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Implementation Science for the Prevention and Treatment of HIV/AIDS

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Abstract

Implementation science is the scientific study of methods to promote the integration of research findings and evidence-based interventions into healthcare policy and practice and, hence, to improve the quality and effectiveness of health services and care. Implementation science is distinguished from monitoring and evaluation by its emphasis on the use of the scientific method. The origins of implementation science include operations research, industrial engineering, and management science. Today, implementation science encompasses a broader range of methods and skills including decision science and operations research, health systems research, health outcomes research, health and behavioral economics, epidemiology, statistics, organization and management science, finance, policy analysis, anthropology, sociology, and ethics. Examples of implementation science research are presented for HIV prevention (prevention of mother-to-child transmission of HIV, male circumcision) and HIV and drug use (syringe distribution, treating drug users with antiretroviral therapy (ART) and opioid substitution therapy). For implementation science to become an established field in HIV/AIDS research, there needs to be better coordination between funders of research and funders of program delivery and greater consensus on scientific research approaches and standards of evidence.

Introduction

Implementation science and operational research have been gaining recognition and support, as evidenced by recent NIH funding announcements,[1, 2] conferences and workshops,[3-5] and the establishment of an academic journal.[6] In the United States, two large integrated health systems have formal organizational initiatives in implementation science: the Veteran's Affairs Center for Implementation Practice and Research Support and the Kaiser Permanente Center for Health Dissemination and Implementation Research. In the global HIV field, implementation science has been recognized by the Framework for Operations and Implementation Research of the Global Fund to Fight AIDS, Tuberculosis and Malaria[7] and the establishment of the William J Clinton Foundation Center for Strategic HIV Operations Research. This paper defines implementation science research and how it differs from dissemination research, describes its evolution, and describes examples relevant to global HIV/AIDS prevention and specific implementation issues relevant to HIV/AIDS in

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drug users. It concludes with a discussion of challenges and opportunities to better establish implementation science as a field in HIV/AIDS research.

Implementation Science Definition

Implementation science is the scientific study of methods to promote the integration of research findings and evidence-based interventions into healthcare policy and practice and hence, to improve the quality and effectiveness of health services and care.[2, 6] Different funders and international organizations use different words to describe this concept, although all specify that this is a research (i.e. scientific) discipline. The U.S. National Institutes of Health (NIH) uses the term "implementation research," the Global Fund and World Health Organization (WHO) uses "operational research," and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and the International AIDS Society (IAS) use "operations research." In this paper, "implementation science" is used to represent all of these terms.

Where is the Science in Implementation Science?

Implementation science is distinguished from monitoring and evaluation by its emphasis on the use of scientific method. PEPFAR has contributed to the confusion between monitoring and evaluation and implementation science by grouping operations research along with monitoring and program evaluation in its 5-year strategy.[8]

Hirschhorn et al. have described the difference between implementation science and monitoring and evaluation as follows: "In general, the objectives of monitoring and evaluation programs and implementation are similar: to understand what is working well, 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."[9]

Implementation science is also different from dissemination research. Dissemination is "the targeted distribution of information and intervention materials to a specific public health or clinical practice audience … to spread knowledge and the associated evidence-based interventions."[2] Dissemination research studies "identify mechanisms and approaches to package and convey the evidence-based information necessary to improve public health and clinical care services."[2] Dissemination is necessary, but it is often not sufficient because interventions that were developed and tested in efficacy and effectiveness trials require local adaptation for implementation.

The origins of implementation science include several quantitative research traditions: operations research, industrial engineering, and management science. Operations research is "the discipline of applying advanced analytical methods to optimize decisions, utilizing mathematical and statistical modeling."[9] Examples of early applications of operations research include research by Babbage in the 19th century that led to the organization of the English postal services, and research during World War II that improved the effectiveness of Allied forces in using radar technology.[4]

Industrial engineering encompasses "the design, improvement and installation of integrated systems of people, materials, information, equipment and energy."[10] Examples include time studies conducted by Taylor in the 19th century and motion studies conducted by the Gilbreths in the early 20th century. These techniques were subsequently combined as time and motion studies that continue to be used to improve the efficiency of work processes.

Management science applies scientific methods more broadly to managerial decisions. In the 19^{th} century, important innovations included developing the concepts of quality control and cost accounting. In the early 20th century, innovations in scheduling and project management by Gantt (the developer of the Gantt chart) led the way towards improved processes for management of complex systems that were later employed by organizations such as National Aeronautics and Space Administration (NASA).

Today, implementation science encompasses a broader range of methods and skills. Examples of methods include state-transition and agent-based simulation models designed to answer questions about feasibility and efficiency and cost-effectiveness; experimental and quasi-experimental studies including cluster-randomized trials and pre/post comparisons of systemic interventions or "packages" of interventions; behavioral economics studies of incentive-based interventions; quality improvement studies that examine the requirements for fidelity versus customization in the field or implement continuous process improvement techniques; and methodological studies that test theoretical models of implementation processes or develop process and outcome measures. Skills required for implementation science research can include decision science and operations research, health systems research, health outcomes research, health and behavioral economics, epidemiology, statistics, organization and management science, finance, policy analysis, anthropology, sociology, and ethics.

Implementation science is a key element of translational research. The NIH-funded Clinical and Translational Science Awards (CTSA) program now encompasses 46 medical research institutions located in 26 states.[11] The CTSAs have adopted the T1-T3 characterization of translational research,[12] in which T1 represents translation from basic science to the clinic, T2 studies comparative effectiveness, and T3 focuses on the "how" of health care delivery using implementation science. An example of these distinctions is the adoption of primary percutaneous coronary intervention (PCI) which includes clinical efficacy results from clinical trials (T1), comparative effectiveness and health services research that established a standard of 90 minutes between arrival in the emergency department and commencement of PCI (T2), and implementation research to identify hospital-based strategies to reduce the time to PCI (T3).[13] Others have expanded the definition of translational research to include T0, basic research that identifies opportunities and approaches to a health problem, and T4 which is translating practice to population health impact through policy.[14, 15]

Examples of Implementation Research in HIV Prevention

Evidence for the effectiveness of protocols for the prevention of mother-to-child transmission (PMTC) of HIV is clear.[16] However, implementation has been challenging.[17] The PEARL study is evaluating PMTC coverage in four East African countries.[18] Using cord-blood surveillance, investigators tracked the coverage "cascade" and identified losses at many stages. Starting with 100% deliveries that were cord-blood positive, 92% were missing information in the folder (chart), 84% were offered an HIV test, 81% were HIV tested, 74% had HIV test results documented in the folder, 71% had documented maternal receipt of nevirapine, 57% had evidence of nevirapine in cord blood, and only 50% had full coverage including treatment of both the mother and the child.[18] Results also varied substantially by site. Each of the losses in the cascade represents a potential point of intervention. A participatory quality improvement project implemented in one rural region in South Africa identified barriers to improvement of several steps in the cascade, developed interventions to address them, and had significant impact in improving performance. Antenatal HIV testing increased from 88% to 98%, CD4 testing of HIV positive mothers increased from 40 to 97%, maternal nevirapine from 57 to 96%, and infant nevirapine from 15 to 68%; 6 week PCR testing also increased from 24 to 68%.[19]

The effectiveness of male circumcision in preventing HIV transmission to heterosexual men has been shown in three large trials conducted in Africa.[20-22] Yet there are substantial barriers to implementation related to organizational and health systems, economics, cultural and environmental factors, social networks, and individual behaviors.[4] A WHO consultation examined operations research implications of several different models for providing male circumcision services, including vertical and integrated health system models. A list of 22 high priority research topics was created, with the five highest being studies of: task-shifting to non-physicians; the effectiveness and cost-effectiveness of different delivery models; counseling strategies to reduce potential risk compensation and unsafe sexual activity immediately following surgery; the acceptability and feasibility of newborn circumcision; and how to build mutually agreeable linkages between traditional circumcisers and the formal health care system.[23] Recent implementation research studies include an evaluation of the number of male circumcision procedures required to achieve optimal competency[24] and the use of a questionnaire and GPS data to strategically locate male circumcision services in Nyanza Province, Kenya[25]

Examples of Implementation Research in HIV and Drug Use

The effectiveness and cost-effectiveness of syringe distribution to injection drug users (IDUs) for prevention of HIV infection have been well established.[26] However, there are important challenges to the implementation of these programs. Attitudes of local law enforcement are critical; for example, in a qualitative study conducted in a Russian city, investigators found that street policing “stop and search” activities inhibited drug users’ willingness to carry injection equipment in public.27 Even when the environment is safe, it is unclear what the target level of coverage should be for syringe distribution to have an impact on local transmission rates. The target rate will vary based on the epidemiologic and behavioral characteristics of the drug using population. In a recent modeling study, Vickerman et al. projected a threshold coverage rate of 15-20% in Svetlogorsk, Belarus and 20% in London.28 Using retrospective data, an intervention in Dhaka, Bangladesh that included needle/syringe exchange and treatment of sexually transmitted diseases for IDUs as well as reduced harassment of drug users by police was estimated to have 31%-81% coverage. This was associated with an estimated 90% reduced HIV incidence among IDUs and an estimated HIV prevalence of 10%, compared to an estimated 42% prevalence had the intervention not been implemented.29

Evidence from prospective cluster-randomized and quasi-experimental studies has also shown the efficacy of providing a package of interventions at the individual and system level. A cross-border project implemented at 5 sites in Vietnam and 4 sites in China worked with law enforcement officials and government officials, and provided sterile injection equipment and peer counsellors. This program was successful in reducing HIV incidence and prevalence among drug users.[30] In a cluster-randomized trial of needle social marketing strategies in 4 communities in China, needle sharing behaviors dropped 62% in the intervention communities compared to the control communities, and there was a statistically significant decline in HIV incidence among IDUs in one intervention township.[31]

Social and structural barriers as well as individual-level behaviors affect access to and use of HIV treatment for substance users.[32, 33] Overcoming such barriers can yield substantial health gains for drug users, and in communities where drugs are fuelling the spread of HIV, drug abuse treatment can have wider benefits for general public health and the community at large. A modeling study of different HIV treatment allocation strategies in St. Petersburg found that a strategy targeting IDUs prevented 40,000 HIV infections over 20 years, 75% of which were estimated to be among non-IDUs. By contrast, a strategy targeting non-IDUs prevented only 10,000 infections. Targeting IDUs actually prevented more non-IDU infections than targeting non-IDUs. A more politically acceptable strategy that targeted non-IDUs and IDUs equally had a less attractive cost-effectiveness ratio than the IDU targeted strategy, but it was estimated to prevent the most infections using the optimistic coverage assumption of 80% for both groups.[34]

In a longitudinal cohort study conducted at opioid substitution therapy (OST) sites in Asia, Eastern Europe, Australia, and Iran, OST was shown to be associated with a reduction in injection risks for HIV.[35] OST in HIV-infected patients is also associated with initiating ART,36 better adherence on ART,37 and improved virologic outcomes.38,[39] Buprenorphine/naloxone treatment is an OST alternative to traditional methadone maintenance treatment.[40] In the U.S., it has substantial advantages in terms of patient acceptability because it can be dispensed at a community pharmacy whereas methadone must be dispensed by a Federally-regulated OST program that frequently requires daily visits by the patient. However, physician adoption of buprenorphine/naloxone in the U.S. has been relatively slow due to regulatory, financial, and attitudinal barriers.[41-43] A pilot study of integrated buprenorphine/naloxone treatment and HIV care found it to be feasible in an HIV clinical care setting.[44] However, routine implementation of such programs in HIV care settings requires changes to care processes and quality assessments, and incurs additional costs that may not be reimbursed under current funding arrangements. These implementation issues are now under study at 10 sites, with support from the HIV/AIDS Bureau of the Health Resources and Services Administration, to create model implementation programs of integrated buprenorphine/naloxone treatment and HIV care.[42]

Challenges and Opportunities

At the Expert Consultation on Implementation Science held by the NIH Office of AIDS Research in July 2009,[4] Dr. Stefano Bertozzi pointed out that although there is increasing recognition of the critical role implementation science can play in improved delivery of HIV/AIDS prevention and treatment, there are several challenges to its broader use. First, because "no one *owns* implementation science" there is insufficient coordination between those funding the research and those supporting delivery. Second, "implementation science necessitates interdisciplinary collaboration and there is a lack of consensus on optimal scientific research approaches in the field." Third, the impact of HIV/AIDS interventions is frequently difficult to determine, particularly for prevention interventions where measures of incidence and behavioral outcomes have limitations. Related to these considerations, researchers and implementers have different expectations about validity and generalizability. Researchers want a high degree of certainty and want to be able to claim broad generalizability. Implementers place value on any information that reduces uncertainty, recognizing that there is a difference between quality and precision. Moreover, the expectation of generalizability of results may not always be possible or necessary. Thus research that will be most valued by implementers may be the least similar to the type of research studies typically supported by NIH.

For implementation science to become an established field in HIV/AIDS research, there needs to be better coordination between funders of research and funders of service delivery and greater consensus on scientific research approaches and standards of evidence. Rigorous implementation science research that is responsive to the needs of implementers can dramatically improve the effectiveness of delivering proven interventions to prevent and treat HIV/AIDS, both globally and locally. With improved funding support, better coordination, and greater scientific clarity, implementation science researchers will be able to deliver on this promise.

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