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**Background**

Because of its accessibility, low cost, low radiation dose exposure, and reasonable diagnostic accuracy, chest radiographs are frequently used for early detection of pulmonary nodules despite their inferiority to low-dose computed tomography (LDCT). Although LDCT has demonstrated a clear benefit for reducing all-cause mortality among high-risk group in lung cancer screening, the high rate of false-positives, low uptake, and the cost of unnecessary diagnostic procedures are important limitations of this approach. The introduction of targeted therapies and immunotherapeutic agents have resulted in a longer duration of overall survival compared with standard chemotherapy. However, these novel therapies are not effective in all patients; thus, early detection remains the most important intervention window for improving patient survival. The emergence of artificial intelligence (AI) as a new tool for assessing medical data implies new opportunities for improving the diagnosis and treatment of various human diseases. In the case of lung cancer diagnosis, coupling AI algorithms with available clinical and biomedical data seems to have the potential to improve lung cancer screening methods. These points lead to a question - Can AI help to provide a "second pair of eyes" for detecting nodules more accurately and earlier in their progression? Hence, this technology review was requested by the Head of Cancer Unit, Disease Control Division, Ministry of Health Malaysia to evaluate the role that AI-based chest x-ray could play in assisting radiologists and to increase the accuracy and efficiency of lung cancer diagnosis.

**Objective**

To evaluate the diagnostic accuracy, efficacy, safety, and economic implication of AI-based chest x-ray for lung cancer screening, and to compare its performance with radiologists.

**Methods**

The following electronic databases were searched through the Ovid interface: MEDLINE (R) ALL 1946 to Jul 29, 2022. Parallel searches were run in PubMed, US FDA and INAHTA database while additional articles were retrieved from reviewing the bibliographies of retrieved articles. The search was limited to articles on human. There was no language limitation in the search. The last search was conducted on 2nd August 2022.

**Results and conclusion:**

**Diagnostic accuracy/ efficacy**

There was substantial fair level of retrievable evidence to suggest that radiologists had better diagnostic performance interpretation with AI algorithm than without for the detection of lung cancer on chest radiographs. Findings in general reported that:

- i. The average sensitivity improved from 66.4% (ranged 45.0%-87.7%) to 74.7% (ranged 55.5%-93.9%) and the number of false-positive findings per radiograph declined from 0.25 (ranged 0.20-0.30) to 0.18 when the radiologists re-reviewed radiographs with AI algorithm. However, specificity was similar with AI-aided (ranged 86.0%-97.0%) and without AI-aided interpretation (ranged 79.0%-96.0%).
- ii. Junior radiologists showed greater improvement in sensitivity

- with AI-aided interpretation as compared with their senior counterparts (12.0%, 95% confidence interval [CI]: 4.0% to 19.0% versus 9.0%, 95% CI: 1.0% to 17.0%) while senior radiologists experienced larger improvement in specificity (mean improvement 4.0%, 95% CI: -2.0% to 9.0%) compared with the junior group (1.0%, 95% CI: -3.0% to 5.0%).
- iii. General physicians benefited more from the use of the AI algorithm than radiologists. The performance of general physicians was improved from 47.0% to 60.0% for sensitivity, from 96.0% to 97.0% for specificity, from 75.0% to 82.0% for positive predicted value (PPV), and from 89.0% to 91.0% for negative predicted value (NPV) while the performance of radiologists was improved from 51.0% to 60.0% for sensitivity, from 96.0% to 96.0% for specificity, from 76.0% to 80.0% for PPV, and from 89.0% to 91.0% for NPV.
  - iv. Artificial intelligence algorithm enhanced the performance of readers for the detection of lung cancers on chest radiographs when used as second reader. Compared to that without AI, the average sensitivity increased significantly for radiology residents (61.0% [95% CI: 55.0% to 67.0%] versus 72.0% [95% CI: 66.0% to 77.0%];  $p=0.016$ ), but specificity was similar with AI ( $p=0.89$ ). For radiologists, average sensitivity was similar ( $p=1.00$ ) but specificity increased with AI (79.0% [95% CI: 77.0% to 81.0%] versus 86.0% [95% CI: 84.0% to 87.0%];  $p<0.001$ ).
  - v. With AI, radiology residents were able to recommend more chest CT examinations (54.7% versus 70.2%,  $p<0.001$ ) for patients with visible lung cancer whereas radiologists recommended significantly less proportion of unnecessary chest CT examinations (16.4% versus 11.7%,  $p<0.001$ ) in cancer-negative patients.
  - vi. For detection of visible lung cancers on the chest radiography in healthy population, the stand-alone AI algorithm performance was comparable to that radiologist with sensitivity, specificity, PPV, NPV, and false-positive rate of 83.0%, 97.0%, 1.3%, 100%, and 3.0%, respectively.

### **Safety**

There was no retrievable evidence on the adverse events or complications related to the use of AI-based chest x-ray for lung cancer screening. Currently, there have been several AI algorithms approved by the United States Food and Drug Administration (FDA) for specific clinical indications, specifically to thoracic radiology. The majority of these algorithms are approved for detection and segmentation of pulmonary nodules. Several algorithms were registered as CE-mark (Class IIa) medical device.

### **Organisational issues**

There was no retrievable evidence in the context of procedural time points and training or learning curve related to AI-based chest x-ray for lung cancer screening. Nevertheless, AI-aided seems to help radiologists to read images effectively and providing complementary interpretation, highlighting areas of the scan requiring particularly close inspection. This information may reduce time to diagnosis, help

avoid fatigue- or workload-induced missed diagnoses, and can be invaluable in helping address shortage of trained radiologists.

**Economic implication**

The cost-effectiveness of AI-based chest x-ray for lung cancer screening has not yet been formally evaluated. However, cost associated to use the technologies generally consists of implementation or integration fee (ranged from £6,000 to £10,000 per centre), annual license and maintenance fee (£60,000), and fixed cost per scan processed (between £0.90 and £1.66 per image) which would be in addition to standard care (£32.73) and it depends on the total patient throughput.