Response to comment by Hopkins et al:

Lung cancer susceptibility, ethnicity and the benefits of CT screening

Following our editorial:

Fulfilling the Dream: Toward Reducing Inequalities in Lung Cancer Screening. Am J Respir Crit Care Med 2015; 192: 125-127 PubMed .

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Response to comment: Lung cancer susceptibility and mortality benefit in lung cancer screening (434 words)

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We thank Hopkins and colleagues for their interest in our editorial(1). We acknowledge the important studies cited which suggest that African-Americans have an increased susceptibility to cigarette smoke and are therefore at higher risk of developing COPD and lung cancer than matched Caucasian individuals (even after considering the impact of other related factors) (*Hopkins et al, this issue*).

We would however like to highlight the difference between lung cancer detection rate and reduction in mortality. While both are related to lung cancer risk and incidence, the latter also addresses factors affecting competing mortality. The paper by Tanner and colleagues that we referred to, reported a more pronounced mortality benefit with LDCT screening compared with chest x-ray in Black compared with non-Black NLST participants(2). This suggests an observed effect of LDCT screening in Black participants over and above that explained by the increase in risk and incidence alone in this ethnic group.

As well as ethnicity, other factors appear to influence lung cancer susceptibility. Gender is another important demographic that influences lung cancer risk and certainly it has been suggested that the cost effectiveness of lung cancer screening is far higher in women compared with men (ICER $46,000 vs. $147,000 (3)). Furthermore, as well as COPD, other comorbidities also increase susceptibility to lung cancer through varying mechanisms. Certainly, HIV and idiopathic pulmonary fibrosis have also been associated with a higher risk of lung cancer even after accounting for smoking history(4, 5).

Another interesting observation is that interval cancers in the NELSON study were associated with increased age, though not smoking status(6). Apart from this study, very little is known about the relative importance of other factors influencing interval cancer incidence with LDCT screening and whether such occurrences may be predicted by evaluating risk in screened individuals. If this were so, screening intervals could be tailored individually by risk.

The relationship between individual lung cancer risk, lung cancer detection, survival benefit of the screened population and cost-effectiveness of lung cancer screening is complex. The current USPSTF criteria(7) for screening eligibility are reasonable at this time, but are likely to be adapted in the future, given the growing evidence base that will in due course inform the medical communities on how best to optimise the harms and benefits of lung cancer screening in individuals with varying risk profiles. Screening may be appropriate at alternative age and risk thresholds, or at more or less frequent

intervals in certain groups. Lung cancer risk and detection rate both need to be balanced with competing mortality in order maintain or exceed the sensitivity and mortality benefit with screening seen in NLST.

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