Repositioning Implementation Science in the HIV Response: Looking Ahead From AIDS 2018

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INTRODUCTION

Implementation science (IS) studies examine ways to deliver health-enhancing tools to those who need them rather than evaluating the efficacy of the tools themselves. IS uses frameworks, outcomes, and methodologies to analyze the behavior of systems, organizations, groups, and individuals. It seeks to close the gap between evidence and practice by identifying delivery strategies that maximize the impact of programs and health systems in the real world. In July 2018, over 15,000 global HIV/AIDS researchers, programmers, policy makers, and activists gathered at the AIDS 2018 in Amsterdam to discuss the current state of the HIV pandemic. “Track E” sought submissions on “innovations and advances in implementation and service delivery and on best strategies for the use of human, financial and other resources for effective and equitable HIV and AIDS responses embedded within broader public health and development frameworks.”

The arsenal of efficacious biomedical tools for HIV prevention and treatment is larger than ever. For example, research at the conference confirmed the high efficacy of antiretroviral therapy (ART) in reducing onward HIV transmission,2,3 providing supporting evidence for the UNAIDS “U = U” campaign (“Undetectable = Untransmittable”). The PARTNER-2 study demonstrated that over 8 years, among 783 gay male couples, no HIV-positive partner with an undetectable viral load infected his HIV-negative partner through 74,567 episodes of unprotected anal sex. Similarly, results from the Prevenir study showed that those taking oral pre-exposure prophylaxis (PrEP) during periods of risk are effectively protected from HIV infection, with no break-through HIV infections among 1435 participants taking event-driven PrEP “on-demand.”4

However, these efficacious tools do not yet benefit all those who need them. IS must close this gap. The importance of this agenda was clear as the conference opened. Long-term, sustainable financing and political will for the HIV/AIDS response seems fragile, emphasizing the need for innovation in efficient, impactful program delivery. The Lancet Commission on “advancing global health and strengthening the AIDS response” urged that implementation of the HIV/AIDS response must be integrated with broader global health efforts,5 while at the same time strengthening the delivery of HIV prevention, as declines in new infections have stagnated.6

SUPPLEMENT ARTICLE

Background: Implementation science (IS) occupies a critical place in HIV/AIDS research, reflected by a scientific track (“Track E”) at the biannual International AIDS Conference. IS seeks to identify health delivery strategies that cost-effectively translate the efficacy of evidence-based interventions for HIV prevention, testing, and treatment into impact on HIV incidence, quality of life, and mortality.

Method: We reviewed the content of Track E, and other presentations relevant to IS, at the 22nd International AIDS Conference held in Amsterdam in 2018. We identified key findings and themes and made recommendations for areas where the field can be strengthened by the 2020 meeting.

Results: Trials of “treat all” strategies in Africa showed mixed evidence of effect. Innovations in HIV testing included expanding self-testing and index testing, which are reaching groups, such as men, where previously testing rates have been low. Adherence clubs and other innovations are being trialed to improve retention in care, with mixed findings. The implementation of pre-exposure prophylaxis for HIV prevention continues but with many challenges remaining in identifying implementation strategies that strengthen demand and support continuation.

Discussion: IS for HIV/AIDS treatment and prevention continues to expand. IS for primary HIV prevention must be prioritized with a dearth of rigorous, intersectoral studies in this area. The weakness of routine data must be addressed. Costing and financing studies should form a stronger component of the conference agenda. Implementation scientists must continue to grapple with the methodological challenges posed by the real-world context for their research.

Key Words: AIDS 2018, implementation science, HIV/AIDS
We critically reviewed HIV/AIDS IS presented at IAS 2018, under 4 themes: the impact of “treat all” strategies in Africa; innovation in delivering HIV testing services and case-detection; implementation strategies to supporting retention in care and treatment; and, optimizing the delivery of primary HIV prevention. We conclude with some thoughts on next steps for the IS agenda as we approach the next International AIDS Conference in 2020.

METHODS

The Track E program included 85 abstracts, including 39 oral abstracts. Materials relevant to Track E were also featured in plenary and cross-track sessions. As the rapporteur team for Track E at the conference, at least one author of this article attended each Track E oral presentation, and we had access to written abstracts, most slides, and video recordings. We summarized the conference in real time over the week of July 23–27, 2018, writing session summaries of all Track E oral abstract sessions and many other sessions of relevance to IS, 4 daily reports, and an oral presentation summarizing findings across Track E. After the conference, we reviewed these materials, agreed on key themes, and identified cross-cutting issues. We summarize here the results from rigorous IS studies presented at the conference, including impact evaluations (with both randomized and nonrandomized designs), process evaluations, economic evaluations, and systematic reviews of program delivery strategies, regardless of scale or geography. We refer to abstracts reported at the conference and, in addition, refer to subsequently published articles where these were available.

RESULTS

Of the 39 oral abstracts in Track E, 8 reported data from nonrandomized evaluation studies, 7 reported data from randomized trials, 6 reported case studies in a “Lessons Learned” format, 5 reported costing or finance studies, 5 reported modeling studies, 4 reported data from principally qualitative research, 2 reported routine data, 1 survey and 1 systematic review.

Theme 1: The Impact of “Treat All” Implementation Strategies in Africa

Since 2015, the WHO has recommended a “treat all” approach, where anyone confirmed as testing HIV positive should begin antiretroviral treatment within 7 days, with the offer of same day initiation, in response to evidence that immediate initiation of ART keeps people alive, healthy, and reduces the risk of transmitting the virus onward. This strategy also means that delivery can be streamlined to be more effective, compared with approaches that required pre-ART follow-up to assess treatment eligibility by CD4 count thresholds. In a cross-track session, 3 cluster randomized trials, all of which launched before this the WHO recommendation, released findings on the implementation and impact of universal test and treat strategies in sub-Saharan Africa. These trials were notable for their large size, and although all 3 studies examined HIV incidence as the ultimate outcome of interest, each examined a different implementation strategy to optimize uptake.

The “Ya Tsie” trial in Botswana reported a reduction in HIV incidence of 31% associated with the delivery of a combination HIV prevention program measured among a cohort of nearly 9000 individuals from communities covering about 10% of the national population. The intervention included home-based and mobile testing and linkage-to-care support, with treatment guidelines changing in both arms of the trial over time toward a treat all approach. The intervention generated a difference in the proportion of all HIV-positive individuals virally suppressed on ART between the arms of the trial. The SEARCH trial in Kenya and Uganda implemented an intervention based on community health fairs, where a “patient-centered multidisease model” was delivered at baseline in intervention and control communities and then over time in intervention communities only. Immediate ART was available throughout the trial in the intervention arm, whereas in the comparison arm, guidelines changed over time. The trial reported improvements in the treatment cascade and reductions in TB and all-cause mortality among both HIV-infected individuals (21% reduction) and all community residents (11% reduction) associated with the intervention. However, there was no difference in 3-year cumulative HIV incidence between the trial arms in cohorts of some 40,000 individuals. Finally, the MaxART trial showed improved retention in care (86% retention at 12 months under intervention compared with 80% retention with standard of care), with no increase in per-patient ART delivery costs, during a stepped-wedge trial of the roll out of facility-based immediate ART initiation in the kingdom of Eswatini. Although not presented at this conference, the results for HPTN 071 (PopART), another large, 3-arm universal test–and-treat study conducted in Zambia and South Africa, were subsequently published in July 2019.

In this trial, both treatment groups received door-to-door interventions including HIV testing and other services. Compared with the standard of care arm, HIV incidence was significantly lower by 30% in the clusters that initiated treatment according to country guidelines (which in the second-half of the trial was immediate ART) but was only 7% lower (nonsignificantly) in the clusters that initiated treatment immediately from the start of the trial.

Theme 2: Innovations in Delivering HIV Testing Services and Case Detection

In addition to the multicomponent “treat-all” trials, the conference saw a range of presentations on innovations in delivering HIV testing services and identifying HIV cases. Engagement with HIV testing is a means to ensure early entry into prevention and care. The Thai Red Cross, for example, showed how HIV testing can not only link HIV-positive key populations to treatment and care but can also be an effective route to link those testing negative, but at risk to HIV prevention services. They stressed the need for frequent and regular testing for key populations to stay negative through linkage and follow-up within the prevention program.
Rates of HIV case detection and repeat HIV testing remain lower among men than women in many settings, particularly sub-Saharan Africa. Consequently, additional HIV testing programs to reach men were shown to be cost-effective (able to identify new cases of HIV at a cost of less than approximately 500 USD per new diagnosis) in a range of settings. In Malawi, male-targeted HIV testing events at weekends in mobile clinics increased the proportion of men tested from 69% in 2014 compared with 78% in 2017. HIV self-testing also provides an important opportunity for screening, by bringing HIV testing services to men. In Kenya, the secondary distribution of 2 additional oral HIV self-test kits by pregnant women aged 18–24 years attending antenatal and postpartum care to their male partners had a large effect on the proportion of these partners tested for HIV, with approximately a 37% higher uptake of HIV testing in the intervention compared with the control group. Rates of couples testing were also higher in the intervention arm (77.8% compared with 38.1%, respectively), as was disclosure of HIV status to partners. In another study in Malawi, community-based distribution of HIV self-tests increased levels of HIV testing in the previous 12 months (68% reported recently testing in the community-based distribution of HIV self-testing kits arm versus 48% testing in the standard of care arm) and had a particularly strong effect among men (65% compared with 42%, respectively). However, despite an increase in testing, there was little evidence that community-based distribution of HIV self-testing kits had an impact on ART initiations. Because HIV self-testing is a first screening step and requires confirmatory testing according (although many self-testers have previously tested) to the Malawi national HIV diagnostic testing algorithm, ensuring linkage to both confirmatory testing and ART for those who test HIV positive is necessary to show effectiveness, and few studies presented data on these critical outcomes, critically among those who test negative on self-testing. Linkages to prevention are as important to linkages to treatment among those who test positive.

The conference also saw reports from programs actively offering HIV tests to the social and/or sexual and/or drug-injecting networks of index cases of HIV infection. One experience was in Ukraine, where an “optimized case finding” delivery model incentivized peer referrals for testing by people testing positive and increased the yield of positive tests from 3.4% to 23.6%.

Theme 3: Implementation Strategies to Support Retention in Care and Treatment

Once diagnosed, people living with HIV need to be linked to care, offered and initiated on an appropriate ART regimen, and then retained on treatment with a suppressed viral load. This is a major challenge for service delivery, especially in fragile and already overloaded health systems and in contexts where poverty and stigma act as barriers.

In Mozambique, data from 10 years of peer support groups involved in community ART distribution and mutual psychosocial support including 2167 patients with HIV attending 13 clinics (over the period from February 2008 to October 2017) showed that 87.5% were retained in care and 76.4% remained in their group. In Zambia, an urban adherence club model that provided off-hours facility access and group-based drug distribution showed that these efforts significantly reduced late drug collection at 7 and 28 days over 12 months compared with standard of care in a randomized trial. In Ethiopia, an approach to improve adherence and reduce the burden on health facilities based on appointment spacing had been increased to 6 months and rapidly scaled up and was found to be acceptable by clients and service providers, whereas in Tanzania, community-based ART delivery through an existing cadre of home-based carers was shown to be acceptable, feasible, and noninferior to existing clinic-based models. Finally, an innovative study from Vancouver among people who use drugs showed that where HIV services were successfully integrated with other health platforms, ART treatment success was facilitated by supporting access to methadone maintenance therapy.

Theme 4: Optimizing the Delivery of Primary HIV Prevention Programs

Implementing HIV prevention programs poses unique challenges and requires multisectoral collaborations to be successful. A modeling study reported at the conference showed that currently the most cost-effective primary prevention tools (including condoms and voluntary medical male circumcision) are funded at only 70% of need. PrEP delivery and the challenges of implementation especially to high-risk groups were a major theme of the conference.

One strategy to strengthen prevention is to improve the use of data to better target efforts. In Kenya, the “prevention roadmap” strategy uses modeled estimates of HIV incidence to geographically segment Kenya into high-, medium-, and low-intensity districts, and programming plans and resources follow this. The PEPFAR DREAMS initiative for prevention of HIV infection among adolescent girls and young women also apply a geographic targeting step at its first stage, before identifying and prioritizing the highest-risk young women for service delivery. Each of these examples was described at the conference, and we anticipate results on the impact of these implementation efforts to be described at future conferences. Data from Zimbabwe and Uganda were used to develop a “prevention cascade” model to help guide prevention efforts not just in terms of where and among whom to prioritize action but what determinants of risk should be targeted.

A number of studies examined PrEP programs. The ACCESS study in Kenya and South Africa concluded that self-perceived risk is an important driver of PrEP Initiation. The study also highlighted a number of missed opportunities to offer PrEP in health facilities. In the PriYA study in Kenya, 22% of young women offered PrEP alongside contraception services initiated it, and uptake was higher among those who had known risk factors for HIV including an STI diagnosis, a partner of unknown HIV status, and the experience of forced sex or violence. As with the ACCESS study, reasons for declining PrEP included low perceived risk and needing to consult a partner. Across a range of studies, it was clear that demand for PrEP needs to be strengthened through better...
messaging and methods for accurate self-assessment of risk, integration with other services and other demand and supply side interventions. Equally complex will be to identify effective strategies to support PrEP continuation, which unlike ART does not need to be lifelong but regularly taken only during periods of risk. A Kenya demonstration project among female sex workers showed significant drop offs in continuation at 1, 3, and 6 months after initiation. The EMPOWER study in South Africa and Tanzania showed initial high uptake of PrEP among young women but subsequent high rates of drop out over 12–15 months and no impact of an adherence club intervention on rates of continuation. Looking forward, potential future products that are longer lasting and may incorporate pregnancy prevention may be more effective and cost-effective in high-risk populations in Africa.

Finally, a small number of studies reported on broader combination prevention approaches. A South African cluster-randomized trial of a parenting intervention combining cash with parenting skills had positive impacts on a number of the psychosocial determinants of risk among adolescents. In another small South African study, adolescent friendly services saw greater uptake of both HIV testing and condoms from adolescents attending these clinics. In Tanzania, a cluster-randomized controlled trial reported a 10-session participatory gender training curriculum delivered to women taking part in a group-based microfinance loan scheme reduced physical intimate partner violence by a third over a 2-year period.

DISCUSSION

“Track E” at AIDS 2018 included an array of implementation strategies to deliver HIV testing, prevention, and treatment services and investigated outcomes ranging from uptake of services to HIV incidence. Yet many questions remain about how best to deliver and evaluate programs in the real world. For example, there were few studies among pediatric or adolescent populations, in humanitarian settings, or that measured viral load among PLHIV. We need to refocus IS on pragmatic approaches that may be less costly, more timely, and provide insight to the program delivery questions.

We highlight 4 areas where we hope to see progress by the International AIDS Conference in 2020. First, we hope to see more on strategies for delivery of primary HIV prevention programs. Track E at AIDS 2018 was dominated by studies on strengthening the treatment cascade. The same urgency has not yet been applied to innovations in the delivery of primary prevention. With stagnating financing and burgeoning populations in many affected countries, the need for treatment for growing numbers of people into the foreseeable future is a widely recognized challenge. By contrast, although we have a range of efficacious prevention tools for uninfected individuals, both old (condoms) and new (voluntary medical male circumcision and PrEP), prevention programs in many settings are still grappling with how best to address demand and supply side barriers so these methods can be optimally scaled. Insofar as prevention has always been a harder sell than treatment, the need for interdisciplinary learning on human behavior is paramount. Research from sociology, psychology, economics, and business can be used to drive many aspects of consumer behavior through an understanding of human social needs and desires, and we must continue to innovate in the HIV response.

Second, economics and financing studies can be strengthened. Costing, cost-effectiveness, and efficiency studies of delivery strategies are essential, but remain rare. Furthermore, there was little research on sustainable approaches to financing the epidemic response. A successful HIV response that optimizes the full tool box of treatment and prevention know-how requires accurate analyses of costs. We do not yet have the economic evidence to understand where and how constrained funds should be spent, and we are failing to develop innovative and robust financing strategies for the long term. Discussions about the place of HIV within broader health system financing with a view to integrating the delivery of HIV prevention, testing, and treatment services with related communicable and noncommunicable diseases were also missing. As people with HIV live longer, diseases of aging will grow in importance, and with the push for universal health coverage, expanding the focus may highlight areas for improving health system efficiencies. Every dollar spent on vertical HIV programs has an opportunity cost. Where programs are not meeting their aims, resources might be better spent elsewhere. This requires an unspiring eye and the inclusion of process, implementation, and outcome evaluations, including costing, as part of any program.

Third, the idea of data-driven programming was common across the conference. However, there is space for vast improvements in routine data systems. The possibilities for IS would be expanded by robust, routine programmatic data systems, including individual identifiers that permit programs to evaluate individual clinical outcomes, and with the ability to course correct for greater impact or efficiency, including better tracking of clinic visits and procedures. At AIDS 2018, it was clear that sufficient investment, coordination, analysis, and harmonization across a myriad of sources of individual data are yet to happen. Rarely are routine HIV data systems sufficient to support rigorous IS. For example, lack of reported repeat viral load tests restricted an assessment of community adherence groups on viral suppression in Mozambique; poor follow-up and missing data limited the ability to assess program quality in community health worker program to trace lost patients in Botswana and in a program to assess the impact of same day diagnosis and treatment on retention of children in care in Uganda. Systems that integrate and securely store unique, universal, health identifiers, and/or identifiable information to facilitate linkage can track patients within and across programs and provide deduplicated individual-level strategic information. Because HIV services are mainstreamed and integrated with other global health efforts, strengthened data systems that form the backbone for supporting and assessing patient care, prevention, and intelligent programming are essential.

Finally, implementation scientists face methodological challenges in undertaking their work and must continue to
innovate. Insofar as IS focuses on real-world, pragmatic research, we have less control over the context of IS research compared with research in basic and clinical science. For example, major changes in international guidelines regarding ART provision were rolled out during the conduct of the implementation trials of universal test-and-treat strategies. As is the case in prevention and clinical science, ethical issues mean that true control groups sometimes cannot be justified, and yet there remains a critical need to develop and refine implementation strategies. The increase in interdisciplinary research, including process evaluations that give rise to understanding of mechanisms of action and potential transferability and scalability of implementation strategies, is encouraging. In addition, we must pursue efficient evaluation methods that obtain high-quality data at a lower cost. Hybrid designs offer one potential method requiring further investigation. We may also choose to pursue a greater focus on evaluations powered on implementation (e.g., coverage and uptake), process, and short-term mediating outcomes, recognizing that it is also incumbent to pre-specify and report these outcomes in trials powered to detect effectiveness. This methodological innovation must continue and gather pace to support the critical IS effort and, thus, the translation of efficacious tools and methods for HIV prevention and treatment into population impact and, ultimately, epidemic control.

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