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Journal club

Evaluation of cardiovascular risk in a lung cancer screening cohort: what value does it bring?

Commentary on:

Ruparel M, *et al*. Evaluation of cardiovascular risk in a lung cancer screening cohort. *Thorax* 2019; 74: 1140–1146.

Context

Lung cancer is the leading cause of cancer-related mortality worldwide [1, 2]. Early detection could decrease mortality and three recent clinical trials aimed to develop and validate personalised risk assessment scores. The National Lung Screening Trial (NLST), the Dutch–Belgian Lung Cancer Screening Trial (NELSON) and the Multicentric Italian Lung Detection (MILD) trial have shown that annual low-dose computed tomography (LDCT) screening reduces mortality [3–6]. Following the successful reduction in lung cancer mortality, the majority of deaths in the LDCT arm were due to cardiovascular disease (CVD), since both lung cancer and CVD are strongly associated with age and smoking history. Ruparel *et al*. [7] investigated the opportunity to assess CVD risk, *via* quantification of coronary artery calcification (CAC), as part of the lung cancer screening (LCS) procedure. The study aimed to assess the prevalence of CAC and cross-examine CAC grading to standardised CVD risk scores (QRISK2) [8] and use of statin medication. LCS-nested risk assessment of CVD could further reduce mortality in a high-risk population at no additional cost.

Methods

The study used participants from the Lung Screen Uptake Trial (LSUT) [9]. The LSUT aimed to increase the number of active or former smokers aged 60–75 years from socioeconomically deprived backgrounds participating in LCS by trialling targeted invitation strategies and was designed to remove the fear and stigma behind a lung cancer diagnosis. 2012 individuals were invited for a LDCT scan. Of these, 1005 individuals responded and 770 participants underwent LDCT. In addition to the LDCT, data collected at the Lung Health Check included self-reported demographics, lifestyle choices (CVD and lung cancer risk factors), history of coronary heart disease (CHD), and general practitioner (GP) attendance in the past year. After data collection, a further 85 participants were excluded due to history of self-reported CHD, and an additional five participants were excluded due to missing QRISK2 score data. Finally, 680 individuals were included in the analysis (figure 1).

CAC grading was achieved using LDCT scans, performed at suspended maximal inspiration. Lung parenchyma was scanned in its entirety in a craniocaudal acquisition. Scans were single read by an experienced team of radiologists, and their

Cite as: Guariglia A, Davies IJ, Kanellakis NI. Evaluation of cardiovascular risk in a lung cancer screening cohort: what value does it bring? *Breathe* 2020; 16: 200204.

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There is a significant opportunity to improve cardiovascular disease (CVD) outcomes in lung cancer screening cohorts with a low-cost, noninvasive assessment of CVD risk, alongside existing assessments https://bit.ly/3a6Ha41

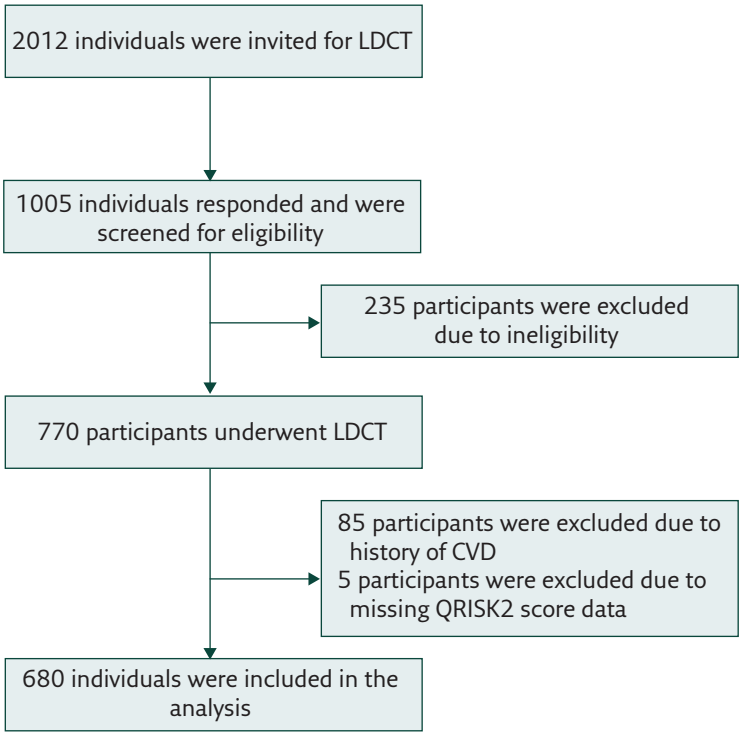

Figure 1 *Flow diagram of the stages and participants who were recruited in the study of Ruparel et al. [7]. Reproduced and modified from [7] with permission.*

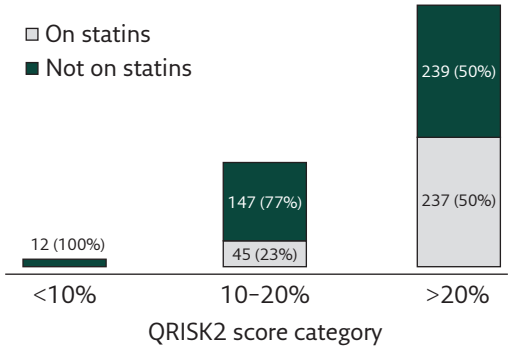

Figure 2 *Graph showing the use of statins among the three QRISK2 groups (<10%, 10–20% and >20%). 77% in the 10–20% and 50% in the >20% groups reported no use of statins despite being in the CVD risk cohort. Data from [7].*

reports provided a visually graded score of CAC across four categories: none, mild, moderate or heavy.

QRISK2 score was used to assess CVD risk from self-reported data. However, it was an estimation of QRISK2 score since serum cholesterol values were not collected and blood pressure values were not available.

Main results

The study confirmed the contributions of various participant characteristics to QRISK2 category. Better educated individuals tended to have lower QRISK2 scores, whereas smoking intensity, smoking duration, body mass index and blood pressure were increased in the high CVD risk QRISK2 categories. There was a high prevalence of CAC in the cohort, with 62% of participants classified as displaying visible CAC. This was "moderate" in 21.3% of participants and "heavy" in 7.2%. The authors reported a positive correlation between CAC grade and QRISK2 category ($p<0.01$), thus confirming previous reports that LCS-eligible individuals have evidence of coronary disease. However, CAC was unable to provide substantial information regarding CVD risk beyond what is provided by the QRISK2 score and could potentially underestimate the risk; 54.7% of participants in the moderate QRISK2 category (10–20%) had no CAC. Finally, there was a large difference between individuals meeting the risk threshold for statin primary prevention and those reporting statin use (figure 2). While 98% of LCS-eligible individuals met the 10% or greater 10-year CVD risk threshold which is required for statin use, only 43.2% reported a history of statin use.

Commentary

Self-reported medical history lacks a high degree of accuracy. However, the alternative, using GP reported prescriptions, would not take into account noncompliance, suggesting that no ideal method of recording medication usage currently exists. CAC visual grading used only broad measures (none, mild, moderate, or heavy) and the scans were only single read by five different radiologists. However, it is stated that the radiologists held many years of experience, the inter-observer agreement for the 5% of scans that were double read was very good and that scoring correlated with formal quantitative Agatston scores [10].

The diversity of trial participants was low. The data obtained only investigates CVD risk in socioeconomically deprived smokers aged 60–75 years, who were disproportionately white and male. Further study of ethnic minority groups would be appropriate, especially due to disproportionate rates of CVD in these populations [11]. In addition, there may be sampling bias: those who respond to the invite are more likely to be health conscious. In agreement with the authors, we believe that this sample is sufficiently representative of participants undergoing LCS procedures and could provide valuable insight.

Perhaps the main criticism of the study findings is the minimal value that CAC scores add to already existing QRISK2 scores, since the majority of participants in the moderate QRISK2 category have a CAC grading of "none". To evaluate its true value, outcome studies comparing correlation between visually graded CAC and QRISK2 score with cardiovascular end-points should be performed. While previous studies have shown that only a small number of participants from LCS cohorts will have

a CVD event, most look at only fatal CHD events, so in future studies, non-fatal coronary events should be studied.

Implications for practice

Given that CVD, alongside lung cancer, is a leading cause of mortality in the economically developed world, an important finding of this paper is the observation that while 98% of participants should be taking statins, less than were half reported to. There are similar observations of low statin use (below 50%) among eligible cohorts with high CVD risk in England and the USA [12] and while not directly assessed in this study, evidence suggests that low adherence is driven by patient dislike and misperceptions surrounding cardiovascular drugs and side-effects [13]. In addition, uptake of National Health Service health check invitations to carry out a CVD risk assessment has been low in the UK [14].

Thus, in order to reduce both lung cancer and CVD related mortalities, there is a clear impetus to develop strategies to improve LCS participation and statin usage among socioeconomically deprived patients. Ruparel *et al*. [7] suggest that CAC screening may provide a valuable opportunity to improve statin adherence within the Lung Health Check. Not only is this a noninvasive technique, but it can be carried out alongside LCS at minimal extra cost, providing a unique opportunity to tackle two diseases with the same procedure. A systematic review of CAC screening studies found that CAC screening can be used as a motivational tool in managing disease risk through medication adherence and potentially lifestyle modification [15]. Thus, showing a participant a visual representation of the calcification of their arteries may add value as a motivational tool, even if it does not add substantial predictive value *per se*.

There is also an opportunity to explore whether CAC screening data can improve adherence to alternative lifestyle interventions, such as physical activity, a healthy diet and smoking cessation, which could be facilitated by wearable or smartphone data collection methods following health checks. This is especially relevant given recent evidence of lifestyle changes following initiation of statin medication [16].

Such studies should consider whether the poor statin compliance observed by Ruparel *et al*. [7] is affected by the low socioeconomic status of participants, and whether CAC screening provides value only in this subset of individuals, compared with the general population at risk of lung cancer. Nevertheless, improving statin compliance in smokers from socioeconomically deprived backgrounds, alongside their increased participation in LCS, is itself an important and desirable goal.

In conclusion, there is great promise for a low-cost, noninvasive parallel evaluation of cardiovascular risk in lung screening cohorts. While the added predictive value of CAC screening beyond QRISK2 remains uncertain, the study does highlight the underusage of statins within this population. Thus, performing CAC screening alongside the standard Lung Health Check could act as a motivational tool to encourage this cohort to undertake measures to reduce CVD risk, such as taking statins. The Lung Health Check programme has the potential to simultaneously reduce rates of CVD and lung cancer mortality within the population.

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Conflict of interest

None declared.

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