NICE National Institute for Health and Care Excellence

DIAGNOSTICS ASSESSMENT PROGRAMME

EarlyCDT Lung for assessing risk of lung cancer in solid lung nodules

Diagnostics Consultation Document – Comments

Diagnostics Advisory Committee date: 17 November 2021

THEME: General comments

Comment number	Name and organisation	Section number	Comment	NICE response
1	UK NSC		Many thanks for providing an opportunity for the UK National Screening Committee (UK NSC) to respond to this consultation. The recommendations appear to be consistent with the evidence base as described in the consultation documentation. The UK NSC advises ministers and the NHS in the four UK countries on all matters relating to population screening. However it is worth noting that the Committee's remit will extend into targeted screening of populations at increased risk of disease. We note that the proposed uses of early CDT are in groups in which nodules have been identified and in which risk of progression has been characterised using current methodologies (Beck +/- Herder). The function of the test is therefore further risk stratification and this may be relevant to populations which have been identified by screening, symptomatic presentation or through incidental detection. At present there is no UK NSC recommended screening programme for lung cancer. However the UK NSC is due to make a recommendation on targeted screening in long term tobacco smokers in 2022. This topic is therefore very timely as risk stratification along the screening and diagnostic pathway would be of major interest should such a programme be recommended. We look forward to future updates in this area.	Thank you for your comment which the committee considered.

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2	Oncimmune	2.4	**EarlyCDT Lung has the potential to improve the rate of cancer diagnosis in the aftermath of the COVID-19 crisis** The ambitions of the NHS Long term Plan for cancer is that by 2028, 75% of people with cancer will be diagnosed at an early stage (stage 1 or 2). If approved early, EarlyCDT Lung can help achieve this target by identifying malignant nodules that would otherwise be overlooked and placed on surveillance. Oncimmune is completely in agreement with the panel's assessment of the intended use of the test. EarlyCDT Lung can be used to complement CT surveillance by enriching patient populations at high risk of lung cancer for biopsy and treatment. The test can, therefore, increase the benefits of CT surveillance and also improve patient outcomes further. In the case of early stage disease, EarlyCDT Lung can offer the added benefit of decreasing CT requirements with a subsequent reduction in NHS resource and waiting times for CT surveillance. This is especially pertinent as we see delays in diagnosis of lung cancer due to COVID-19, which are likely to have a significant impact on the loss of life.	Thank you for your comment which the committee considered.

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THEME: Diagnostic accuracy

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3	Oncimmune	**3.2 Report Inclusion Criteria** Key inclusion criteria for sensitivity estimation were: • Persons with solid pulmonary nodules identified by CT scanning, who may be eligible for further diagnostic testing. • Malignancy confirmed by biopsy or surgical resection; benign nodules confirmed by clinical follow-up of at least one year. • Studies reported diagnostic accuracy data, or any data on the	**The diagnostics consultation document states that the evidence of the diagnostic accuracy of EarlyCDT Lung in people with lung nodules is limited.** **Additionally, the EAG diagnostics assessment report concluded that the evidence was insufficient to draw any firm conclusions as to diagnostic accuracy and while EarlyCDT Lung appears to have poor diagnostic accuracy, this is uncertain because the evidence is so limited.** • Oncimmune are in agreement with the EAG that the evidence assessed was insufficient to draw firm conclusions. Oncimmune also believe in the highest standard of evidence and reporting and strongly request that the 20% estimate is removed from the Diagnostics assessment document, as the estimate is uncertain, based upon limited and ineligible evidence. None of the five studies selected by the EAG used to estimate diagnostic performance satisfied the EAG's own assessment inclusion criteria. In particular, no cohort explicitly performed EarlyCDT Lung after identification of pulmonary nodules. Three of the studies (EarlyCDT LCS, US and Hong Kong) were not published to a standard suitably high enough for the purpose, being only non-peer-reviewed conference abstracts or posters. The remaining two studies (HIPAA and German RCT) are stated by EAG as being at high risk of bias.	Thank you for your comment which the committee considered. The committee decided to keep the external assessment group's estimate of diagnostic accuracy in section 3.2 of the diagnostics guidance document, but added further detail on the source of data used to emphasise its uncertainty. It also added the 95% confidence intervals to the company's accuracy estimate, which was previously omitted.

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		clinical impact of the technology. • Therefore, the assessment excluded the following types of study: - Unpublished studies (stated in the Main Report Abstract) - Screening studies - Case-control studies - Retrospective samples	The EAG diagnostic assessment report states in the 'Strengths and Limitations' section, 3.4.3, that 'analysis was limited by lack of data, with only two fully published studies, and potential for risk of bias and poor generalisability. This meant there was little scope for statistical analysis, and a lack of robustness in results. The EAG considers that the existing evidence is too limited to draw any firm conclusions on the diagnostic accuracy of EarlyCDT Lung'. Basing the 20% sensitivity estimate on a set of ineligible studies is not appropriate. Reports of this nature are placed in the public domain, and placing a sensitivity estimate in the public domain which is based upon uncertain and limited evidence would be extremely damaging and unjust. **As the EAG conclude that no firm conclusions can be made for diagnostic accuracy, we request that the 20% sensitivity estimate be removed from this report and any other documentation that will be publicly or widely available.**	

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THEME: Ongoing studies

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4	Oncimmune	3.4	**The EAG report identified 2 potentially relevant ongoing studies of EarlyCDT Lung:** 1. **The 'China study'** – this study is not applicable to this report as this study is for an alternative product which has been developed specifically for the Chinese market 2. **The 'US study'** – this small study is now complete and is likely to be published in the next year There is, however, another ongoing study, not identified, which is relevant and summarised below: <u>iDx Lung Health Trial</u> • [redacted] • [redacted] • [redacted]	Thank you for your comment which the committee considered. The external assessment group highlighted that this study was discussed at the committee meeting. The iDx lung health trial is testing the value of EarlyCDT Lung for cancer screening and might not include people with already identified pulmonary nodules. The committee decided to update section 3.4 of the diagnostics guidance document to highlight that the study in China is evaluating a different product. Further detail on the US study was also added to section 3.4. The committee were unable to add further detail on the iDX Lung Health Trial as the provided details are contained in the study protocol which is currently marked confidential.

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			[redacted] • Funded by Innovate UK, the study is sponsored by University Hospitals Southampton NHS Trust and the coordinating centre is Southampton Clinical Trials Unit. • [redacted] The study protocol is available upon request.	
5	Oncimmune	3.7	**The EAG report concluded that no studies of EarlyCDT Lung in the target population reported health-related quality of life outcomes.** [redacted]	Thank you for your comment which the committee considered. The committee were unable to add further detail on the iDX Lung Health Trial as the provided details are contained in the study protocol which is currently marked confidential.

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6	Oncimmune	3.8	**The EAG report concluded no direct trial evidence was found on how EarlyCDT Lung impacts on long-term patient outcomes, such as lung cancer related mortality and morbidity, morbidity associated with other diagnostic tests or procedures, and overall and disease-free survival.** [redacted]	Thank you for your comment which the committee considered. The committee were unable to add further detail on the iDX Lung Health Trial as the provided details are contained in the study protocol which is currently marked confidential.

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THEME: Research recommendations

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7	Oncimmune	4.1	**The EAG report recommended further research on:** • **The accuracy of EarlyCDT Lung, and the validity of the risk models used to combine EarlyCDT Lung results with the Brock and the Herder risk models** • **The impact of EarlyCDT Lung on clinical management decisions** While the iDx Lung Health Trial may provide some evidence towards the accuracy, risk model and impact on clinical management decisions, Oncimmune is in agreement with the panel's conclusion that further research is required. We are, therefore, eager to work with NICE to support further research. We would like to highlight that EarlyCDT Lung specimen collection by finger stick is validated for use. This means that finger stick collection packs can be sent directly to patients to collect their own blood at home. The blood can then be posted back for testing using standard mail routes, without the need for any refrigeration during transport (much like COVID-19 PCR tests can be). In light of the impact the COVID-19 pandemic has had on current NHS practices and waiting times, this specimen collection method could be particularly beneficial for gathering further evidence through research studies, and for any future integration of the test into the NHS.	Thank you for your comment which the committee considered.

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			This approach could, for example, be used to access Lung Health Check patient cohorts, in addition to those already being accessed via the iDx Lung Health Trial. This could provide a very cost and time efficient option, using existing cohorts in NHS trials, to support this research.	
8	Oncimmune	4.2	**The Diagnostics Consultation Document recommends a large retrospective audit, or, dependent on existing data, a prospective data collection.** Oncimmune would appreciate information on the timescale to complete the research described, as and when available. Gaining a recommendation for EarlyCDT Lung from NICE is extremely important not only to the test's and Oncimmune's success, but this could have a real impact on patient outcomes, especially in light of COVID-19's impact to the NHS and cancer diagnosis and treatment.	Thank you for your comment which the committee considered. The committee discussed that the research proposed will be considered by the NICE Medical Technologies Evaluation Programme research facilitation team for developing specific research study protocols as appropriate. Currently, guidance is reviewed 3 years after publication or sooner if new evidence becomes available.