Budgetary impact of using BPaL for treating extensively drug-resistant tuberculosis


INTRODUCTION

The increasing burden of drug-resistant tuberculosis (TB) is a significant public health concern. Particularly, the problem of providing appropriate treatment to those with extensively drug-resistant TB (XDR-TB)—defined for the purpose of this study as patients with multidrug resistant TB (MDR-TB), whose TB strains are also resistant to at least one of the four first-line drugs (isoniazid, rifampicin, ethambutol and streptomycin) and at least one of the four second-line drugs (fluoroquinolones, second-line injectable agents, second-line oral agents, and at least one of aminoglycosides)—is a major concern. The rapid adoption of the BPaL regimen to address the high drug-resistant TB burden in countries fighting against a high drug-resistant TB burden can lead to significant programmatic and clinical challenges in managing patients with XDR-TB in high DR-TB burden countries.

Methods

- Per-patient treatment cost of BPaL regimen was compared head-to-head with the conventional XDR-TB treatment regimen for respective countries based on cost estimates primarily assessed using microcosting method and expected frequency of each TB service. The 5-year budget impact of gradual introduction of BPaL against the status quo was assessed using a Markov model that represented patient’s treatment management and outcome pathways.

Results

- The cost per patient completing treatment with BPaL was US$7142 in Indonesia, US$4782 in Kyrgyzstan and US$7152 in Nigeria—57%, 78% and 68% lower than the conventional regimens in the respective countries. A gradual adoption of the BPaL regimen over 5 years would result in a 5-year average national TB service budget reduction of 17% (US$128 780) in XDR-TB treatment-related expenditure in Indonesia, 15% (US$700 247) in Kyrgyzstan and 32% (US$1 543 047) in Nigeria.

Conclusion

Our study demonstrates that the BPaL regimen can be highly cost-saving compared with the conventional regimens to treat patients with XDR-TB in high drug-resistant TB burden settings. This supports the rapid adoption of the BPaL regimen to address the significant programmatic and clinical challenges in managing patients with XDR-TB in high DR-TB burden countries.

Key questions

- What is already known?
  - Conventional treatment for extensively drug-resistant tuberculosis (XDR-TB) is highly costly to both the health systems and to the patients—posing significant challenges in treatment adherence and ultimately treatment outcomes.
  - A 6-month novel regimen (bedaquiline, pretomanid and linezolid; BPaL) containing three oral medications—pretomanid, bedaquiline and linezolid—developed by the Global Alliance for TB Drug Development (TB Alliance) received regulatory approval from the US Food and Drug Administration in 2019, and the WHO announced it recommends its use under operational research conditions.

- What are the new findings?
  - Our study is the first study to empirically assess costs of health service components for patients with XDR-TB and quantify the budget impact of switching to the BPaL regimen in three geographically diverse high drug-resistant TB burden countries.
  - On a per-patient basis, the BPaL regimen can be two-to-five fold cheaper to treat patients with XDR-TB compared with the conventional regimens.
  - Gradual adoption of BPaL would result in an average reduction of between 15% and 32% in budgets required to manage patients with XDR-TB.

- What do the new findings imply?
  - Our study demonstrates that the BPaL regimen can be highly cost-saving compared with conventional regimens to treat patients with XDR-TB.
  - Our study supports the rapid adoption of the BPaL regimen in countries fighting against a high drug-resistant TB burden.
resistant to at least one fluoroquinolone and a second-line injectable agent—is alarming. The global number of reported XDR-TB patients increased to 12,350 in 2019 compared with 10,800 in 2017. This number likely still reflects a substantial underestimate given the need for advanced drug susceptibility testing. Although XDR-TB treatment coverage has improved, treatment completion rates remain low at 30% with a considerable proportion of patients with XDR-TB dying (26%), failing treatment (18%) or lost to follow-up (LTFU) (18%). In addition, high costs and long treatment duration associated with the conventional XDR treatment regimens may pose financial challenges for both the National TB Programmes (NTPs) and patients with XDR-TB. As such, these financial burdens can impede the progress towards the 2030 end TB targets.

The low treatment success is attributable to the complexity and challenges associated with the conventional XDR-TB treatment regimens. A typical XDR-TB treatment lasts at least 20 months requiring lengthy hospitalisation during the intensive phase and use of at least seven drugs, including 6 months daily administration of injectable drugs that may result in patients experiencing adverse events. Likewise, conventional XDR-TB treatment is highly costly to both the health systems and to the patients—both out-of-pocket and in productivity losses—posing significant challenges in treatment adherence and ultimately treatment outcomes. Given these concerns, promising trial results of a 6-month novel regimen (bedaquiline, pretomanid and linezolid; BPaL) containing three oral medications—pretomanid, bedaquiline and linezolid—developed by the Global Alliance for TB Drug Development (TB Alliance) provides a hopeful outlook in managing patients with XDR-TB.

The results of the Nix-TB clinical trial evaluating the BPaL regimen showed 89% treatment efficacy in patients with XDR-TB and 92% in patients who had MDR-TB treatment intolerance (to regimens available in South Africa 2015–2017) or failed MDR-TB treatment, with insignificant differences in adverse events to other regimens containing linezolid. Furthermore, the BPaL regimen proved to be equally effective in both HIV-negative patients and people living with HIV on antiretroviral therapy.

In August 2019, BPaL received regulatory approval from the United States Food and Drug Administration and the WHO announced it recommends its use under operational research conditions. In 2020, the regimen was granted conditional marketing authorisation by European Medicines Agency. Given favourable clinical trial outcomes and regulatory approvals for its wide use, it is equally important to understand the potential cost trade-offs and budget impact of introducing BPaL alongside the continued use of the conventional XDR-TB treatment regimens in various epidemiologic and operational settings. We conducted empiric cost and budget impact analyses from a health service provider perspective of introducing the BPaL regimen alongside the use of conventional regimens for XDR-TB treatment in three high MDR-TB burden countries.

METHODS

Study overview

This study was conducted in Indonesia, Kyrgyzstan and Nigeria, which are among the 30 high-burden countries for MDR-TB. The number of laboratory-confirmed patients with XDR-TB in these countries was 33,109 and 16, respectively, in 2019. We collected the projected number of patients with XDR-TB who were anticipated to start using BPaL during 2020–2024 from a separate study (submitted for publication), in which we conducted semistructured interviews with NTPs in the three countries to gather in-depth information on country targets and planned regimens for DR-TB treatment (table 1).

We compared costs and budget impact concerning the use and introduction of BPaL regimen to the conventional regimens in each country to treat patients with XDR-TB. Conventional regimens included bedaquiline and linezolid with four to six additional anti-TB drugs administered over at least 20 months (online supplemental table S1). For the BPaL regimen, we assumed a duration of 6 months for the full course of treatment.

Cost analysis

We first conducted a landscape analysis, in close collaboration with the NTP staff, to identify key health services and utilisation frequencies necessary to assess empiric unit cost estimates and per-patient costs to treat patients with XDR-TB in the respective countries. Health service costs were primarily assessed based on the bottom-up costing method, multiplying empirically measured direct and indirect use of resources by unit prices/cost estimates necessary to complete each service process (online supplemental table S2). For resource use and cost data that were not possible to empirically collect at each study site, we reviewed literature (including estimates from World Health Organization Choosing Interventions that are Cost-Effective (WHO-CHOICE)), price catalogues, financial records service utilisation statistics (online supplemental Cost Analysis). These costs were estimated using top-down method, where estimated service-specific total costs were divided by service use/volume. Capital costs including buildings, equipment, vehicles and furniture were annualised using a discount rate reflecting the economics in each country (5% in Kyrgyzstan, 3% in Indonesia and Nigeria) and the standard assumption of respective useful life for each capital good. All costs were assessed as 2019 US$ adjusted for inflation for cost data available in years other than 2019. Cost data collected in local currency were converted to the 2019 US$ estimates using the Oanda currency converter. All cost data were collected using a modified version of a validated Excel-based tool developed by the Management Sciences for Health for the USAID-funded TB CARE 1 project, led by KNCV.
Perpatient costs in treating and monitoring patients with XDR-TB for each regimen were assessed assuming full adherence to the national guideline and algorithm in each country. These estimates were calculated based on identified frequency or quantities of key health services and medical commodities (eg, drugs) consumed by one patient with XDR-TB throughout the entire TB care cascade from the point when the patient was initiated on treatment. Each health service utilisation frequency was then multiplied by service unit cost to arrive at the total per-patient cost. Costs of drugs were categorised into intensive and continuation treatment phases. Prices of TB drugs for Kyrgyzstan and Nigeria were based on the Global Drug Facility (GDF) Medicines Catalog from November 2018. In Indonesia, the GDF catalogue was used for imipenem/cilastatin, whereas the prices of all other drugs except for pretomanid were extracted from the national e-catalogue, which is the NTP procurement
parameters over the 5-year period until they reached one of the treatment outcome states.

Sensitivity analysis
We conducted one-way sensitivity analyses of key parameters to determine the robustness of our model results regarding the average cost per BPaL treatment completed and the average net budget impact. We varied: (1) the timeline of introducing BPaL (+1 year), (2) the population eligible for the BPaL regimen (±20%), (3) reducing the dosage of linezolid with 50% in the BPaL regimen as being studied in the ZeNix trial, and (4) reducing the frequency of outpatient consultations to weekly instead of daily.

Ethical statement
This manuscript structure follows the Consolidated Health Economic Evaluation Reporting Standards statement checklist which is based on the format of the CONSORT statement checklist.

Patient and public involvement
The National Tuberculosis Programs of all countries endorsed this study. No patient was involved in generating the research questions or the outcomes measures, nor were they involved in designing the study, or developing the models. No patient was consulted on interpretation or writing up the results. The results will be disseminated to the National Tuberculosis Programs. There are no plans to disseminate the results to patients or the community.

RESULTS
Cost per patient treated
Unit costs, types and service utilisation frequencies of key health services necessary for XDR-TB care varied across the three countries assessed in our study (online supplemental table S2). The cost per patient treated when fully adherent with the BPaL regimen was US$4559 in Indonesia, US$2255 in Kyrgyzstan and US$4109 in Nigeria (figure 1). In Indonesia, drugs constituted 70% of the total cost of the BPaL regimen, versus 49% in Kyrgyzstan and 27% in Nigeria. In Kyrgyzstan, hospitalisation constituted 24% of the total cost of the BPaL regimen, and in Nigeria outpatient consultations 51%. The cost per patient treated with the respective conventional regimens was US$11 046 in

Figure 1 The drug and treatment management costs (in US$) per XDR-TB patient 100% adhering to the conventional regimens and BPaL by country. BPaL, bedaquiline, pretomanid and linezolid; XDR-TB, extensively drug-resistant tuberculosis.

The drug and treatment management costs (in US$) per XDR-TB patient 100% adhering to the conventional regimens and BPaL by country. BPaL, bedaquiline, pretomanid and linezolid; XDR-TB, extensively drug-resistant tuberculosis.

Indonesia, US$13,374 in Kyrgyzstan and US$15,042 in Nigeria (figure 1). For Indonesia and Kyrgyzstan, drugs constituted the largest percentage of the total cost of the conventional regimen (68% and 81%, respectively), whereas in Nigeria, outpatient consultation was the largest cost relatively with 46%.

### Cost per treatment completed

The cost per treatment completed among patients treated with BPaL was on average US$7142 in Indonesia, US$4782 in Kyrgyzstan and US$7152 in Nigeria (table 2). These costs were 57%, 78% and 68% lower, respectively, when compared with the cost of completing treatment with conventional regimens, US$16,732 in Indonesia, US$21,714 in Kyrgyzstan and US$22,021 in Nigeria (table 2). In our sensitivity analysis, reducing the dosage of linezolid with 50% reduced the average cost per BPaL treatment completed to US$6026 (–16%) in Indonesia, to US$4,517 (–6%) in Kyrgyzstan, and to US$6,900 (–4%) in Nigeria (figure 2A, online supplemental figures S2A and figure S3A). Reducing DOT to weekly visits reduced the average cost per BPaL.

### Table 2  Annual costs and cost per treatment completed by treatment regimen Indonesia, 1000 US$

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BPaL, bedaquiline, pretomanid and linezolid.
Adoption of the BPaL regimen would result in an average reduction in the net budget required to manage XDR-TB in the respective countries. Of all the health systems service components, BPaL drug costs constituted the largest contributor to the overall cost-savings. Across the three countries included in this study, using BPaL would result in at least 57% (and as high as 90%) reduction in per-patient drug costs compared with the current regimens to treat XDR-TB. This was primarily due to a reduction in the number of drug types and shortened duration of treatment for the BPaL regimen compared with conventional regimens. Furthermore, procurement prices of key drugs used to treat XDR-TB largely contributed to the difference in cost-savings across the three countries. For example, the unit cost used for one tablet of bedaquiline was US$5.71 in Indonesia, which is more than two times as high as the price charged through GDF. Similarly, the unit cost of one tablet of linezolid was US$6.39, which is more than five times higher than the price charged through GDF. In Indonesia, it is anticipated that these key drugs for XDR-TB treatment will be not procured through GDF for the foreseeable future. Likewise, Indonesia had highest per-patient cost of XDR-TB treatment using BPaL (US$4559), resulting in lowest absolute cost-savings compared with other countries.

Another notable contributing factor to the cost-savings associated with the BPaL regimen was the reduction in health service utilisation required to manage treatment of patients with XDR-TB. If the BPaL regimen would be used in the three countries, we anticipate that the number of visits to clinics for outpatient consultation, number and types of patient safety and treatment monitoring tests would be dramatically reduced due to simplified standardised drug regimen and a 14-month reduction in treatment duration compared with the conventional XDR-TB treatment course. Furthermore, if factoring in programmatic (eg, simplified procurement and supply chain management) and operational (decentralisation of XDR-TB treatment) benefits of the simplified and standardised treatment regimen, we expect that the economic case for adopting BPaL regimen would become more favourable. In our sensitivity analyses, we showed that the average costs per BPaL treatment completed in Indonesia were most sensitive to halving the dosage of linezolid, which showed to be efficacious and more tolerable in the ZeNIX trial. Prescribing BPaL to the other WHO-recommended patient populations, patients who are either unable to tolerate or failed MDR-TB treatment would increase quantifying the budget impact of switching to the recently FDA-approved pretomanid-containing BPaL regimen in three geographically diverse high DR-TB burden countries. On a perpatient basis, the BPaL regimen can be two-to-five fold cheaper to treat patients with XDR-TB compared with the conventional regimens, assuming full adherence to the respective care paths outlined in the respective NTP guidelines. We showed that gradual adoption of BPaL would result in an average reduction of between 15% and 32% in budgets required to manage patients with XDR-TB in the respective countries.
the reduction in the net budget (figure 2B). Increasing the speed of BPaL roll-out would reduce the XDR-TB-related expenditure, particularly when the proportion of patients with XDR-TB being enrolled on BPaL would increase over the years.

Our findings should be interpreted in light of the following limitations. First, because the BPaL regimen is a novel regimen that has not yet been widely adopted or studied in large scale, we primarily relied on the data available from the Nix trial to populate the BPaL treatment parameters in the model. Some parameter values in the model may, therefore, have been optimistic in a simplified model structure that may not fully capture the complexities of the XDR-TB patient care. For example, in our study, we used 1.4% LTFU rates of BPaL regimen as reported in the Nix trial. In reality, LTFU rates may be higher, and this would result in higher cost estimate per patient completing BPaL treatment, reducing the overall cost-savings associated with the introduction of BPaL regimen. Second, while we accounted for the impact of adverse events on treatment outcomes and overall treatment costs, we assumed types of adverse events, and management of adverse events would be similar between the two regimens (eg. 10% of the patients would require hospitalisation due to myelosuppression for both regimens). As such, we did not assess costs specific to managing adverse events, resulting from respective XDR-TB treatment. If frequency and types of adverse events associated with the programmatic use of BPaL regimen are higher compared with the conventional regimen, we expect that the overall cost-savings for BPaL regimen will also subsequently be reduced. While uncertainties around these parameters did not impact our overall cost-saving and budget impact estimates for BPaL, ‘real-world’ cost implications may be more significant on overall costs associated with the introduction and use of BPaL regimen. These factors are being evaluated in on-going operational research projects in various settings by the TB Alliance and KNCV.

Second, the overall cost and budget estimates for BPaL introduction were estimated based on the anticipated number of patients who will be initiated on the BPaL regimen in the respective years between 2020 and 2024 in each country. As our study was done prior to the FDA approval, we took a conservative approach in estimating these numbers with the key stakeholders from the NTP in the respective countries. Likewise, if countries take more rigorous and inclusive approach to introducing the BPaL regimen, we expect that the overall cost-savings and budget impact be greater than what was projected in our analyses. Third, in our budget impact analyses, we did not consider initial diagnostic costs and the costs associated with the implementation when transitioning to the novel regimen. While we expect that initial diagnostic process will not change for the decision to initiate patients BPaL, if the diagnostic process becomes simplified for BPaL, this would further favour adoption of BPaL regimen. Furthermore, while we expect that the costs associated with the implementation of the new regimen are an important factor, if the regimen can be scaled-up and maintained for the longer term, these costs will be marginalised. However, these implementation costs will vary considerably depending on the operational conditions, training needs, coverage and speed of implementation to the lower levels of health systems. Therefore, we encourage future studies to thoroughly investigate programmatic and implementation costs for introducing new treatment regimens for TB. Finally, as our analyses were restricted to the health service provider perspective, we did not factor potential patient benefits and cost that could result from the simplified treatment regimen for XDR-TB. We encourage future studies to empirically assess patient perspective costs and benefits of simplified standardised regimens for DR-TB.

CONCLUSION

Our study demonstrates that the BPaL regimen can be highly cost-saving compared with conventional regimens to treat patients with XDR-TB. While further evidence on costs from the patient perspective would provide an important complementary evidence to our work, findings from our study support the rapid adoption of the BPaL regimen in countries fighting against a high drug-resistant TB burden with limited health system capacity.

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REFERENCES
10 United States Food and Drug Administration. Briefing document Pretomanid tablet, 200 Mg, meeting of the antimicrobial drugs Advisory Committee (AMDAC) 2019.
26 Conradie F. High rate of successful outcomes treating highly resistant TB in the ZeNix study of pretomanid bedaquiline and alternative doses and durations of linezolid IAS. Berlin, Germany, 2021.