

Abstract

Breath analysis is an exciting and innovative field that has demonstrated potential to dramatically increase survival rates by detecting diseases at earlier stages when treatment options are more effective, as well as enabling better management of chronic illnesses improving the health span of patients.

However, there is a lack of understanding and commercially available solutions needed to achieve reproducible and reliable data within the breath analysis community. This results in poor data comparability, inhibiting this important innovation from realising its full potential [1,2].

- Traceable and accurate quantification are key to underpinning data comparability and data confidence.
- Traceability and accuracy are ensured through calibration using primary reference materials, developed, maintained and disseminated by National Metrology Institutes like NPL.

NPL's expertise in gas metrology and standardisation can be repurposed for the medical sector to accelerate the uptake of breath analysis into routine clinical practice.

The need for early diagnostic tools

- Early-stage diagnosis is one of the most important factors affecting patient outcomes, particularly for diseases such as cancer.
- Providing new diagnostic techniques to enable earlier detection will support the NHS Long Term Plan goal of saving 55,000 lives per year by early detection of cancer [3].
- A colorectal cancer case study demonstrates the need for early diagnosis [4,5].

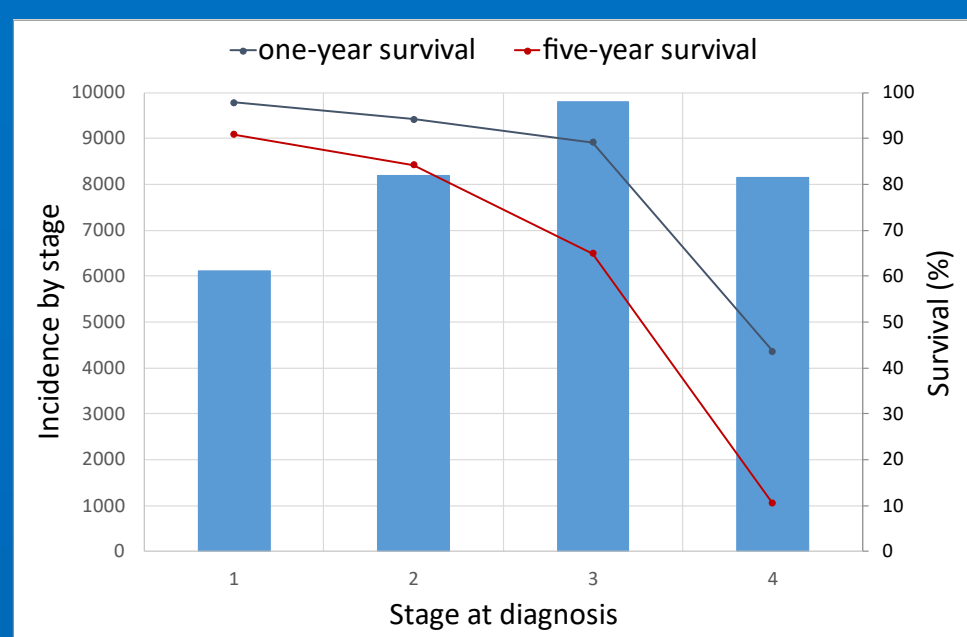


Figure 1. Incidence and survival of cancer cases by stage at diagnosis. 1-year survival rate more than doubles from 44 % to 98 % when diagnosed at stage 1 compared to stage 4. Based on a graphic created by Cancer Research UK.

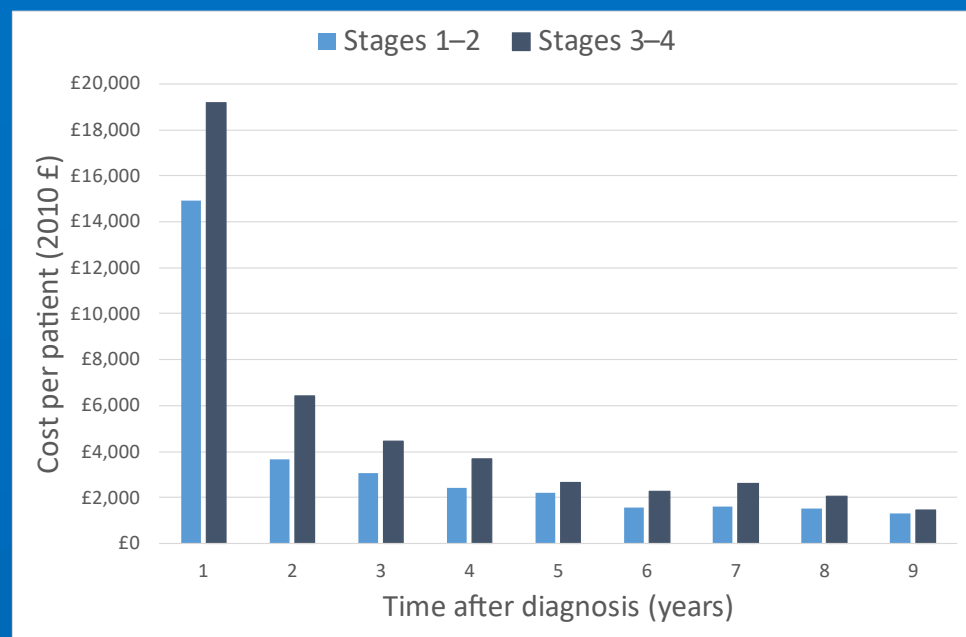


Figure 2. Cost per patient by number of years after diagnosis. Stage 3 and 4 diagnosis have an increased cost when compared to stage 1 and 2 diagnosis for each year after diagnosis.

Breath analysis for early disease diagnostics

- The breath analysis market has grown exponentially over the last two decades, as evidenced by the increase in peer reviewed publications and the number of clinical trials involving breath analysis [6].
- This hasn't translated into routine clinical practice
- Poor data comparability resulting in a lack of clinical confidence is a contributing factor [1,2] which NPL is perfectly positioned to address.

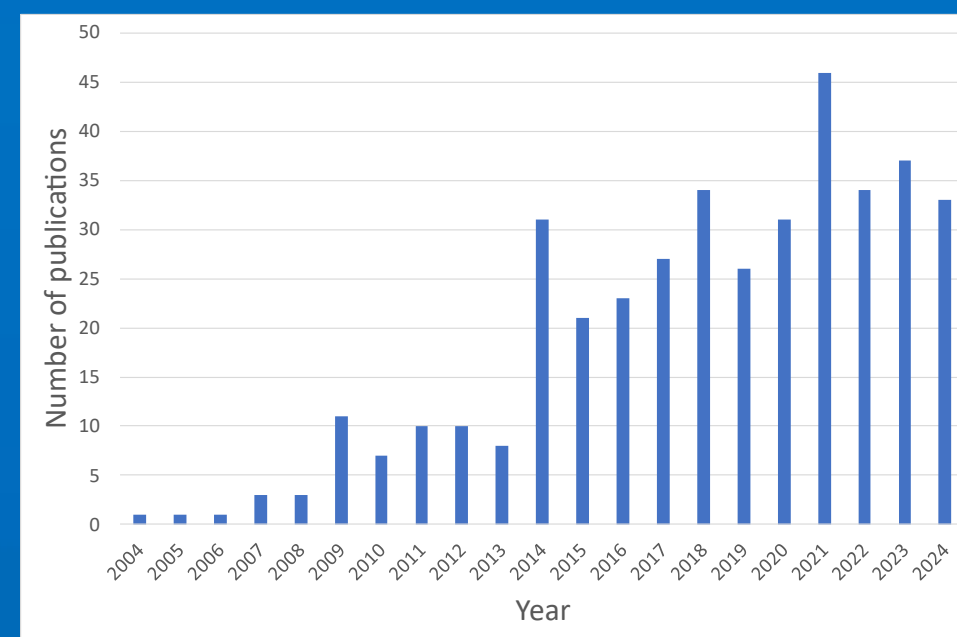


Figure 3. Number of hits in a PubMed search for "breath analysis disease detection" between 2004 and 2024 showing an increase in publications over the last two decades.

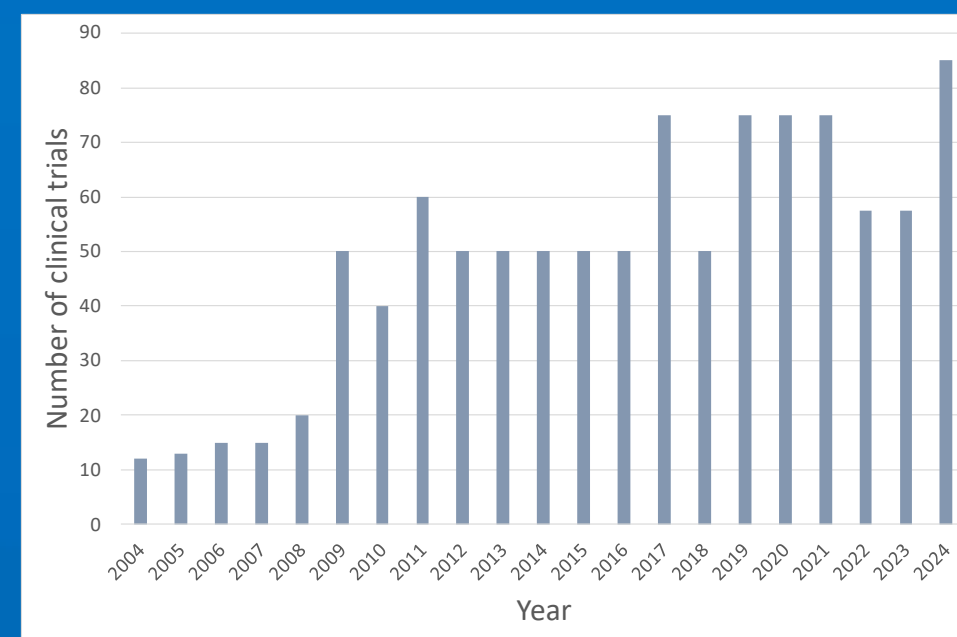


Figure 4. Number of clinical trials between 2004 and 2024 showing an increase in clinical trials over the last two decades. Credit: Owlstone Medical

Recent work at NPL

NPL delivered a Government Office of Technology Transfer Knowledge Asset Grant Fund (GOTT KAGF) project which engaged with academic and industrial stakeholders to review the barriers that negatively impact data comparability and clinical confidence in the breath analysis industry. The common findings from the stakeholder engagement are as follows:

- There is a lack of breath-specific reference materials available commercially.
- Regulatory bodies often do not know what criteria are needed to certify new breath analysis technologies.
- Breath is a challenging matrix to measure with the biomarkers of interest typically being present at low concentrations (nmol / mol or pmol / mol) compared to other compounds commonly found in exhaled breath (μmol / mol) [7].
- Patient to patient variability and contamination from exogeneous sources make identifying and quantifying biomarkers relevant to specific diseases very challenging.

Strategy for Enabling Clinical Confidence

NPL have developed an implementation strategy to exploit the findings from the GOTT project. This involves repurposing our Knowledge Assets in the following areas to maximise impact in the breath analysis community:

- Expertise in the development, preparation, analytical validation, control, dissemination and use of traceable gas reference materials that includes a wide range of volatile organic compounds (VOCs) and inorganic gases relevant to breath analysis.
- Expertise in considerations for accurate sampling and analysis of trace components in gas materials.
- Expertise in driving and delivering the development of international consensus such as through CEN and ISO standardisation committees.
- Expertise in the development and operation of interlaboratory comparison exercises, participation in which is essential for institutions wanting to demonstrate their capabilities against internationally recognised standards.

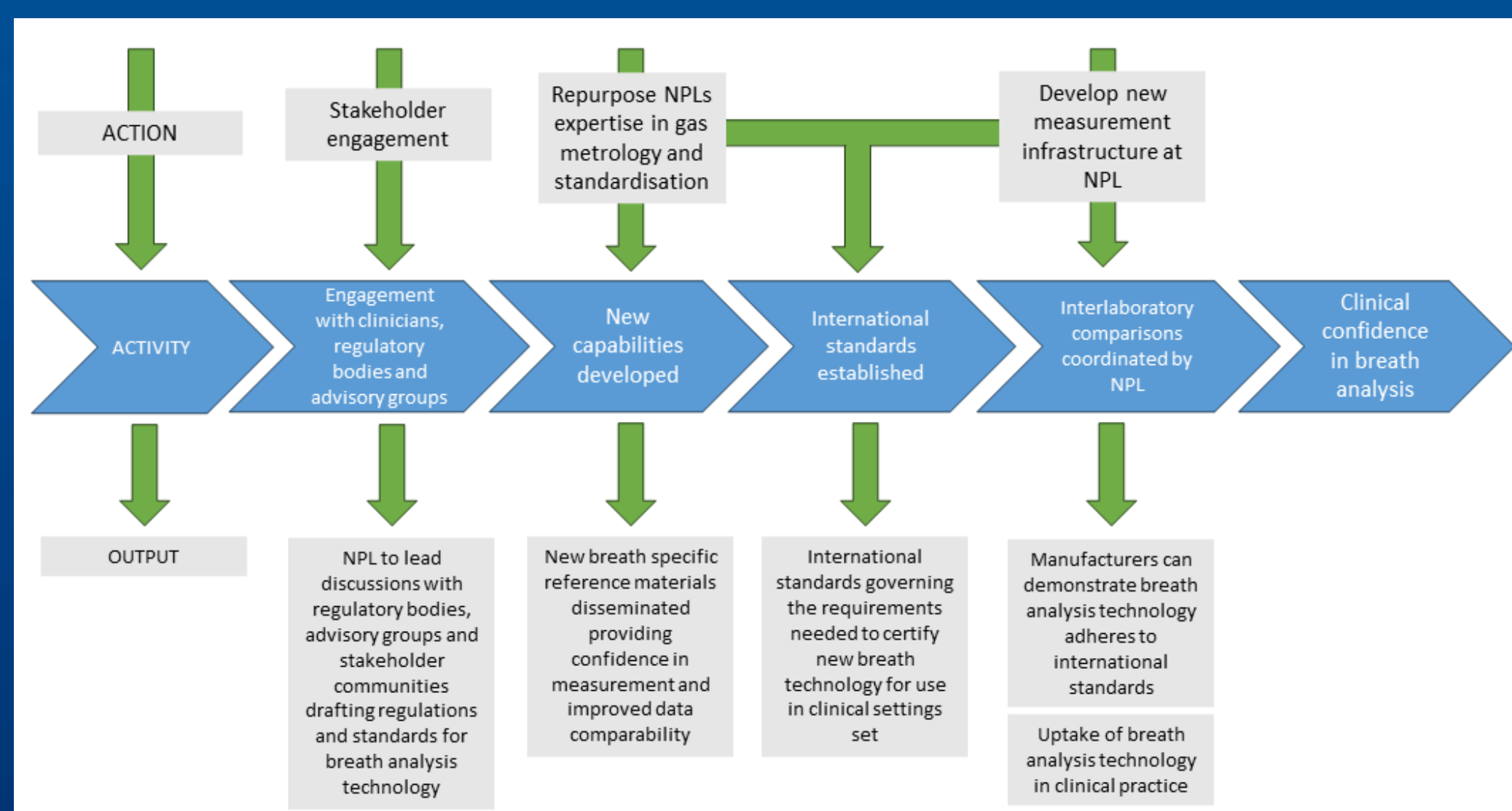


Figure 5. Implementation strategy developed by NPL in accelerate the uptake of breath analysis into routine clinical practice.