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**Background**

Tuberculosis (TB) is a preventable disease caused by *Mycobacterium tuberculosis*, primarily affecting the lungs and spreading through the air. Despite being curable, TB was the second leading cause of death from a single infectious agent worldwide in 2022, after COVID-19, causing almost twice as many deaths as HIV/AIDS. Southeast Asia accounted for the largest proportion of TB cases in 2021. Malaysia is categorised as an intermediate TB burden country, and detection rates are still below WHO estimates, indicating a need for more proactive case finding, especially among high-risk groups.

Breath test analyse breath specimen in two ways, chemically and physically. Chemical technique in the analysis which identify chemical interaction between volatile organic compounds (VOCs) and sensor surface. Physical method quantify a molecule's physical characteristics such as size, shape and charge of the breath molecules. There is a need for a rapid, low-cost, easy-to-use diagnostic method to ensure effective screening and control. There is growing interest in the use of breath tests as a screening method for TB. This technology review aims to evaluate the effectiveness, safety of breath test in diagnosing TB following a request from a Pathologist (Medical Microbiologist) in Hospital Sultan Abdul Halim, Sungai Petani.

**Objective**

The objective of this technology review was to assess the accuracy, effectiveness, safety, and economic implication of breath test in diagnosing tuberculosis in patients suspected of having TB.

**Methods**

The following electronic databases were searched through the Ovid interface: MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions 1946 to January 08, 2024, HTA Full-text Journals, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to March 6, 2024, EBM Reviews - ACP Journal Club 1991 to February 2024, EBM Reviews - Cochrane Clinical Answers February 2024, EBM Reviews - Cochrane Central Register of Controlled Trials February 2024. Parallel searches were run in MISC (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 13<sup>th</sup> March 2024. Among the tools used to assess the risk of bias and methodological quality of the articles retrieved is the ROBIS and Critical Appraisal Skill Programme (CASP) checklist. All full text articles were then graded based on guidelines from the US/Canadian Preventive Services Task Force.

**Results and conclusion:****Efficacy/ effectiveness**

There was fair level of retrievable evidence on breath test showing its varying performance in diagnosing tuberculosis.

**Breath test (electronic nose)**

Breath test using electronic nose showed good pooled diagnostic accuracy. However, the performance of electronic nose was varied in four diagnostic accuracy studies included in this review. Sensitivity and specificity ranging from 52.3% to 90.8% and 36.4% to 99% respectively. The studies included in this review varies in terms of type of electronic nose used and population tested.



**Breath test (other than electronic nose)**

The performance of breath test other than electronic nose was good in diagnosing TB with sensitivity and specificity ranging from 80.4% to 95.7% and 80.3% to 91.3% respectively, and AUC performance ranged from 0.867 to 0.935.

**Safety**

There was limited evidence retrieved on the safety of breath test. Breath tests was not associated with treatment-related adverse events during the sessions or the follow-up. The United States Food and Drug Administration (US FDA) has not yet approved breath testing for tuberculosis. The electronic nose [REDACTED] device is claimed as having CE approval, indicating compliance with European regulatory standards.

**Organisational issues**

All the practices regarding the test analysis including the pre-examination, examination, post-examination, safety and training of staff or operator shall follow international or local guidelines such as Malaysian Standard, MS ISO 15189:2014, Specific Technical Requirement for Accreditation of Medical Microbiology Laboratories (STR 2.5) and National Policy and Guidelines for Point of Care Testing by Ministry of Health Malaysia.

**Economic implication**

No cost-effectiveness study retrieved on breath test to diagnose Tuberculosis. Nevertheless, the estimated price for laboratory-based automatic thermal desorption-gas chromatography-mass spectrometer (ATD-GC-MS) was near [REDACTED], whereas a more accessible point-of-care device, using a portable gas chromatograph coupled to a surface acoustic wave detector (ATD-GC-SAW), is priced lower at around [REDACTED].

**Conclusion**

A fair level of retrieved evidences has demonstrated that point-of-care (POC) breath test has moderate to good diagnostic accuracy in detecting TB in high incidence setting.

No safety issue has reported with the use of this device. No cost effectiveness study retrieved on this device.