting (https://shouldiscreen.com/English/lung-cancer-risk-calculator). The micro-simulation study raised a lot of questions regarding patient selection. Screening is in fact a complex process, which requires careful consideration of the balance of the benefits and harms. The adoption of the USPSTF recommendations are based on current best evidence, but may result in nearly half of the low-risk cases being unable to gain benefit or having more disadvantages in screening. Adopting the author's the rule of thumb to help detailed SDM based on individual lung cancer risk and personal preference can allow the screened person to benefit from the benefits of screening.

This is an important study to show that for those with shorter life expectancy and at lower risk, preference plays an important role in whether to receive screening or not. However, one shoe doesn't fit all, and there are several limitations in this microsimulation study since the assumptions might not hold, especially for Asian population. The generalizability of the results to Asian population may be questionable. First, the risk models Dr. Caverly *et al.* used to predict patient-specific annual incidence of lung cancer may lose predictive accuracy in Asian population. Second, the assignment of histology of incident lung cancer cases was based on the PLCO (Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial), but the pattern of histology of incident lung cancer cases among the Americans is different from that among the Asians. Third, the cancer survival was based on SEER lung cancer data, which is again U.S. based, and is different from the lung cancer survival in Asia. Forth, the life expectancy in the U.S. is very different from the life expectancy in other countries. Fifth, patients' preference may be affected by the potential out-of-pocket costs of treatment, which varies from country to country. Thus, given what this microsimulation showed, we know that both life expectancy, risk of lung cancer, and patients' preference are all important, but implementation of these cutoffs in clinical practice, especially in Asian countries, should be warranted.

However, most of the current research is aimed at the design of screening for heavy smoking high-risk populations. However, in recent years we have known that the proportion of patients non-smoking lung cancer among lung cancer patients is greatly increased, especially in Asia (12,13). Currently, there are no criteria or risk-prediction model to select high-risk individuals for lung cancer in never smokers. Some studies have shown that the risk of non-smoking lung cancer correlated with family history of lung cancer, female sex and environment exposure, which was not taken into consideration in this paper (14,15). It is also well recognized that heritable risks and genetic contributions are highly associated with risk of lung cancer among patients with non–smoking-related lung cancers (16-18). However, the cost-effectiveness analysis of lung cancer screening among non-smoking populations participating in lung cancer screening is still inconclusive due to controversy about the pros and cons of lung cancer screening in this population. In the future, a large-scale study was conducted to predict lung cancer risk with integration of genomic (liquid biopsies with ctDNA Detection) and clinical features (clinical profile and LDCT characteristics of the pulmonary suspicious nodules) in never-smoker may be needed (19-22).

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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