

## Feasibility of GeneXpert® Edge for Tuberculosis Diagnosis in Difficult-to-Reach Populations: Preliminary Results of a Proof-of-Concept Study

Marcelo Cordeiro-Santos,<sup>1,2,3\*</sup> Jair dos Santos Pinheiro,<sup>3,4</sup> Renata Spener-Gomes,<sup>1,2</sup> Alexandra Brito de Souza,<sup>1,2</sup> Maria Gabriela de Almeida Rodrigues,<sup>1,2</sup> Jayne Marina Pinto da Silva,<sup>1</sup> Jaqueline Silva Jesus,<sup>1</sup> Daniel Souza Sacramento,<sup>4</sup> Artemir Coelho de Brito,<sup>5</sup> Mayara Lisboa Soares de Bastos,<sup>6</sup> Allyson Guimarães Costa,<sup>1,2</sup> and Anete Trajman<sup>6</sup>  
<sup>1</sup>Fundação de Medicina Tropical Dr. Heitor Vieira Dourado (FMT-HVD), Manaus, Amazonas, Brazil; <sup>2</sup>Universidade do Estado do Amazonas, Manaus, Amazonas, Brazil; <sup>3</sup>Universidade Nilton Lins, Manaus, Amazonas, Brazil; <sup>4</sup>Secretaria Municipal de Saúde, Manaus, Amazonas, Brazil; <sup>5</sup>Ministério da Saúde do Brasil, Brasília, Brazil; <sup>6</sup>Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil

**Abstract.** GeneXpert® Edge (GX-Edge) is a new point-of-care platform not yet tested in the field. In this proof-of-concept study conducted for the diagnosis of tuberculosis in communities living alongside two large rivers of the Brazilian Amazon, we demonstrate that GX-Edge implemented in boats to offer onsite testing is a feasible strategy to investigate potentially devastating diseases such as tuberculosis in difficult-to-reach populations, such as riverside communities.

Located in the heart of the Amazon rainforest, Amazonas is the Brazilian state with the highest incidence rate of tuberculosis (TB), 75.9/100,000 inhabitants, more than the double of the national average.<sup>1</sup> About 1% of the 2 million inhabitants of Manaus, the state capital, live in riverside communities by the Negro and the Amazon rivers (Figure 1), a difficult-to-reach population.

Xpert® MTB/RIF is a molecular test endorsed by the WHO in 2010 for the rapid diagnosis of TB and rifampicin resistance.<sup>2</sup> The cartridge generation Ultra has higher sensitivity for pulmonary TB, 89.2% as compared to 77.9% of Xpert® MTB/RIF.<sup>3</sup> The test is run in the GeneXpert® system, which can also detect other infectious agents such as the respiratory syncytial virus and influenza viruses. Recently, a SARS-CoV-2 cartridge was approved by the U.S. Food and Drug Administration.<sup>4</sup> GeneXpert® is not considered a point-of-care test because it requires laboratory infrastructure, including electricity supply. Launched in 2018, the GeneXpert® Edge (GX-Edge) is a new generation platform meant to be used by health services with limited infrastructure. GX-Edge is a single-slot platform (one test per cycle), powered by a charged battery or electricity, and uses a 2-in-1 tablet/laptop and a compact printer. However, its feasibility and acceptability have not yet been tested in the field.<sup>5</sup>

The AmazonEdge project is a 2-year prospective study designed to analyze the feasibility, acceptability, and impact of GX-Edge in riverside communities on the outskirts of Manaus. The protocol was approved by the Research Ethics Committee in Fundação de Medicina Tropical Dr. Heitor Vieira Dourado (process #3.719.859) on September 13, 2019. The Committee waived the researchers from obtaining informed consent because health assistance was carried out as per routine, and the procedure had the potential to expedite TB diagnosis and treatment, with no foreseen harm. Compensation for study participation was not offered.

Residents of all riverside communities by the Negro and the Amazon rivers have been assisted by two existing fluvial primary healthcare facilities of Manaus Health Department since

2012. Boats travel alternately alongside the rivers for 10 days monthly. Services include TB diagnosis and treatment. Residents with respiratory symptoms of any duration are identified by the community leaders of each village 24–48 hours before the boat's scheduled arrival and referred to their health services. Sputum samples are collected on site and transported to the reference TB laboratory in Manaus for GeneXpert® processing. In 2017, 381 sputum samples were collected, in six of which *Mycobacterium tuberculosis* DNA was detected. Because of the trip routine, the delay between sputum collection and test results was, in average, 15 days. Medication is then provided during the following trip, which results in further delay for treatment initiation, despite the 2-hour result device.

During the first phase of this ongoing study, we evaluated the feasibility of the platform in this scenario. Residents referred for productive cough of any duration were included in the study if sputum was provided. The GX-Edge system was installed in both boats, and Ultra tests were carried out on site for all participants. Remaining sputum aliquots of each sample were kept at 2–8°C storage in dry ice in boxes with temperature control during the remaining of the trip and then transported to the reference laboratory in Manaus to confirm the results by solid culture (Löwenstein–Jensen medium) for *Mycobacterium tuberculosis* and by a second Ultra test. Healthcare professionals in the boats were trained to immediately start TB treatment if the test was positive; the boats were equipped with a fixed dose combination of the standard regimen in Brazil (rifampicin, isoniazid, pyrazinamide, and ethambutol).

During six trips performed between January 8, 2020 and March 26, 2020, 39 eligible persons from 21 riverside communities were identified, and all provided sputum. The mean ( $\pm$ SD) age was  $44 \pm 19$  years, 63% were male, and 5% were indigenous. None had TB and no error results were reported. All negative results were confirmed in aliquots successfully kept between 2°C and 8°C, as per temperature registries. The fully charged battery was sufficient to perform four TB tests daily, which met the demand of each community. The battery was charged between communities using the boats' generator. The study is currently on hold because of the COVID-19 pandemic.

Based on these very preliminary findings, we believe that the use of the GX-Edge platform in mobile transportation such

\* Address correspondence to Marcelo Cordeiro-Santos, Fundação de Medicina Tropical Dr. Heitor Vieira Dourado (FMT-HVD), Av. Pedro Teixeira, 25, Dom Pedro, Manaus, Amazonas, Brazil. E-mail: marcelocordeiro@uea.edu.br

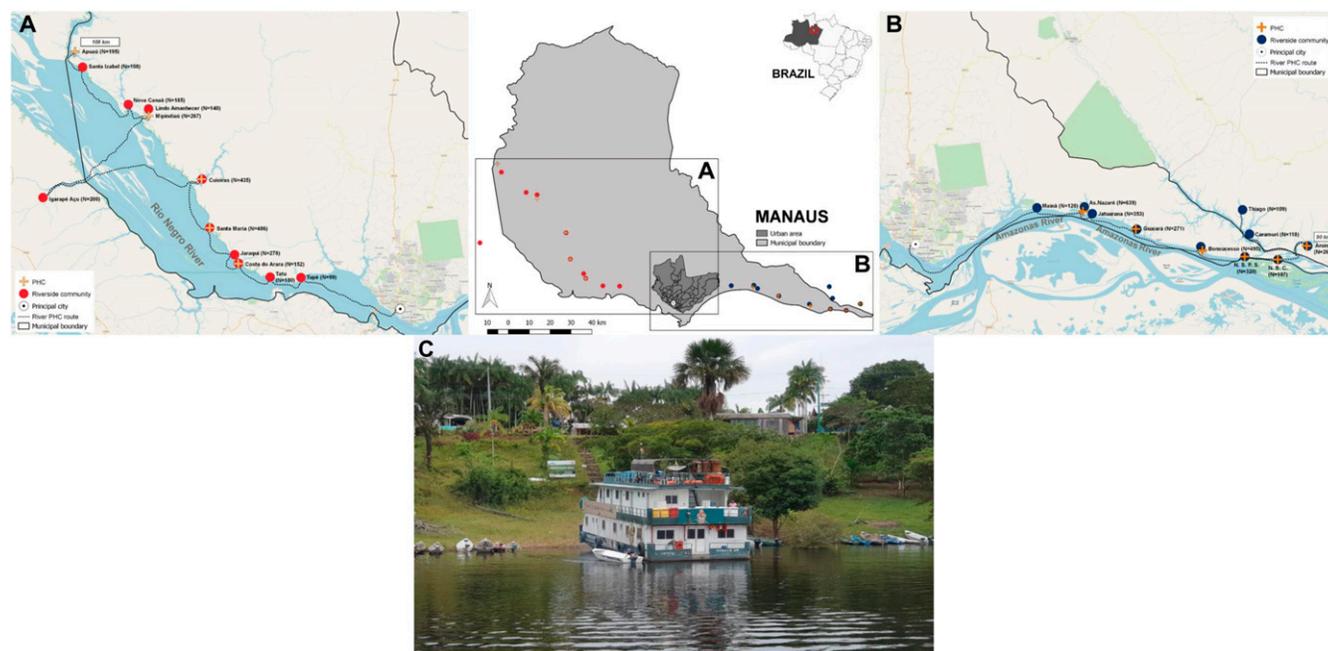


FIGURE 1. Spatial distribution of primary healthcare centers in Manaus city, Amazonas State, Brazil. (A). Riverside communities of the Negro River; (B). riverside communities of the Amazon River; (C). fluvial primary health care. This figure appears in color at [www.ajtmh.org](http://www.ajtmh.org).

as these boats is a feasible strategy to investigate TB and possibly other infectious diseases in difficult-to-reach populations, such as riverside communities. At this moment where COVID-19 is rapidly spreading in Amazonas State from the capital to the interior, namely, to riverside and indigenous communities, our experience with TB testing could be assessed for other potentially devastating diseases. Avoiding displacement of remote populations to urban areas is essential to protect vulnerable populations, offer rapid diagnosis and treatment, and ultimately save lives. The acceptability and impact of the GX-Edge for diagnosing TB in this population remain to be explored. We intend to resume the study as soon as possible.

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Authors' addresses: Marcelo Cordeiro-Santos, Renata Spener-Gomes, Alexandra Brito de Souza, Jayne Marina Pinto da Silva, Jaqueline Silva Jesus, and Allyson Guimarães Costa, Fundação de Medicina Tropical Dr. Heitor Vieira Dourado (FMT-HVD), Manaus-AM, Brazil, E-mails: [marcelocordeiro@uea.edu.br](mailto:marcelocordeiro@uea.edu.br), [renataspenergomes@gmail.com](mailto:renataspenergomes@gmail.com), [xandra.bsouza@gmail.com](mailto:xandra.bsouza@gmail.com), [jaympinto@gmail.com](mailto:jaympinto@gmail.com), [ilanesj@gmail.com](mailto:ilanesj@gmail.com), and [allyson.gui.costa@gmail.com](mailto:allyson.gui.costa@gmail.com). Jair dos Santos Pinheiro and Maria Gabriela de Almeida Rodrigues, Universidade do

estado do Amazonas, Manaus-AM, Brazil, E-mails: [jpsantos.jair@gmail.com](mailto:jpsantos.jair@gmail.com) and [rodriguesgabriela016@gmail.com](mailto:rodriguesgabriela016@gmail.com). Daniel Souza Sacramento, Secretaria Municipal de Saúde, Manaus-AM, Brazil, E-mail: [dsacramento.am@gmail.com](mailto:dsacramento.am@gmail.com). Artemir Coelho de Brito, Departamento de Condições Crônicas e Infecções Sexualmente Transmissíveis, Ministério da Saúde do Brasil, Esplanada dos Ministérios, Brasília-DF, Brazil, E-mail: [artemir.brito@saude.gov.br](mailto:artemir.brito@saude.gov.br). Mayara Lisboa Soares de Bastos and Anete Trajman, Instituto de Medicina Social, Universidade do Estado do Rio de Janeiro, Maracanã, Rio de Janeiro-RJ, Brazil, E-mails: [mayara\\_bastos@yahoo.com.br](mailto:mayara_bastos@yahoo.com.br) and [atrajman@gmail.com](mailto:atrajman@gmail.com).

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