Software with artificial intelligence derived algorithms for automated detection and analysis of lung nodules from CT scan images

ERRATUM

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This document is intended to replace pages 54, 62, 168, 206, 227, 234, 235 and 241 of the original EAG assessment report for software with artificial intelligence derived algorithms for automated detection and analysis of lung nodules from CT scan images, which contained a few inaccuracies or typographical errors identified by the consultees and commentators involved in the consultation phase of this assessment.

Page number	Correction
54	Changed from "… for use in asymptomatic populations." to "… for screening, diagnosis and monitoring of lung cancer." (Text taken from Veolity's User Guide).
62	Removed * for Veolity as the company clarifies that the indication does cover symptomatic population.
168	Replaced "*Incidental population – AI-RAD Companion Chest (Coreline Soft) (1 study)*" with "*Incidental population – AI-RAD Companion Chest (Siemens Healthineers) (1 study)*"
206	Corrected the expected number of people with actionable nodules.
227	To reflect the uprated treatment costs used in the model.
234	Deleted the columns for the surveillance population.
241	Replaced "Table 54 presents … in a symptomatic population." with "Table 54 … in an incidental population."
245-246	Change to the incremental QALYs where the time to read and report a scan is altered.

The amended pages follow in order of page number below.

Veolity (MeVis)

Veolity is a CE-marked (class IIa medical device) software. It can detect, measure and assess the growth of lung nodules in low-dose and regular dose CT scans that include the complete chest, with and without contrast. The software is compatible with slice thickness of up to 3 mm. Veolity is indicated for screening, diagnosis and monitoring of lung cancer. Users can interact with the software by adding and dismissing nodules in the analysis and editing the findings of the software. With input from the user, the software also calculates the malignancy risk of the nodules using the Brock model. Veolity's current detection algorithm only detects solid nodules. A new version of the software (Veolity 2.0) is planned for the beginning of 2022. This version will detect solid and sub-solid nodules. Usually, 2 updates or functional upgrades per year are planned. Existing versions will continue to be supported. Veolity includes rules for reporting following the BTS guidelines for the investigation and management of pulmonary nodules[11] and integrates with the PACS. The company states that usually 4 to 6 hours of training are needed for radiologists to learn how to use Veolity. The software is commercially available to the NHS, distributed in the UK by SynApps Solutions.

Veye Lung Nodules (Aidence)

Veye Lung Nodules is a CE-marked (class IIb medical device) software. It can detect, measure and assess the growth of solid and sub-solid lung nodules in low-dose or standard dose CT scans where both lungs are visible, with and without contrast. The software is compatible with slice thickness of up to 3 mm. Veye Lung Nodules is intended for use in people aged 18 and over. Users can dismiss nodules found by the automated analysis but editing the findings is not possible. Users can add nodules, but the software will not measure the volume of user-added nodules. The software is updated frequently. Veye Lung Nodules includes rules for reporting following the BTS guidelines for the investigation and management of pulmonary nodules.[11] The software integrates with, and findings of the software are visible within, PACS. The company expects radiologists to attend a 1-hour training session before using the technology. The software is commercially available to the NHS.

VUNO Med-LungCT AI (VUNO)

VUNO Med-LungCT AI is a CE-marked (class IIa medical device) software. It can detect, measure and assess the growth of solid and sub-solid lung nodules in low-dose chest CT scans. It is intended for use in lung cancer screening populations. The software integrates with PACS.

Error! Reference source not found. for details). Reference lists of included studies and a selection of recent, relevant systematic reviews identified via the database searches were checked. Forwards citation tracking from key publications of included studies (to identify citing papers) was also undertaken, using Science Citation Index (Web of Science) and Google Scholar.

Study eligibility criteria

Studies that satisfied the following criteria were included:

Population	<u>All questions</u> People who have no confirmed lung nodules or lung cancer and who are not having staging investigations or follow-up imaging for primary cancer elsewhere in the body, who have a CT scan that includes the chest: • because of signs or symptoms suggestive of lung cancer (symptomatic population); • for reasons unrelated to suspicion of lung cancer (incidental population); • as part of lung cancer screening (screening population). People having CT surveillance for a previously identified lung nodule (surveillance population). Where data permits, the following subgroups may be considered: • Patient's ethnicity; • People who have a CT scan: (1) with or without contrast; (2) using a low-dose or a standard dose; (3) of solid nodules or sub-solid nodules; • For the incidental population, by reason for CT scan.
Target condition	<u>All questions</u> Lung nodules or lung cancer
Intervention	<u>All questions</u> CT scan review by a radiologist or another healthcare professional using any of the following software for automated detection and analysis of lung nodules: • AI-Rad Companion Chest CT (Siemens Healthineers) • AVIEW LCS+ (Coreline Soft) • ClearRead CT (Riverain Technologies)* • contextflow SEARCH Lung CT (contextflow)** • InferRead CT Lung (Infervision)* • JLD-01K (JLK Inc.) • Lung AI (Arterys) • Lung Nodule AI (Fujifilm) • qCT-Lung (Qure.ai) • SenseCare-Lung Pro (SenseTime) • Veolity (MeVis) • Veye Lung Nodules (Aidence) • VUNO Med-LungCT AI (VUNO) * Indication for use specifies use in asymptomatic population, therefore the software cannot be assessed in symptomatic population. ** Indication for use specifies use in symptomatic population, therefore the software cannot be assessed in incidental or screening populations. Please note: specific indications for use for some of the technologies are unclear because only information in the public domain was available.

Table 1. Characteristics of correctly detected nodules in a mixed population from China obtained via convenience sampling.[58]

Nodule type	Nodule size	Reference standard	Correctly detected nodules		
			Stand-alone software	Reader 1 – Unaided	Reader 2 – unaided
Total	All	6,363	4,484	2,562	3,617
Solid	≤6 mm	53.4%	50.0%	49.5%	47.1%
	>6 mm	4.1%	5.1%	8.1%	5.1%
	All	57.5%	55.1%	57.6%	52.3%
Sub-solid	≤5 mm	20.8%	19.6%	13.1%	20.8%
	>5 mm	6.8%	7.9%	10.0%	10.1%
	All	27.6%	27.5%	23.1%	30.9%
Calcified	NR	5.1%	6.6%	6.0%	5.1%
Pleural	NR	9.8%	10.7%	13.3%	11.7%

NR, Not reported.

Four studies reported on characteristics of true positive nodules detected by stand-alone software,[49, 64] by software-assisted readers,[54] and/or by the reference standard[30, 54, 64] without a comparator. These non-comparative results are reported in **Appendix 5, section** Error! Reference source not found.**.**

Additional true positive nodules detected by software compared to unaided reading (1 study)

Incidental population – AI-RAD Companion Chest (Siemens Healthineers) (1 study)

The study by Rueckel et al. included 105 consecutive patients who received a whole-body CT scan in the emergency department of a single German hospital.[47] Retrospective reading by stand-alone software (AI-RAD Companion Chest CT prototype, Siemens Healthineers) detected three additional true positive nodules compared to the original radiologist report (17% of CT scans have been originally reported by a board-certified radiologist alone, the other 83% CT scans have been commonly reported by a radiology resident and a board-certified radiologist). All three additional nodules detected measured at least 6 mm, with the largest nodule being 8 mm.

False positive nodules (4 studies)

Four studies reported on characteristics of false positive nodules detected by stand-alone software in a random screening population,[46] an incidental population[47] and mixed populations,[45, 64] respectively. No study compared characteristics of false positive nodules between readers with and without concurrent software use.

Table 2. Scenario analysis results based on cost per person with an actionable lung nodule correctly identified (screening population)

Strategy	Expected total costs (£)	Incremental costs (£)	Expected number of people with actionable lung nodules	Incremental number of people with actionable lung nodules	ICER (£) per person with actionable lung nodules
Base-case					
AI-assisted radiologist reading (ClearRead CT)	127,600	-	149.3	-	-
Unaided radiologist reading	130,500	2,900	123.8	-25.5	Dominated
Prevalence of detecting actionable lung nodules from 0.206 to 0.2823 (estimate reported in another NELSON lung cancer screening trial)[3]					
AI-assisted radiologist reading (ClearRead CT)	127,600	-	204.7	-	-
Unaided radiologist reading	130,500	2,900	169.7	-35	Dominated
Time taken to read and report CT scans- assumed to be 10 minutes for both AI-assisted and unaided image analysis					
Unaided radiologist reading	130,500	-	123.8	-	-
AI-assisted radiologist reading (ClearRead CT)	132,500	2,000	149.3	25	78
Time taken to read and report CT scans- assumed to be 10 minutes for AI-assisted and 8 minutes for unaided image analysis					
Unaided radiologist reading	125,600	-	123.8	-	-
AI-assisted radiologist reading (ClearRead CT)	132,500	6,900	149.3	25.5	270
CT, computed tomography; QALY, quality adjusted life-year					

6.4.4 Discussion

The preliminary model provides a relatively straightforward approach to assessing cost-effectiveness of AI-assisted detection and analysis of lung nodules for chest CT scan images. However, a major

Multidisciplinary team	£146	National schedule of NHS costs 2020/21 (CDMT_OTH other cancer MDT meetings)
Guided needle biopsy	£1670	NHS reference schedule (DZ71Z- minor thoracic procedure, guided needle biopsy)
PET scan	£1161	RN01a- PET-CT of one area, 19 years and over
Treatment		
Stage I	£18,705	Bajre et al., 2017[72]
Stage II	£21,312	
Stage III	£23,922	
Stage IV	£14,909	
CT, computed tomography; PET-CT, positron emission tomography and computed tomography; PSSRU, Personal Social Services Research Unit		

7.4.6 Utility values

The utility values that were used to derive the quality adjusted life years (QALYs) for people with lung cancer were mainly obtained from Bajre et al.,[72] which were originally obtained from Naik et al., 2015. Briefly, these authors collected health-related quality of life information using the EQ-5D questionnaire from 1760 Canadian ambulatory cancer patients and reported utility values by stage at diagnosis. Among the participants with lung cancer (N=128), patients with stage I, II, III and IV diagnoses had utility estimates of 0.81, 0.77, 0.76 and 0.76, respectively. For people without a lung nodule, we assigned a utility value of 0.855 (Rickets et al., 2020).

In the base-case, we assumed that there is a –0.063 disutility for people with a non-nodular structure incorrectly identified as a nodule (false positive during detection of a lung nodule). In the model, we assumed that these non-nodular structures will be discharged at the first CT surveillance (i.e., at three months or one year). Also, we assumed that people under CT surveillance with lung nodules that were later diagnosed as benign, there would be a disutility of –0.063 lasting until the person was discharged. People without lung nodules and those with benign nodules were assumed to have utility values representing UK-specific general population norms.

We assumed that a disutility of –0.2 associated with undergoing a biopsy with a duration of three months.

Table 3. Summary of intermediate outcomes from the full model

Results	Symptomatic		Incidental		Screening	
	AI-assisted	**Unaided**	**AI-assisted**	**Unaided**	**AI-assisted**	**Unaided**
Correct detection of any lung nodules	808.0	645.5	110.7	88.4	422.5	371.6
Correct detection of actionable nodules	481.8	333.4	58.6	42.5	223.8	178.7
Lung cancer detected at first presentation	7.0100	6.5510	1.3985	1.0810	5.3351	4.5423
Cancer detected at 3-month CT surveillance	1.9230	3.6700	0.2181	0.3506	0.8326	1.4732
Cancer detected at 1-year CT surveillance	2.3120	1.2360	0.2233	0.1796	0.8523	0.7546
Cancer detected at 2-year CT surveillance	1.9060	0.758	0.1563	0.1227	0.5964	0.5158
Cancer detected at 4-year CT surveillance	2.3600	0.6140	0.1893	0.1105	0.7225	0.4642
Cancers detected	15.5120	12.8290	2.1850	1.8440	8.3420	7.7500
Cancers missed (<5mm)	2.2823	2.8212	0.3702	0.3673	1.4129	1.5433
Cancers missed (no lung nodule detected)	0.5641	4.992	0.0773	0.7069	0.3461	1.7816
Cancers missed (slow growing)	4.1302	1.8466	0.5879	0.3023	2.2439	1.2701
Cancers missed	6.9770	9.6600	1.0353	1.3764	4.0029	4.5950
Total cancers	**22.489**	**22.489**	**3.2203**	**3.2204**	**12.345**	**12.345**

(InferRead CT Lung)					
No disutility associated with false positive nodules during detection or disutility associated with undergoing CT surveillance					
Unaided radiologist reading	715,450	-	6385.86	-	-
AI-assisted radiologist reading (InferRead CT Lung)	816,520	101,080	6393.81	7.95	12,709
CT, computed tomography; QALY, quality adjusted life-year					

8.1.2 Incidental population

Cost per correct identification of a person with actionable lung nodules

Error! Reference source not found. presents the estimates of the costs and additional people correctly identified with an actionable nodule with the use of AI-assisted radiologist reading compared to unaided radiologist reading in an incidental population. These results show that AI-assisted radiologist reading (InferRead CT Lung) is approximately £4,000 cheaper and expected to correctly identify an additional 16.1, resulting in the unaided reading strategy being dominated.

Scenario analyses

Table 4. Scenario analysis results based on cost per QALY (incidental population)

Strategy	Expected total costs (£)	Incremental costs (£)	Expected QALYs	Incremental QALYs	ICER (£) per QALY
Base-case					
AI-assisted radiologist reading (InferRead CT Lung)	229,210	-	6571.19	-	-
Unaided radiologist reading	231,640	2,430	6573.63	2.44	996
Prevalence of detecting any lung nodules (0.1300 to 0.3800)					
AI-assisted radiologist reading (InferRead CT Lung)	356,490	-	6541.56	-	-
Unaided radiologist reading	381,670	25,180	6538.59	-29.6	Dominated
Time taken to read and report CT scans- assumed to take 12 minutes for AI-assisted and unaided					
Unaided radiologist reading	223,910	-	6573.63	-	
AI-assisted radiologist reading (InferRead CT Lung)	229,210	5,300	6571.19	-2.44	Dominated
Time taken to read and report CT scans- assumed to take 15 minutes for AI-assisted and 12 minutes unaided					
Unaided radiologist reading	223,910	-	6573.63	-	
AI-assisted radiologist reading (InferRead CT Lung)	236,580	12,670	6571.19	-2.44	Dominated
People with benign nodules discharged at 2-year CT surveillance (solid nodules) and 4-year CT surveillance (sub-solid nodules) in both strategies					
Unaided radiologist reading	231,900	-	6573.58	-	-

AI-assisted radiologist reading (InferRead CT Lung)	232,540	640	6570.46	-3.11	Dominated
No disutility associated with false positive nodules during detection or disutility associated with undergoing CT surveillance					
AI-assisted radiologist reading (InferRead CT Lung)	229,210	-	6583.58	-	-
Unaided radiologist reading	231,640	2,430	6582.69	-0.89	Dominated
CT, computed tomography; QALY, quality adjusted life-year					