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Response to comment on: "Low-dose computed tomography screening for lung cancer in people with workplace exposure to asbestos"

We thank Professor Harris et al. [1] and Professor Barbone et al. [2] for their comments to our paper on low-dose computed tomography screening for lung cancer in people with workplace exposure to asbestos.

Our case-control study [3] derives from a lung cancer screening study in which participants were selected for their strong smoking history. Exposure to asbestos was not a selection criteria and, although it was confirmed by interview in the 216 identified exposed subjects, the level of exposure was probably low, as indicated by the low prevalence of pleural plaques (10.2%). In contrast, 61.1% of participants in the ARP study [1], including 34% non-smokers, have pleural plaques. Harris et al. point out that the detection rate of lung cancer was similar in the two studies (around 0.5 per 100 person-years), suggesting that higher cumulative asbestos exposure in the ARP study might have offset higher smoking exposure in the COSMOS study, providing support to occupational LDCT screening in non-smokers exposed to asbestos. We would like to highlight that the number of subjects in our case control study was very small and that the detection rate, based on a single cancer case, was lower than that reported in the whole COSMOS population (1.1%) [4].

We did not include data from the study by Barbone et al. [2] as they were published after the ending date (April 1st 2018) of our literature search.

We agree that the low numbers of non-smokers exposed to asbestos who received LDCT screening and that have been reported in the literature do not allow drawing firm conclusions about the efficacy of lung cancer screening in this group. However, we reported data from the nine available published reports including a total of 1891 non-smokers and only 6 of them were diagnosed with lung cancer through LDCT screening [3]. The pooled detection rate was only 0.1% with an upper 95% limit of 0.4%, although it was slightly higher in two of the reports: 0.6% in an early report of the ARP study (2 lung cancers diagnosed among 325 screened individuals) [5] and 0.7% in a Japanese study (3 lung cancers diagnosed among 452 screened individuals) [6]. Harris et al. now report 4 lung cancer cases diagnosed among 596 screened corresponding to a detection rate around 0.5 per 100 person-years [1].

Of interest, a recent report published after the preparation of our review suggest that LDCT screening may be an effective strategy to reduce lung cancer mortality in never-smokers in Asia [7]. This is in contrast with the current recommendation in the United States that are based on microsimulation modeling and indicate that never-smokers should not be screened [8–10].

We acknowledge that cost-effectiveness may not be an acceptable criteria to decide whether occupational lung cancer screening is viable in workers exposed to asbestos. On the other hand, we lack robust information on false positive findings of LDCT screening in subjects at low risk of cancer, which may counterbalance the low efficacy of LDCT screening, especially among asbestos-exposed population with high prevalence on non-malignant radiological findings. Other potential harms to consider, even if mitigated by recent evidences [11], include incidental findings, over diagnosis, radiation exposure, and psychological distress.

We did not proposed to unconditionally exclude asbestos-exposed never or "light" smokers from occupational lung cancer screening program, but to monitor them to gather more information about risks, exposure levels, signs of disease such as presence of interstitial changes, genetic predisposition or presence of additional risk factors, as proposed by Harris et al. [1]. It should be noted that, these follow-up activities towards both active and retired workers with exposure to asbestos are also included in the 2014 Helsinki criteria [12] where it is indicated that recommended follow-up routines, principally focused on non-malignant asbestos-related disease, may differ among countries but usually are based on exposure evaluation, disease history, pulmonary function tests and chest radiograph. In this regard, the same document highlighted that in recent years the LDCT has been identified as useful tool in the early diagnosis of asbestos-related disease thus suggesting its use in the follow-up schema of asbestos exposed workers in order to facilitate early detection of asbestos-related lung cancer [12].

However, according to the 2014 Helsinki criteria the use of LDCT screening should be reserved to (i) workers with any asbestos exposure and a smoking history equal to the entry criteria of the US national lung screening trial (NLST) study and to (ii) workers with asbestos exposure with or without a smoking history, which alone or together would yield an estimated risk level of lung cancer equal to that in the entry criteria of the NLST study. Therefore, it is evident that the inclusion of asbestos-exposed workers never or 'light' smokers in LDCT screening program should be based on an accurate exposure assessment that in turn should be obtained by means of reliable work histories that provide the most practical and useful measure of occupational asbestos exposure (for example, in our study we administered a structured questionnaire to all subjects who indicated an asbestos exposure in order to identify and evaluate occupational exposures) [12,13].

In conclusion, we could only reiterate that further work is required to stratify risk profiles of the never-smoking population and to determine the benefits and harm of LDCT in never-smokers. In detail, future studies aimed at assessing risk estimation for lung cancer screening eligibility will have to focus especially on the complex interactions between asbestos exposure and other risk factors for lung cancer.

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Declaration of Competing Interest

Giulia Veronesi has financial relationships with Medtronic, Abmedica and Versurgical for consultation and proctoring. All other authors have no conflict of interest to declare.

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Patrick Maisonneuve*
Division of Epidemiology and Biostatistics, IEO European Institute of Oncology IRCCS, Milan, Italy
E-mail address: patrick.maisonneuve@ieo.it.

Sergio Iavicoli
Italian National Insurance Institute for Workplace Injuries (INAIL), Department of Occupational and Environmental Medicine, Epidemiology and Hygiene, Rome, Italy

Giulia Veronesi
Division of Thoracic and General Surgery, Humanitas Clinical and Research Center, Rozzano, Milan, Italy

* Corresponding author.