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Operational Research for the 3 by 5 Initiative

Introduction

The World Health Organization (WHO) promotes an evidence-based approach to public health. To date, most of the experience and evidence about the treatment of HIV/AIDS with combination drug therapy has been generated in industrialized countries, where physician-led, individual case management is the standard model of care. Unfortunately, relatively few of these data are of immediate relevance to the delivery of antiretroviral therapy (ART) in resource-constrained settings.

UNAIDS and WHO have established the 3 by 5 target and announced that closing the treatment gap is a global health emergency. It is therefore clear that an incomplete evidence base on how to most effectively implement ART in resource-limited communities *cannot* be a constraint to emergency approaches to close the treatment gap in line with the 3 by 5 target. In contrast, lack of knowledge mandates "learning by doing"—the implementation of an operational research agenda of relevance and importance for ART programmes.

As treatment programmes go to scale, it is critical to derive data about what works, and what does not work and why, as fast as possible. This is implicit in the 3 by 5 strategy, where one of the two strategic elements in Pillar 5 "The rapid identification and re-application of new knowledge and successes" is to continuously learn by doing—with ongoing evaluation and analysis of programme performance and a focused operational research (OR) agenda.

The Operational Research agenda for 3 by 5

The 3 by 5 Initiative has therefore developed a focused and relevant operational research agenda which has six areas of activity:

1. **to coordinate and help develop an appropriate operational research agenda relevant to the needs of ART programmes.** The capacity to do research in many resource-limited countries is constrained and it is important to coordinate activities. It is also essential to focus work on the issues relevant to scale-up. Consensus will be developed with programme managers about the immediate needs and will then be regularly reviewed by a small ad-hoc committee as data and evidence are generated, and new issues emerge.

2. **to seek data on the impact of scaling up ART on prevention and at-risk behaviour; on mitigation; and on stigma and discrimination.** While we expect treatment to accelerate prevention, it is important to provide clear evidence that this does indeed happen, and seek ways to maximize any synergies. It is also critical to identify rapidly whether any negative interactions occur, and take urgent steps to stop them (see the technical briefing on Accelerating prevention). Such work can best be done in communities already involved in research. Many of these groups have already come together in a WHO-funded meeting, an OR agenda has already been mapped out and will commence when funds are made available early in 2004.

3. **to identify ways to define the externalities of ART scale-up on health systems performance.** While we anticipate the resource inputs and capacity strengthening necessary to scale up ART in line with 3 by 5 targets will strengthen health systems, it is important to provide clear evidence that this does indeed happen, and seek ways to facilitate it. It is equally important to identify where the opposite is happening and ways to minimize any negative impacts. An internal think tank in WHO has already started to map out the issues involved and will define the basic OR agenda and the relevant research partners in early 2004.

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4. **to identify ways to cost ART programmes and to link costs to impact and effectiveness.** The sterile debate about whether treatment or prevention is more cost-effective is redundant with the universal recognition that a comprehensive approach is the only acceptable programme design to implement. Nevertheless, solid cost data and cost-effectiveness analysis must be conducted to help develop sustainable systems and their long-term financing. By the end of January 2004 the basic OR agenda will be defined and the research partners identified.

5. **to improve programme design and find better tools to reduce risky behaviour and drug resistance, based on the analysis of data.** The results of all the OR and other strategic information-gathering activities need to be analysed rapidly with a view to what works, what does not work and why. The capacity of research groups in the South will be developed to enable most data analysis to be done nationally.

6. **to incorporate new knowledge rapidly back into ART programme policy and practice.** Research within the 3 by 5 Initiative must be focused and contribute immediately to the improvement of operations. Data and new knowledge need to be fed back rapidly both to the centres where the OR is carried out (an ethical obligation), but more widely to any programmes facing a similar situation. This core activity of WHO underpins the entire OR approach.

Clinical trials and Operational Research

Some evidence is best derived from clinical trials and indeed some data can only reliably come from a trial where individuals are randomized to different interventions. Many clinical trials groups with considerable experience of ART trials in industrialized settings are actively forming partnerships with research groups in high-burden countries, and developing the research infrastructure necessary to do large and multi-centre trials.
Some of the more obvious topics are already being pursued by these established research teams. For instance, several clinical trials of different drug regimes, or ways to implement treatment with structured interruptions of treatment, are under way. One trial is comparing laboratory-guided patient management with clinical management alone. Other funded trials will seek to determine how treatment reduces HIV transmissibility.

The immediate issues for the 3 by 5 operational research team here are:

- to foster collaboration and coordination of the various research teams and partnerships to avoid unnecessary duplication and academic competition;
- to review how comprehensively the clinical trials agenda is covered;
- to ensure that the clinical trials agenda being pursued is really the most appropriate to ART programmes as they scale up; and
- to fill in any clear and strategically important gaps in the research agenda.

Strategic information and Operational Research

There is a clear complementarity and inter-relationship between monitoring and evaluation (M&E), some specific surveillance activities and operational research. All derive "strategic information", new knowledge and data that will make up the evidence base on ART delivery in resource-limited settings.

- Programme performance will be monitored and evaluated regularly, and analysis of how different and heterogeneous approaches to the delivery of ART compare to one another will be of immediate significance (see the technical brief on Monitoring and Evaluation)

- Drug resistance surveillance will show the extent of this problem and how well programmes contain it; and careful analysis should be able to reveal the determinants that influence the evolution and spread of resistance and thus what to do to minimize its emergence (see the technical brief on Drug resistance surveillance).

Regardless of where the data come from, all need to be analysed in terms of what can be done to improve programme performance and impact.

Milestones: **OR agenda defined in 25 national programme committees to scaling up access to ART by June 2004.**

50 OR projects funded and in progress in at least 25 countries by December 2004.

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