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Operational research for improved tuberculosis control: the scope, the needs and the way forward

C. Lienhardt,* F. G. J. Cobelens†

* Stop TB Partnership & Stop TB Department, World Health Organization, Geneva, Switzerland; † Centre for Poverty-Related Communicable Diseases, Amsterdam Institute of Global Health and Development, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

SUMMARY

The promotion of research is one of the main components of the World Health Organization's Stop TB Strategy, which includes 'programme-based operational research (OR)' and 'research on introducing new tools into practice'. The importance of OR in improving tuberculosis (TB) control was recognised a long time ago, and historical OR studies have been instrumental in the development of major strategies for TB control. Although a growing number of OR projects are being conducted in the world today, little is known about their results or their likely impact on TB control programmes. As funding organisations increasingly recognise the need for OR, we propose a rational framework to conduct OR, which covers a spectrum from local setting-oriented to international policy guiding research, and determines the rele-

vance, replicability and generalisability of the results. OR in TB control is aimed at 1) improving programme performance; 2) assessing the feasibility, effectiveness and impact of new strategies or interventions on TB control; and 3) collecting evidence to guide policy recommendations on specific interventions. This requires strengthened capacity to plan and conduct OR in low-income countries and appropriate support to conduct both nationally and internationally led OR projects. Suggestions are made for potential steps for improved purpose-driven OR, which may help to improve TB control locally and inform policy recommendations internationally.

KEY WORDS: operational research; implementation; capacity building

ONE OF THE MAIN COMPONENTS of the World Health Organization (WHO) Stop TB Strategy is the promotion of research, which includes conducting 'programme-based operational research' and 'research on introducing new tools into practice' (Table 1).¹ Recent history has shown that well-conducted operational research (OR) projects can lay the ground for major advances in tuberculosis (TB) control. Careful observation and analysis of TB programme data have fed the conceptualisation of new or adjusted programmatic approaches that were subsequently implemented and evaluated for their impact on TB control. For example, the observation in the early twentieth century of the incremental yield of serial sputum smears led to a policy of three serial smears for ruling out smear-positive pulmonary TB being recommended by the WHO and the International Union Against Tuberculosis and Lung Disease (The Union).^{2,3} Carefully conducted observational studies in several low-income countries later showed that the incremental yield under routine conditions was less than observed in these earlier studies,^{4,5} and the policy was consequently re-

vised to two serial smears, resulting in huge savings in terms of human resources and workload. Similarly, the experience of a number of national programmes assisted by The Union in Africa during the 1980s showed the feasibility of effective TB case management in low-income countries. These documented observations provided the basis of a new approach to TB control,⁶ which was then adopted by the WHO as the core of its DOTS strategy.⁷ This operational work had a profound impact on shaping modern TB control, and has been translated into policy in the poorest and most afflicted countries in the world over the past two decades.⁸

International and national funding agencies have long recognised the importance of OR for improving TB control, and support a wide array of projects addressing a large range of issues. An increasing number of countries also now recognises its importance; according to the 2008 WHO Global TB Report, 89 countries, including 20 of the 22 high-burden countries, have reported research activities related to TB control (compared with 49 countries in 2006) for a

Table 1 The six components of the Stop TB Strategy¹

- 1 Pursue high-quality DOTS expansion and enhancement
 - Secure political commitment with adequate and sustained financing
 - Ensure early case detection and diagnosis through quality-assured bacteriology
 - Provide standardised treatment with supervision and patient support
 - Ensure effective drug supply and management
 - Monitor and evaluate performance and impact
- 2 Address TB-HIV, MDR-TB and the needs of poor and vulnerable populations
 - Scale up collaborative TB-HIV activities
 - Scale up prevention and management of MDR-TB
 - Address the needs of TB contacts, and of poor and vulnerable populations
- 3 Contribute to health system strengthening based on primary health care
 - Help improve health policies, human resource development, financing, supplies, service delivery and information
 - Strengthen infection control in health services, other congregate settings and households
 - Upgrade laboratory networks and implement the Practical Approach to Lung Health
 - Adapt successful approaches from other fields and sectors, and foster action on the social determinants of health
- 4 Engage all care providers
 - Involve all public, voluntary, corporate and private providers through public-private mix approaches
 - Promote use of the International Standards for Tuberculosis Care
- 5 Empower people with TB, and communities through partnership
 - Pursue advocacy, communication and social mobilisation
 - Foster community participation in TB care, prevention and health promotion
 - Promote use of the Patients' Charter for Tuberculosis Care
- 6 Enable and promote research
 - Conduct programme-based operational research
 - Advocate for and participate in research to develop new diagnostics, drugs and vaccines

TB = tuberculosis; HIV = human immunodeficiency virus; MDR-TB = multidrug-resistant TB.

total of almost 400 projects.⁹ These projects addressed the basic elements of DOTS (49 countries), collaborative TB-HIV (human immunodeficiency virus) activities (39 countries), multidrug-resistant (MDR-TB) and extensively drug-resistant TB (XDR-TB) (39 countries), Practical Approach to Lung Health (10 countries), and social mobilisation and community involvement (22 countries). Research into risk factors for TB, including tobacco and diabetes, and the introduction of new technologies in TB control programmes has also been reported.

However, although increasing numbers of projects are being carried out worldwide, their impact on TB control may be questioned. Little is known about their relevance (do they address recognised gaps in TB programme performance?), their completion (how many are finally reported to relevant audiences?), and constraints or barriers in carrying them out. Only a minority of the OR projects carried out are reported in the international medical literature. As this limits their dissemination, few OR projects are of benefit outside the settings in which they were conducted. This may reflect a lack of motivation in submitting research manuscripts on the part of researchers, a lack of interest on the part of journal editors to pub-

lish OR papers or the lack of writing skills required for publication. It may also reflect poorly designed or conducted research: there seems to be a widely spread misconception that, contrary to well-designed epidemiological research or randomised controlled trials, OR escapes scientifically rigorous investigation and evaluation.

As a result, it is often difficult to assess whether operational studies have had an impact on TB control programmes and led to beneficial changes in programmes and the organisation and infrastructure of health systems. As the global landscape for support to programmes and programme-related research is changing, it is important to revisit the fundamentals of OR and address key questions regarding its practicalities, so as to propose pragmatic ways to optimise and rationalise OR for improved TB control.

DEFINITION OF OPERATIONAL RESEARCH

Many definitions have been proposed for OR. According to Last's *Dictionary of Public Health*, OR is 'the systematic study of the way in which organisations function. [. . .] OR includes health services research that aims at evaluating health services, outcomes and process by which services are provided. It involves epidemiology, economics and social and behavioural sciences'.¹⁰ The WHO defines OR as 'the use of systematic research techniques for programme decision-making to achieve a specific outcome. OR provides policy makers and managers with evidence that they can use to improve programme operations'.¹¹ In 2005, Laserson et al. gave a focused definition of OR in TB as '[research] intended to provide managers, administrators, and policy makers with the information that they need to improve service delivery activities and plan future ones'.¹² Zachariah et al. recently defined OR as 'the search for knowledge on interventions, strategies, or tools that can enhance the quality, effectiveness, or coverage of programmes in which the research is being done'.¹³

These and other definitions show common ideas but also the diversity of focus with regard to the objectives of OR (why are studies performed?), its research methods (how are they performed?) and its scope (what level of policy decisions should they impact?). From a TB perspective, the objective of OR is generally not only to help TB control managers to improve programme operations, but also to provide policy makers with empirically derived or evidence-based answers to address problems in service delivery. OR methods include quantitative and qualitative health service evaluations as well as observational epidemiology studies. However, while for some authors randomised controlled trials are not part of OR methods,¹³ others do include randomised trial designs (such as cluster randomised controlled trials) to assess effectiveness.¹⁴ Finally, the scope of OR suggested by these definitions ranges from an exclusive focus on locally relevant research conducted to address locally

defined problems, to a recognition of the potential impact on global policy recommendations.¹⁵

Rather than taking a position from among these views, we propose that OR for TB control covers a range of objectives, methods and scopes. Instead of addressing this from the perspective of the contentious realm of OR, we propose to start with the identification of research needs for improving TB control, rather than asking what OR should entail. The role of OR in TB control would then be to fill gaps in research between the development and evaluation of new interventions under ideal conditions and the optimisation of the use of and access to such interventions—whether new or existing.

SPECTRUM OF OPERATIONAL RESEARCH

OR may be regarded as covering a spectrum of objectives, methodological options and scope of increasing relevance and generalisability (Figure). At one end of the spectrum, OR is purely setting-oriented and aims at assessing the quality of and access to services, identifying ways in which they can be improved or evaluating the feasibility of locally set approaches or interventions. At the other end, the objective is to assess the effectiveness of interventions when they are implemented and the impact of TB control interventions (e.g., on health outcomes, policy or people's livelihoods). OR studies thus aim at collecting relevant information needed to guide policy making and develop strategies on a global scale. It should be noted that research aimed at studying the effects of, for example, a new drug or vaccine under ideal trial conditions (generally known as efficacy studies) would not be regarded as part of OR.¹³

Logically, methodological options follow these objectives, and range from observational studies that can have important qualitative components (e.g., among small groups of patients or health care workers using direct observation of practice, focus group discussions or in-depth interviews)^{16,17} to comparisons of interventions in which the primary outcomes would be determined by quantitative methods.^{14,18}

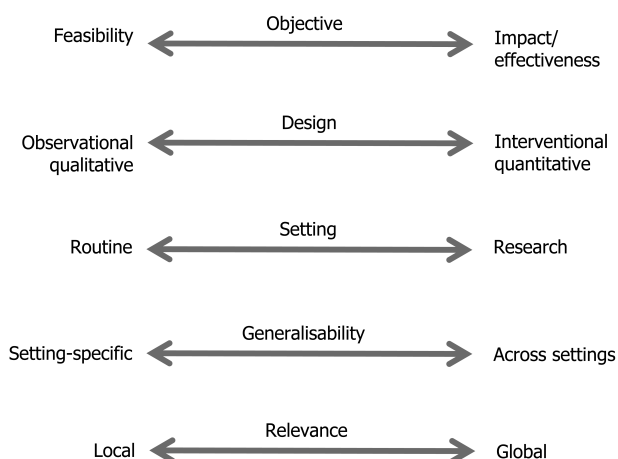


Figure The scope of operational research.

The range in objectives and methodologies also reflect ranges in scope. An important factor is generalisability, i.e., the extent to which results may be applied to settings beyond that in which the data were collected. At one end of the spectrum are studies and study questions for which generalisability is limited, such as studies of health care delivery in which highly specific, local conditions play a decisive role (e.g., determinants of patient satisfaction in the utilisation of TB diagnostic services). This does not present a problem, as studies are intended to provide locally relevant solutions to locally defined problems. On the other end of the spectrum, for studies aiming to collect relevant information needed to guide policy making and develop strategies at a global scale, generalisability to other settings is key. These include studies that measure the impact or effectiveness of new interventions, e.g., new diagnostic tools or treatment regimens, or clinical algorithms for excluding TB disease in patients eligible for isoniazid preventive treatment (IPT). As the local conditions in which studies are conducted influence the effect of the intervention, it is important to distinguish the elements that are setting-specific from those that are valid across settings when interpreting the results. Careful description of the setting in the study report will help policy makers to determine to what extent the results will be applicable to their own setting. Alternatively, similar study protocols can be executed in various settings. By compiling a single multisetting database and using analytical approaches for assessing heterogeneity, such as multi-level (hierarchical) analysis, one can distinguish between setting-specific and general effects.

From the above, the ultimate relevance of an operational study ranges from local to global, determined by the importance of the study question, the observations made and the generalisability of its findings, and is dependent on the quality of the design and the methods used.

A PRAGMATIC PERSPECTIVE OF OPERATIONAL RESEARCH IN TB CONTROL: DEFINING RESEARCH NEEDS

Along this spectrum, a wide range of study types may be used according to the objectives pursued and the scale of research. In pragmatic terms, OR should be defined following an assessment of what is ultimately needed. This can be categorised as research for 1) improving programme performance and outcomes; 2) assessing the feasibility, effectiveness or impact of new strategies or interventions on TB control; or 3) collecting data to guide policy recommendations on specific interventions.

Research to improve programme performance and outcomes

Often regarded as the classical realm of OR, the goal of research to improve programme performance and

outcomes is to assess deficiencies in TB control programmes and identify causes that are amenable to improvement using technical or managerial interventions. Research questions are therefore setting-oriented, and results are setting-specific. Actors are primarily TB programmes and/or researchers commissioned for the studies, and users are health care providers and/or programme managers. The scale is local or national. Despite limited generalisability, the methodological issues may be relevant to other high-burden countries, and publication of the results is useful to provide examples.

A wide variety of approaches may be adopted, including audit-like studies and locally relevant hypothesis-generating studies. Research questions are generated following the identification of problems or challenges encountered in programme activities, and are based on a review of locally collected surveillance or programme-based data or on qualitative studies that use properly defined methods.^{16,17} They may also aim at identifying specific risk factors or the causal effect of given variables, using case-control or cohort (retrospective or prospective) study designs.¹⁸ These can lead to testing targeted interventions aimed at improving local TB control performance, such as methods to increase case detection,^{19,20} improve treatment adherence²¹ or encourage collaboration with the private health sector.²² Disciplines such as health economy can also contribute to the assessment of projects and interventions.²³

Studies of new interventions to improve TB control

New strategies or interventions are needed to improve TB control. These include the effective and efficient use of new tools (diagnostics, treatment, vaccines), as well as of novel algorithms or combinations of tools, or new approaches to care delivery. Once the efficacy of new interventions has been established in relevant trials or validity studies, OR needs to be conducted to determine the conditions/requirements under which these interventions can be implemented by assessing their effectiveness, acceptability, feasibility and affordability under routine programme conditions. This type of OR (sometimes also referred to as implementation research) aims at understanding local, setting-specific factors relevant for the successful introduction of new interventions, as well as factors that apply across settings.²⁴ It thus fills the gap between setting-oriented OR and internationally generalisable research for global policy making. Actors are primarily TB programmes and/or researchers commissioned for the studies. Users include policy makers, care providers and/or programme managers in the country where the study is conducted, and also those of other countries with similar epidemiological patterns and health care systems. The scale ranges from national to regional/international. Studies are therefore best conducted in several countries/settings, and reported in such a way that TB programme managers and policy

makers can use the results to adapt the tested implementation strategy to their own setting. The above-mentioned studies on the incremental yield of sputum smear examination are a good example of this use of OR, as are recent studies from Botswana that evaluated IPT under routine conditions.²⁵

Studies to inform international policy recommendations

It is increasingly recognised that decision making with regard to new interventions should be based on evidence.²⁶ Initial evaluations of new interventions under controlled conditions (clinical, laboratory) need to be complemented by assessments under real life, programme conditions to show that they are beneficial when scaled up.²⁷ Thus, for new diagnostics, once their accuracy has been proven using validity studies, 'demonstration' studies should be performed to evaluate their use in populations and assess their potential impact and cost-effectiveness. Patient-relevant outcomes, such as reduced treatment delay, improved cure rates, quicker recovery of the ability to work and lower risk of relapse and drug resistance, are increasingly recognised as important criteria in deciding whether, and how, to adopt new tools and interventions.²⁸ In addition, it is important to establish their potential impact on TB epidemiology (e.g., transmission), health services and health policy so as to inform policy recommendations.²⁹

Actors are primarily researchers working in collaboration with TB programmes. Users are (international) policy makers. These studies are conducted on a regional or global scale. As generalisability across settings is of primary importance, the choice of study locations is dictated by the representativeness of the setting in terms of epidemiological patterns and health systems, as well as local research capacity to produce high-quality data. While research is being carried out within TB control programmes, there is generally a need for additional research capacity (e.g., laboratory, clinical, data management). Rigorous methods should be used, driven by results from safety, efficacy and demonstration studies, and can include Phase IV trials, cluster randomised trial designs, cost-effectiveness studies and impact evaluation studies.^{30,31} By executing similar study protocols in various countries, data can be compiled into a single database and analysed for comparisons across countries. An example of such evaluation is the recent multicountry demonstration study on the Xpert MTB-RIF assay (Cepheid, Sunnyvale, CA, USA) and the cost-effectiveness analysis based on its results (C Boehme, personal communication).

FUNDING OPERATIONAL RESEARCH: A CHANGING LANDSCAPE

According to the Treatment Action Group (TAG),³² US\$34 million (6.8%) of the US\$510 million invested in TB research and development by more than

70 reporting organisations worldwide in 2008 were for OR, defined as epidemiological studies or randomised controlled studies of existing interventions, or targeted evaluation of new or existing interventions. Although this does not cover all types of OR projects conducted, it indicates that only a limited proportion of funding is available for OR compared to that for more tool-specific development research. For all the tools developed, however, knowledge about their potential impact and ways to optimally incorporate them into existing TB control strategies is crucial. Lack of sufficient funding for OR will therefore severely delay the implementation of new and better tools.

There is a wide range of public and private sources of funding for improving TB control programme operations, including bilateral and multilateral donors, non-governmental organisations, international organisations and private funds. While major funding institutions (such as National Institutes of Health/National Institute of Allergy and Infectious Diseases, the Bill and Melinda Gates Foundation, the European Commission) primarily support 'upstream' technological research and development, increasing attention is currently being paid to 'downstream research', with funding opportunities for improving the use of existing technologies (e.g., increased case finding, simplified treatment monitoring) or new tools (operational requirements and cost-effectiveness of new technologies). New opportunities are arising, such as the Wellcome Trust initiative to strengthen research capacity in Africa,³³ or the recently launched President's Emergency Plan for AIDS Relief (PEPFAR) Phase II, which states that 'study proposals [. . .] are encouraged to focus on bringing evidence into practice to improve service delivery and outcomes'.³⁴

Although not included in the TAG report, the Global Fund to Fight AIDS, Tuberculosis and Malaria (The Global Fund) is a major funder of TB control programmes in high-burden countries. The Global Fund explicitly states that up to 10% of country proposal budgets should include monitoring, evaluation and OR. The proportion of grants including an OR component has increased from 19% in Rounds 1–5 to 58% in Round 7, highlighting the importance of OR in national TB programmes (NTPs). However, this provision does not seem to be used optimally in some countries, due to limited local capacity for conducting OR, absence of coordination mechanisms at country level to involve suitable research collaborators,³⁵ or lack of capacity to access and handle funds for OR ('absorptive capacity'). The latter may limit the demand for funding and in turn, through a vicious cycle, reduce its availability.

All of this underscores the importance of capacity building with NTPs to manage and conduct OR projects in high-burden countries. NTPs themselves should be recipients of funds for OR so that priorities for OR are set by themselves rather than by research institutes. In this respect, international funding or-

ganisations, such as the Global Fund, could have an important role to play.

ASPECTS OF CAPACITY BUILDING

Despite international interest in OR and broad consensus regarding its importance in TB control, the reality is that very little research is conducted or published from resource-limited settings where the greatest burden of TB is found.³⁶ Capacity to conduct OR within NTPs is often limited due to lack of expertise, infrastructure, staff, funds, policy cycle and/or a professional culture supportive of the critical questioning of performance that OR entails. According to a recent workshop organised by the Stop TB Partnership Research Movement, the main reasons for this lack of capacity are that OR is often not embedded in Programme Strategy Plans, that there is no focal person in programmes directly responsible for OR, and that OR projects often do not yield clear results to improve programme performance (see Stop TB Partnership website www.stoptb.org).

Building the OR capacity of NTPs should address three levels: institutional, human resource and collaboration. The creation of an environment conducive to the performance of OR is key to improvement at NTP level. NTP managers should be convinced of the benefits of ongoing monitoring and evaluation to improve programme performance and increase ownership of results. A core OR capacity should therefore be implemented at the NTP or the Ministry of Health (MoH) levels, while collaboration with governmental research institutes, local universities and non-governmental organisations should be forged to support the organisation research projects. NTPs should therefore include staff members who are capable of planning and conducting OR projects, and even if they do not participate in the studies themselves, they should at least be the lynch pin between the NTP and the collaborating research partners.

Training in OR should provide a theoretical background in research methods as well as practical experience with fieldwork. It should, at a minimum, include capacity training for quantitative research (linked to monitoring and evaluation), including protocol development, ethical approval, data collection and analysis, paper writing and publication. Additional training could include qualitative research, economics and social science, although it might be better to seek collaborative partnerships with groups that have expertise in these areas. There are multiple schemes for building capacity in OR, from short, ad hoc in-country training courses to overseas academic training, from distance learning to 'on-the-job' training, etc. Mentorship programmes are increasingly being proposed, which offer the advantage of accompanying selected candidates through various levels of training, coupled with on-the-job training and practical experience.³⁷ Career perspectives for research

trainees adds to staff retention, e.g., through 'OR fellowships'.

HOW TO REALISE OPERATIONAL RESEARCH: THE NEED FOR A CONCERTED EFFORT

Promoting the use of rational, objective-driven OR in TB control, in our view, means that research needs along the entire 'OR spectrum' must be addressed, from local to international level. This implies that fruitful local experience should feed international recommendations that, in turn, should be adapted to local needs and constraints.

An example of the latter is the recently reaffirmed WHO recommendation, based on a series of clinical trials and systematic reviews, for wide implementation of IPT.³⁸ Although based on solid evidence, little guidance has been offered on how to implement this policy locally, leaving NTPs facing complex issues such as how to confirm TB infection, how to rule out TB disease, or how to achieve an effective link between TB and HIV/AIDS (acquired immune-deficiency syndrome) control programmes. Another example is the use of novel diagnostic tools or approaches, such as front-loaded microscopy, fluorescence microscopy or non-commercial culture-based methods for the diagnosis of drug-resistant TB, recently recommended by the WHO, that need to be integrated into health services. Novel and creative thinking is needed to address gaps between policy recommendation and implementation, between local needs and the larger perspective, and to set up clear directions for research. A broad, concerted effort is urgently needed to develop OR capacity, allocate appropriate resources and encourage all actors to work together.³⁹

Thus, at the national level, NTPs should be encouraged to create their national research agenda reflecting the research priorities based on local needs.^{40,41} Coordination mechanisms should be established at the national level to provide clear strategies to establish research priorities and determine the allocation of resources necessary to address these, involving NTP managers, MoH decision makers as well as local and international partners and donors. Targeting of resources in a concerted manner will ultimately optimise OR projects so that the results can be of direct benefit to NTPs and patients. As the ultimate relevance of OR is to contribute to the improvement of TB control performance and influence policy change,⁴² it is essential that policy makers be involved at an early stage, when planning the study, so that they are aware of the questions addressed and of the expected findings.⁴³

At the international level, there is a need to identify priorities that can guide funding institutions to target in OR needs. On this basis, in November 2009, the Stop TB Partnership Research Movement, the WHO Stop TB Department and the Global Fund initiated a process of 'promotion and rationalisation of operational research for TB control', which included an ex-

pert group meeting, a workshop, the commissioning of a systematic review on OR and wide consultation with the main stakeholders, including the Stop TB Partnership Working Groups.⁴⁴ The objective was to critically address the increasing need for improved and rationalised OR in TB control, define gaps and identify key areas where evidence was lacking for proper implementation of existing and innovative technologies and novel service delivery models. The definition of priority areas was discussed, particularly with regard to their use in countries that would apply to the Global Fund rounds as well as to other grant calls. As a result, five key areas were identified in which knowledge gaps using either existing or novel technologies hamper proper implementation of TB control activities. These are 1) access to, screening for and diagnosis of drug-susceptible, MDR and XDR-TB; 2) development of sustainable collaboration with all practitioners for TB care and control; 3) prevention and treatment of TB in HIV-infected patients; 4) optimal access to and delivery of treatment and retreatment of drug-susceptible, MDR and XDR-TB; and 5) OR capacity building. For each of these, problems relating to the present situation were identified and prospects for potential improvement/solutions were developed (Table 2). The list of critical questions to be addressed to improve TB control at national and international levels in each of these five areas was the basis for the inclusion of OR as a well-characterised component of research and development within the newly launched Global Plan to Stop TB 2011–2015.⁴⁵

Given the above, we suggest that the promotion and rationalisation of OR in TB control could furthermore be based on the following three steps: 1) creation of an OR agenda in collaboration with key partners and stakeholders, based on local agendas and results of systematic reviews; 2) development of a global OR database that would list projects and detail their objectives, study populations, methods to be used, and the expected results and outputs; this would provide extensive information on what is being done and where in the world, and help track studies and their results, and could thereby make research outcomes transparent and widely accessible to programme managers, policy makers and researchers; 3) development of multicentre/country OR proposals to address common challenges (such as the identification of the optimal combination of diagnostic tools at all levels of the health services to increase case finding) using similar study protocols and collecting data in a comparable manner. The development of functional research platforms grouping partner countries and international organisations is a proposed model to scale up OR both at the national and international levels, and will provide ample information for policy making.

CONCLUSION

Operational research in TB control covers a wide range of objectives, methodologies and scopes, depending

Table 2 List of priorities in operational research

Goal: To conduct research aimed at improving TB control performance and developing interventions that result in improved policy making, better implementation of health systems and more efficient methods of service delivery		
Description	Major activities	Scope*
To improve access to and use of diagnostic services to increase early case detection and improve the diagnosis of drug-susceptible TB, MDR- and XDR-TB and TB associated with HIV	Conduct research on the socio-economic and qualitative barriers that influence TB diagnosis at patient and health provider level and identify the most effective interventions for overcoming these barriers	1
	Research on ways to bring diagnostic services closer to the community (decentralisation, active case finding, mobile systems, etc.) and how to integrate them into the general health system	1
	Research aimed at improving the screening of suspects and high-risk groups, identifying which populations/high-risk groups should be screened, what they should be screened for and how they should be screened	1
	Research on service delivery to find out how to introduce new tools in current health systems; what their contribution to improved case detection and treatment of drug-susceptible and drug-resistant TB would be; and how TB diagnostic services could be integrated with other diagnostic services	2
	Research on the ideal combination of diagnostic tools to be introduced and what determines the appropriateness of particular combinations for particular national programmes/health services	2
To foster operational research for sustainable public-public and public-private partnerships for TB care and control	Evaluation of the post-scale-up impact of a new test, including public health and societal consequences	3
	Improve and scale up existing approaches to engage all health care providers	1
	Monitor contributions of different provider groups to TB care and control	1
	Encourage the involvement of as yet unengaged providers	1
To address priority operational research questions to improve implementation of joined TB-HIV control activities	Develop and assess responses to changing involvement of diverse providers in TB care and control	1
	Encourage the introduction of regulatory approaches, such as mandatory TB case notification, certification and accreditation, and restricting access to anti-tuberculosis drugs to collaborating care providers	1, 2
	Investigate how to optimise links between TB and HIV/AIDS programmes	1
	Investigate means to improve decentralisation and integration of access to TB treatment and ART	1, 3
	Assess the validity of TB screening algorithms in HIV-infected persons in different settings	2
	Research on how to improve adherence to IPT	1, 2
To investigate methods to improve access to and delivery of treatment for drug-susceptible, MDR- and XDR-TB patients and encourage community participation	Research on the optimal timing for IPT in relation to ART	3
	Investigate how to reduce mortality in TB-HIV co-infected patients	3
	Optimise infection control to reduce TB transmission	1
	Identify reporting gaps and develop dynamic feedback systems to improve and monitor service delivery	1
	Research to assess factors that affect health-seeking behaviour and treatment adherence and test means to improve adherence and reduce default rates	1
	Identify ways to empower users, families and communities	1
To enhance capacity building for operational research within programmes	Research on retreatment regimen and amplification of drug resistance	3
	Identify risk factors for drug-resistant TB	1, 3
	Define and evaluate strategies for integration/scale-up of drug-resistant TB management into TB control programmes	1, 3
To enhance capacity building for operational research within programmes	Address issues related to capacity strengthening for operational research to ensure that countries have the capacity to perform TB-related operational research to improve programme performance	1
	Assess the impact of various operational research training models	3
	Assess means of sustaining capacity and retaining trained staff in programmes	1

Source: adapted from Stop TB Partnership⁴⁵ and Marais et al.³⁹

* Scope of operational research: 1 = improving programme performance and outcomes; 2 = assessing the feasibility, effectiveness or impact of new strategies or interventions on TB control; 3 = collecting data to guide policy recommendations on specific interventions (see p 8).

TB = tuberculosis; MDR-TB = multidrug-resistant TB; XDR-TB = extensively drug-resistant TB; HIV = human immunodeficiency virus; AIDS = acquired immune-deficiency syndrome; ART = antiretroviral treatment; IPT = isoniazid preventive treatment.

on the needs it addresses. These needs include improvement of programme performance; feasibility, effectiveness and impact of new strategies or interventions in TB control; and evidence to guide policy recommendations on specific interventions.

Strengthening the capacity to plan and conduct OR in low-income countries has risen up the international agenda, as has support for nationally led OR projects. The development of local and national OR agendas are a prerequisite to conducting objective-driven OR projects and ensure their uptake by the authorities concerned. The establishment of an international OR database and the development of OR platforms bringing together partner countries and international organisations may help improve the quality

of OR projects and enhance their impact on national and international policy making. Funders should be encouraged to invest in sustainable research, including OR that is built into the framework of programmes, particularly in areas where the disease burden is high and resources and time are limited.

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R É S U M É

Promouvoir la recherche est une des composantes essentielle de la Stratégie « Halte à la Tuberculose » de l'Organisation Mondiale de la Santé, qui inclue la recherche opérationnelle (RO) intégrée aux programmes de lutte et la recherche pour l'introduction de nouveaux outils dans la pratique quotidienne. L'importance de la RO pour améliorer la lutte contre la tuberculose (TB) est reconnue depuis longtemps, et des études historiques ont joué un rôle majeur dans la mise au point des stratégies majeures de lutte mondiale contre la TB. Un nombre croissant de projets de RO est actuellement mené dans le monde, mais on ne connaît pas tous les résultats de ces projets, ni s'ils ont eu un impact sur les programmes de lutte contre la TB. Comme les organismes donateurs tendent à reconnaître de plus en plus l'importance de la RO, nous proposons un cadre rationnel pour mener ces projets, qui couvre un spectre large—depuis la RO menée au niveau du programme pour en améliorer sa performance,

jusqu'à la RO menée au niveau international afin de guider le développement des recommandations de santé publique. La reproductibilité et la capacité de ces projets à être généralisés dépendra du niveau de cette RO. De manière générale, la RO est menée dans les trois domaines suivants : 1) améliorer la performance des programmes de lutte ; 2) évaluer la faisabilité, l'efficacité et l'impact des nouvelles stratégies ou interventions ; et 3) collecter les données nécessaires au développement de recommandations de santé publique sur l'utilisation de telle ou telle intervention. Cela demande un renforcement des capacités afin de planifier et mener des projets de RO dans les pays à faibles ressources et un soutien financier approprié afin de mener ces projets au niveau national et international. Des suggestions sont faites sur les diverses étapes de la RO qui permettra une amélioration de la lutte contre la TB au niveau national et influencera la mise au point des recommandations au niveau international.

R E S U M E N

Fomentar la investigación es uno de los principales componentes de la estrategia Alto a la Tuberculosis de la Organización Mundial de la Salud, que comprende la 'investigación operativa (IO) con enfoque programático' y la 'investigación sobre la introducción de nuevos instrumentos en la práctica cotidiana'. Durante mucho tiempo se ha reconocido la importancia de la IO en el progreso del control de la tuberculosis (TB) y los estudios históricos de este tipo han contribuido en forma decisiva al desarrollo de las principales estrategias encaminadas a controlar la TB. Aunque en la actualidad se llevan a cabo un número creciente de proyectos de IO, se conoce poco acerca de sus resultados o de su posible repercusión en los programas de lucha contra la TB. Dado que los organismos que proveen financiamiento admiten cada vez más la necesidad de IO, se propone a continuación un marco racional para la realización de IO, desde la centrada en los entornos locales hasta la investigación desti-

nada a orientar las políticas internacionales; este marco establece la pertinencia, la reproducibilidad de los estudios y la factibilidad de generalizar sus resultados. La IO en materia de control de la TB busca: 1) mejorar el desempeño de los programas; 2) evaluar la factibilidad y la efectividad de las nuevas estrategias e intervenciones y su repercusión en el control de la TB; y 3) recoger datos fidedignos que orienten la formulación de recomendaciones normativas sobre intervenciones específicas. Estos objetivos exigen el fortalecimiento de la capacidad de planeación y de puesta en práctica de la IO en los países de bajos ingresos y el respaldo oportuno a la realización de estos proyectos de escala nacional e internacional. Se aportan además sugerencias sobre los pasos que pueden optimizar las investigaciones con fines concretos, que contribuirán al progreso local del control de la TB y documentarán las recomendaciones normativas en el ámbito internacional.