Report From the Expert Consultation on Implementation Science Research

A Requirement for Effective HIV/AIDS Prevention and Treatment Scale-Up

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1.0 Executive Summary

Scientific knowledge and financial resources available to prevent and treat HIV/AIDS have expanded considerably over the last decade. Yet the knowledge base regarding how to deliver interventions efficiently and effectively, transfer interventions from one setting or population to another, and make informed choices between competing interventions has not kept pace with the growth of HIV/AIDS services globally. This gap in the transference of research findings to full-scale program delivery is impeding the success in prevention, care, and treatment programs in both the numbers of persons reached and the effect on health outcomes. Implementation science research provides us with an opportunity to address this implementation gap by reducing the unknowns in program delivery and by developing models that increase the public health impact of HIV/AIDS prevention, treatment, and care services.

The roots of implementation science are found in operations research, an area of study originally developed for military, industrial, and government applications, but it is now increasingly used in global health practice. Classic operations research uses a variety of advanced analytic tools to improve practices or production, whereas implementation science is a broader term for a field of study in which multiple disciplines—including epidemiology, sociology, and health economics—come together to achieve improvements in population health. Researchers conducting studies under the umbrella of implementation science are not testing the efficacy of a potential intervention, but rather seeking to improve the effectiveness of a proven strategy or treatment. Improving effectiveness means researchers may need to use study designs that will not always allow them to strictly control all variables, which, in turn, may affect the generalizability of results. This potential weakness is balanced, however, by the value of implementation science research: the ability to contribute to program development and scale-up, thus illuminating problems and testing new approaches to the application of results from controlled research settings.

Based on landmark clinical research studies, we know how to reduce HIV transmission and effectively treat persons living with HIV/AIDS. However, in settings where the burden of HIV is high, where financial and human resources are low, or where cultural and social norms affect health-seeking behaviors, these definitive research results have yielded low-to-moderate returns when results are transferred into HIV/AIDS programming or service delivery. For example, male circumcision and prevention of mother-to-child transmission have not been implemented effectively in many settings. Using implementation science research, we have an opportunity to identify barriers within these types of interventions and simultaneously test a potential solution to increase the effectiveness of program investments.

In response to the growing imperative for analyses to inform and improve uptake of proven interventions, and to scale up HIV/AIDS programs, the Office of AIDS Research (OAR) at the National Institutes of Health (NIH), in collaboration with the Pangaea Global AIDS Foundation, convened an expert consultation in July 2009 in Cape Town, South Africa, to provide a forum for discussion and identification of research priorities in the field of implementation science as they relate to the NIH mission. The central question addressed through this consultation was how researchers and program implementers can work within the field of implementation science to achieve substantial positive impacts in public health and to make recommendations on the role of NIH in reducing the

research-to-implementation gap. Recommendations were made for implementation science research in the following areas:

- Prevention of mother-to-child HIV transmission;
- Engaging and retaining individuals in HIV/AIDS care;
- Integration of primary health care and HIV/AIDS services;
- Structural interventions (determinants of risk; service utilization);
- Human resources and health systems; and
- Scaling up proven interventions (male circumcision, co-trimoxazole, isoniazid).

In addition to specific research priorities, recommendations from the consultation included necessary changes in practices and the organization of the implementation science field, as well as steps to ensure appropriate review of research funding applications; developing implementation science research methodologies and standards of practice; coordinating research activities with implementing agencies, setting clear priorities for the field; developing mechanisms for disseminating research results; and initiating training opportunities for researchers and implementers in the field.

2.0 Introduction

Scientific knowledge and financial resources available to prevent and treat HIV/AIDS have expanded considerably over the last decade, and yet, the collective knowledge and well-documented experience on how best to deliver proven interventions, to transfer interventions from one setting or population to another, or to make informed choices between competing interventions are lacking. The translation of scientific knowledge to effective and efficient program implementation can be referred to as the "implementation gap."

In recent years, the implementation gap has become a critical barrier in efforts to reduce HIV incidence and attain treatment and health outcome goals. Efforts to bridge the gap and scale up interventions proven effective in clinical trials have led to the rise of operations research, impact evaluations, and more rigorous monitoring and evaluation designs in the field of HIV/AIDS. Implementation science is an umbrella term that can be used to encompass various forms of research focused on reducing the implementation gap, making it possible to improve health outcomes at a population level, and increasing the public health impact of HIV/AIDS prevention, treatment, and care services.

In the health domain and in the field of HIV/AIDS research, numerous institutions, multilateral entities, and foundations have been engaged in supporting and/or conducting implementation science activities for several years. The Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), World Bank, and World Health Organization have identified the importance of implementation science in scaling up interventions and meeting internationally established prevention and treatment goals. Within the U.S. public sector, the National Institutes of Health (NIH), the Office of the U.S. Global AIDS Coordinator (OGAC), the U.S. Agency for International Development (USAID), and the Centers for Disease Control and Prevention (CDC) all have active implementation science portfolios, and all have articulated the importance of this form of research in answering field-based questions where environment, economics, culture, gender, behavior, and social circumstances complicate service delivery.

Organizers of international HIV/AIDS conferences are increasingly including sessions highlighting the results of operations research (a precursor to implementation science research), reflective of the growing recognition that this area of science is important in successful scale-up of HIV/AIDS and related health services globally. As the global leader in supporting AIDS research, NIH has a role to play in implementation science. In July 2009, the NIH Office of AIDS Research (OAR), in collaboration with the Pangaea Global AIDS Foundation, convened a consultation in Cape Town for discussion on implementation science research among experts in the field of HIV/AIDS research and program implementation. OAR, located in the NIH Office of the Director, is responsible for coordinating the scientific planning, budgetary, legislative, and policy elements of the NIH AIDS research program, and for promoting collaborative research in national and international settings. All the NIH Institutes and Centers support AIDS and AIDS-related research. The NIH has a significant interest in implementation science research. As the scientific knowledge in HIV prevention and treatment continues to expand, the gap between discovery and implementation increases, undermining the progress needed in resource-poor settings domestically and abroad.

In Cape Town, Dr. Jack Whitescarver, NIH Associate Director for AIDS Research and Director of OAR, explained that the goal of the consultation was to consider opportunities and priorities for implementation science research and the unique contribution the NIH could make to reduce the research-to-implementation gap. Dr. Nancy Padian, Chair of the consultation, emphasized the importance of the implementation science field, especially in the area of AIDS research. She outlined the format of the consultation, which included plenary presentations and a series of breakout group discussions. The following report reflects the key points made in presentations and group discussions at the consultation and summarizes recommendations for future NIH support.

2.1 The Origins and Application of Implementation Science *(Chris Collins)*

As a precursor or cousin to implementation science, operations research has its roots in 19th century analysis of sorting, pricing, and transportation processes in the English postal services. The scale, effectiveness, and efficiency required in operations to support World War II activities spurred significant development of the field; today, operations research is used widely in industry and government.

Scale, effectiveness, and efficiency are essential for controlling the global AIDS epidemic, both in prevention and in treatment. With a large and ever-expanding body of scientific knowledge, the importance of narrowing the gap between what is known about efficacious treatment and prevention interventions and their effective delivery in the field has grown. With the application of operations research to the field of health, multiple definitions of the term have emerged. A framework document on operations research developed by the Global Fund in collaboration with other international health agencies states, “Any research producing practical, usable knowledge…which can improve program implementation…regardless of the type of research…falls within the boundaries of operations research.”

Classic operations research emphasizes the use of advanced analytic tools, such as mathematical and statistical modeling, so that the greatest efficiency in manufacturing an item or delivering a service can be achieved. This approach has a role in the health sector, where such techniques can be employed in selected instances, as in the most efficient design of an operating theater. However, in

the health sector, a broader range of disciplines, including epidemiology, anthropology, sociology, statistics, political science, policy analysis, health economics, and ethics is often needed to answer important questions. Implementation science applies to all these disciplines and encompasses a wide range of health research activities, including:

- Comparisons of two or more established interventions;
- Different approaches to delivering a health intervention;
- Strategies to encourage uptake of available services;
- Improved processes to guide implementation and program management;
- Adaptation of interventions to new populations and settings;
- Cost-effectiveness modeling; and
- Improved methodologies to implement interventions at scale.

Implementation science should be distinguished from other areas of health research. For example, clinical research focused on establishing the efficacy of health interventions in controlled settings or on monitoring and evaluation of program delivery falls outside the scope of implementation science. By contrast, implementation science can be used to successfully identify the optimal and most efficient solutions to implementation and operational challenges, resulting in strong programs and achieving good health outcomes. It encompasses various forms of research design and crosses disciplines—for example, impact evaluation and classic operations research—as long as a clear research question has been identified.

2.2 Improving Population Health: The Utility and the Challenges in the Application of Implementation Science *(Stefano Bertozzi)*

There is increasing recognition of the critical role implementation science can and must play in improved and broader delivery of HIV/AIDS prevention, treatment, and care services. However, several challenges remain for its use in health and the field of HIV/AIDS research, including those related to coordination, interdisciplinary collaboration, scientific design, validity of results, and generalizability of results.

There is a variety of other reasons why implementation science currently is not being supported or utilized at the level needed. First, no one *owns* implementation science. The work largely comprises disjointed, small-scale efforts with little coordination between those funding the research and those supporting service delivery. Second, implementation science necessitates interdisciplinary collaboration, and there is a lack of consensus on optimal scientific research approaches in the field. Third, as a complex health issue, the HIV/AIDS epidemic is difficult to address and the impact of interventions is frequently difficult to determine. This is particularly true in the area of prevention, where measures and proxies to determine incidence and behavioral outcomes are limited or poor. Fourth, the expectation of generalizability, central in biomedical and clinical research, may not be possible or necessary in much of implementation science research, because results may point to lessons that are applicable to only a single program, country, or region.

Lastly, there is a mismatch between expectations of researchers who report implementation science results and implementers who are the end users of these results. Scientists generally want to produce results that have a high degree of certainty. From the perspective of the end users or implementers, any information that reduces uncertainty in their day-to-day decisionmaking has value. A shift in

thinking to value the output of research designs in less tightly controlled, real-world circumstances has an impact on both studies considered for funding and the application of results generated through research.

Although challenges exist generally in advancing the field of implementation science, there are specific issues that are of greater significance to NIH's implementation science research agenda. In seeking to answer how implementation science can be used to improve the delivery of evidence-based interventions and to improve health outcomes, key questions are: what implementation science activities are consistent with NIH's mission and expertise; what unique role could NIH assume in advancing translation of research into better health outcomes; and how can the NIH optimize its engagement in implementation science? In making this determination, it is important to recognize that the most valuable implementation science research may deviate from the type of research studies typically supported by the NIH.

In public health, perfection is often the enemy of the good. Implementation science and operations research within the context of health are labels often used to describe "soft research," in which quality and reliability of results are questioned. In the case of implementation science, there may be a need to balance scientific *rigor* with the ability to conduct research that may have the most useful outcomes with the most positive impact. In some cases, a less rigorous study may produce greater expected public health benefit.

In this context, the term *rigor* should not be taken to imply a lower *quality* of research. Rather, because of the nature of the questions implementation science examines, this form of research often may not produce results with the same *precision* that other forms of research can. The rigor of a study can be preserved; the level of certainty that is sought from the research should be determined in advance, but with a larger confidence interval. Within implementation science, the effects of the context in which the study is conducted are not controlled or eliminated. A study can be rigorous if it focuses on tracking outcomes of an intervention with a clear description of the context and how the context may help or hinder achievement of the outcomes. When evaluating the value of implementation science, these unique issues concerning rigor and precision should be debated and understood.

OAR should determine its priorities for implementation research by evaluating expected costs and benefits of potential research projects. The *best* research design may not be optimal, to the extent that better is more expensive, if funds are unavailable, or the design is infeasible in the context of the intervention. Potential benefits of implementation research can be measured in part by: the prevalence of *bad* practices that need to be improved; the degree to which results may actually change practice; and the magnitude of the potential improvement in practices. Implementation research that is particularly relevant and/or appropriate to the NIH includes *modeling* of implementation strategies and *comparison* of implementation strategies. In these areas, implementation science research can evaluate both specific interventions and program design and management issues.

Establishing implementation science as a necessary and credible field will mean mentoring a new generation of researchers, increasing venues and mechanisms for disseminating findings, forging collaborations between classic researchers and program implementers, identifying unique roles for

lead organizations in global health delivery and research, and creating a strategic approach to identification of implementation research priorities.

2.3 Methodological Tools to Improve the Quality and Utility of Implementation Science

As the field of implementation science grows, so does the need to find ways to increase quality and efficiencies in the research design and data collection systems. Through tools and standardized metrics, implementation science research activities could be coordinated across similar settings, leading to national or regional results and an ability to inform decisionmaking in HIV/AIDS interventions at these levels. In this context, "regional" refers to a collection of countries linked by language, culture, economies, and proximity.

2.3.1 Application of Technology to Improve Health Outcomes *(Dennis Israelski)*

Communications technology is transforming clinical and public health practice. The availability of technology tools that enhance communication and collaboration in resource-limited settings has the potential to add significant power to implementation research. Incorporating these new technologies in the design of implementation science research can facilitate information flow and knowledge sharing among researchers and providers, as well as improve efficiencies, the quality of data collected, and, ultimately, health outcomes. Mobile technologies are one example of how the general widespread uptake in technology can be used to benefit research. Currently, there are approximately 3 billion cell phones in use, and 64 percent of users are in low- and middle-income countries. It is estimated that by 2012, half of all individuals in the remotest areas will have mobile phones. Mobile phones can enable health care workers to provide real-time information in areas where health clinics and trained professionals are unavailable, with the potential to: increase access to information for hard-to-reach populations; improve the ability to diagnose and track diseases; and allow for timely public health information as the basis for action.

With widespread adoption of mobile technology in resource-limited countries, there will be a corresponding increase in the use of tools for group communication. Mobile technologies (Short Message System, Global Positioning System) allow for: sharing of group-specific information; coordination of field outreach; and geo-location, mapping, and visualization of events in communities where the research is taking place. Tools that allow synchronization of different database platforms (e.g., Epi Info™, Access®, Oracle®) create opportunities for countrywide health information systems that could in turn simplify needs assessments, provide rationale for donor portfolio management, connect interventions, enhance efficiencies of large-scale interventions, and allow for patterns of successful practice to emerge. Allowing data to be automatically synchronized between databases, spreadsheets, Web sites, applications, phones, personal digital assistants, and maps can be expected to improve the level of detail available in the data collected and the data analyses. Implementation science research is poised to examine the functionalities of new technology tools, improving and informing clinical and program-level

decisionmaking, and integrating use of information communication technology in research design.

2.3.2 Using the Results of Implementation Science Research: The World Bank's AIM-AIDS Program *(Arianna Legovini, presented by Stefano Bertozzi)*

National and regional data on the effectiveness of HIV/AIDS interventions are of significant importance to national ministries of health, regional health consortia, and multilateral donors. The World Bank's Africa HIV/AIDS Impact Evaluation Program (AIM-AIDS) seeks to build country-level evidence on the effectiveness of large-scale HIV interventions, to expand the technical capacity of national AIDS authorities, and to improve the evidence-base for decisionmaking. The principal tool of the AIM-AIDS program is impact evaluation, which is defined as "counterfactual analysis to isolate the causal effect of an intervention on an outcome." The program is now working across 19 national AIDS authorities.

Using implementation science as the tool, the AIM-AIDS program enables World Bank staff and national authorities to test implementation alternatives and deliver *just-in-time* operational advice to improve program effectiveness. A major strength of AIM-AIDS is that it is a multicountry program, allowing it to run a coordinated policy and programming learning agenda, to improve comparability and generalizability of research findings, to harmonize measurements used in research, and to promote exchange and knowledge-sharing between developing countries.

3.0 Applying Implementation Science to Specific Topic Areas

Moving from a general overview of implementation science, the utility and need for an expanded effort in this area may best be illustrated by looking at specific HIV/AIDS service delivery challenges as they exist in the field currently. Following are three areas in which a health intervention has been proven effective, but implementation has either faltered or multiple, significant challenges for implementation have emerged. Additional implementation research could be of significant benefit to scaling up efforts or improving the health outcomes of interventions widely implemented but experiencing suboptimal results.

3.1 Prevention of Mother-to-Child Transmission *(Laura Guay)*

Scientifically, the knowledge of how to prevent mother-to-child HIV transmission (PMTCT) has been well documented. Widespread uptake of PMTCT programs around the world has yielded uneven results, with large reductions in transmission documented in only some regions. However, rates of vertical transmission remain unacceptably high in many resource-limited settings, and the research-to-implementation gap remains. Implementation science research is urgently needed to identify the reasons for the implementation gap—policy, social, economic, clinical, behavioral—and to alter or tailor how interventions are structured and delivered. Implementation science research that identifies how to overcome barriers to programming and define feasible alternatives also will help in building the case to health ministries and donors for expanded PMTCT programming.

The multiple services or interventions within the PMTCT area can be viewed as a sequence or a *cascade* of interventions, culminating in the successful prevention of HIV transmission from the pregnant women to her infant. The concept of a cascade is useful in thinking about implementation science research because it breaks an intervention into smaller, incremental components, each of which presents particular challenges and for which different implementation strategies may be most effective. PMTCT services lend themselves to the cascade concept because of the multiple, distinct steps required to make the intervention effective: from accessing antenatal care in general, to counseling and testing, to antiretroviral therapy (ART) delivery, and to followup postnatal services. At each step of the service sequence, women are lost to the program. Implementation science research is needed to help determine how best to recruit and then retain women at each point in the cascade of both antenatal and PMTCT services.

The central question in PMTCT delivery is not which treatment regimen is best, but which implementation strategy will produce the highest improvement in health outcomes. With PMTCT and other prevention programs, it is essential to understand the factors that lead to successful implementation. Implementation science is needed to examine ways to maximize functionality and to test alternative approaches to PMTCT intervention.

3.2 Male Circumcision *(Fred Wabwire-Mangen)*

Male circumcision (MC) is one of the oldest surgeries performed. There is now overwhelming evidence demonstrating the efficacy of MC as an HIV prevention intervention. Between 2005 and 2007, three efficacy studies showed a prevention effect ranging from 5 percent to 60 percent among those who were circumcised.

While the efficacy results are impressive, the challenges in designing a service delivery program are significant. With considerable effort invested in international dialogue and planning for service delivery, program implementers have been met with numerous challenges in implementing MC in many countries in sub-Saharan Africa. The hurdles to scale up take many forms, including limits on the ability of community organizations and health systems to make the service available, economic constraints, cultural concerns, and the complexities of human behavior.

The gap between research findings and wide-scale implementation can be separated into two distinct gaps—one between research results and development of appropriate policies, and the other between the policy and actual implementation of the intervention.

The prospect of wide delivery of MC raises numerous questions that implementation science is well positioned to address.

- In the research findings-to-policy gap:
  - Who should deliver MC?
  - Who should be circumcised?
  - What surgical procedures should be used?
  - What training is needed?
  - Is posttrial surveillance required?

- In the policy-to-implementation gap:
  - Is the population ready for circumcision as a public health intervention?
  - What capacity exists in health systems to implement this intervention?
  - What delivery strategy is appropriate?

While delivery of MC has taken longer than many would have liked, countries across sub-Saharan Africa are now moving forward with policy development, situation analysis, training, and expanded delivery of the intervention.

3.3 HIV Treatment as a Prevention Strategy *(Julio Montaner)*

In general, existing prevention strategies have thus far attained suboptimal results in containing the HIV pandemic. New approaches to prevention are needed. Investments in social, behavioral, and technological prevention research continue to push to find proven and sustainable means of significantly reducing HIV incidence. However, there is an urgent need for expanded research to test the potential of HIV treatment as a prevention intervention. Within this context, is there room for using implementation science research to further knowledge about a concept or theory and not necessarily a discrete program or intervention?

It has been well documented that highly active antiretroviral therapy (HAART) stops HIV replication, reducing levels of HIV in the blood and sexual fluids. There is a growing body of evidence to indicate that lower HIV levels are strongly associated with reduced likelihood of HIV transmission. Research on mother-to-child transmission, discordant couples, and injection drug users (IDUs) has demonstrated the prevention impact of HAART. Cost-effectiveness research has demonstrated significant cost savings to be realized from the number of estimated HIV infections averted due to increased delivery of HAART. An article published in *The Lancet* (November 2008) presented a mathematical model of universal testing and immediate HIV treatment of those identified as HIV seropositive. The model indicated that, over time, the HIV infection rate would fall significantly due to reductions in viral load in people living with HIV, lessening the risks of further transmission as thresholds of coverage are obtained.

The concept of treatment as prevention requires more extensive study. There are several questions and concerns that need to be addressed, including the potential for toxicity and drug resistance resulting from early treatment in the course of HIV disease, protection of individual rights of health decisionmaking if health authorities seek to use HAART to prevent HIV transmission, the many logistical challenges of earlier and expanded treatment delivery, costs of the intervention, and possible erosion of the prevention impact over time.

The goal of current studies in this area is not to test changes in treatment strategies for people living with HIV, but rather to understand changes in HIV incidence that result from improved access and more effective delivery of treatment to those who are in medical need.

4.0 Identifying Research-to-Program Gaps

Important next steps to advance the use of implementation science in HIV/AIDS services include identifying research-to-program gaps that require new knowledge and consideration of how

implementation science is supported and organized. The following sections include gaps discussed and identified by the consultation participants in the areas of care and treatment interventions, prevention interventions, and economic and impact evaluation.

4.1 Care and Treatment Interventions

In the area of HIV care and treatment services, seven priority areas were identified in which knowledge generated from implementation science research could catalyze programmatic scale-up and greater public health benefit.

4.1.1 The care cascade—recruitment and retention: Health services research on various program models (disease integration, role of primary health care delivery, access points) and social sciences research on the application of health behavior theory and the resulting individual response and behaviors, including treatment adherence.

4.1.2 Health clinic systems or operations: Achieving efficiencies and quality in human resources (utilization and training), streamlining care, meeting patient needs and expectations, and managing chronic care.

4.1.3 Sustaining organizational and provider behavior change: Workforce recruitment and retention (why providers leave or stay), evidence-based approaches to workforce development, and promoting change in health care provider attitudes and client relationships.

4.1.4 Integrating HIV and primary care: Strengthening primary care services, integrating HIV services, and improving access to primary care through HIV care delivery sites; expansion of HIV care services by using a family care approach model; and integration of HIV/tuberculosis (TB) coinfection treatment services.

4.1.5 HIV treatment as HIV prevention—research on the *test-and-treat* model: Understanding the prevention impact of treatment on HIV incidence; determining the degree to which the presence of treatment in communities provides an incentive for voluntary counseling and testing; and test-and-treat programs in special populations.

4.1.6 Preserving ART regimens: Determining when to switch HIV treatment regimens, including monitoring of treatment failure and utilizing available laboratory methods in decisionmaking; risk factors for late initiation of ART; and community- or peer-led adherence strategies.

4.1.7 Surveys and surveillance: Establishing appropriate measures and mechanisms for demographic population surveys in order to characterize local epidemics to inform strategic treatment scale-up, and population coverage/sentinel populations/ surveillance.

For a more complete list of potential areas discussed for implementation science research in care and treatment, see Appendix A.

4.2 Prevention Interventions

In the area of HIV prevention, the following gap areas were identified:

4.2.1 Behavioral disinhibition: Within existing prevention services, the importance of and identification of strategies to minimize the effect on HIV transmission.

4.2.2 Combination prevention: Evaluation of "kitchen sink" interventions versus costs of disaggregated "one-at-a-time" activities.

4.2.3 Cascade approach to identify implementation science research questions in: PMTCT, test-and-treat, MC, harm reduction for IDUs, microbicides, and preexposure prophylaxis.

For a more complete list of implementation issues at each point in the PMTCT cascade and other health areas, and a list of potential implementation science research areas in prevention interventions, see Appendix B.

4.3 Economic and Impact Evaluation

In the area of economic and impact evaluation, the following gap areas were identified:

4.3.1 Incentives: Patient incentives—value to patients (effective, efficient) and performance-based financing.

4.3.2 Economics of integrating health systems: Optimization of health care packages, and how to fund them from different funding sources.

4.3.3 Task shifting: Economic evaluation and impact on health outcomes.

4.3.4 Optimal models of care: Identifying and choosing between models of care (public health needs versus a "Cadillac" of services).

4.3.5 Program evaluation as part of the design of the intervention: Definition of outcomes of interest, and design of standardized instruments/tools.

5.0 Using Implementation Science to Achieve the Greatest Public Health Impact

Dr. Padian emphasized that the goal of the consultation was to identify specific priority implementation science research areas in which an NIH research contribution could have the most substantial public health impact. The final discussion was structured to facilitate participants to generate the "whats" (specific priority implementation science research areas or ideas for support) and the "hows" (practices, methodologies, and tools for implementation science research; and changes in NIH planning and decisionmaking of research priorities) of advancing the NIH implementation science research agenda on HIV/AIDS.

The following subsections provide a synthesis of recommended priority research areas of inquiry and structural change. Detailed research questions are found in Appendices A and B.

5.1 Recommended Research Priorities for the NIH

Across all discussant groups, three significant issues were identified as top priorities in which implementation science research could facilitate programmatic change and progress.

5.1.1 PMTCT: Significant improvement in the effectiveness of PMTCT programs is a high priority. Implementation science research is an appropriate mechanism to investigate implementation issues and barriers to attaining 95 percent coverage of HIV-seropositive pregnant women through each step in the intervention cascade, to optimize effectiveness and efficiency of services.

5.1.2 Engaging and retaining people in care: Bringing people into systems of care earlier in the course of HIV infection and retaining them in a positive cycle of interventions are crucial to maximizing prevention opportunities, preserving the efficacy of first-line ART, and improving individual and population health outcomes. Examples of research opportunities include:

- Testing of models to optimize coverage of care services;
- Comparing models of service provision and adherence support;
- Delineating key issues that result in suboptimal clinical outcomes;
- Identifying appropriate portals for HIV testing; and
- Identifying specific strategies related to familial and cultural issues that affect retention of pediatric and adolescent clients.

5.1.3 Integration of primary health care and HIV/AIDS services: Using implementation science research, it is crucial to investigate how provision of HIV/AIDS prevention, treatment, and care services can be integrated into and can strengthen primary and other health care systems. Examples of research opportunities include:

- Innovative approaches to integrating multiple health services to improve general health outcomes, and
- Determining where integration of services is advisable and where stand-alone approaches are more appropriate.

In addition to the above top priorities, four areas of research inquiry also were identified as high priorities to achieving improvements in HIV transmission reduction and positive health outcomes for HIV-seropositive individuals.

5.1.4 Proven interventions to scale: In both prevention and treatment, implementation science research can advance the understanding of how to take to scale an intervention with demonstrated effectiveness. Areas of particular interest and need are prevention for adolescents, strategies to reduce concurrent sexual partnerships, and male circumcision. In the clinical realm, identification of cost-effective strategies to optimize the increased uptake of co-trimoxazole and isoniazid therapy, and cervical cancer and anemia screening programs were highlighted. Can methods or strategies be developed for rapid scale-up

that can be applied to a wide variety of settings? Can component analysis of efficacious interventions be used to identify crosscutting elements of success?

5.1.5 Optimal treatment approaches to coinfections: Major coinfections or comorbidities of HIV/TB and HIV and drug use need close investigation of how to integrate services, early identification/detection of comorbidities, prioritization of care and treatment needs, and cross-training of health care providers. High-quality treatment of TB and drug use is essential to successful HIV prevention and treatment. Impact data on integrated clinical and community models of care and on the use of treatment as prevention among communities of IDUs are needed.

5.1.6 Structural interventions: Research is needed to evaluate methods of manipulating social, environmental, policy, economic, and other societal variables in order to reduce HIV transmission and acquisition, as well as to increase the use and optimization of health care services. Priority populations include men who have sex with men; IDUs in Europe and in Central and Eastern Asia; Africans in high-incidence countries; incarcerated persons; and members of racial and ethnic minorities. The integration of service provision into economically disadvantaged urban populations, particularly addressing adolescents, also is a priority.

5.1.7 Human resources and health systems: Research is needed to assess the safety, efficiency, and effectiveness of alternative staffing approaches, including task shifting, task sharing, and involvement of informal health care providers. Improving and retaining quality of services provided, through a focus on systems strengthening, will demonstrate what system improvements will yield the greatest health outcomes. Testing models that use communication technology to strengthen data flow and analysis should be prioritized.

5.2 Recommendations for the NIH for Furthering the Field of Implementation Science Research

A number of issues emerged through discussions of the types of research needed to address the implementation gap and specific content gaps. Gaps or issues identified were related to: interagency coordination, priority setting, handling of research applications, and standardizing methodologies and implementation science research tools. Because implementation science research is in a developmental phase, process or structural issues are important because they will either help or hinder the implementation and the quality of the research that will be conducted. The following discussions represent the main thematic areas recommended for consideration by the NIH.

5.2.1 Coordination among agencies and researchers: Coordination of implementation science research efforts is required among funding agencies and between researchers and program implementers. Successful implementation science research depends on the involvement of experienced researchers alongside experienced service providers. This is required at both the agency level and within the field. For the NIH to better engage in implementation science, research should be closely coordinated with service provider agencies both internal and external to the United States (Agency for Healthcare Research

and Quality, OGAC, Health Resources and Services Administration, CDC, USAID, Global Fund, the United Nations system).

The NIH should work with donor agencies and implementers to identify opportunities for collaboration as programs are being planned. Ideally, funding for services and implementation science research would be coordinated across organizations. For example, the President's Emergency Plan for AIDS Relief (PEPFAR) funding could be leveraged through existing NIH grants to conduct more sophisticated implementation science research projects by NIH researchers working at PEPFAR sites. The NIH, CDC, and in-country academic institutions might collaborate on particular studies, taking advantage of the unique perspectives of each agency/institution involved.

5.2.2 Setting priorities: HIV/AIDS programs could benefit from the establishment of clear funding priorities for implementation science research. Country-identified or regional priorities informed by experiences of suboptimal program implementation may lead to conducting research that has the highest potential of informing and affecting program change to realize improved health outcomes.

5.2.3 Appropriate review of applications: Implementation science research applications should be reviewed by individuals with expertise in the field. Utilizing existing study sections for review may unfairly disadvantage implementation science research applications. The NIH should consider establishing a study section in its Center for Scientific Review dedicated to implementation science proposals. This would preserve the relevance of such research applications, streamline the review process, and allow for the rapid awarding of grants.

5.2.4 Developing methodologies and practice: A variety of efforts are needed to further define and develop the field of implementation science, including: developing a common taxonomy; reaching consensus on expected rigor and precision in results; developing quality standards for data collection that could facilitate data sharing across programs; developing adaptive research designs; coordinating data systems with linkages between clinical, behavioral, and biological data sets; identifying strategies to improve effectiveness and efficiencies of relevant networks through the use of information and communication technologies; and achieving consensus on ethical guidelines for implementation science research.

5.2.5 Assessment of findings and dissemination of results: Speed is an essential element of a successful approach to implementation science. Rapid assessment of intermediary and final study results, along with the quick dissemination of findings, is necessary to ensure the utility of the research in improving program design and implementation. Forums for disseminating results are needed—either the adaptation of existing forums or development of new ones.

Implementation science research may produce what is considered "imperfect" information that does not meet stringent criteria and may not be definitive enough to be published in a peer-reviewed journal. Identifying alternative mechanisms to disseminate

information will be important in getting the most value out of investments in implementation science research. Integrating implementation science research at the annual PEPFAR Implementers' meeting and International AIDS Society conferences will increase coverage of the field.

5.2.6 **Training:** Formal training opportunities need to be strengthened in low- and middle-income countries. Appropriate incentives and funding for training implementation science experts to further develop the field require consideration.

6.0 Conclusion and Next Steps

The expert consultation held in Cape Town was an important step in OAR's effort to develop a coordinated trans-NIH research agenda and strategy on HIV/AIDS implementation science. The consultation provided an opportunity for researchers and implementers to discuss and debate a wide range of issues, including the definition of implementation science research, current applications of this form of research, key opportunities for additional research, and ideas for changing the way implementation science research is supported, organized, and utilized.

The recommendations from this consultation will be presented to the Office of AIDS Research Advisory Council, which provides advice to the Director of OAR on the planning, coordination, and evaluation of AIDS research and training activities. OAR then will work closely with the key NIH Institutes and Centers to determine how best to implement the recommendations resulting from this consultation.

APPENDIX A

Research-to-Program Gaps and Priorities for Research in Care and Treatment

- Recruiting and retaining patients in care
  - Health services research—determining which program models are successful in keeping people in care (linking data across programs, tracking loss to followup)
  - Social sciences research—health behavior theory, individual responses and behaviors

- Creating clinic efficiencies
  - Human resources—availability, training, and retention
  - Streamlining care
  - Patient needs/expectations
  - How best to manage chronic care

- Sustaining organizational and provider behavior change
  - Recruitment of workforce
  - Evidence-based approaches for workforce development
  - Understanding why people stay in or leave the workforce

- Incorporating HIV care into primary care
  - Community care delivery expanded to include HIV prevention, care, and treatment with related services (sexually transmitted infections, family planning, prenatal care, malaria)
  - How prevention gets integrated into primary care
  - Family approach to care (pediatric well-child care)
  - Optimize methodologies for delivery of health services, its coverage, and geographic mapping; and assess the effectiveness of these services

- Treatment as prevention
  - Universal diagnosis and treatment—feasibility studies conducted in a small community on provision of a comprehensive spectrum of services, from testing to access to care
  - Preventive effect of treatment on HIV incidence and secondary outcomes (individual, family, and community levels)
  - Test-and-treat programs in special populations, including assessment of mental health and substance use
  - Determining the degree to which the presence of treatment in a society provides incentives for voluntary counseling and testing
  - Preparation for use of preexposure prophylaxis

- Maximizing clinical outcomes
  - Monitoring treatment failure
  - Laboratory methods available

  - Clinical loss to followup—how to reduce and reasons for loss
  - Adherence to treatment regimens, including self-reporting
  - Tuberculosis (TB) and HIV coepidemics—how to implement interventions and their effectiveness that address TB in the context of HIV
  - Risks factors for late initiation of antiretroviral therapy
  - Providing treatment in prisons

- Laboratory testing and clinical monitoring
  - Implemented on a large scale and effectiveness of this approach assessed
  - Improving linkages between laboratories and clinics

- Modeling and cost assessments of new technologies for testing and treatment.

APPENDIX B

Research-to-Program Gaps and Priorities for Research in Prevention

- Effective interventions for prevention of mother-to-child-transmission (PMTCT), but:
  - Insufficient numbers of pregnant women are identified as HIV-infected prior to labor and delivery, so they are not able to take advantage of existing interventions (including retesting in pregnancy).
  - Pregnant women who are identified are not assessed early enough to establish if they need treatment for their own health.
  - Women do not receive prophylaxis in a timely fashion during pregnancy ("wait" to 28 weeks or do not start if >28 weeks).
  - More effective "complex" prophylaxis is not provided—why and how to overcome barriers?
  - Women who receive prophylaxis may not take it (there is a need to determine why this occurs).
  - How to implement antiretroviral (ARV) programs to prevent postnatal mother-to-child-transmission because there are proven interventions (e.g., infant prophylaxis) now available.
  - How to optimize infant feeding counseling.
  - How to link diagnostic testing effectively with PMTCT, including point-of-care testing.
  - Implementation of family planning/contraceptive provision into maternal postnatal care.

- Combination prevention—multilevel intervention—areas of "cascade" to develop interventions:
  - Identification of HIV-infected individuals in the general population.
  - Identification of core high-risk individuals who are unaware of their HIV serostatus; community outreach to high-risk individuals to increase their frequency of HIV testing (including repeat testing); also, how to identify discordant couples; and issues of access and retention.
  - Identification of acute infections (e.g., using new assay formats).
  - Community mobilization/outreach for HIV-infected individuals who are not yet identified—implement interventions already known to work.
  - HIV-infected persons not in care—treatment engagement interventions.
  - HIV-infected persons in care and not on antiretroviral therapy (ART)—work with providers to increase testing.
  - HIV-infected individuals in care, on ART, but who are not adherent (or substance users)—screening for nonadherence, mental health.
  - HIV-infected individuals in care, on ART, with controlled viral load, but have problems with retention in care.
  - Combination interventions compared to single interventions, including biomedical, behavioral, and structural interventions to see if there is any impact.

- Treatment as prevention:
  - Superimpose social marketing and prevention in HIV-infected individuals.
  - Evaluate the impact on community viral load and HIV incidence.
  - ART in discordant couples—how complete is access for discordant couples?

- Harm reduction—most effective combination of interventions to address substance use in the United States and internationally.
  - Need to evaluate harm reduction quickly among drug users.
  - Introduction of methadone programs in resource-limited settings—how to potentiate ARV treatment and affect viral load?

- Behavioral intervention studies for couples—learning about engaging couples in prevention; using findings from one area of research and applying them to another.

- Antenatal voluntary counseling and testing: What is the optimal way to enhance identification of HIV-infected pregnant women?
  - Compare antenatal clinic testing with community-based interventions to increase awareness in a variety of ways and to bring testing closer to "home" than "clinic" (e.g., mobile van testing, lay-based counseling, home testing).
  - Compare antenatal clinic testing to community-based interventions targeted at men to encourage couple counseling and testing to decrease the number of HIV-infected babies.

- Determination of the need for and provision of therapy: How can CD4 evaluation be integrated into antenatal care to allow rapid initiation of therapy in pregnant women who need treatment for their own health?
  - Compare current standard of care to an approach that includes highly active antiretroviral therapy through antenatal clinics (task shifting to nurse).

APPENDIX C

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