INT J TUBERC LUNG DIS 19(12):S32–S38

http://dx.doi.org/10.5588/ijtld.15.0482

From availability to uptake: planning for the introduction of new, child-friendly anti-tuberculosis formulations

S. Malhotra,* I. Ursu,† R. Ghoneim,‡ P. Paredes Jodrey,‡ M. Soucy Brown,‡ M. Barr-DiChiara§

*Global Alliance for TB Drug Development, New York, New York, USA; †Mapping Health, London, UK; ‡Management Sciences for Health, Arlington, Virginia, §Independent Consultant, Brooklyn, New York, USA

SUMMARY

BACKGROUND: Assessing the state of country readiness for the introduction of new, child-friendly anti-tuberculosis formulations can highlight potential bottlenecks, facilitate early planning, and accelerate access to appropriate treatment for children with tuberculosis (TB).

METHODS: To understand pathways and potential obstacles to the introduction of new pediatric formulations, we performed a desk review of key policy documents and conducted 146 stakeholder interviews in 19 high-burden countries.

RESULTS: Issuance of World Health Organization (WHO) guidance serves as the trigger for considering adoption in most countries; however, the degree of alignment with WHO recommendations and duration of introduction processes vary. Endorsement by experts and availability of local evidence are leading criteria for adoption in upper-middle- and high-income countries. Ease of administration, decreased pill burden, and reduced treatment costs are prioritized in low- and lower-middle-income settings. Countries report an average of 10 steps on the path to new treatment introduction, with core steps taking between 18 and 71 months.

CONCLUSIONS: The process of new treatment introduction is complicated by diverse country processes, adoption criteria, and evidence requirements. Challenges differ between low- and middle-to-high-income countries. Responsiveness to the unique hurdles faced across settings is important in ensuring a sustainable market for improved pediatric anti-tuberculosis treatment.

KEY WORDS: introduction; adoption; timelines; access; pathways

IN RECENT YEARS, there has been a call to action to mobilize political will and resources for the neglected epidemic of childhood tuberculosis (TB). The need for improved, child-friendly treatment for both drug-susceptible and drug-resistant TB has been identified as a cornerstone of this agenda.[1] Real and perceived concerns about the size of, and fragmentation in, the pediatric TB market, however, have engendered commercial inertia. These factors have contributed to the current access crisis, whereby even 5 years after World Health Organization (WHO) issuance of guidance on optimal dosing for the treatment of TB in children, there are no quality-assured, correctly dosed, child-friendly TB formulations on the global market.[2,3]

In the absence of child-friendly treatment options, providers and parents have been forced to crush adult pills or use existing, inappropriately dosed pediatric formulations to treat children with TB, options that have been shown to increase the risk of poor treatment outcomes, non-adherence, and loss to follow-up among children.[4–6]

Since 2013, a new initiative spearheaded by the Global Alliance for TB Drug Development and the WHO has brought together commercial partners, policy makers, donors, national TB programs (NTPs), and child health stakeholders to catalyze the market for child-friendly anti-tuberculosis treatment. Through this effort, it is expected that appropriately dosed, dispersible, fixed-dose combinations (FDCs) for the treatment of drug-susceptible TB will be available through the Global Drug Facility (GDF) by late 2015.

Before improved treatments can translate into better outcomes in children with TB, they must be made available to pediatric patients in high-burden countries (HBCs) throughout the world.[7] Lessons learned from previous treatment introductions suggest that the process of country introduction and scale-up is often poorly defined, and associated timelines are protracted.[6] Suppliers report that slow country uptake, erratic procurement, and fragmented demand for pediatric TB products contribute to manufacturing inefficiencies and wastage, deterring

Correspondence to: Shelly Malhotra, Global Alliance for TB Drug Development, New York, NY 10005, USA. Tel: (+1) 646 616 8673. Fax: (+1) 212 227 7541. e-mail: shelly.malhotra@tballiance.org
Article submitted 2 June 2015. Final version accepted 8 September 2015.

Table 1 Interview affiliations

	Organization							
Country	NTP	Health Ministry	Procurement	Regulatory	WHO	Expert	NGO	Total
Afghanistan	1	1		1		1	1	5
Bangladesh	1		1	2	1			5
Brazil	2	1	1	1	1	1		7
Cambodia	5			4	1		2	12
China	1		1	1	1	5		9
Democratic Republic of Congo	1			1	1	1	2	6
Ethiopia	1	3	1	2	1			8
India	2				1	3		6
Kenya	2	1	1	1	1	2		8
Myanmar	1	2	1		1			5
Nigeria	2	1	2		1	1	1	8
Pakistan	1		1	1	1	1		5
Philippines	5	1	2	1	1	1		11
Russia	2		2	1	1	1		7
South Africa		1	1			5	1	8
Tanzania	4	1	1	1	1			8
Thailand	4		3	1	1	3		12
Uganda	1	1	1	1		1		5
Viet Nam	6	1			2	1	1	11
Total	42	14	19	19	17	27	8	146

NTP = National Tuberculosis Program; WHO = World Health Organization; NGO = non-governmental organization.

further investment in the childhood TB treatment market.

This article assesses the state of country readiness for the introduction of new pediatric TB formulations and identifies potential bottlenecks on the road to introduction, implementation, and scale-up of new anti-tuberculosis formulations. Clarifying adoption and introduction pathways can facilitate efforts to navigate hurdles, supporting a healthy market for life-saving therapies for children with TB.

METHODS

To understand pathways and potential obstacles to the introduction of new treatments for childhood TB, we conducted qualitative research in 19 of 22 HBCs (Table 1). Three HBCs—Indonesia, Mozambique, and Zimbabwe—were excluded from the study due to time and capacity constraints.

An initial literature review of key policy documents, including national TB strategic plans, TB treatment guidelines, essential medicines lists (EMLs), procurement manuals, regulatory guidelines, budgets, grant plans, and program reviews, was performed. Findings were entered into a standardized data form. Informant interviews were then conducted to validate and expand upon findings from the desktop review. Interviewees were identified through a combination of purposive and snowball sampling. Predetermined criteria included selection of representatives from the NTP, WHO country office, national regulatory authority, procurement office, and the essential medicines committee of each country. Representatives were then asked to identify additional individuals and organizations involved in TB program decision making, such as TB technical working group members, professional societies, development partners, non-governmental organizations, civil society, and 'experts'.

Interview tools were developed and refined by the research team. Interviewers were then trained in the administration of the study tool, a structured questionnaire covering topics such as policy change processes, evidence requirements, decision-making criteria and influencers, procurement and regulatory requirements, and planning sequences and timelines.

In all, 146 interviews were conducted between December 2014 and April 2015 (see Table 1 for affiliations). Interviews were conducted in person in all countries, with the exception of China, Russia, and a subset of interviews in Myanmar. Informed consent was obtained verbally using a standard script. Ethics committee involvement was not required, as the scope of inquiry was institutional processes rather than individuals. Data from interviews were entered directly into an Excel template (MicroSoft, Redmond, WA, USA), cleaned, and validated. Data were then aggregated, coded, and analyzed by the core study team. Results were compared and discrepancies were discussed and resolved by the team.

Study limitations include the potential for recall error or personal bias in the data, given the relatively small sample size per country. These risks were mitigated through triangulation of findings with data from the published literature, and by purposively sampling diverse institutional representatives to

enable multiple perspectives. Limitations also include the study's almost exclusive focus on the public sector TB market, given its disproportionate relevance for TB control efforts (Table 1).

RESULTS

Treatment introduction processes

Stakeholders were asked to describe the steps involved in introducing new TB treatments in their respective countries. The average number of procedural steps reported by participants was 10 (range 7–13), with introduction processes in most countries commencing upon issuance of WHO guidance on new treatments (Table 2). Updates to national treatment guidelines, guideline dissemination, forecasting, procurement transition, and training are core elements of the introduction process across all HBCs; WHO EML inclusion and GDF product availability are less central to the introduction processes in most countries (Table 2).[8]

Timelines associated with introduction vary significantly across HBCs. Reported transition times for a few key steps—including registration, national guideline change, forecasting, and procurement—range from <2 years in countries such as Afghanistan, Bangladesh, and the Democratic Republic of Congo (DRC) to >5 years in countries such as China and South Africa, with a median time across HBCs of 24 months (2 years) (Figure 1).

Of 19 countries participating in the study, 18 reported provisions in place that potentially shorten regulatory timelines. This included 8 countries with fast track registration procedures, 3 that allow regulatory exemptions, and 7 with both fast track and waiver provisions. On the other hand, additional procedural and planning processes across all countries, and requirements for local clinical, cost-benefit, or pilot studies in a subset of countries—including Russia, India, China, South Africa, Uganda, and Viet Nam—serve to further prolong introduction timelines.

Policy adoption criteria

The WHO consistently serves as a catalyst for considering treatment adoption across HBCs. While WHO guidance serves as a trigger for consideration of new treatments in 15 of the 19 countries surveyed, the degree to which countries accept WHO endorsement as a proxy for local review processes differs between low- and middle-to-high-income countries (Figure 2). Although important, WHO recommendation alone is insufficient to trigger guideline change among upper-middle-income and high-income countries (UMICs and HICs), such as South Africa, Thailand, Russia, and China and in India, where endorsement by experts and availability of local evidence on new treatments are seen as priority criteria for adoption (see Appendix for a full listing of countries by World Bank income classification).

Among most low- and lower-middle-income countries (LIC/LMIC), limited capacity to independently execute additional studies and the cascade of influence through funding agencies, such as the Global Fund to Fight AIDS, TB, and Malaria (The Global Fund), drive close alignment with WHO guidelines. Practical considerations, such as decreased pill burden, ease of administration, and reduced costs of treatment, are reported to be leading influencers of treatment adoption in these settings (Figure 2).

Of 19 HBCs participating in the study, 15 (79%) have adopted into national treatment guidelines either the WHO's 2010 'Rapid Advice' or its 2014 dosing recommendations for treatment of drug-susceptible TB in children;[3,9] however, the four countries that have not as yet officially adopted WHO dosing recommendations—Brazil, China, DRC, and India—represent 47% of the estimated burden of pediatric TB across the HBCs and 49% of the burden among countries participating in the study (Figure 3).[10]

Market readiness for new pediatric TB formulations

Existing preferences for treatment of drug-susceptible TB in children may have a bearing on country receptiveness to new pediatric TB formulations. Country practices are currently divided between those that use pediatric FDCs (63%), those that use loose pediatric drug formulations (16%), those that split or crush adult tablets (11%), and those that use a mixture of product types (11%) to treat childhood TB (Figure 4). While there are signs that attitudes may be shifting, experts in countries such as Russia, China, and India have historically been reluctant to implement FDC formats, given either providers' preferences for individually tailored dosing approaches or the lack of locally generated evidence on FDC effectiveness. The majority of countries (84%), however, report an eagerness to switch to pediatric FDCs, once appropriately dosed treatments are available (Figure 4).

Procurement channels for first-line drugs (FLDs) for children and adults are currently divided between quality-assured and non-quality-assured, locally and globally supplied networks. Of the 19 countries surveyed, seven (37%) report exclusively securing quality-assured FLDs through the GDF. A recent study suggests that procurement volumes of FLDs for children through the GDF platform reflect approximately 12% of notified pediatric TB cases in the HBCs.[11] The remaining countries report procuring FLDs through national or international competitive bidding, or a mixture of approaches (Figure 5). Among nine countries procuring some or all FLDs locally, seven report regulatory or procedural provisions prioritizing locally sourced drugs (Figure 5).

Table 2 Reported steps from new treatment availability to introduction

Countries	Steps*												
	WHO recommends	WHO adds to EML	National treatment guidelines updated	Dissemination of new guidelines	Addition to national EML	Product registration	Training	Product quality surveillance	Pharmacovigilance	Product available through GDF	Forecasting/ procurement	Other steps†	Total number of steps
Afghanistan	√	√	√	√	√	√	√			√	√		9
Bangladesh	√	√	√	√	√	√	√	√	√	√	√	√ √	13
Brazil	√		√	√	√	√	√	√	√		√	√	10
Cambodia	√		√	√	√		√	√	√	√	√		9
China			√	√	√	√	√				√	√	7
Democratic Republic of Congo	√	√	√	√	√	√	√	√	√	√	√		11
Ethiopia	√	√	√	√	√	√	√	√	√	√	√		11
India			√	√		√	√	√	√		√	√	8
Kenya	√	√	√	√	√	√	√	√	√		√	√ √	12
Myanmar	√		√	√			√				√	√ √ √	8
Nigeria	√	√	√	√	√	√	√	√	√	√	√		11
Pakistan	√	√	√	√	√	√	√	√	√	√	√		11
Philippines	√		√	√	√	√	√	√	√		√	√	10
Russia			√	√	√	√	√				√	√ √	8
S Africa	√	√	√	√	√	√	√	√	√		√	√	11
Tanzania	√	√	√	√	√	√	√	√	√	√	√	√	12
Thailand	√		√	√	√	√	√	√	√		√	√	10
Uganda	√	√	√	√	√	√	√	√	√	√	√		11
Viet Nam	√	√	√	√	√	√	√	√	√	√	√	√ √	13
Total countries	16	11	19	19	17	17	19	15	15	10	19	18	

* The sequence of 'steps' represented in the table is not indicative of the order of processes in specific countries.
† Each √ represents one step. Potential steps mentioned include technical committee review, import license, local clinical trial, budget approval, approval by the Global Fund to Fight AIDS, Tuberculosis and Malaria, among others.
WHO = World Health Organization; EML = Essential Medicines List; GDF = Global Drug Facility.

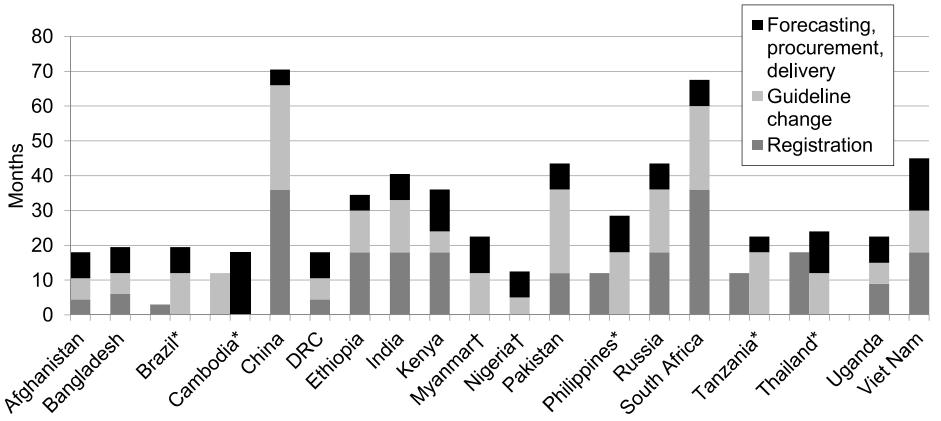

Figure 1 Estimated median time for key steps toward product availability. *Indicates that more than one of these processes may occur in parallel. †Stakeholders report that registration is not required as a condition for introduction of new anti-tuberculosis drugs. DRC = Democratic Republic of Congo.

DISCUSSION

Readiness for the introduction of new pediatric TB formulations is marked by country-level demand, the presence of a receptive policy environment, and the existence of a pathway for the rapid introduction of new treatment formulations. The criteria for the adoption of new treatments differ across low- and middle-to-high-income countries. While WHO guidance serves as the primary trigger for considering the adoption of new anti-tuberculosis treatment formulations across settings, the degree of alignment around WHO recommendations and the duration of national policy adoption processes vary significantly. Among UMICs and HICs, such as South Africa, Thailand, Russia, and China, and in India, both treatment endorsement by experts and the availability of local evidence on new treatments are seen as critically influencing adoption. Donor requirements in most LIC and LMIC settings, on the other hand, drive convergence around WHO-recommended treatments.

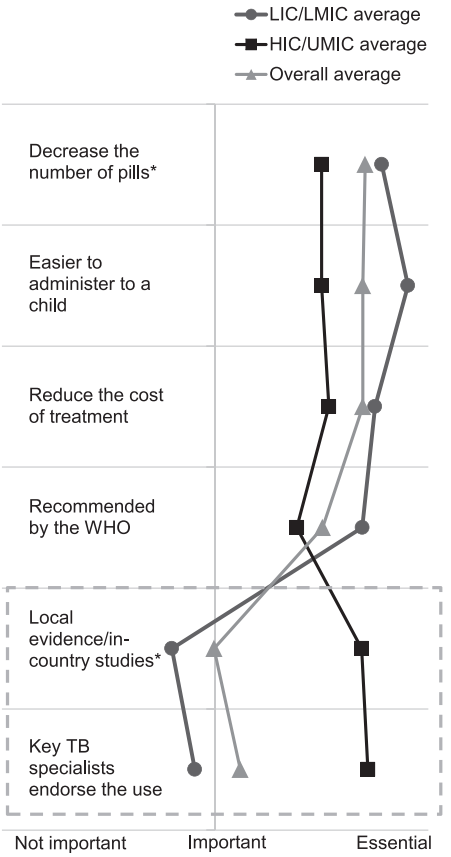

Figure 2 Key criteria for treatment adoption. *Myanmar data on the number of pills and Brazil data on local evidence not available. WHO = World Health Organization; LIC = low-income country; LMIC = low-middle-income country; HIC = high-income country; UMIC = upper-middle-income country.

Interview participants reported standard timelines for drug registration, guideline change, forecasting, procurement, and delivery of new treatments as ranging from 18 to 71 months across the HBCs. Strong expressions of interest in the new FDCs (84% of countries) and expedited regulatory provisions for treatments of public health priority (95% of countries) highlight the potential to accelerate time-to-market for forthcoming child-friendly anti-tuberculosis formulations in some settings; however, additional country-specific procedures in other settings — such as requirements for EML inclusion, product quality testing, pharmacovigilance, and generation of local clinical and non-clinical evidence—further prolong introduction timelines.

Procurement practices for pediatric TB treatments currently remain fragmented across formulation types and procurement channels, and while most countries have adopted WHO dosing guidance, those countries that have not represent approximately half of pediatric TB cases. For small treatment markets, such as the market for first-line pediatric TB formulations, convergence of procurement practice around WHO-recommended treatments and quality-

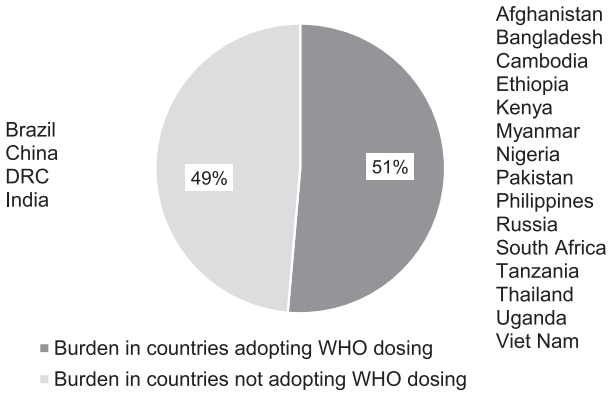

Figure 3 Burden in countries per WHO guideline adoption status. WHO = World Health Organization; DRC = Democratic Republic of Congo.

assured supply through platforms such as the GDF can drive affordability by facilitating demand consolidation to foster manufacturing economies of scale. As home to almost half of all new adult and pediatric TB cases in the 22 HBCs, middle-to-high-income HBCs, such as the BRICS countries (Brazil, Russia, India, China, and South Africa), are also critical in driving solutions to the childhood TB problem.[10] The current non-alignment of some middle- and high-income countries with WHO treatment recommendations and hurdles to introduction—related to slow policy change processes, localized evidence requirements, trade protections, and arduous regulatory provisions—hinder the rapid integration of new treatments in these settings. Failure to capture such a significant portion of the treatment population poses a fundamental threat to both affordability and market sustainability, and can deter further commercial investment in this and other small but essential public health markets.

Identifying opportunities to promote harmonization of treatment practices and requirements across high-, middle-, and low-income TB-endemic settings—including greater mutual recognition of strin-

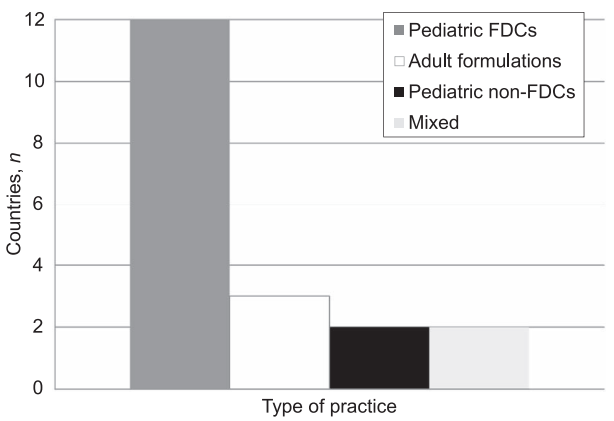

Figure 4 Formulation practices. FDC = fixed-dose combination.

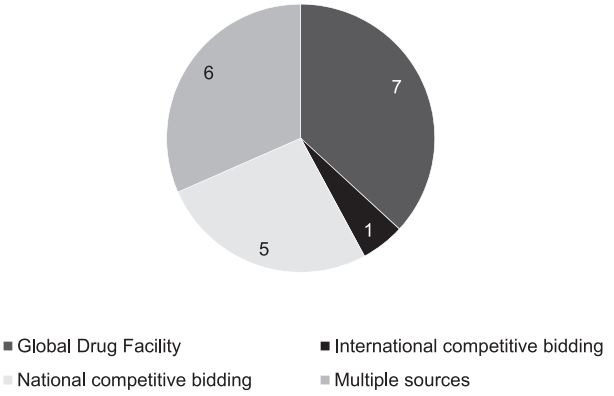

Figure 5 Source of country first line drug supply.

gent regulatory authority or WHO prequalification standards and alignment around normative treatment recommendations—could help accelerate access to life-saving treatments for childhood TB. The recent agreement of BRICS Health Ministers to collaborate in scaling up research on, and access to, new TB treatments represents an important step in the right direction; however, continued political will and resources will be needed.[12]

CONCLUSIONS

Before improved treatments can translate into better outcomes for children with TB, they must be made available to pediatric patients across the TB-endemic world. The process of treatment introduction and scale-up is complicated by a variety of country-specific introduction processes, adoption criteria, and administrative and evidence requirements. The challenges faced differ significantly between low- and middle-to-high-income countries. Clarifying adoption and introduction pathways can facilitate efforts to navigate hurdles and support a healthy market for life-saving therapies for children with TB. In addition, the development of strategies that are responsive to the unique hurdles faced across settings is important in accelerating access to, and ensuring a sustainable market for, new pediatric TB treatments.

Acknowledgements

The research team would like to thank all the stakeholders who contributed their time and insights. This study would not have been possible without the data collection efforts of participating staff and consultants, including V Anyebe, Z Ghowsi, S Bashar, V Nakiganda, C Breyer Bonilla, K Payne, S Kakaveya, S Rotolo, J Mbo, A Liben, A N Muturi, H Henry, M I Quelapio, M Dalenogare, C N Kamalandua, B M Gibe, H Qureshi, C Kagoma, Z Ni, and M Root. We are grateful for the guidance and helpful comments of C Scott, D Lee, M Spigelman, A Brands, E Robertson, C Owuna, and C Pero.

Conflicts of interest: SM is employed by the Global Alliance for TB Drug Development, whose activities are aimed at developing and making available improved therapies for TB. RG, PP, and MS are employed by Management Sciences for Health (Arlington, VA, USA), which provides technical assistance with drug management

in many of the high-burden countries. Other authors declare no conflicts of interest.

The financial sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of this report.

References

1 World Health Organization, Stop TB Partnership, the International Union Against Tuberculosis and Lung Disease, Centers for Disease Control and Prevention, United States Agency for International Development, United Nations Children's Fund, the Treatment Action Group (TAG). Roadmap for childhood TB: towards zero deaths. WHO/HTM/TB/2013.12. Geneva, Switzerland: WHO, 2014.
2 UNITAID. Tuberculosis medicines technology and market landscape 2014. Geneva, Switzerland: UNITAID, 2014.
3 World Health Organization. Rapid advice: treatment of tuberculosis in children. WHO/HTM/TB/2010.13. Geneva, Switzerland: WHO, 2010.
4 Swaminathan S, Rekha B. Pediatric tuberculosis: global overview and challenges. Clin Infect Dis 2010; 50 (Suppl 3): S184–S194.
5 Nataprawira H M, Wonoputri N. Obstacles facing tuberculosis treatment in children from a developing country: a hospital-based study. Am J Epidemiol 2014; 2: 8–12.
6 Adams L V, Craig S R, Mmbaga E J, et al. Children's medicines in Tanzania: a national survey of administration practices and preferences. PLOS ONE 2013; 8: e58303.
7 Wells W A, Konduri N, Chen C, Lee D, Ignatius H R, Gardiner E, Schwalbe N R. Tuberculosis regimen change in high-burden countries. Int J Tuberc Lung Dis 2010; 14: 1538–1547.
8 Stop TB Partnership Task Force on Retooling. New technologies for tuberculosis control: a framework for their adoption, introduction and implementation. WHO/HTM.STB/2007.40. Geneva, Switzerland: WHO, 2007.
9 World Health Organization. Guidelines for national tuberculosis programmes on the management of tuberculosis. WHO/HTM/TB/2014.03. 2nd ed. Geneva, Switzerland: WHO, 2014.
10 Dodd P J, Gardiner E, Coghlan E, Seddon J A. Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modeling study. Lancet Glob Health 2014; 2: e453–459.
11 Scott C, Gardiner E, de Lucia A. Availability of pediatric tuberculosis treatment: an analysis of supply and demand. Int J Tuberc Lung Dis 2015; 19 (Suppl 1): S17–S22.
12 Stop TB Partnership. BRICS Health Ministers make historic commitments in the fight against TB. Geneva, Switzerland: Stop TB Partnership, WHO, 2014. http://www.stoptb.org/news/stories/2014/ns14_081.asp Accessed September 2015.

APPENDIX

World Bank Country and Lending Group Classifications, 2015[1]

Low-income economies	Afghanistan, Bangladesh, Cambodia, Democratic Republic of Congo, Ethiopia, Kenya, Myanmar, Tanzania, Uganda, Zimbabwe
Lower-middle-income economies	India, Nigeria, Pakistan, Philippines, Vietnam
Upper-middle-income economies	South Africa, Brazil, Thailand, China
High-income economies	Russian Federation

Reference

1 World Bank. Country and lending groups. Washington DC, USA: World Bank, 2015. data.worldbank.org/about/country-and-lending-groups. Accessed September 2015.

RESUME

CONTEXTE : Evaluer le niveau de préparation du pays à l'introduction de nouvelles formulations pour la tuberculose (TB) acceptables par les enfants peut mettre en lumière des goulots d'étranglement potentiels, faciliter une planification précoce et accélérer l'accès à des traitements appropriés pour les enfants atteints de TB.

MÉTHODE : Pour comprendre le cheminement et les obstacles potentiels à l'introduction de formulations TB pédiatriques correctement dosées, nous avons réalisé une revue approfondie des principaux documents de politique et conduit 146 entretiens avec des parties prenantes dans 19 des 22 pays les plus touchés (HBC).

RÉSULTATS : La publication de la guidance de l'Organisation Mondiale de la Santé (OMS) sert de premier déclencheur pour envisager l'adoption dans la majorité des HBC ; cependant, le degré d'alignement avec les recommandations de l'OMS et la durée des procédures d'introduction dans le pays varient. L'approbation par des experts et la disponibilité de preuves locales relatives aux nouveaux traitements sont les critères principaux d'adoption dans les HBC à revenu moyen supérieur et élevé. La facilité d'administration, la réduction du nombre de comprimés et la réduction du coût du traitement sont les priorités des pays à revenu faible ou intermédiaire. Les pays font état d'une moyenne de 10 étapes dans la procédure d'introduction de nouveaux traitements, les étapes principales prenant entre 18 et 71 mois.

CONCLUSION : Le processus d'introduction de nouveaux traitements et leur expansion sont compliqués par un ensemble de procédures d'introduction spécifiques à chaque pays, par les critères d'adoption, et les besoins de preuves. Les défis diffèrent entre les pays à revenu faible et moyen et ceux à revenu élevé. Les stratégies qui répondent aux obstacles particuliers affrontés dans différents contextes sont importantes pour assurer un marché durable afin d'améliorer le traitement anti-tuberculeux de l'enfant.

RESUMEN

MARCO DE REFERENCIA: La evaluación del grado de preparación de un país para la introducción de nuevas formulaciones de medicamentos antituberculosos adaptados a los niños pone de manifiesto los eventuales cuellos de botella del procedimiento, facilita una planificación temprana y acelera el acceso a los tratamientos apropiados para los niños con diagnóstico de tuberculosis (TB).

MÉTODOS: Con el propósito de comprender los mecanismos de introducción de las formulaciones pediátricas con dosis apropiadas y los posibles obstáculos que pueden surgir, se llevó a cabo una revisión exhaustiva de los principales documentos normativos y se realizaron entrevistas a 146 interesados directos en 19 países con alta carga de morbilidad (HBC) por TB.

RESULTADOS: La publicación de las directrices de la Organización Mundial de la Salud (OMS) constituye el principal incentivo de la adopción de nuevos tratamientos en la mayoría de los HBC; sin embargo, el grado de cumplimiento de estas recomendaciones y la duración de los mecanismos de introducción en los países varía en los diferentes entornos. La aprobación por los expertos y la existencia de datos fidedignos locales sobre los nuevos tratamientos son los criterios fundamentales de la adopción en los países con alta morbilidad e ingresos medios altos y altos. En los países con ingresos medios bajos y bajos se da prioridad a las consideraciones prácticas como la facilidad de administración, una baja cantidad de comprimidos y el bajo costo del tratamiento. Los países notifican un promedio de 10 etapas en el procedimiento de introducción de los nuevos tratamientos y las etapas básicas duran 18–71 meses.

CONCLUSIÓN: La introducción y la ampliación de escala de los nuevos tratamientos se dificultan por la diversidad de mecanismos, criterios de adopción y la exigencia de datos fidedignos en cada país. Los obstáculos difieren de manera significativa en los países de ingresos bajos e ingresos medios a altos. Las estrategias sensibles a las dificultades específicas encontradas en los diferentes entornos son importantes para garantizar un mercado sostenible para mejorar el tratamiento contra la TB pediátrica.