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## Short Communication

# Cost analysis of GenoType® MTBDRplus and GenoType® MTBDRsl at the State Laboratory of São Paulo, Brazil

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## ABSTRACT

**Background:** We aimed to evaluate the costs of GenoType® MTBDR*plus* and MTBDR*sl* incurred during the diagnosis of first- and second-line drug-resistant tuberculosis (TB) in São Paulo, Brazil.

**Methods:** Mean and activity-based costs of GenoType® were calculated in a referral laboratory for TB in Brazil.

**Results:** The mean cost value and activity-based cost of GenoType® MTBDR*plus* were USD 19.78 and USD 35.80 and those of MTBDR*sl* were USD 54.25 and USD 41.85, respectively.

**Conclusions:** The cost of GenoType® MTBDR*plus* was reduced owing to the high number of examinations performed and work optimization.

**Keywords:** Line Probe Assay. Multidrug-resistant tuberculosis. Molecular diagnosis. Mean Cost. Tuberculosis.

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (MTB) is a major global health concern. Approximately 6.4 million new cases of TB were reported in 2021[1]. Although Brazil is not a high-burden country for multidrug-resistant TB (MDR-TB), the underdetection of these cases has reached 67.1% according to World Health Organization (WHO) data[1]. The COVID-19 pandemic has negatively affected the search for people with drug-resistant tuberculosis (DR-TB) and the transmission of resistant strains, with a possible increase in primary resistance. In 2022, 1,104 new cases of DR-TB were diagnosed in Brazil[2].

Most patients with drug-sensitive TB can be treated with shortened first-line regimens with high efficacy. However, in recent years, the increasing number of cases of MDR-TB, which is characterized by resistance to the most effective drugs, such as rifampicin (RIF) and isoniazid (INH), and extensively drug-resistant TB (XDR-TB), which is resistant to drugs such as INH, RIF, and second-line drugs (fluoroquinolone, bedaquiline, and/or -linezolid), has become a threat to public health. MDR-TB and XDR-TB require long, expensive, and less effective treatments; furthermore, these TB forms are associated with a high occurrence of adverse effects and mortality[3].

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**Conflict of Interest:** All authors declare no conflict of interests.

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To improve the fight against TB, the WHO has advocated the use of molecular methods to detect MDR-TB and XDR-TB since 2008[4]. The early and adequate diagnosis of MDR/XDR-TB is key to achieving the "End TB Strategy," which defines goals to be met for the prevention, care, and control of TB from 2016 to 2035[5,6].

Cost refers to the value of all the resources invested in performing an activity, including evaluation via diagnostic tests[6]. The mean cost was calculated by dividing the total cost by the quantity produced in the analyzed time interval. Activity-based cost (ABC) analyzes the direct and indirect costs appropriate for complex organizations that consume resources heterogeneously, providing greater accuracy in determining testing costs[7].

The accuracy and cost of conventional and molecular methods for the diagnosis of MDR-TB have been described in several countries[8-10], including Brazil[11-13]. However, data on the costs incurred with the use of molecular tests in Public Health Laboratories are scarce, and the information obtained can be used to optimize resource management health services in countries with a unified health system, such as Brazil, particularly with the recent incorporation of GenoType® MTBDR*plus* and GenoType® MTBDR*sl*[14].

Therefore, the objective of this study was to evaluate the mean cost and ABC of the GenoType® MTBDR*plus* and GenoType® MTBDR*sl* tests for the detection of MDR/XDR-TB in clinical isolates at the State Referral Laboratory of Public Health, Brazil.

Cost analysis was performed at the State Laboratory of Public Health of the State of São Paulo, Instituto Adolfo Lutz (IAL). The mean and ABC for the laboratory diagnostic tests GenoType® MTBDR*plus* and MTBDR*sl* (Hain Lifescience, Nehren, Germany), which detect resistance to RIF and INH and second-line drugs (quinolones and injectable drugs, capreomycin, kanamycin, and amikacin), respectively, were calculated according to the data points "infrastructure," "human resources," "inputs," and "equipment."

For such analyses, MTB clinical isolates from the laboratory network in the state of São Paulo, which produce cultures to detect resistance to first- and second-line drugs, were evaluated by the IAL. Initially, the MTB clinical isolates were subjected to the GenoType® MTBDR*plus* test to detect resistance to INH and/or RIF. Isolates resistant to any of these drugs were subjected to a GenoType® MTBDR*sl* test using the same DNA. In total, 600 GenoType® MTBDR*plus* and 45 GenoType® MTBDR*sl* tests were included in the analysis. Data were collected from May 2020 to May 2021 and the evaluation was performed as described in the Cost Technical Manual[7]. The authors declare no conflict of interest.

The costs are expressed in US dollars (USD) according to the conversion rate of USD 1.00 = R$ 5.27 as established by the Brazil Central Bank in December 2022. This study was approved by the Research Ethics Committee (CAAE number: 21762719.6.1001.5257) and followed the recommendations of the Ministry of Health[15].

**Figure 1.** Components of the mean cost and activity-based cost (ABC), where the "Inputs" consisting of the largest component of the mean cost in the GenoType® MTBDR*plus* and "human resources" in the GenoType® MTBDR*sl* are observed. The biggest component for ABC was "human resources" in both trials.

**Table 1.** Total values of the mean cost and activity-based cost (ABC) in US dollars and reais (official Brazilian currency). The mean cost was lower than the ABC in the GenoType® MTBDR*plus* and higher in the Genotype® MTBDR*sl*.

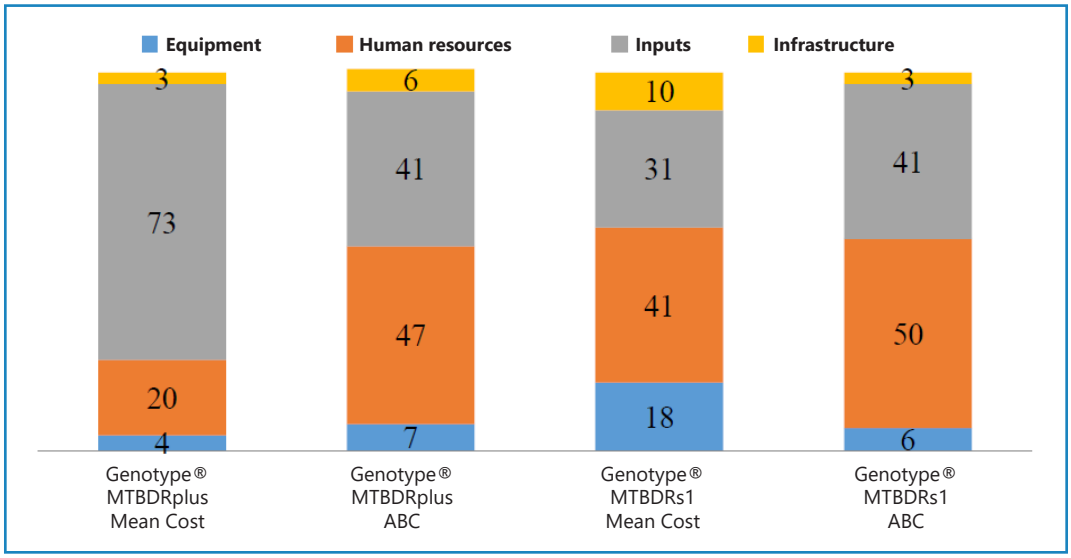


**FIGURE 1:** Components of mean cost and activity-based cost (ABC) of Genotype® MTBDR*plus* and MTBDR*sl* (%).

**TABLE 1:** Mean cost and activity-based cost.

| Method | Samples/Month | Mean Cost (US$) | Mean Cost (Real) | ABC (US$) | ABC (Real) |
|---|---|---|---|---|---|
| Genotype® MTBDR*plus* | 600 | 19.78 | 104,26 | 35.80 | 188,64 |
| Genotype® MTBDR*sl* | 45 | 54.25 | 285,82 | 41.85 | 220,57 |

USD 1.00 = R$ 5,27; ABC: activity-based cost.

By calculating the mean cost and ABC, the lower cost of the GenoType® MTBDR*plus* was observed in relation to MTBDR*sl* owing to the optimization of the work during both tests in the IAL. The "input" was the component with the greatest impact on the mean cost in the GenoType® MTBDR*plus* in relation to MTBDR*sl*. Because the DNA extracted is reused when resistance is detected in the GenoType® MTBDR*plus*, there are fewer "inputs" in the MTBDR*sl*.

"Human Resources" was the component with the greatest impact on ABC in both GenoType® MTBDR*plus* and MTBDR*sl*, as the process is not fully automated. These results are similar to those of Soares et al. for a study conducted in a tertiary referral hospital in Minas Gerais, Brazil[11].

ABC analysis better reflects costs by providing the true value of the examinations, whereas the mean cost depends on the number of tests performed[7]. The mean cost of GenoType® MTBDR*sl* was higher than that of GenoType® MTBDR*plus* because a smaller number of second-line tests were performed (45 per month). This shows that an increase in the number of tests performed leads to lower costs, consistent with the workload of the IAL, which has a high demand for these tests. A similar result was observed in Minas Gerais, where the mean cost was higher than the ABC owing to the small number of tests performed[13].

GenoType® has been incorporated into the Brazilian Unified Health System for the rapid detection of MDR-TB since July 2021; however, few cost studies have been conducted in public health referral laboratories before its incorporation. Although a cost-effectiveness analysis was not performed in this study, another study carried out by the same group showed that the turnaround time (TAT) for the release of MDR isolates is shorter when compared to susceptibility testing with the MGIT 960 system, therefore being dominant in a cost-effectiveness analysis[11].

Certain Brazilian studies have also evaluated ABC as a diagnostic method; for the identification test, bacilloscopy had an ABC of US$ 6.01 and a subsidized Xpert of US$ 10.86[12]. For the cost evaluation of sensitivity methods, the GenoType® MTBDRplus molecular test was US$ 48.38[12] and, in our study, the ABC of GenoType was US$ 35.80; the difference are due to the differences in the laboratories where the studies were performed. The phenotypic methods had higher costs, with US$ 76.56 for the sensitivity test for each drug using BACTEC MGIT 360 and US$ 136.80 for the proportion method[11].

In a study conducted in a tertiary hospital in China, the costs were lower in the diagnosis of MDR-TB using GenoType® owing to the reduction of the TAT for result release, but the authors did not include the costs of the multiple components[9]. In another study conducted in Russia[10], the use of GenoType® in routine DR-TB investigations, compared with the use of MGIT 960, was associated with a lower cost and greater success in the treatment of DR-TB.

It is important to emphasize that, in Brazil, variations in the dollar exchange rate and the commercialization of the first- and second-line Genotype® kits by a single company are factors that impact the increase and oscillation of costs.

A limitation of this study is the accuracy of the molecular tests obtained in the IAL, which were not analyzed. In addition, these values cannot be extrapolated to other locations because each laboratory has differences in the components analyzed.

Cost calculations are important and should be used in decision-making by managers and administrators to evaluate the incorporation of diagnostic tests in health institutions. ABC in particular is the best method of evaluating the costs of techniques to provide the real value of testing.

In the present study, we conclude that the costs of GenoType® MTBDR*plus* were lower than those of GenoType® MTBDR*sl* owing to the high number of MTBDR*plus* tests performed in the IAL and work optimization.

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