Cost-effectiveness of BPaLM/BPaL regimen for Multi-drug resistant, rifampicin resistant tuberculosis, India

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Policy Brief

Summary

Current options for treating tuberculosis (TB) that is resistant to rifampicin (RR-TB) are few, also regimens are often long and poorly tolerated. Following recent evidence from the TB PRACTECAL trial, countries are considering programmatic uptake of 6-month, all-oral treatment regimen, BPaLM. We conducted an economic evaluation to assess whether the introduction of BPaLM/BPaL regimen under National Tuberculosis Elimination Programme (NTEP) in India for the treatment of MDR/RR-TB is a cost-effective strategy. A Markov model was used to estimate the incremental cost-effectiveness of two regimens containing Bedaquiline, Pretomanid and Linezolid (BPaL) with and without moxifloxacin (BPaLM). These two regimens are compared with the current mix of (Longer regimen – 58% and shorter regimen – 42%) standard of care (SOC) regimen to treat MDR/RR-TB from the Indian health system perspective. We estimated the total costs and quality-adjusted life years (QALYs). Our findings indicate that BPaL based regimen are likely to be more cost effective than the current mix of (Longer regimen – 58% and shorter regimen – 42%) standard of care (SOC) regimen standard of care (SOC) regimen. Probability sensitivity analysis showed that when compared to standard of care, BPaLM and BPaL were more cost effective in 96% and 91% of the simulations respectively. In Cost Threshold Analysis, BPaL was found to be cost saving if the price is reduced to 29% than the current price and BPaLM was found to be cost saving if the price is reduced to 8% than the current price. A cost effectiveness analysis was performed from an Indian healthcare perspective. BPaL based regimens are cost effective and patients with MDR/RR-TB can be treated in six months duration. Evidences suggest to consider programmatic uptake of BPaL/BPaLM.

Background

Multi Drug Resistance TB (MDR-TB) is a global public health concern as it threatens the progress made in TB care and control. It is a growing public health concern since it requires more complex treatment than drug-sensitive TB and incurs more cost. MDR-TB is a type of TB that is resistant to at least two first-line anti-TB drugs i.e., Isoniazid and Rifampicin. Pre-XDR-TB is TB in which resistance to Rifampicin (MDR/RR-TB) and any fluoroquinolone are detected.[1] Extensively Drug Resistant Tuberculosis (XDR-TB) TB caused by *Mycobacterium tuberculosis* strains that fulfil the definition of MDR/RR-TB and which are also resistant to any fluoroquinolone and at least one additional Group-A drug (Group A drugs are the most potent group of drugs in the ranking of second-line medicines for the treatment of drug-resistant forms of TB using longer treatment regimens and comprise levofloxacin, moxifloxacin, bedaquiline and linezolid).[2] Treatment and management of drug-resistant TB is costly to the health system and patients (with high hospitalization rates for long periods and

Problem Statement

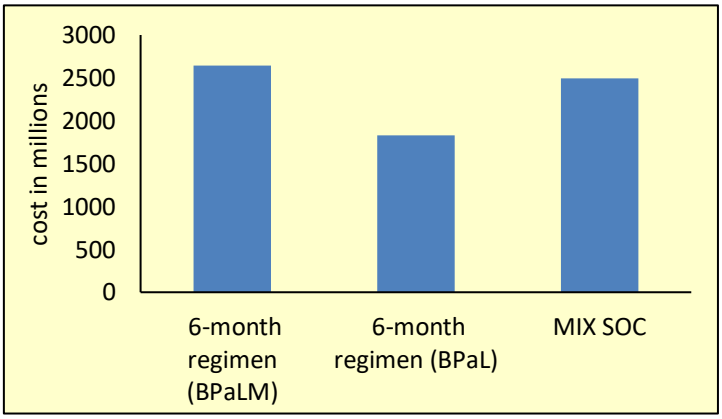
Available treatments are also difficult for patients to use due to the complex and significant side effects and adverse events as well as the number of drugs prescribed, often including a combination of injectables and oral medications. India with an annual incidence of 2.6 million TB cases is striving to accelerate the incorporation of evidence based new interventions in its National Tuberculosis Elimination Programme (NTEP) to achieve the TB elimination goal by 2025. The estimated incidence of MDR/RR-TB in 2021 for the country was 119,000 (ranged 93,000-145,000).[3] Several new initiatives have been undertaken to control TB more efficiently and shortening of TB treatment duration is considered an important strategy to achieve the TB elimination Goals. In Bangladesh, where a 9-month shorter regimen resulted in a treatment success rate of 87.9%.[4] Similarly assenting experiments were then conducted by Cameroon and Niger, with the treatment success rates of over 89% in each country.[5] The first randomized controlled trial study on the short-term therapy of MDR-TB was released in 2019 by Nunn et al.[6] The standardized shorter regimen of 9–11 months (composed of 7 drugs) with a treatment success rate of 78.8% was proved to be non-inferior to the long-term program recommended by the World Health Organization in 2011. It has released and updated guidelines for MDR-TB in 2018 that introduced shorter regimen as an option for patients who have not been previously treated for more than one month with second-line medicines or have no evidence of resistance to fluoroquinolones and second-line injectable drugs after reviewing the results of the STREAM study and other observational studies.[7]

The findings of the Nix TB trial were reported by Conradie F et al, in 2020 where three-drug regimen given orally to patients with XDR-TB for 26 weeks, consisting of Bedaquiline, Pretomanid, and Linezolid (BPaL), at the end of the therapy 90% of the patients had a favorable outcome.[8] It suggests that the combination of Bedaquiline, Pretomanid, and Linezolid led to a favorable outcome in a significant number of patients who were fluoroquinolone resistant. Zenix TB trial was reported by Conradie F et al,[9] in 2022. In the Zenix trial, a total of 181 participants were enrolled, a total of 84 to 93% of the participants across all four bedaquiline, pretomanid, linezolid treatment groups had a favorable outcome. The overall risk–benefit ratio favored the group that received the three-drug regimen with linezolid at a dose of 600 mg for 26 weeks, with a lower incidence of adverse events reported and fewer linezolid dose modifications TB-PRACTECAL evaluated the safety and efficacy of all oral regimens (24 weeks) for the treatment of MDR-RR TB containing BPaL plus moxifloxacin (BPaLM) which highlighted that both BPaL and BPaLM was non-inferior to the accepted standard care with respect to primary composite outcomes of 89% and 52% of the patients respectively, had a favorable outcome. Considering the evidences from the above clinical trials, in December 2022, WHO recommended (i) a 6-month treatment regimen composed of Bedaquiline, Pretomanid, Linezolid (600mg), and Moxifloxacin (BPaLM) regimen in place of the 9-month or longer (18-month) regimens in MDR/RR-TB patients, (ii) the use of the 9-month all-oral regimen rather than longer (18-months) regimen is suggested in patients with MDR/RR-TB and in whom resistance to fluoroquinolones has been excluded.

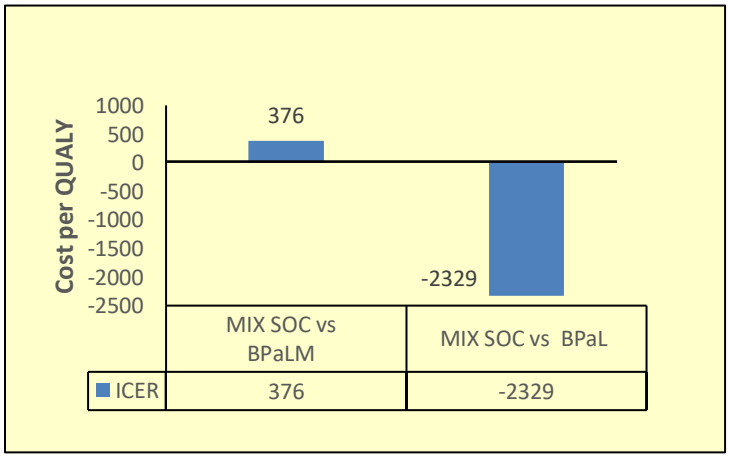
Treatment for adult smear-positive drug-resistant

Strategies	Drugs	Regimen	Duration	Population
Intervention - BPaL	Bedaquiline (Bdq) Pretomanid (Pa) Linezolid (Lzd)	(6-9) Bdq Pa Lzd	6-9 months	Adult aged ≥14 years smear positive MDR/ RR-TB Individuals
Intervention - BPaLM	Bedaquiline (Bdq) Pretomanid (Pa) Linezolid (Lzd) Moxifloaxacin(M)	(6-9) Bdq Pa Lzd M	6-9 months	Adult aged ≥14 years smear positive MDR/ RR-TB Individuals
Comparator (SOC)	Bedaquiline (Bdq) Levofloxacin (Lfx) Clofazimine (Cfz) Pyrazinamide(Z) Ethambutol(E) Isoniazid(Hh) Ethionamide(Eto)	(4-6) BdqLfx, Cfz, Z, E, Hh, Eto	Shorter 9-11 months and longer 18- 21 months, current mix of (Longer regimen 58% and shorter regimen 42%) standard of care (SOC) regimen	Adult aged ≥14 years smear positive MDR/ RR-TB individuals

Costs to treat MDR/RR-TB patients by different regimens



Incremental Cost-Effectiveness Ratio



Key Messages

- India with an annual incidence of 2.6 million TB cases is striving to accelerate the incorporation of evidence based new interventions in its NTEP to achieve the TB elimination goal by 2025.
- The estimated incidence of MDR/RR-TB in 2021 for the country was 119,000 (93,000-145,000).
- Several new initiatives have been undertaken to control TB more efficiently and shortening of TB treatment duration is considered an important strategy to achieve the TB elimination Goals.
- Treatment and management of drug-resistant TB is costly to the health system and patients (with high hospitalization rates for long periods and high drug costs).
- Available treatments are also difficult for patients to use due to the complex and significant side effects and adverse events as well as the number of drugs prescribed, often including a combination of injectable and oral medications.

Key Messages

- World Health Organization released and updated guidelines for MDR-TB in 2018 that introduced shorter regimen as an option for patients who have not been previously treated for more than one month with second-line medicines or have no evidence of resistance to fluoroquinolones and second-line injectable drugs after reviewing the results of the STREAM study and other observational studies.
- There is now consistent evidence that 6-month Bedaquiline based regimens are likely to be effective than the current regimen.

Conclusion

The new shorter Bedaquiline regimens BPaL is cost-saving and BPaLM is cost-effective as compared to the current mixed standard of care regimen. BPaLM can be made cost saving by procurement of drugs and thoroughly monitoring the patients for adverse drug reactions before it turns severe in order to reduce the hospital related costs. Programmatic uptake of these regimens could improve treatment success rate for MDR/RR-TB and free up resources for investment in other areas of TB programmes.

The policy brief is based upon the Health Technology Assessment of "Assessing the cost-effectiveness of the new treatment BPaLM/BPaL for Multi-drug resistant, rifampicin resistant, tuberculosis (MDR-RR-TB) as compared to the shorter oral Bedaquiline containing regimen under the National Tuberculosis Elimination Programme (NTEP)" by Regional Resource Centre for HTA In, ICMR-National Institute for Research in Tuberculosis, Chennai

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