Research for Change: Using Implementation Research to Strengthen HIV Care and Treatment Scale-Up in Resource-Limited Settings

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The expansion of human immunodeficiency virus (HIV) care and treatment in Africa and other resource-limited settings has begun to mitigate the impact of the acquired immunodeficiency syndrome pandemic. As this expansion has occurred, critical research has been conducted that has helped to define best practices and establish guidelines in HIV care. However, despite this research, a tremendous gap exists between the actual delivery of care and those strategies with proven efficacy in the clinical research setting: the program-implementation gap. The field of implementation research has the potential to fill this knowledge gap and to address the barriers to the effective replication of evidence-based interventions in local settings. This article reviews the current understanding of the field of implementation research and discusses its association with other areas of health services research, clinical research, and quality management work. Opportunities for conducting implementation research are proposed, and future steps to develop the field are outlined.

The expansion of HIV care and treatment in Africa and other resource-limited parts of the world has been an important step forward in mitigating the impact of the AIDS pandemic on individuals, communities, and nations. The immediate challenge—getting HIV care and treatment programs started—has largely been met worldwide. These early treatment efforts have had a range of success; the approaches have been as varied as the environments in which they have been tried. The 3 challenges now facing the global community and national governments involve: (1) how to most effectively scale up HIV treatment from thousands to millions; (2) how to ensure quality; and (3) how to sustain large public treatment programs over time, given limited resources. Key questions include: (1) which models of delivery of care are effective in various settings, (2) which interventions should be expanded and replicated, (3) how human and financial resources are affected by the scale-up, and (4) how effective these approaches will be once they are implemented across diverse sites and areas.

The scale-up process has been facilitated by research. Examples of new knowledge developed to help define the optimal approaches to scaling up HIV treatment in resource-limited settings have included: (1) pilot programs that have explored a particular model of care delivery [1–4]; (2) evaluations of novel drug regimens and laboratory monitoring strategies [5–8]; (3) assessments of barriers unique to care in marginalized populations and in resource-limited settings, including HIV testing strategies [9]; (4) financial resource analyses, including cost studies and cost-effectiveness models [10, 11]; and (5) human resource analyses, including assessments of the impact of health care worker shortages locally or globally [12].

In many cases, standard methods of clinical research—from prospective cohorts and randomized, controlled trials to cost-effectiveness analyses—have pointed the way toward successful implementation of HIV care and treatment [1, 5–8, 10, 11, 13–15]. Al-
though traditional approaches to clinical research in HIV care and treatment will remain critical to HIV treatment scale-up, there is a tremendous gap between a research finding and making an effective service available to sick people living amidst poverty and broken health systems; this gap is known as the “program-implementation gap.”

We often assume that interventions with proven efficacy in a clinical research setting will be easily replicated on a larger scale in real-world settings. However, for many diseases, including measles, malaria, tuberculosis (TB), and HIV disease, the implementation of proven interventions has lagged. Research to identify and address the barriers to effective replication of evidence-based interventions in public programs has lagged even further [16]. One example is the efficacy of directly observed therapy to improve adherence to and cure rates associated with TB treatment. Although model programs have reported high rates of success, reports from most national TB treatment programs document much lower rates of cure, raising questions about how implementation failed and the potential risk of drug-resistant TB [17].

The global investment in programs to expand HIV prevention, care, and treatment services has grown to nearly 10 billion dollars per year. Translating findings from clinical research studies and pilot programs into effective design and implementation of national programs is vital to maximizing the benefit of this immense investment. However, little is known about which interventions are effective at scale-up and over time. As a consequence, it is essential that research be conducted to determine (1) how HIV care and treatment interventions that have been proven to be effective in pilot settings are designed and implemented and (2) how to translate the findings from clinical trials into broader practice.

IMPLEMENTATION RESEARCH

Fixsen and colleagues from the National Implementation Research Network noted, “It has been well documented in many disciplines that major gaps exist between what is known as best practices and what is actually done” [18, p. 2]. As Sanders and Haines [16] have delineated it, implementation research, as a subset of health services research, addresses multiple components of health systems, including their policies, processes, structures, and resources. Because of this broad scope, there are areas of overlap between areas of implementation research and health systems research, operations research, outcomes research, decision analysis, program evaluation, and quality improvement initiatives. Therefore, implementation research is perhaps best seen as a subdiscipline driven by a specific research agenda: to improve health services in the context of practical constraints. It applies methodologic rigor borrowed from other areas of health services research to address implementation questions. It strives to develop new knowledge about how health services are delivered and how they can be most effectively implemented within the context of local, real-world constraints.

Although the disciplinary boundaries remain imprecise, what is more important than a formal definition of implementation research is a need to better define the optimal approaches that can answer the following key questions: What is happening, is it what is expected or desired, and why is it happening this way? [19]. Some work has already begun to define the role of certain methods and approaches in implementation research, but much remains to be done [20–23].

EXAMPLES OF IMPLEMENTATION RESEARCH

The effectiveness and efficiency of programs and services as implemented depend on a range of factors, including the site, environment, provider, and patient or target populations. Research into implementation has identified some of the factors associated with better or more-effective HIV care, as implemented according to established guidelines in high-income settings. Studies have included evaluation of a quality improvement effort in federally supported HIV clinics across the United States [24]; the quality of care provided by an experienced HIV care provider [25]; and continued disparities between the care received by women and the care received by men [26].

Work in more resource-limited settings has provided evidence of the power of applying rigorous health services research methods to programs as implemented. One example was reported by the Quality Assurance Project/Russia, which evaluated the implementation of a multicomponent program to improve the management of arterial hypertension [27]. The research included cost analyses and addressed service utilization questions beyond traditional quality assessment. The data were able to provide valuable lessons relevant to how the program could be expanded within the local constraints in Tula Oblast, Russia, and to assess the potential impacts on health services and costs.

IMPLEMENTATION RESEARCH IN THE SCALE-UP OF HIV CARE AND TREATMENT

There has been a growing body of work in implementation research examining the expansion of HIV care and treatment. These studies have begun to describe the successes and gaps in HIV care in a number of areas, including provision of antiretroviral agents, screening for TB, and prevention of mother-to-child transmission (PMTCT) [27–30].

With only 11% of HIV-infected pregnant women receiving prevention interventions in 2006, PMTCT, in particular, has been the focus of a rapid increase in implementation research [31]. A study of the efficacy of 1 PMTCT program across 3 districts in South Africa found considerable variability in the care provided [32]. The researchers were able to identify both
patient factors and site factors associated with successful implementation, highlighting challenges of effective implementation of evidence-based interventions in the context of local constraints. They noted that identifying and addressing causes of inequalities in how programs are implemented, as well as assessing the effectiveness of the programs, was critical to optimizing the impact of PMTCT interventions.

Implementation research on breast-feeding by HIV-infected mothers has also contributed to a better understanding of the gaps between clinical trial results and the results noted when these interventions are translated into guidelines and implemented in constrained settings [33, 34]. In Botswana, for instance, formula-fed infants had higher rates of illness than did breast-fed infants during a large outbreak of diarrheal disease [34]. The importance of understanding the impact of local constraints—in this case, a lack of access to clean water—on the outcomes of a program provides context for policy decisions and program design. To reach the low levels of HIV transmission seen in clinical trials, governments will have to invest in safe water. Implementation research allows such decisions to be based on data from the actual settings in which the interventions will be delivered, rather than based solely on abstraction from pilot programs or trials.

Distinguishing Implementation Research from Related Approaches to Optimizing Delivery of Health Interventions

Because implementation research is a discipline defined more by its agenda than by its methods, it is useful to compare implementation research with its related disciplines. Each of these approaches will lead to new knowledge regarding how best to deliver HIV care in resource-limited settings and will guide implementation research studies.

Clinical research. The field of HIV care, treatment, and prevention is constantly changing and progressing, driven in large part by clinical studies designed to expand understanding of HIV/AIDS and effective approaches for its treatment and prevention. Clinical research seeks to develop new knowledge and understanding about health care and treatment not limited by the constraints found in the real-world context of health care delivery. Recent examples include data on circumcision and prevention, newer approaches to PMTCT, and the management of women who receive treatment with single-dose nevirapine [15, 35, 36]. Implementation research plays an important role in increasing our understanding of how to translate clinically effective practices into systems of care and treatment that incorporate the challenges of local environment and resources. Moreover, there are many areas of HIV care and treatment for which randomized trials are neither feasible nor ethical [37]. In these settings, implementation research also is an essential step to expand knowledge for optimal approaches in local settings [29, 30].

Operations research. Confusion reigns in distinguishing implementation research from operations research. "Operations research," a term borrowed from process engineering, has been defined as the discipline of applying advanced analytical methods to optimize decisions. Research questions in the field of operations research generally take the following form: How can a set of operations be optimized, given a specific set of constraints? Generalized, these questions arise in many fields, ranging from manufacturing to airline scheduling, to computer network design, to health service delivery. As an interdisciplinary science, operations research utilizes analytic methods in mathematical and statistical modeling to support decision making for complex, real-world problems, focusing on how operations are put into place and executed in an organization or system. For HIV care in resource-limited settings, classic operations research has been used to address questions of facility siting and capacity, commodity forecasting, and resource allocation, as well as vaccine efficacy [38–41]. More broadly, operations research has been used in important studies of barriers to access and barriers to implementation, as well as to guide the design of national and local HIV treatment interventions [42, 43]. Implementation research provides the crucial link between the findings of operations research on how to optimize a system of care and treatment and the effective application of these findings in a local program.

Cost-effectiveness. There are many examples where mathematical models that include cost-effectiveness analyses of existing programs have been useful in guiding the development of policies and guidelines for HIV care and treatment [10, 11]. As with any model, the accuracy of its findings will depend entirely on how well it reflects real-world conditions. Thus, the outcomes of HIV treatment programs based on the guidelines and policies suggested by models will always need to be studied once implemented, to determine whether the assumptions made for the mathematical models hold true in the nonidealized locations where services are delivered.

Monitoring and evaluation. Significant efforts are also already under way to strengthen the monitoring and evaluation of care and treatment scale-up efforts, with a number of countries and donors investing in these efforts. In general, the objectives of monitoring and evaluation programs and implementation are similar: to understand what is working as well as what is not working and why. However, most monitoring and evaluation activities necessarily focus on measuring the services provided rather than on the barriers to implementation. The scientific rigor of implementation research broadens the scope of monitoring and evaluation activities, to understand the etiology of gaps between expected results and observed outcomes.

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Quality improvement. The field of quality measurement and improvement has also contributed to progress in the expansion of HIV care, treatment, and prevention. Quality assessment—that is, measurement of the current level of performance relative to established standards—identifies areas for quality improvement at the site and program level. Measuring quality of care is difficult in resource-limited settings, where the demands of providing care leave minimal time or resources to assess and improve care. However, quality improvement activities are necessary to ensure that care is provided as designed, with outcomes, as planned, that meet acceptable standards for effective care and service delivery [44].

Despite these constraints, there are examples of quality assessment and improvement efforts having been implemented in a number of areas of medical care in resource-limited settings [45–47]. There is also a growing effort to examine and improve the quality of HIV services as provided. Groups such as the Quality Assurance Project, the Institute for Healthcare Improvement, the Region Center for Quality in HIV Care, and others have been working in selected areas to measure and improve the quality of HIV services. However, although quality improvement includes data collection and analysis, it is not necessarily designed to scientifically approach questions of how and why programs and systems are implemented.

Although all of these areas of work are essential to the scale-up of HIV care and treatment worldwide, and, although these areas should be further strengthened, we argue that the broader scope of implementation research is often missing from the spectrum of activities designed to improve treatment. One important element that is central to implementation research but may be peripheral to other approaches is that programs operate within local constraints. A better understanding of what models and which systems work best in the local constraints of a specific setting and for different target populations is essential to improve the efficiency of scale-up efforts.

Opportunities for implementation research

It is essential to be able to identify and understand gaps in efficacy between clinical trials or pilot programs and the programs implemented on the basis of these trials or recommended guidelines. There are many opportunities for implementation research to further facilitate and strengthen the expansion of HIV prevention, care, and treatment, including antiretroviral therapy (ART) (Appendix). For example, even at sites supported by a single program and using similar guidelines, data showed heterogeneity of services as delivered across sites and identified multiple areas where improvement was needed, in addition to opportunities for cross-site learning [27, 32].

A better understanding of the levels of quality in the setting of rapid expansion is important to identify the models and systems best able to provide effective care as the expansion continues and to provide assistance to efforts for which strengthening is needed. Further work to better define the site, provider, and patient population characteristics that are associated with the differences in quality and effectiveness of services is urgently needed to both improve these sites and disseminate this information to programs at the local and national level that are planning ongoing expansion. Training has been a major activity to ensure scale-up of quality of care, and implementation research to determine optimal approaches and effectiveness for transfer of knowledge and skills is equally important [48]. Another key role of implementation research is to evaluate the efficacy and safety of circumcision as a prevention intervention when replicated across multiple sites as a response to recent study results and the recommendation of the Joint United Nations Programme on HIV/AIDS [49]. Similar work is needed to continue to better understand optimal approaches to the feeding of infants, management of pregnant women who are in need of ART, replication of adherence interventions, and the impact on outcomes of newer models that integrate HIV and TB care. Other areas include the effect of integration of routine “opt-out” HIV testing, task shifting, quality and effectiveness of care, pediatric adherence strategies, and many other areas.

What are the next steps?

There is a critical need for a practical and public health–oriented approach to measuring, understanding, and improving services as implemented and the programmatic characteristics associated with successful translation of clinical trial results into care settings. This approach must include the development of appropriate research studies that can evaluate aspects of implementation, including feasibility, fidelity, and outcomes, without overburdening programs as they provide desperately needed services. There also needs to be an increased focus on further definition and development of optimal study design, appropriate methods of statistical analysis, and integration of the multiple disciplines required to understand and improve implementation. To accomplish this goal, implementation research needs to become an integral part of the research agenda—as central as clinical trials in the development of evidence-based guidelines and program design. Finally, increased funding and institutional support for collaborations between academic research and public health programs directly involved in scale-up and implementation are required to provide the platform from which these efforts can be initiated. Adequate budgetary provision for implementation research to improve program delivery has been included in previous Global Fund rounds, in World Bank projects, and in the President’s Emergency Plan for AIDS Relief strategies, as well as in national plans. These efforts should be applauded and continued.
In addition to the implementation gap, there is a well-known information gap in global health. Efforts should also be focused on disseminating the findings from implementation research studies widely and translating them into policies and program designs. Identifying who will implement the necessary changes and deciding how this will be accomplished will need to be integrated into the planning and improvement processes. One possible model is the Quality Enhancement Research Initiative funded through the U.S. Veterans Affairs Research and Development Service [50]. The program works to maximize the quality and outcomes of services provided through the Veterans Affairs system by systematically implementing evidence-based approaches to care and clinical research findings into clinical practice. The structure, process, and outcomes of these efforts are then evaluated to determine whether the program efforts have achieved the desired goals. The underlying principle is that “practice needs to determine the research agenda, and research results determine interventions that improve quality of patient care” [50]. The intersection of clinical research and clinical service needed in the scale-up effort for prevention of HIV infection, care, and services provides the opportunity to apply this principle to strengthen and enhance ongoing and new efforts.

CONCLUSION

Experience in expanding HIV care and treatment continues to strengthen as efforts increase. However, research to understand how HIV interventions that have been proven to be effective in trial settings can be implemented in real-world, local settings and how to scale pilot treatment programs to include larger numbers of people remains less developed. The hypothesis-driven approaches and methodological rigor more fully developed in biological and medical sciences need to be expanded within the field of implementation research. Only by carefully studying and understanding the gaps between what was planned and what has happened, as well as which populations did or did not benefit and why, can we better understand how to effectively expand HIV treatment to people and communities in need. Quantitative and qualitative methods drawn from health systems research, operations research, outcomes research, and decision analysis, as well as the data collection, analysis, and process improvement methods drawn from program evaluation and quality improvement initiatives, can and should be integrated into a robust science. The growth of implementation research as a mature discipline will improve our ability to learn from past experience. As a discipline focused on translating results from laboratories, clinical research, and pilot programs, implementation research will assist health care providers and policy makers in their efforts to address the needs of patients affected by HIV infection and other diseases worldwide.

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APPENDIX

SAMPLE IMPLEMENTATION RESEARCH QUESTIONS

- How do we balance the need to provide quality, effective care with the reality of local resource limitations? How do the optimal approaches differ on the basis of environment, site, and target populations?
- What is the optimal balance needed between resources to provide health care services and resources allocated to conduct implementation research to evaluate and learn from experience?
- How does the model of care and the way it has been implemented predict sustainability and quality? What are the challenges in replicating the model in other settings? How should these challenges be identified and addressed?
- In settings where standards of care exist, why aren’t they followed and why don’t they result in the desired health outcomes?
- What variables determine whether program goals have been met?

References


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