



IMPLEMENTATION RESEARCH IN TDR: CONCEPTUAL AND OPERATIONAL FRAMEWORK



UNDP/World Bank/WHO
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RATIONALE FOR IMPLEMENTATION RESEARCH

There are many examples of potentially effective disease control products that have had only limited impact on the burden of disease because of inadequate implementation resulting in poor access. Insecticide-impregnated nets (ITNs) have been shown to reduce overall child mortality by 15-60% in field trials. But implementing ITNs on a large scale has proven difficult and only a fraction of African children at risk have access to the protection of an ITN. Available antimalarials could greatly reduce child mortality in Africa if given promptly when needed, but recent situation analyses in several African countries showed that less than 10% of children with symptoms of malaria had access to appropriate treatment within 24 hours after the onset of fever. TDR studies suggest measures that can improve prompt delivery of antimalarial drugs at the household and community levels – e.g. training of shopkeepers and innovative packaging of antimalarial drugs – and home management of febrile illness can improve child survival. But these interventions have not yet been implemented on a large scale.

Praziquantel was a breakthrough for schistosomiasis control. Though initially too expensive, the price has now come down but treatment coverage remains poor in Africa, the continent with the largest schistosomiasis burden. Single-dose diethyl carbamazine (DEC) and ivermectin were shown to be effective for large-scale treatment of lymphatic filariasis and they are now the recommended drug regimen, in combination with albendazole, for the global elimination programme. But it is proving difficult to achieve a sufficiently high treatment coverage to ensure elimination of transmission. Simple interventions based on regular washing of affected limbs with soap and water can greatly reduce the suffering of patients with elephantiasis, but it is not evident how to ensure effective implementation of this intervention on a large scale.

All the above products have successfully completed the classical R&D process, and have been put on the shelf of proven disease control products. But they failed to have their full potential impact because of major implementation problems that impeded

access. Research on these products ceased too early. It is now agreed that research should not stop after providing the proof of principle for a product, or after demonstrating its effectiveness in selected situations, but that it has an additional critical role to play in helping solve major implementation problems. Experience has shown that implementation research can make a major difference and help ensure that proven control products have the intended health impact. Examples are the development of community-directed treatment (ComDT) for onchocerciasis, and development of home-management for uncomplicated malaria. These examples used to be exceptions but under its 2000-2005 strategy, TDR is addressing implementation research as an integral part of the research process. TDR supports implementation research for proven and currently available control products, and is preparing for implementation research on new products that would have a significant impact on disease burden if access can be assured, such as rectal artesunate for malaria or miltefosine for leishmaniasis. ■

OBJECTIVE OF IMPLEMENTATION RESEARCH

The overall objective of implementation research is to significantly improve access to efficacious interventions against tropical diseases by developing practical solutions to common, critical problems in the implementation of these interventions.



In order to achieve this objective, Implementation Research will:

1. **Identify common implementation problems, and their main determinants, which prevent effective access to interventions, and determine which of these problems are susceptible to research;**
2. **develop practical solutions to these problems and test whether new implementation strategies based on these solutions, can significantly improve access under conditions of routine disease control;**
3. **determine in collaboration with partners the best way to introduce these new implementation strategies into the health system and facilitate their full-scale implementation, evaluation and modification as required.**

Implementation research will focus on diseases for which a disease control tool (or package of tools) is available and proven to be efficacious, and that has the potential to greatly reduce the burden of disease if the major implementation problems could be resolved and access be improved. Access is defined as the facility with which disease-affected populations can obtain relevant components of specific public health interventions. Access reflects both the supply of and the demand for the intervention. ■



CRITERIA FOR IMPLEMENTATION RESEARCH

Implementation Research covers a broad research area. TDR will need to set clear priorities for implementation research and develop very focused research activities. To help guide the prioritization process, TDR's Scientific and Technical Advisory Committee (STAC) has defined the following criteria for implementation research to be undertaken by TDR:

- **Research need for disease control**

Implementation research should address priority problems for disease control that are amenable to research. The need for research on these problems should have been clearly expressed by disease control programmes.

- **Researchable questions**

TDR's mandate is research and there needs to be a clear distinction between implementation research and routine activities of disease control and programme implementation, such as monitoring and evaluation. Implementation research will require clearly defined researchable questions that can be addressed by scientific methods, it

being understood that the exact definition of research questions may require exploratory research. The proposed research should also offer a good prospect for innovative solutions to disease control problems.

- **Expected health gain**

Implementation research aims at improving access in order to maximize the impact of interventions on poor and marginalized populations. A major criterion for prioritizing implementation research products should therefore be the expected ultimate health gain for the poor. This emphasis on health gain also implies focusing on a limited number of priority areas to ensure the timely development of a solid evidence base for more effective implementation strategies and thus build momentum for their application, rather than focusing on a large number of small isolated issues that are unlikely to have significant health impact.

- **Possibility to extrapolate to other settings and diseases**

Priority will be given to research for which the results will be relevant for

other settings and health systems, and for other diseases and control strategies. Location-specific problems would not be covered by implementation research and would require the development of local solutions through operational research undertaken within the context of a national control programme. However, if similar problems would occur in several different locations or settings, there may be an underlying generic researchable problem that would justify implementation research efforts. Most implementation research may initially be disease specific, but a research proposal will receive higher priority if it is likely that the research findings can be extrapolated to other diseases.

- **Focus on process and outcome indicators**

The aim of implementation research is to improve access, and the evaluation of new and improved implementation strategies will therefore focus on process and outcome indicators of access, such as the percentage of children with fever receiving appropriate treatment within 24 hours. STAC

deemed the specific focus on process and outcome indicators a necessary and appropriate step which would facilitate up-scaling of interventions. It recommended that the question of access be de-coupled from the question of health impact: both may be important but they will generally require a different study design.

Implementation research is a concept that is still evolving in TDR. Further experience is needed to better define the optimal boundaries, the most effective division of labour with local operational research, and how research capacity building can be undertaken most effectively to optimize the impact of research on disease control. ■

GENERAL OPERATING PRINCIPLES

Implementation research requires a different mode of operation than in other research areas in TDR. The following are general operating principles that are characteristic for implementation research:

• Active link to disease control

Implementation research will need active links to disease control in order to properly understand implementation problems, to ensure that proposed solutions are appropriate, and to accelerate uptake of these solutions in disease control. This requires links with health services and disease control programmes in endemic countries, as well as active interaction with regional and global disease control initiatives where such exist, e.g. Roll Back Malaria, Stop TB, Global Programme for Elimination of Lymphatic Filariasis, African Programme for Onchocerciasis Control, etc.

• Rapid response to needs of disease control

Implementation problems require urgent solutions and implementation research needs to respond rapidly to

the priority needs of disease control. If the development of new solutions takes too long, sub-optimal solutions may get implemented that would be difficult to change at a later stage. Hence, implementation research must be rapid and responsive, as well as flexible and proactive.

• Partnership

Successful implementation of interventions requires the involvement of many partners, and special efforts must be undertaken to ensure that implementation research becomes an effective and respected member of such partnerships. Partnerships are important to implementation research as a source of information on developments in disease control implementation, and as a major target audience for reporting the findings and recommendations of implementation research, and for implementing the solutions.

• Involvement of disease endemic country scientists

Implementation research requires active involvement of researchers >

from endemic countries. It provides them with an important opportunity to broaden their experiences and skills in implementation research. Implementation research will provide additional support as required (e.g. through skills training or protocol development workshops, etc.) to strengthen the research capacity of national scientists and disease control staff. The main focus will be on "learning by doing".

- **Involvement of endemic country health professionals**

Equally important is involvement of health professionals in the area of health systems development, programme implementation and disease control who can help ensure that the research focuses on the major implementation bottlenecks and who will be essential in translating research findings into improved implementation in real life.

- **Smooth and flexible interaction with other research areas of TDR**

This is of particular importance for interaction with the Steering Committee

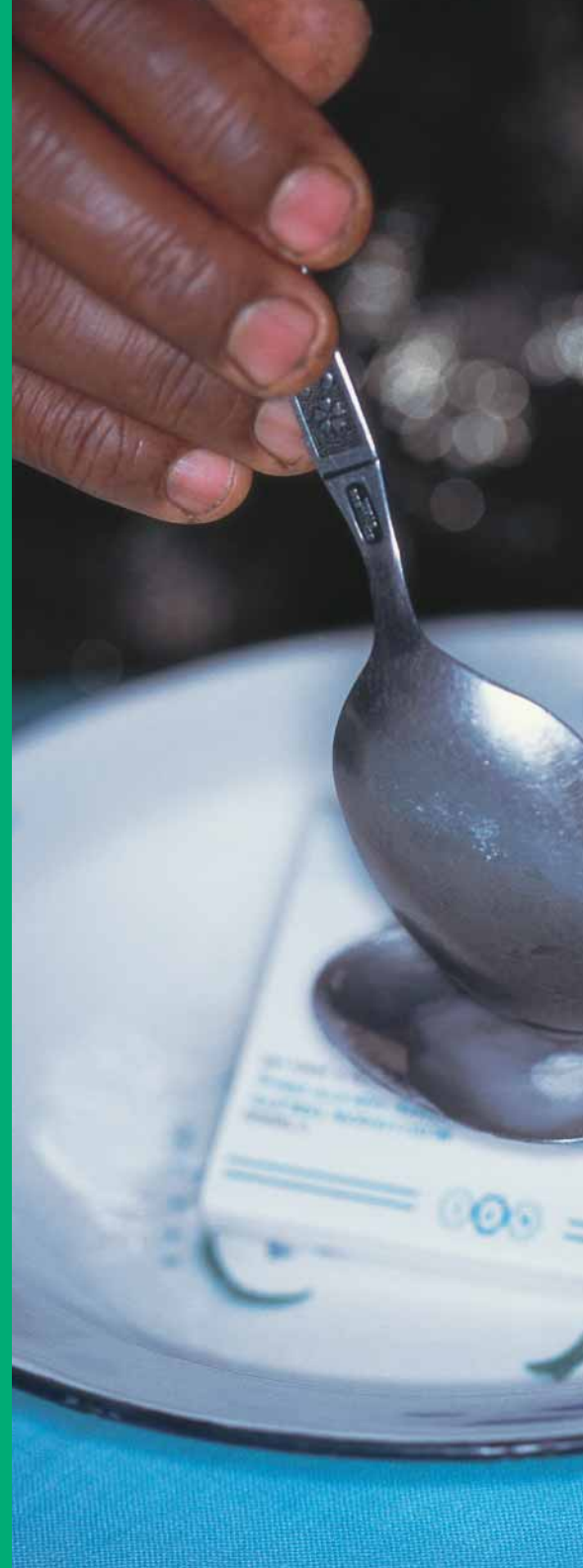
on Proof-of-Principle research, which funds research into the effectiveness of new and improved intervention methods, and for interaction with Research Capacity Strengthening.

- **Collaboration with TDR co-sponsors**

Implementation research will actively collaborate with TDR's co-sponsors, especially at the implementation level where there are important opportunities for synergy between TDR's research and the co-sponsors' support to large-scale implementation initiatives. Implementation research will also work closely with related WHO programmes and with all concerned WHO offices at country and regional levels.

- **Active marketing of results**

The available disease control tools and the results of implementation research must be actively marketed at all levels: international, national, provincial, district and community. This will require special implementation research activities to develop cost-effective ways to market research findings. ■





CHALLENGES



Implementation research will bring many new challenges. Developing a good understanding and building collaboration with endemic communities, national health systems, Ministries of Health, and WHO regional offices, while at the same time remaining well connected with research and academic institutions, will require building bridges between experts that do not traditionally work well together. The staff profile of TDR may need to be modified to include more experts in public health, health systems and disease control programme management.

Implementation research could become expensive and labour intensive

particularly since real life challenges occur during large-scale implementation of control strategies. The balance between what resources are directly attributable to control and which ones to research, and how control programmes will contribute, will need careful consideration.

New ways of fundraising may need to be developed, especially for diseases for which TDR does not have a tradition of implementation research. Start-up funds may need to be identified to enable TDR to demonstrate its capability for implementation research for those diseases, and establish its comparative advantage, before significant additional funding can be secured.

PRODUCT PORTFOLIO FOR IMPLEMENTATION RESEARCH

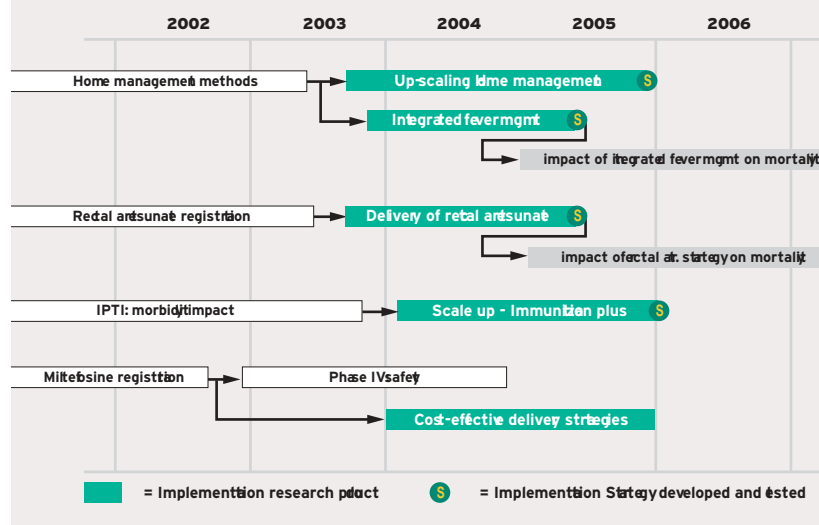
The Scientific and Technical Advisory Committee endorsed the above framework for implementation research during its meeting of February 2003 and requested TDR to clearly show how the planned implementation research activities fit in the overall research effort of the Programme.

TDR's overall research priority setting process is based on a comprehensive consultative analysis of research needs and research opportunities. The resulting priorities are summarized in the Strategic Emphasis Matrix which includes the strategic emphases for implementation research. A portfolio of research products defines the specific research activities that TDR plans to undertake to address the strategic emphases. The Strategic Emphasis Matrix and the product portfolio are regularly reviewed and updated according to new research needs and opportunities. In January 2003, the product portfolio for implementation research was updated to reflect the refocusing on issues of access. The implementation research portfolio for the 2004/2005 biennium is described below.

In discussing the product portfolio, it is useful to differentiate between two types of implementation research:

1. Implementation research that is the next logical step for products in the TDR research pipeline that are or will soon be ready for implementation and for which there are important research questions on how they should be implemented and
2. Implementation research on TDR tools that have been developed in the past and that are now the cornerstone of tropical disease control but for which there are major obstacles to large-scale and sustained access.

Figure 1. IR as the next and final phases of products in the TDR pipeline



The current products in the Implementation Research portfolio are listed in Table I (see pages 12-13), which shows for each product the main research questions, current or potential partners and the resources required. **Figure I** shows the timelines for the type 1 products and indicates to which other products in the TDR research pipeline they correspond.

Implementation research is the next step in the research pipeline for four major TDR products: two drugs that were recently or will soon be registered (rectal artesunate and miltefosine), one intervention method Intermittent Preventive Treatment in infants (IPTi) for which the proof of principle is being demonstrated in terms of morbidity impact, and one implementation method (home management of malaria) that has been shown effective in improving access to appropriate antimalarial treatment at the community level and in reducing malaria mortality.

The home management approach has been adopted by Roll Back Malaria, but as the previous studies were done at

small scale, there remain important questions about its effective up-scaling through the public health system. Hence, one implementation research product will focus on this issue in the context of up-scaling in RBM lead countries in Africa. The studies on home management have also led to the concept of community-based integrated fever management, combining treatment against malaria and pneumonia. There remain many questions to be resolved about how this can be implemented effectively without jeopardising access to malaria home management while ensuring proper use of antibiotics. This is the subject of another implementation research product. Similar questions on how to deliver the drug at the community level are the subject of the implementation research on rectal artesunate.

All products shown in Figure I are expected to produce tested implementation strategies within 2-3 years and these will then be made available to Ministries of Health and control programmes. The tools on which these interventions are based have all been

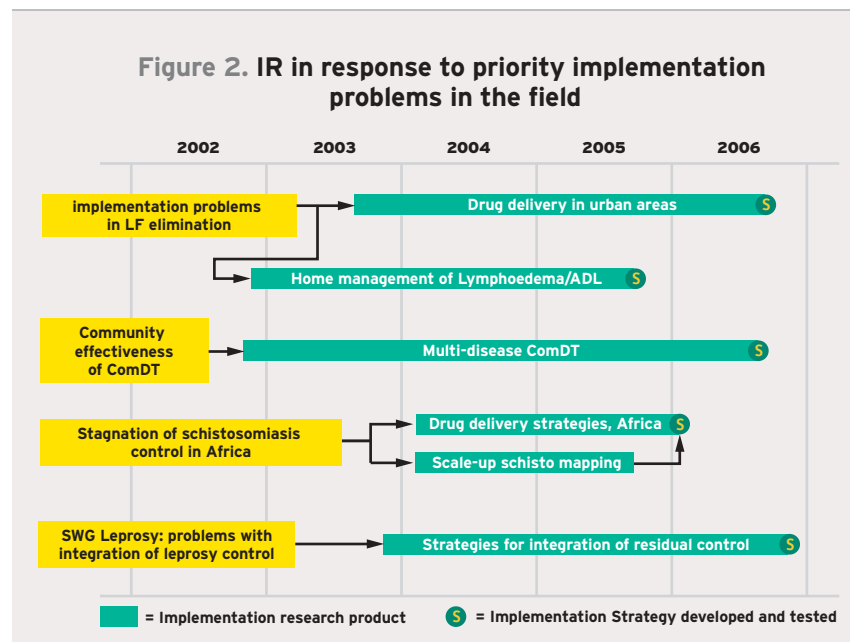
shown to be efficacious in reducing morbidity. However, this information may not be considered sufficient to justify large-scale implementation of rectal artesunate and integrated fever management and it is planned to undertake trials of their effectiveness in reducing child mortality, once the implementation strategy has been worked out.

The implementation research products in Figure I cover all major products that are approaching the end of the development phase in the TDR research pipeline, with the exception of Lapdap, where the main questions relate to its effectiveness and safety, and which is therefore covered by another research activity outside implementation research. Access to artesunate combination treatment will be covered by implementation research on home management.

Figure 2 (see page 10) shows the timelines for the type 2 products, and the major implementation problems they respond to. Three of the diseases are in TDR's disease category III for which the "control strategy is proven >

effective, disease burden falling and elimination is planned". For these diseases, TDR's overall strategic emphasis is on improved implementation strategies, and hence they feature prominently in the implementation research portfolio.

The tools used in the interventions in Figure 2 have all been developed previously by TDR, i.e. single-dose DEC or ivermectin +/- albendazole for lymphatic filariasis, ivermectin for onchocerciasis, praziquantel for schistosomiasis and MDT for leprosy. Significant progress is being made with control of the diseases concerned, but there remain major implementation challenges for which research input is urgently required. The need for research has been clearly expressed by those responsible for implementation and this strong demand for research greatly facilitates the necessary collaboration between research and control. The implementation research products for lymphatic filariasis and onchocerciasis have already been started although some, e.g. on community level management of lymphoedema/ADL,



on a very limited scale due to lack of funds. The research on multi-disease ComDT is a response to both a challenge (sustained annual ivermectin treatment over a period of decades) and an opportunity (the success with community-directed treatment for onchocerciasis providing a possible model for integrated delivery of community-based interventions). This is an example where implementation

research for one disease may contribute to health sector development in general and to improved implementation for other diseases. The implementation research products for schistosomiasis and leprosy have not yet started due to lack of funds.

The research questions that all these products address are summarized in Table I. There are two types: questions

on how to implement and ensure effective access by those in need, and questions on how to bring the interventions to scale within the context of the health system constraints in endemic countries. Both are critical and both need to be addressed if TDR's research is to have the intended impact.

Table I also shows that there are established or anticipated links with the relevant international disease control/elimination initiatives and selected Ministries of Health. Furthermore, the concerned WHO programmes are involved and contribute to the planning and implementation of the research activities.

The main problem for Implementation Research is that of funding. Funds are currently only available for 5 of the 11 implementation research products, and for none of those do the available funds meet the requirement. The best funded product is that on up-scaling of malaria home management, for which 70% of the required funds have been secured from TDR's undesignated

funds. But only 30% of the required funds are available for the product on sustainable management of lymphoedema/ADL, a level at which the product cannot be properly implemented. For 6 of the 11 products, no funds have yet been identified.

TDR has been successful in developing efficacious interventions for targetted tropical diseases. The remaining challenge is to ensure access to these interventions by those who need them. Implementation Research will be critical to make this happen.



Table 1. List of Implementation Research products with the corresponding research questions and pa

Product title	Main research question
Scale-up of effective home management of malaria	What factors hinder/promote scaling-up of home management system at large scale? Which factors determine sustainability? Is home management equally feasible/acceptable using new technologies?
Integrated management of childhood fevers at the community level	Is an integrated intervention for malaria and pneumonia feasible? How should it be implemented to achieve high coverage?
Strategies and impacts of deployment of rectal artesunate in highly-endemic malarious areas	How and where at household/community level should the intervention be deployed? What training/supervision is needed for persons who diagnose and administer? What health education best supports referral and treatment?
Scale-up of "Immunization Plus" with UNICEF in 4 countries of West Africa	What is the effect of adding IPTi on acceptability of, and coverage of, immunization? What is the cost-effectiveness of IPTi?
Cost-effective delivery strategies for new drugs against visceral leishmaniasis	What are the most appropriate and cost-effective ways for delivering drugs? How to ensure high levels of compliance?
Drug delivery strategies for lymphatic filariasis elimination in urban areas	What are the main reasons for low treatment coverage in urban areas? Can these problems be overcome with a community development approach?
Strategies for sustainable and affordable management of lymphoedema and associated ADL	How can simple methods for lymphoedema/ADL management be made sustainable? Are alternative strategies?
Community-directed integrated delivery of interventions for major health problems in Africa	Is ComDT a feasible and effective approach for the integrated delivery of interventions? What are the advantages and disadvantages, and what measures to improve it?
Strategies for improved delivery of praziquantel at the community level	How can praziquantel treatment be scaled up in different settings? How feasible/cost-effective is the use of existing mechanisms?
Scaling-up mapping of urinary schistosomiasis for nationwide planning of control	How can the educational system be involved in mapping? What mapping/spatial analysis strategy should be used?
Strategies for integration of leprosy control into the regular public health services	What are the major obstacles to integration of leprosy services? How to improve case detection, compliance, disability prevention and referral?

	Current/potential partners
management of malaria. What is the most cost-effective and sustainable distribution strategy? What adaptations are needed for IEC and in urban settings? Are more effective/expensive drugs?	RBM, MoH, AFRO, WHO/MAL
Intervention in children feasible and acceptable to communities? How to ensure adherence by caregivers? How to make the intervention sustainable?	UNICEF, MAL, CAH
How can the drug be made available for optimal access? How to diagnose, treat, provide referral advice, monitor treatment? How to provide advice?	RBM, MAL, EDM
How to ensure compliance with EPI (including EPI coverage) and how can it be optimized?	UNICEF
How to improve detection of patients, delivering miltefosine to the most affected groups and	MoH India, CPE
How to improve access in urban areas? How to develop and partnership strategy?	ICMR, NICD, CPE
How can the intervention be brought to scale? How feasible, cost-effective and	CPE
How to improve integrated delivery of community-based interventions? What modifications are needed?	APOC, RBM
How to improve access in endemic regions in Africa? How to develop mechanisms for other diseases?	SCI, CPE
How to improve access to schistosomiasis using the red urine questionnaire?	SCI, CPE
How to improve access to services and what are possible solutions that can sustain adequate levels of access, referral?	International NGOs, CPE

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