

Repositioning Implementation Science in the HIV response: Looking ahead from AIDS 2018

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Abstract

Background

Implementation science occupies a critical place in HIV/AIDS research, reflected by a full scientific track (“Track E”) at the bi-annual 22nd International AIDS conference. Implementation science 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 implementation science, at the 22nd International AIDS conference held in 2018 in Amsterdam. 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 trialled 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

Implementation science for HIV/AIDS treatment and prevention continues to expand. The weakness of routine data systems must be addressed. Implementation science for primary HIV prevention must be prioritised with a dearth of rigorous, intersectoral studies in this area. Costing and financing studies could 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.

Introduction

Implementation science (IS) studies examine programmes that deliver health-enhancing tools to those who need them, rather than evaluating the efficacy of the tools themselves. Implementation science uses frameworks, outcomes and methodologies to analyse the behaviour of systems, organisations, groups and individuals. It seeks to close the gap between evidence and practice by identifying delivery strategies that maximise the impact of programmes and health systems in the real world¹. In July 2018, over 15,000 global HIV/AIDS researchers, programmers, policy makers and activists gathered at 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 ART in reducing onward HIV transmission²³, 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 breakthrough 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. It is the role of implementation science to 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 appears fragile, emphasising the need for innovation in efficient, impactful programme 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 efforts⁵, while at the same time strengthening the delivery of HIV prevention, as declines in new infections have stagnated⁶.

We critically review HIV/AIDS implementation science presented at IAS 2018, grouped under four 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, optimising the delivery of primary HIV prevention. We conclude with some thoughts on next steps for the implementation science agenda as we approach the next International AIDS Conference in 2020.

Methods

The Track E programme included 85 abstracts, including 39 oral abstracts. Material relevant to Track E was also featured in plenary and cross-track sessions. As the rapporteur team for Track E at the conference, at least one author of this paper attended each Track E oral presentation and we had access to written abstracts, most slides and video recordings. We summarised 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 implementation science, four daily reports and an oral presentation summarising findings across Track E⁷. Following the conference, we reviewed these materials, agreed on key themes and identified cross-cutting issues. We summarise here the results from rigorous implementation science studies presented at the conference, including impact

evaluations (with both randomised and non-randomised designs), process evaluations, economic evaluations and systematic reviews of programme delivery strategies, regardless of scale or geography. We refer to each abstract reported at the conference, and in addition refer to subsequently published papers where these were available.

Results

Of the 39 oral abstracts in Track E, eight reported data from non-randomised evaluation studies, seven from randomized trials, six reported case studies in a “Lessons Learned” format, five reported costing or finance studies, five reported modelling studies, four principally qualitative research, two reported routine data, one a survey and one systematic review.

Theme 1: The impact of “Treat All” implementation strategies in Africa

Since 2015, WHO has recommended a “treat all” approach, where anyone confirmed as testing HIV positive should begin antiretroviral treatment within seven days, with the offer of same day initiation. This recommendation is in response to evidence that immediate initiation of ART has been shown to keep people alive, healthy and reduces the risk of transmitting the virus onwards⁸. This strategy also means that delivery can be streamlined to be more effective, compared to approaches that required pre-ART follow-up to assess treatment eligibility by CD4 count thresholds. Three cluster randomised trials, all of which launched before this 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 three studies examined HIV incidence as the ultimate outcome of interest, each examined a different implementation strategy to optimise uptake.

The ‘Ya Tsie’ trial in Botswana reported a statistically significant reduction in HIV incidence of 31% associated with the delivery of a combination HIV prevention programme measured among a cohort of nearly 9000 individuals from communities covering about 10% of the national population^{9,10}. 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, towards a treat all approach. The intervention generated a large 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-centred multi-disease model” was delivered at baseline in intervention and control communities, and then over time in intervention communities only^{11,12}. Immediate ART was available throughout the trial in the intervention arm, while 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 to 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 Eswatini¹³. Although not presented at this conference, the results for HPTN 071 (PopART), another large, three-arm universal test and treat study conducted in Zambia and South Africa were subsequently published in July 2019¹⁴. In this trial, both treatment groups received door-to-door interventions including HIV testing and other services. Surprisingly, compared to 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 were immediate ART), but was only 7% lower (non-significantly) in the clusters that initiated treatment immediately from

the start of the trial. A range of analyses across all four studies are now underway to inform future implementation efforts.

Theme 2: Innovations in delivering HIV testing services and case-detection

In addition to the multi-component “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 be also an effective route to link those testing negative but at risk to HIV prevention services¹⁵. They stressed the need for frequent and regular testing for key populations to stay negative through linkage and follow up within the prevention programme.

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 programmes 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 settings¹⁶. In Malawi, male-targeted HIV testing events at weekends in mobile clinics increased the proportion of men tested from 69% in 2014 compared to 78% in 2017¹⁷. HIV self-testing also provides an important opportunity for screening, by bringing HIV testing services to men. In Kenya, the secondary distribution of two additional oral HIV self-test kits by pregnant women aged 18 to 24 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 to the control group¹⁸. Rates of couples-testing were also higher in the intervention arm (77.8% compared to 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 to 42%, respectively)¹⁹. 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 programmes 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 “optimised case finding” delivery model incentivised peer referrals for testing by people testing positive and increased the yield of positive tests from 3.4% to 23.6%²⁰.

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 ten years of peer support groups involved in community ART distribution and mutual psychosocial support including 2,167 patients with HIV attending 13 clinics (over the period Feb 2008 to Oct 2017) showed that 87.5% were retained in care and 76.4% remained in their

group²¹. 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 to standard of care in a randomised trial²². In Ethiopia, an approach to improve adherence and reduce the burden on health facilities based on appointment spacing had been increased to six-months and rapidly scaled up, and was found to be acceptable by clients and service providers²³, while in Tanzania community-based ART delivery through an existing cadre of home-based carers was shown to be acceptable, feasible and non-inferior to existing clinic-based models^{24,25}. 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 therapy²⁶.

Theme 4: Optimising the delivery of primary HIV prevention programmes

Implementing HIV prevention programmes poses unique challenges and requires multi-sectoral collaborations to be successful. A modelling study reported at the conference showed that currently, the most cost-effective primary prevention tools (including condoms and VMMC) are funded at only 70% of need²⁷. PrEP delivery and the challenges of implementation especially to high risk groups was a major theme of the conference.

One strategy to strengthen prevention is to improve the use of data to better target our efforts. In Kenya the “prevention roadmap” strategy uses modelled 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 applies a geographic targeting step at its first stage, before identifying and prioritizing the highest risk young women for service delivery. Each of these examples were 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 prioritise action, but what determinants of risk should be targeted^{28,29,30}.

A number of studies examined PrEP programmes. The ACCESS study in Kenya and South Africa concluded that self-perceived risk is an important driver of PrEP Initiation³¹. 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 violence³². 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 following initiation³³. 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 continuation³⁴. 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 Africa⁷.

Finally, a small number of studies reported on broader combination prevention approaches. A South African cluster randomised trial of a parenting intervention combining cash with parenting skills had

positive impacts on a number of the psychosocial determinants of risk among adolescents ³⁵. In another small South African study, adolescent friendly services saw greater uptake of both HIV testing and condoms from adolescents attending these clinics ³⁶. 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 two-year period ³⁷.

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 programmes in the real world. Taking the long view to sustainability, now is the time to refocus implementation science on pragmatic approaches that may be less costly, more timely and which provide insight to the program delivery questions that remain.

We highlight four 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 programmes. 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. In contrast, although we have a range of efficacious prevention tools for uninfected individuals, both old (condoms) and new (VMMC, PrEP), prevention programmes 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 ³⁸, the need for interdisciplinary learning on human behaviour is paramount. Decades of research from sociology, psychology, economics and business have been used to drive many aspects of consumer behaviour through an understanding of human social needs and desires, and we must continue to innovate in the HIV response.

Second, economics and financing studies at AIDS 2018 can be strengthened. Costing, cost-effectiveness and efficiency studies of delivery strategies are essential, but remain rare. Further, 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 non-communicable 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 programmes has an opportunity cost. Where programmes are not meeting their aims, resources might be better spent elsewhere. This requires an unsparing 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 implementation science would be expanded by robust, routine programmatic data systems, including individual identifiers that

permit programmes 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, co-ordination, analysis and harmonisation across a myriad of sources of individual data has yet to happen. Rarely are routine HIV data systems sufficient to support rigorous implementation science. For example, lack of reported repeat viral load tests restricted an assessment of community adherence groups on viral suppression in Mozambique ²¹; poor follow-up and missing data limited the ability to assess program quality in community health worker programme to trace lost patients in Botswana ³⁹, and in a program to assess the impact of same day diagnosis and treatment on retention of children in care in Uganda ⁴⁰. Systems that integrate and securely store unique, universal, health identifiers and/or identifiable information to facilitate linkage, can track patients within and across programmes and provide de-duplicated individual-level strategic information. As 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 implementation science focuses on real-world, pragmatic research, we have less control over the context of implementation science research compared to research in basic and clinical science. For example, a major change in international guidelines regarding ART provision was 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 lower cost. Hybrid designs offer one potential method requiring further investigation⁴¹. We may also choose to pursue a greater focus on evaluations powered on implementation (e.g. coverage, 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 implementation science 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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