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Western Pacific Regional Green Light Committee: progress and way forward

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SUMMARY

The Western Pacific Regional Green Light Committee (rGLC WPR) was established in 2011 to promote the rational scale-up of programmatic management of drug-resistant tuberculosis (PMDT). We reflect on its achievements, consider the challenges faced, and explore its potential future role. Achievements include the supervision and support of national PMDT action plans, increased local ownership, contextualized guidance, and a strong focus on regional capacity building, as well as a greater awareness of regional challenges. Future rGLC activities should include (1) advocacy for high-level political commitment; (2) monitoring, evaluation, and supervision; (3) technical support and contextualized guidance; and (4) training, capacity building, and operational research. Regional activities require close collaboration with both national and global efforts, and should be an important component of the new Global Drug-resistant TB Initiative.

1. Introduction

Multidrug-resistant tuberculosis (MDR-TB; cases infected with *Mycobacterium tuberculosis* that is resistant to isoniazid and rifampicin) is a major threat to global gains in TB control. The management of MDR-TB is more difficult than that of drug-susceptible TB. It requires specialized laboratory diagnostics, a long duration of treatment with expensive and toxic drugs, careful monitoring of treatment progress, and addressing frequent adverse drug reactions. Programmatic management of drug-resistant TB (PMDT) requires considered planning and adequate and well-trained human resources, together with strong political commitment for institutional support and funding security.

The original Green Light Committee (GLC) was formed in 2000 to provide technical assistance to DOTS (the internationally recommended strategy for TB control) programmes and to promote the rational use of and improve access to concessionally priced, quality-assured, second-line anti-TB drugs.[1] The GLC assisted many countries in setting up pilot PMDT projects and established the principles for responsible MDR-TB management in resource-limited settings. Best practice guidelines detailing the choice of regimens were published in 1996 to guide clinicians on TB treatment, but the first guidelines on PMDT were published by the World Health Organization (WHO) in 2006, and included experiences from different GLC projects.[1] In 2009, a ministerial meeting in Beijing of 27 countries with a high burden of MDR-TB called for urgent action to reduce the imminent threat of the emergence and spread of drug-resistant TB.[2] World Health Assembly resolution WHA 62.15 focused on the prevention and control of drug-resistant TB, and was approved by the Sixty-second World Health Assembly in

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2009. The resolution encouraged high-level political commitment and adequate funding allocation, together with the development of global, regional, and national action plans.[3]

A revised global framework to support PMDT was developed in 2010. The framework recognized the need to improve access to diagnosis and treatment, and to limit the transmission of drug-resistant TB. It called for the establishment of decentralized regional structures to enhance country engagement, oversight, and support.[4] In 2011, the Western Pacific Region Green Light Committee (rGLC WPR) was established to assist member countries with rational scaling up of PMDT. The rGLC WPR was mandated to provide inputs to national strategies/action plans for PMDT scale-up, oversee the provision of technical assistance to countries, review monitoring mission reports and surveillance data, improve access to and rational use of quality-approved medicines, and promote advocacy for regional PMDT scale-up. We provide a brief overview of rGLC WPR activities, reflect on its achievements and challenges, and explore its potential future role.

2. Structure of the rGLC

The rGLC initiative shifted the focus from 'regulation and control' to 'support and assistance', with a strong emphasis on regional ownership, increased involvement of country representatives, and local capacity building. Member countries were at different stages of PMDT implementation with consequent diverse needs, ranging from the Philippines with the earliest GLC-approved programme[5] to settings without any PMDT experience.

An rGLC secretariat was established at the WHO Regional Office for the Western Pacific in Manila, and an expert committee contributing the following skill sets was convened: development and review of PMDT scale-up plans; clinicians with experience in managing drug-resistant TB, including paediatric and HIV-infected patients; patient support, nursing care, and case-holding strategies; drug management; laboratory aspects; infection control; epidemiology and surveillance and information systems; and communication and advocacy. A call for applications was made for the selection of individuals to serve as members on the rGLC WPR for a period of 2 years. Interested applicants were asked to respond with a motivation letter, a copy of their curriculum vitae, and a covering letter emphasizing their relevant MDR-TB experience, specific technical expertise, and the constituency to be represented. The selection was made by a committee comprising the Stop TB Partnership (STP), the MDR-TB working group of the STP, and the WHO. The selection was based on clear criteria, which included a rational distribution of areas of expertise and experience, previous GLC experience, geographical and gender distribution, and constituency represented. Preference was given to applicants from and/or with extensive experience in the Western Pacific Region. Members were selected for an initial 2-year term, with provision for at least half of the members to secure a second term in order to ensure continuity.

The rGLC mechanism is not only an expert committee, but a partnership of the Committee, countries, technical organizations, and donor agencies (Figure 1). The Committee performs an overseer role and the Secretariat ensures coordination. The mechanism encourages countries to share their experiences and taps into the expertise of various technical organizations for specific technical assistance to the country as relevant. Donor agencies provide funding support for scaling up PMDT and receive updated status information on programme implementation through the mechanism.

3. Size of the challenge and key activities

Globally in 2013, a total of 300 000 (range 230 000–380 000) among notified TB cases were estimated to have MDR-TB,[6] with

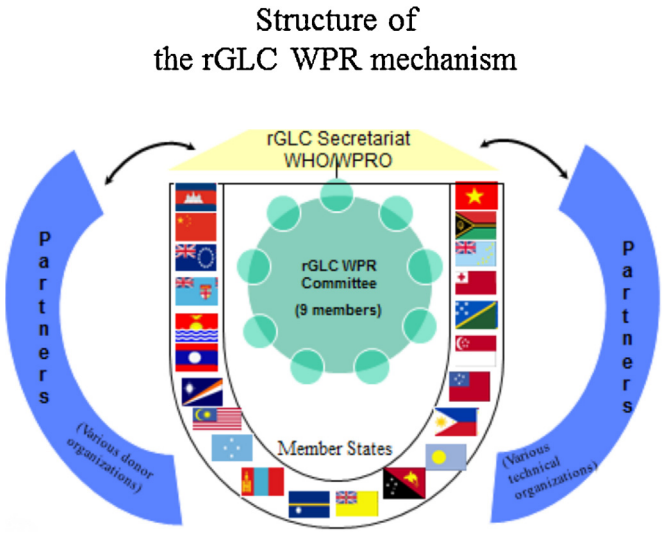

Figure 1. Structure of the Western Pacific Regional Green Light Committee (rGLC WPR).

nearly one quarter (71 000, 95% confidence interval (CI) 47 000–94 000) of them in countries of the WHO Western Pacific Region. The Region includes countries with high MDR-TB case-loads, such as China, Viet Nam, and the Philippines, and remote Pacific Island nations with very small and irregular case-loads.[7] Table 1 summarizes the estimated MDR-TB case-numbers in the countries of the Western Pacific Region.

Key activities of the rGLC WPR have included assistance with the formulation of national PMDT action plans, PMDT programme evaluation, critical review of mission reports, establishing and administering a quality-assured second-line drug repository for small Pacific Island nations, and contributions to regional capacity building with ongoing strategic and technical guidance. Technical support has included all aspects of programme performance, with particular emphasis on quality assurance of laboratory protocols, treatment, and case management.

The expert committee has had regular teleconferences and bi-annual face-to-face meetings. Meetings have been arranged to coincide with regional TB events, which has minimized costs and allowed rGLC members to interact with country programme managers, raise awareness of MDR-TB, and provide expert advice. These interactions have increased mutual understanding of both country and regional TB control challenges, and have provided opportunities for addressing these challenges.

The Secretariat has coordinated monitoring missions to all countries with a high MDR-TB burden and has arranged critical reviews of country reports within strict timelines. Priority recommendations have been clearly communicated and progress reviewed during subsequent visits. In addition to the routine monitoring missions, special technical assistance missions have been arranged to address country-specific challenges, such as clinical audit tools, pharmacovigilance, protocol development for the management of extensively drug-resistant TB (XDR-TB; MDR with additional resistance to fluoroquinolones and one or more of the second-line injectable agents), etc. Regional training of trainers and consultant courses on PMDT and drug management have been organized, as well as in-country training on the clinical aspects of MDR-TB management.

A workshop exploring pragmatic ways of strengthening and harmonizing the regulation of TB medicines in the Region has taken place, involving national TB programmes (NTPs), national medicine regulatory authorities (NMRAs), technical partners, and other key stakeholders. This workshop served as an entry point for

overall strengthening and harmonization of regulations for all medicines in the Western Pacific Region. Clinical consultation on MDR-TB case management has been provided for Pacific Island countries and areas, and a rotating stockpile of second-line anti-TB drugs maintained for their use. To address programmatic problems, seek alternative approaches, and improve programme performance, the Secretariat has been involved in various operational research projects in collaboration with NTPs and other stakeholders. Recognizing the important role of the private sector within the Region, the Secretariat has developed a 'private sector assessment tool' and has piloted the tool. rGLC has also worked with governments on the introduction and protection of novel TB drugs.[8]

4. Achievements

An important outcome of decentralization of the GLC has been the development of a regional pool of experts for PMDT support and scale-up. Their involvement has increased regional capacity, reduced mission expenses, and improved the feasibility of recommendations. It has stimulated greater local ownership of the MDR-TB problem, encouraging countries to critically assess the performance of all PMDT activities, irrespective of Global Fund support or GLC approval. Regional analysis of the drug resistance TB situation has been performed to assist all stakeholders to understand the situation better.[7] Assessment of GLC-approved and non-approved programmes has demonstrated that non-approved programmes fare much worse, but has also emphasized the unmet patient demand and the need for private sector engagement. The analysis of the procurement and sales data of anti-TB drugs from both the public and private sectors in the Philippines has shown that an enormous quantity of anti-TB drugs have been channelled through the private market outside the purview of the NTP.[9] The analysis of private sector contributions to PMDT in the Philippines has facilitated the agenda for responsible private sector involvement.[10]

PMDT should not be a stand-alone programme. The siloing of PMDT activities has been a major barrier to enhanced local oversight, ownership, and responsible programme expansion. PMDT should be part and parcel of routine TB programme activities and part of the overall health-care system. The rGLC WPR has advocated for and encouraged integration of the PMDT with overall TB control activities by organizing rGLC meetings with other TB-related events, participating in joint programme reviews, and coordination with other sectors such as NMRAs, maternal and child health programmes, paediatricians, and others.

Oversight by the rGLC WPR has ensured optimal value extraction from country missions. All reports have been critically reviewed with clear formulation of feasible and prioritized recommendations. Challenges and bottlenecks have varied according to the different stages of PMDT implementation, requiring different types of technical assistance (Figure 2). The rGLC has benefited from the existing close relationships between the WHO Regional Office and member countries, which has enhanced the articulation of local priorities and needs. The decentralized rGLC model has been found to be more accessible and has created a platform for sharing experiences (both frustrations and successes), strengthening local ownership and encouraging innovative local solutions. Enrolment statistics since 2011 confirm that an increasing number of patients have accessed care (Table 2), despite major financial constraints.[11] The rising trend demonstrates the readiness for PMDT scale-up, and the credit for the progress made belongs to the respective countries. However, considerable unmet needs remain.

5. Challenges

Although local ownership at the TB programme level has improved, national prioritization remains low and the domestic resources allocated to PMDT are grossly inadequate. In 2013, of the expenditure on PMDT in the countries in the WHO Western Pacific Region, 18.4% was from domestic sources, with the remaining 81.6% from external grants.[7] The gap between the estimated number of MDR-TB patients and those receiving adequate care grows wider. Despite a steady increase in PMDT enrolment, cases treated in 2013 represented only16% of all estimated MDR-TB cases among notified pulmonary TB cases.[6,7] Without greatly increased domestic investment, the long-term sustainability of donor-funded programmes is a serious concern. Major funding shortfalls demonstrate the need for greatly increased advocacy and strong regional political commitment to contain the spread of MDR-TB. High- and middle-income countries need to increase domestic resources. Innovative health financing (health insurance, social protection schemes, etc.) may play an important role. However, it is to be noted that considerable donor support will still need to be continued for low-income countries.

Among the total estimated number of MDR-TB cases, 25% (18 000, 95% CI 15 000–21 000) are among retreatment cases and 75% (53 000, 95% CI 47 000–75 000) among new TB cases,[7] posing a major challenge to enhanced case detection. Due to limited funding, MDR-TB detection in many countries is focused exclusively on retreatment cases, or even those failing the retreatment regimen, since these groups have the highest

Table 1
Estimated numbers of MDR-TB cases among notified pulmonary TB cases in countries of the Western Pacific Region[a,b]

	MDR-TB among new TB cases			MDR-TB among previously treated TB cases			Total MDR-TB cases	
	n	(95% CI)	%	*n*	(95% CI)	%	*n*	(95% CI)
China	45 000	(35 000–55 000)	6	9200	(7800–11 000)	26	54 000	(48 000–61 000)
Philippines	4400	(3100–6000)	2	4100	(3000–5500)	21	8500	(6900–10 000)
Viet Nam	3000	(1900–4100)	4	2100	(1500–2600)	23	5100	(4100–6100)
Republic of Korea	780	(600–980)	3	1200	(850–1600)	14	1900	(1600–2300)
Papua New Guinea	560	(340–800)	5	570	(480–650)	24	1100	(890–1400)
Cambodia	320	(160–580)	1	180	(68–370)	11	510	(270–740)
Mongolia	33	(16–59)	1	210	(180–240)	34	240	(210–280)
Lao People's Democratic Republic	160	(96–230)	5	65	(56–75)	24	220	(160–290)
Japan	110	(63–160)	<1	100	(72–130)	10	200	(150–260)
Western Pacific Region	53 000	(31 000–75 000)	4	18 000	(15 000–21 000)	22	71 000	(47 000–94 000)

CI, confidence interval; MDR-TB, multidrug-resistant tuberculosis.
[a] Source: Global TB database (http://www.who.int/tb/country/data/download/en/).
[b] Restricted to those with a case-load of more than 50 patients.

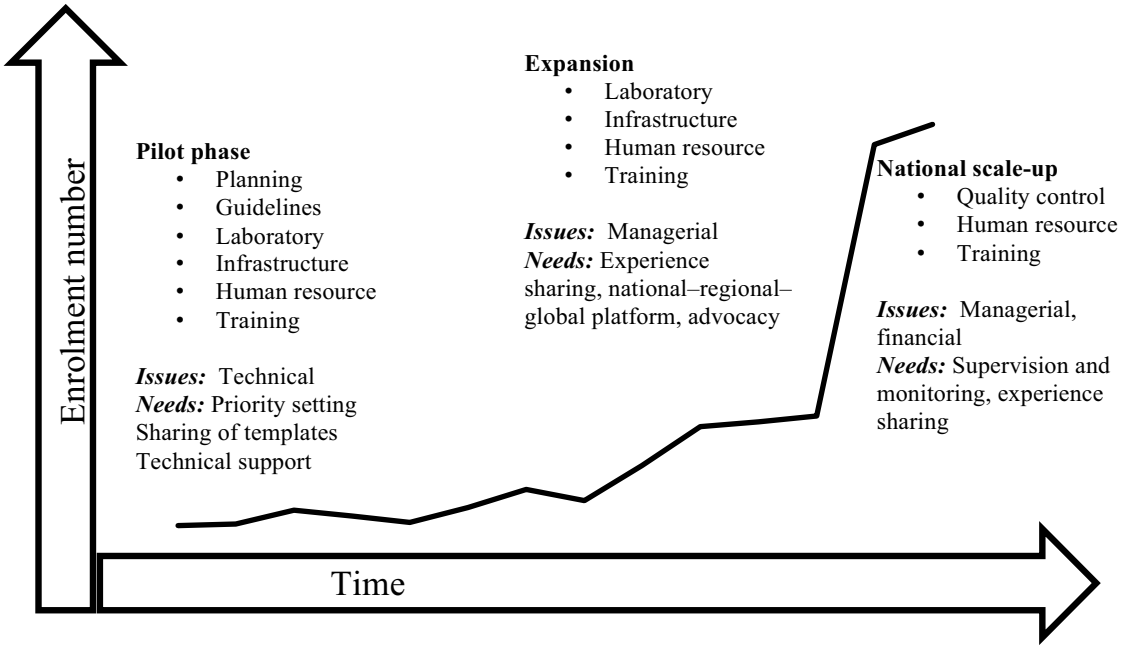

Figure 2. Thematic diagram of technical support requirements during different phases of PMDT scale-up.

likelihood of drug-resistant disease. However, the majority of the MDR-TB burden is occurring among new cases and this trend is likely to increase if ongoing transmission of MDR-TB is not contained. Broadening the presumptive MDR-TB criteria to include all new cases has substantial funding implications. The development of rapid diagnostic tools is paving the way for a rapid increase in the number of diagnosed MDR-TB patients, but those diagnostic tools need to be used properly—different diagnostic algorithms will have different impacts in different country settings. Health economic evaluation (such as cost-effectiveness analysis) of different models will help countries to choose the best model for themselves. Countries need to be pragmatic and tailor their responses to the local epidemic and available resources.

Poor treatment outcomes of MDR-TB cases remain a major concern. Treatment success for the 2011 cohort was only 52% in the Region.[7] Although comparable to the global average (48%),[6] better outcomes are required and can be achieved. Achieving optimal outcomes is essential to retain enthusiasm for PMDT expansion, and for patients, their communities, and governments to retain faith in the value of this important public health programme. Low success rates may be a consequence of transitioning from pilot projects to nationwide expansion, with high loss to follow-up. This poses a serious risk of amplifying drug resistance, and the underlying reasons require thorough evaluation. The fact that some countries have performed well – Cambodia and Viet Nam have consistently achieved treatment success in more than 70% of cases[6,7] – demonstrates the importance of sharing best practices and learning from each other.

Yet another challenge is that PMDT will generate XDR-TB. The risk can be minimized with ongoing surveillance of local drug resistance profiles, optimization of standard treatment regimens, and meticulous attention to all the programmatic factors outlined above. The provision of treatment for XDR-TB, palliative care, and infection control measures needs to be strengthened to address this challenge. It reiterates the need for PMDT scale-up to be based on a well-functioning DOTS programme, with proven readiness and the necessary country commitment. If basic DOTS programmes are dysfunctional, then every effort must be made to correct this in order to reduce the risk of multiplication of resistance and protect future treatment options. Undesirable channelling of resources from DOTS programmes may weaken the base of PMDT. Suboptimal PMDT within a poorly functional DOTS programme may pose more public health risk than benefit.[12,13]

Other obstacles identified are limited human resources, inadequate diagnostics, and misalignment of diagnostic and treatment capacity, especially with the roll-out of the Xpert MTB/RIF test in many countries. A particular challenge within the Region has been the size and unregulated nature of the private sector. The long-term sustainability of programmes has been threatened by donor dependence. Unrealistic donor-driven targets may have unintended consequences, such as fragmenting service delivery and encouraging inaccurate reporting to save face. The delicate balances between ambition, vision, reality, and feasibility, together with the ability to measure progress and gaps, have to be considered at all times.

Table 2
Yearly enrolment into programmatic management MDR-TB (PMDT) programmes in the Western Pacific Region[a,b]

Country	Year			
	2010	2011	2012	2013
Cambodia	38	57	110	121
China	1222	1155	1906	2184
Laos	2	2	9	4
Mongolia	156	126	171	192
Philippines	548	2397	1918	2262
Papua New Guinea	0	60	82	145
Viet Nam	101	578	713	948

MDR-TB, multidrug-resistant tuberculosis.
[a] Source: Global TB database (http://www.who.int/tb/country/data/download/en/).
[b] Data for high TB-burden countries only.

6. Future role

The rGLC WPR has overseen major progress in PMDT scale-up during its initial years. It has also generated greater awareness of regional challenges and has encouraged local solutions to these problems. Countries need continuous support, regular monitoring,

and a forum for sharing experiences throughout the pilot, expansion, and nationwide scale-up phases. Quick changes are fraught with danger if the basic groundwork has not been consolidated.

The rGLC WPR needs to ensure its own relevance and sustainability into the future. Future activities aim to cover the following priority areas: (1) providing strategic oversight and advocacy to improve high-level political commitment, as evidenced by action plans at different levels of the country as appropriate and increased domestic funding; (2) maintenance of essential monitoring, evaluation, and supervision activities, as well as providing a platform for sharing experiences; (3) provision of technical support and contextualized guidance, including assistance with the introduction of new drugs and regimens; and (4) training and capacity building, including basic operational research.

Regional initiatives should be dynamic and responsive to the needs of member countries, but retain a focus on the priority areas outlined. This requires close collaboration with global efforts and ought to be a key component of the newly consolidated Global Drug-resistant TB Initiative (GDI).[14] Funding of rGLC WPR activities depends on the Global Fund cost-sharing mechanism, with contributions from the United States Agency for International Development (USAID) and Japan. Secure funding into the future will sustain and improve current support efforts.

Conflict of interest: This article is an expression of the views of the Secretariat and members of the Western Pacific Regional Green Light Committee.

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