DETECT-ION

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CLARION

Point-of-Care Breath Diagnostics

Delivers Laboratory-Quality Results for Malaria and Tuberculosis Diagnostics in LMIC

WHITE PAPER

Executive Summary

CLARION, Detect-ION's point-of-care breath diagnostics platform, has been field-validated for the first time in a low- and middle-income country (LMIC) setting, yielding breath-based diagnostic tests for two of the world's highest-burden infectious diseases.

Detect-ION deployed the CLARION breath diagnostics platform at Makélékélé Hospital in Brazzaville, Republic of Congo, as part of the MATTHIAS (MAlaria and Tuberculosis breaTH dIAgnoStics) study funded by Gates Foundation: the first of its clinical validation of using breath volatile organic compounds (VOC) for diagnosis for malaria and tuberculosis (TB) in a co-endemic, resource-limited field setting.

Operating directly at the point of care, CLARION collected and analyzed exhaled breath from confirmed malaria-positive, TB-positive, and healthy control subjects, achieving 74% sensitivity and 77% specificity for malaria, and 90% sensitivity and 83% specificity for TB. Critically, the VOC biomarker signatures predictive of each disease were found to be biochemically distinct and non-overlapping, demonstrating that CLARION resolves independent, disease-specific molecular fingerprints from exhaled breath, even within a population where both diseases co-occur.

These findings establish three things of strategic importance: first, that breath-based VOC diagnostics are clinically viable in real-world field conditions; second, that CLARION's analytical architecture can simultaneously address multiple high-burden infectious diseases; and third, that the platform's diagnostic signal orthogonality lays the evidentiary foundation for a future multiplexed CLARION diagnostic: a single screening tool capable of co-screening malaria and TB from one breath specimen, at the point of care in near real time.

Problem Statement

Malaria and TB remain among the most devastating infectious diseases worldwide, with their greatest burden falling on sub-Saharan Africa (**Figure 1**). The World Health Organization estimates that malaria generated approximately 249 million cases and more than 600,000 deaths in 2022 alone[1], while TB continues to affect roughly 10.6 million people each year[2]. Despite meaningful advances in recent decades, persistent diagnostic gaps continue to undermine elimination efforts, particularly in resource-constrained settings where conventional diagnostic infrastructure is difficult to sustain.

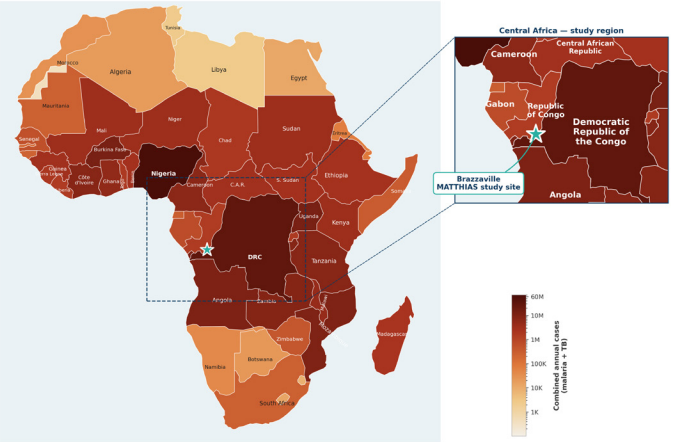


Figure 1. Geographic context of the MATTHIAS study. The Republic of Congo, highlighted within the African continent, sits at the epicenter of the world's highest dual burden of malaria and TB, making Brazzaville an epidemiologically deliberate choice for CLARION's first field validation.

Existing diagnostic modalities present substantial practical limitations in these environments. Microscopy, rapid diagnostic tests (RDTs), and molecular platforms such as GeneXpert each carry dependencies on specimen temperature stability, storage, and transport, trained laboratory personnel, and reliable supply chains that many endemic regions cannot consistently support. Malaria RDTs are further compromised by false-negative rates and the growing prevalence of *Plasmodium falciparum* strains harboring *hrp2/hrp3*[3,4] gene deletions, rendering the most widely deployed antigen-based tests unreliable. TB diagnostics face an equally challenging frontier, where patients with low bacillary loads routinely evade detection[5], sputum collection remains clinically difficult and inconsistent, and processing times extend diagnostic timelines by hours.

The Mission

Non-invasive breath analysis represents a potentially transformative shift in how both diseases are detected and managed at the population level. A validated breath-based diagnostic platform would eliminate the specimen collection barriers, cold-chain dependencies, and infrastructure overhead that currently exclude the most vulnerable patients from timely care. By enabling accurate, point-of-care detection from exhaled breath (requiring no needles, no sputum, and no laboratory), such a technology could extend diagnostic reach to remote clinics, community health workers, and mobile screening programs operating at the margins of existing healthcare systems. Earlier and more accurate identification of both malaria and TB cases would allow treatment to begin before disease progression and transmission, reducing the clinical severity of individual cases and lowering the per-patient cost of care. At a system level, redirecting healthcare expenditure away from late-stage treatment and repeated inconclusive diagnostics toward accurate early intervention could meaningfully stretch limited health budgets, ultimately translating fewer resources into more lives saved across the populations that bear the greatest burden of both diseases.

The Breath Quagmire and Detect-ION's Solution

Breath analysis as a diagnostic concept has been explored for decades yet has never achieved clinical mainstream adoption, and the biomedical community has seen this before. In the early 1980s, genomic sequencing carried extraordinary clinical promise and extraordinary barriers in equal measure. Platforms were room-sized, expensive, and specialist-operated. Protocols were unstandardized, reproducibility was poor, and the signal-to-noise problem seemed intractable. The promise was never in doubt; the instrument was the bottleneck. It was only with the arrival of next-generation sequencing (NGS) that standardized, reproducible measurement became possible at scale[6] - and with it, the clinical translation the field had long promised.

Breath analysis finds itself in the same quagmire. Traditional GC-MS platforms, the gold standard of VOC analysis, are large, expensive, and incompatible with point-of-care deployment. Breath collection protocols remain unstandardized, reproducibility across cohorts is poor, and isolating disease-specific VOC signatures from ambient contamination and metabolic noise has kept the field rich in biomarker candidates but chronically short on deployable solutions[7]. This has not been for lack of scientific interest - but for lack of a standardized measurement engine. CLARION is that engine that brings laboratory-grade breath analysis to the point of care, pairing standardized collection protocols with the analytical rigor needed to cut through noise and identify clinically actionable VOC signatures. Where NGS broke the genomics bottleneck, CLARION is designed to break this one.

Unlike traditional breath analysis where field collection and laboratory analysis are separate and logistically complex stages, CLARION integrates breath collection, chromatographic separation, mass spectrometric detection, and preliminary data analysis into a single point-of-care instrument (**Figure 2**). What currently requires sorbent tubes, shipping logistics, cold storage, and a trained scientist is collapsed into a 10-minute result, delivered at the bedside, in the rural clinic, or in the hands of a community health worker in the field. Other approaches that sidestep this pipeline, including those built on sensor architectures such as metal oxides, may also offer the logistical simplicity for deployment but forfeit the compound-level resolution that GC-MS provides for clinical decision-making. As a miniaturized GC-MS platform engineered specifically for decentralized deployment, CLARION brings laboratory-grade analytical specificity directly to the settings where diagnostic need is greatest and existing solutions have never reached. Where decades of breath biomarker research have produced compelling science without a viable delivery mechanism, CLARION provides the platform that finally makes clinical translation possible.

CLARION removes the final barrier between breath science and clinical reality by standardizing measurements where none existed before.
A portable, low-cost platform that doesn't just unlock diagnostics, it accelerates the science.

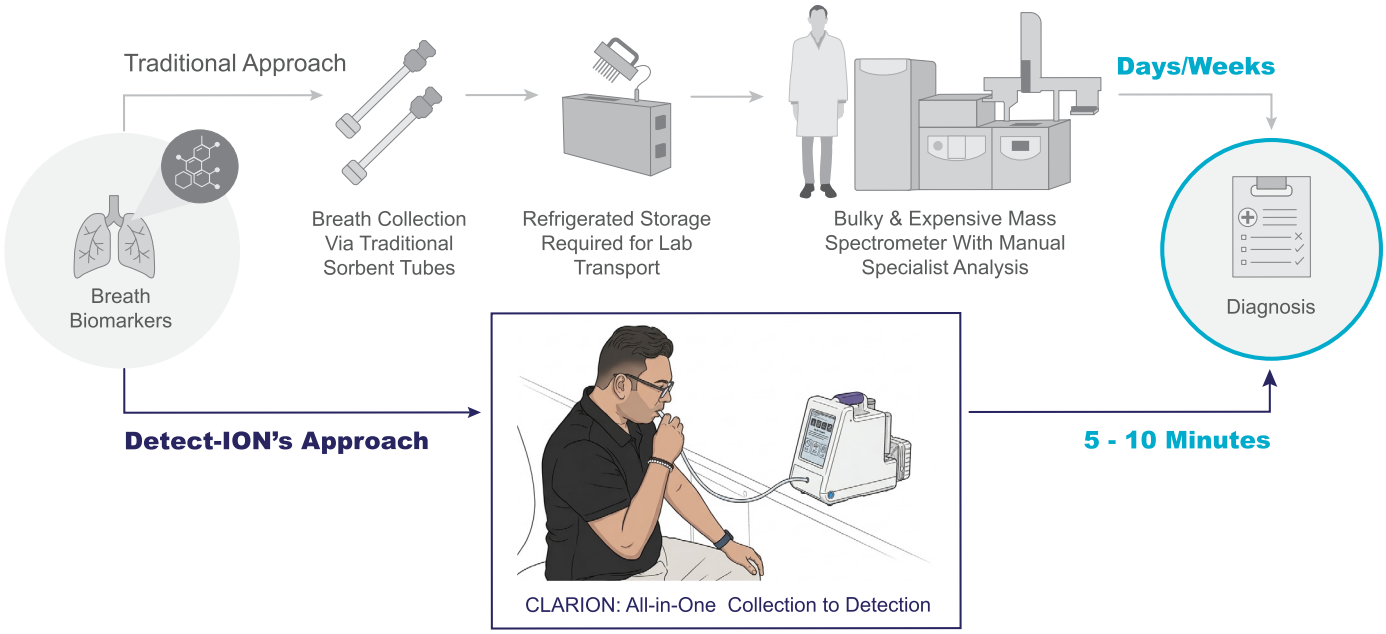


Figure 2. CLARION's integrated workflow reduces diagnostic time from days/weeks to under 10 minutes while eliminating sample transport and laboratory dependencies.

MATTHIAS Clinical Study

Validating breath biomarker diagnostics requires more than controlled laboratory conditions; it demands real-world deployment in the environments where both diseases are most prevalent and diagnostic infrastructure is most strained. To that end, Detect-ION deployed an early-stage variant of the platform, CLARION-α, directly in the field. Brazzaville, the capital of the Republic of Congo, was selected as the study site for deliberate scientific and epidemiological reasons: the city carries a high dual burden of malaria and TB, operates within a healthcare infrastructure representative of the broader sub-Saharan African context and hosts institutional partners capable of supporting rigorous clinical research. Significantly, engaging a site where both target diseases co-circulate within the same population allowed CLARION-α to be stress-tested against the precise diagnostic ambiguity (overlapping symptom presentations, co-infections, and variable pathogen loads) that any real-world breath diagnostic platform must be able to resolve. The resulting clinical investigation, designated the MATTHIAS study, was conducted in two phases (Human Trial 1 [HT-1] and Human Trial 2 [HT-2]) between August and December 2025 at Makélékélé Hospital in Brazzaville, as described in **Table 1**. The study was executed in collaboration with Labyrinth Global Health (LGH), whose established regional presence and clinical research infrastructure were instrumental in enabling site access and study execution, and through LGH's partnership with the Laboratoire National de Santé Publique (LNSP), the Republic of Congo's national public health laboratory (**Figure 3**).

Figure 3. Detect-ION team visiting the Brazzaville site to train local partners and clinicians on the CLARION-α system.

Figure 4. A subject in Brazzaville exhaling into the CLARION-α system to provide a specimen for subsequent breath analysis during HT-1.

This collaboration ensured that reference diagnostics were conducted to national laboratory standards, lending the study both scientific rigor and local institutional credibility. The cross-sectional design enrolled adults presenting with symptoms suggestive of malaria or TB, and quantitative polymerase chain reaction (qPCR) and GeneXpert served as reference standards against which CLARION-α's breath-based VOC detection was benchmarked. In parallel, paired breath specimens were collected; first a specimen was collected and analyzed in CLARION-α (as shown in **Figure 4**) and then another collected on sorbent tubes and archived for independent analysis by high-resolution mass spectrometry (HRMS) back at Detect-ION's lab in Tampa, FL. This provided an orthogonal analytical layer to corroborate CLARION-α's VOC findings and strengthen the evidentiary foundation of the dataset.

Table 1. MATTHIAS study design, summarizing cohort composition, reference standards, and VOC biomarker validation methods.

	HT-1: Malaria	HT-2: TB
Dates	Aug - Oct 2025	Nov - Dec 2025
Positive cases	18 malaria-positive	48 TB-positive
Controls	96 malaria-negative	55 TB-negative
Reference standard	qPCR	GeneXpert MTB/RIF PCR Assay
VOC biomarker validation method	Agilent QTOF HRMS	Agilent QTOF HRMS

MTB/RIF: Mycobacterium tuberculosis/rifampin assay; QTOF: quadrupole time-of-flight.

Data Analysis

CLARION-α's on-site analytical capability enabled breath VOC detection in near real-time, with instrument data transmitted back to Detect-ION's laboratory in Florida for concurrent analysis by the data science team as the study progressed. Simultaneously, breath specimens collected on sorbent tubes underwent site-level decontamination protocols before being shipped to the Detect-ION facility for HRMS processing, providing an independent corroborating dataset against which CLARION-α's outputs were validated. Back in the Detect-ION lab, a rigorous multi-stage data processing pipeline was applied to the full breath dataset: background subtraction to isolate endogenous VOC signals from ambient and instrumental noise, signal denoising to improve spectral clarity, and systematic feature extraction to identify candidate VOC biomarkers across the cohort. The resulting feature sets were then subjected to multivariate statistical analysis to develop and internally validate diagnostic classification models for both malaria and TB, setting the stage for the key performance findings that follow.

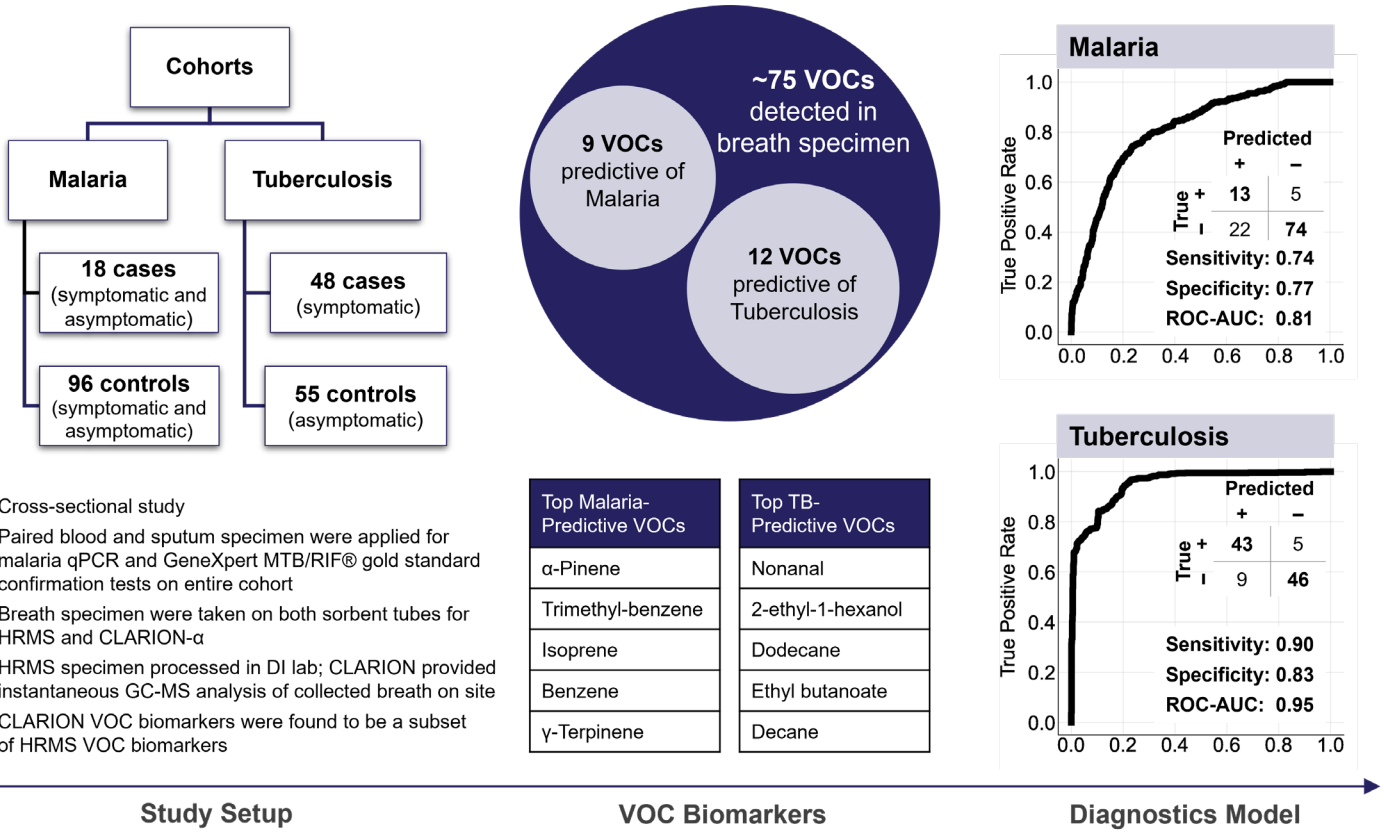
Key Results

VOC Biomarker Discovery and Validation

The HRMS analysis of archived sorbent tube specimens played a pivotal role in anchoring the biological interpretation of CLARION-α's outputs. HRMS's superior mass accuracy and resolving power enabled unambiguous molecular identification of flagged VOCs, assigning precise molecular formulae and structural candidates to compounds that CLARION-α identified as diagnostically relevant, transforming candidate signals into chemically characterized biomarkers. Of equal significance was a finding that emerged from leave-one-out cross-validation of the predictive models: the VOC signatures for malaria and TB were biochemically distinct from one another. Despite the symptomatic overlap between the two diseases during their early phases and the co-endemic nature of the study population, each condition was predictable using a discrete, non-redundant biomarker fingerprint (**Figure 5**). This molecular separability demonstrates that CLARION-α is not detecting a generalized host response to infection but resolving disease-specific metabolic perturbations, a prerequisite for any breath diagnostic intended to operate in settings where malaria and TB co-circulate and clinical differentiation between them is consequential.

Diagnostics Model Accuracy Based on Breath VOC Biomarkers

CLARION-α demonstrated meaningful diagnostic performance across both target diseases, seen in **Figure 5**.



- Cross-sectional study
- Paired blood and sputum specimen were applied for malaria qPCR and GeneXpert MTB/RIF® gold standard confirmation tests on entire cohort
- Breath specimen were taken on both sorbent tubes for HRMS and CLARION-α
- HRMS specimen processed in DI lab; CLARION provided instantaneous GC-MS analysis of collected breath on site
- CLARION VOC biomarkers were found to be a subset of HRMS VOC biomarkers

Top Malaria-Predictive VOCs	Top TB-Predictive VOCs
α-Pinene	Nonanal
Trimethyl-benzene	2-ethyl-1-hexanol
Isoprene	Dodecane
Benzene	Ethyl butanoate
γ-Terpinene	Decane

Figure 5. MATTHIAS study overview showing cohort enrollment, VOC biomarker discovery (~75 VOCs detected with 9 malaria-predictive and 12 TB-predictive compounds), and diagnostic model performance achieving receiver operating characteristic area under the curve (ROC-AUC) of 0.81 for malaria and 0.95 for TB.

Beyond classification performance, the biological validity of CLARION-α's findings was firmly established. The VOC biomarkers driving both diagnostic models aligned closely with compounds reported in the published breath analysis literature: for malaria, detected compounds including α-pinene, benzene, terpinene, and isoprene reflected VOCs found in infected individuals' breath and in prior peer-reviewed studies[8,9] and known mosquito attractants[10], while for TB, nonanal, dodecane, and decane similarly corresponded to established literature-validated biomarkers[11,12]. Importantly, the predictive VOC signatures identified by CLARION-α were independently corroborated by the HRMS analysis of archived breath specimens. The key biomarkers flagged by the CLARION models appeared as a consistent subset within the HRMS-derived feature set, providing orthogonal confirmation that the platform is detecting real disease signal rather than instrument artifacts.

One breath sample. Two diseases. No cross-interference. CLARION shows the potential for a single non-invasive sample to simultaneously screen for malaria and TB without compromising specificity.

Vision: Scaling Breath Diagnostics for Global Impact

The MATTHIAS study represents Detect-ION's first clinical validation of breath-based VOC diagnostics for malaria and TB in a real-world, co-endemic field setting; and marks an exciting starting point rather than a finish line. The findings from CLARION-α inform a clear and deliberate development roadmap. Building on the analytical architecture validated in Brazzaville, Detect-ION has developed CLARION-β, a next-generation prototype explicitly engineered for remote and decentralized deployment. Where CLARION-α was designed to prove science, CLARION-β is designed to deliver on-site highly specific diagnostics at scale.

The strategic shift embedded in CLARION-β's design philosophy is fundamental: rather than requiring patients to travel to centralized healthcare facilities, CLARION-β will go to the patients (**Figure 6**). Optimized for portability, operational simplicity, and deployment resilience in low-infrastructure environments, the platform can function in the hands of community health workers, mobile screening teams, and field clinicians operating far beyond the reach of hospital laboratories. CLARION-β will invert the traditional diagnostic model and directly address the last-mile access problem, bringing timely diagnosis to the highest-burden populations.

Figure 6. Envisioned deployment of CLARION-β, reflecting Detect-ION's commitment to translating rigorous breath biomarker science into a platform that is not only analytically capable, but physically deployable where it matters most.

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