Breath analysis for disease detection: what conditions have been validated?

Breath Analysis for Disease Detection: Where Clinical Validation Stands

Breath analysis has been explored across many diseases, but only a **small subset** has fully validated, widely approved clinical tests. Most conditions are still in research or early validation phases.

Diseases with Established Clinical Breath Tests

Well-accepted / approved tests

Disease / indication	Breath target & status	Citations
Helicobacter pylori infection	**Urea breath test** (^{13}C/^{14}C-urea), in routine clinical use	(Haworth et al., 2022; Bajo-Fernández et al., 2024; Binson et al., 2021)
Small intestinal bacterial overgrowth, carbohydrate malabsorption, gut microbiome function	**Hydrogen and methane** breath tests, widely used for GI disorders	(Haworth et al., 2022; Sharma et al., 2023; Binson et al., 2021)

FIGURE 1 Conditions with widely used clinical breath tests

These are described as among the **few breath-based diagnostics currently available and in widespread clinical use** (Haworth et al., 2022; Binson et al., 2021).

Conditions with Strong Research but Limited/No Full Validation

- **Cancers:** Especially **lung cancer**, gastric cancer, and others; many VOC panels and sensor/e-nose studies show good discrimination, but remain largely at discovery/validation stages, not routine care (Pham & Beauchamp, 2021; Zheng et al., 2024; Khoubnasabjafari et al., 2021; Nakhleh et al., 2016; Brinkman et al., 2024; Amann et al., 2014; Pereira et al., 2015).
- **Respiratory diseases:** Asthma, COPD, pulmonary infections, interstitial lung disease, pulmonary hypertension; robust research and promising classification, but breath VOCs are **not yet standardized or fully validated for clinical diagnosis** (Zheng et al., 2024; Ibrahim et al., 2021; Nakhleh et al., 2016; A. et al., 2024; A. et al., 2021; Zhao & Meng, 2024).
- **Non-cancer GI and liver disease:** GERD, Barrett's esophagus, IBD, IBS, coeliac disease, cirrhosis, fatty liver; 24 VOC studies reviewed, all exploratory or early-stage, with **no clinically validated VOC biomarker** yet (Haworth et al., 2022; Sharma et al., 2023).
- **Cardiovascular, renal, metabolic, neurodegenerative disorders, arthritis, diabetes:** Numerous pilot studies and panels reported, but again **no routinely used VOC-based diagnostic tests** (Haworth et al., 2022; Pham & Beauchamp, 2021; Kaloumenou et al., 2022; Khoubnasabjafari et al., 2021; Van Der Schee et al., 2015; A. et al., 2021).
- **Infectious diseases (TB, invasive aspergillosis, C. difficile, malaria, SARS-CoV-2):** Multiple proof-of-concept and early clinical studies; some COVID-19 breathalyzer systems have provisional approvals in specific jurisdictions, but broad, fully validated adoption is still limited (Haworth et al., 2022; Pham & Beauchamp, 2021; Zheng et al., 2024; Kaloumenou et al., 2022; Amann et al., 2014; Binson et al., 2021).

Why So Few Validated Conditions?

Reviews emphasize bottlenecks: **non-standardized sampling/analysis**, small and heterogeneous cohorts, environmental confounding, and limited external validation. As a result, **very few endogenous breath VOC biomarkers have reached full clinical validation**, despite extensive research across many diseases (Haworth et al., 2022; Chan et al., 2020; Zheng et al., 2024; Khoubnasabjafari et al., 2021; Ibrahim et al., 2021; Bajo-Fernández et al., 2024; Van Der Schee et al., 2015; Binson et al., 2021).

Conclusion

Clinically validated, widely used breath diagnostics are currently confined mainly to **H. pylori urea breath tests** and **hydrogen/methane tests for gut function**. For most other conditions—including cancers, chronic lung diseases, GI, liver, cardiovascular, metabolic, and neurodegenerative diseases—breath analysis is promising and often accurate in studies, but VOC biomarkers remain in discovery or early validation stages rather than fully established clinical diagnostics.

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