

SCIENCE TO PROGRAM IMPACT

OVERVIEW

A strong focus on the linkage between research findings and program activities is the foundation of the U.S. Centers for Disease Control and Prevention's (CDC) successful public health impact. Scientific excellence, integrity, and public health ethics are at the core of the CDC mission. CDC leadership and support for the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) and its activities around global tuberculosis (TB) have contributed to broader scientific knowledge, as related to global health. Over the past 15 years, global HIV and TB experts at CDC have developed over 2,000 scientific protocols supporting the collection and reporting of data to guide, monitor, and evaluate programs.

CDC'S ROLE

CDC serves as a leader in the production of top-notch science to inform program development and improve public health impact worldwide. As part of its global HIV and TB program, CDC ensures compliance with global public health standards regarding scientific integrity and human protections in both data collection and service delivery. This is accomplished by overseeing the review and approval of scientific information products; providing training, capacity-building, and technical assistance on protection for human subjects and scientific ethics; and monitoring regulatory compliance. These activities ensure that high quality research is conducted, that the rights and well-being of study participants are protected, that data collected are accurate, complete, and verifiable from source documents; and that such studies are in compliance with approved protocols, their standard operating procedures, guidelines for Good Clinical Practice and Good Laboratory Practice, and all applicable regulatory requirements.

To strengthen the link between public health research and practice in CDC's global HIV and TB programs, CDC coordinates, develops, and oversees several different operational research initiatives, including Public Health Evaluations, Implementation Science, Key Population Implementation Science, and Combination Prevention Impact Evaluations. The purpose of these activities is to yield knowledge that will enhance the delivery of services and maximize the population-level impact of HIV prevention, care, and treatment services provided in the 44 PEPFAR-supported country and regional offices, as well as those initiated at CDC headquarters.

ACCOMPLISHMENTS / RESULTS

CDC-supported implementation science has resulted in public health program developments that strengthen and expand the global prevention and treatment landscape for TB and HIV. Among these are advances in the access to and accuracy of HIV testing; the development and scale-up of models for HIV treatment services, including methods to improve retention and adherence to antiretroviral treatment (ART); the expansion of voluntary medical male circumcision services (VMMC); innovations in the prevention of mother-to-child transmission (PMTCT); the impact of integrating HIV services into those for antenatal care and TB; and the development of model HIV testing and treatment services for key populations.

Numerous specific examples highlight the critical role performed by CDC, working in partnership with local research partners, in advancing PEPFAR goals. Data from implementation science research on provider-initiated testing and counselingⁱ in Botswana contributed to widespread introduction of routine testing into PMTCT programs across Africa. A detailed multi-country study of the PMTCT cascadeⁱⁱ yielded data that provided the basis for further evaluation of these programs. Evaluation of home-based testing and counseling in Ugandaⁱⁱⁱ that included analyses of cost-effectiveness^{iv} led to expanded implementation of home-based testing, which has been adopted in many other countries. A CDC project that developed methodologies for costing analysis of ART programs in five countries led the way for the systematic expenditure analysis that is routinely utilized throughout PEPFAR; this type of analysis is now a central component of country operational planning.^v A randomized trial that demonstrated the effectiveness of cell phone text messaging in improving ART adherence and virologic suppression contributed to its widespread introduction into programs.^{vi} A multi-country study of risk factors for low ART retention demonstrated the higher success rates among programs that provide for community-delivery of ART, which supported their further expansion.^{vii} A study of TB diagnostic algorithms among persons with HIV^{viii} and of the cost-effectiveness of expanding TB diagnostic testing^{ix} contributed to new guidance from the World Health Organization (WHO) on TB/HIV management. CDC's development and field evaluation of new assays for use of dried blood spots for monitoring ART resistance^x and viral load^{xi} are now in increasingly widespread use. Scientific protocols used to monitor scale-up of VMMC,^{xii} PMTCT Option B+,^{xiii} and the WHO Test and Start guidelines^{xiv} have demonstrated progress in each of these areas while also providing data that highlight critical challenges in reaching adolescents^{xv} and men^{xvi} that need to be addressed in every country program. Recent studies demonstrate the cost-effectiveness of demand creation strategies for VMMC,^{xvii} the comparative impact of different cervical cancer treatment approaches on cervical HIV shedding,^{xviii} the potential for index client testing to facilitate active case-finding of persons with HIV infection,^{xix} and the reduction in community-level HIV incidence that can be attained through a combination prevention approach that includes the provision of ART for all persons with HIV infection.^{xx}

CDC country offices are staffed with global HIV and TB experts who work closely with local and international research partners to develop operational research capacity at local universities and other institutions. The alignment of CDC scientific experts in country offices with local implementing partners plays a crucial role in facilitating the rapid translation of research findings into HIV and TB programs.

As of 2018, critical information and findings from CDC-supported work have been shared through over 4,000 information products, including more than 1,600 manuscripts published in peer-reviewed journals, over 1,300 abstracts presented at scientific conferences, and over 1,000 other publications, such as surveillance reports, technical guidance, and training materials. CDC has also provided technical consultation to support the publication of over 100 documents published by WHO and UNAIDS, including technical guidance documents to support the implementation of national HIV and TB programs.

-
- ⁱ Centers for Disease Control and Prevention (CDC). Introduction of Routine HIV Testing in Prenatal Care --- Botswana, 2004. *MMWR Morb Mortal Wkly Rep.* 2004 Nov 26;53(46):1083-6.
- ⁱⁱ Stringer EM1, Ekouevi DK, Coetzee D, Tih PM, Creek TL, Stinson K, Giganti MJ, Welty TK, Chintu N, Chi BH, Wilfert CM, Shaffer N, Dabis F, Stringer JS; PEARL Study Team. Coverage of nevirapine-based services to prevent mother-to-child HIV transmission in 4 African countries. *JAMA.* 2010 Jul 21;304(3):293-302. doi: 10.1001/jama.2010.990.
- ⁱⁱⁱ Lugada E, Levin J, Abang B, Mermin J, et al. Comparison of home and clinic-based HIV testing among household members of persons taking antiretroviral therapy in Uganda: results from a randomized trial. *J Acquir Immune Defic Syndr.* 2010 Oct;55(2):245-52. doi: 10.1097/QAI.0b013e3181e9e069.
- ^{iv} Menzies N, Abang B, Wanyenze R, et al. The costs and effectiveness of four HIV counseling and testing strategies in Uganda. *AIDS.* 2009 Jan 28;23(3):395-401. doi: 10.1097/QAD.0b013e328321e40b.
- ^v Menzies NA, Berruti AA, Berzon R, et al. The cost of providing comprehensive HIV treatment in PEPFAR-supported programs. *AIDS.* 2011 Sep 10;25(14):1753-60. doi: 10.1097/QAD.0b013e3283463eec.
- ^{vi} Lester RT(1), Ritvo P, Mills EJ, et al. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. *Lancet.* 2010 Nov 27;376(9755):1838-45. doi: 10.1016/S0140-6736(10)61997-6. Epub 2010 Nov 9.
- ^{vii} Koole O, Tsui S, Wabwire-Mangen F, Kwasigabo G, et al. Retention and risk factors for attrition among adults in antiretroviral treatment programmes in Tanzania, Uganda and Zambia. *Trop Med Int Health.* 2014 Dec;19 (12):1397-410. doi: 10.1111/tmi.12386. Epub 2014. Sep 17.
- ^{viii} Cain KP, McCarthy KD, Heilig CM, et al. An algorithm for tuberculosis screening and diagnosis in people with HIV. *N Engl J Med.* 2010 Feb 25;362(8):707-16. doi: 10.1056/NEJMoa0907488.
- ^{ix} Abimbola TO(1), Marston BJ, Date AA, et al. Cost-effectiveness of tuberculosis diagnostic strategies to reduce early mortality among persons with advanced HIV infection initiating antiretroviral therapy. 2012 May 1;60(1):e1-7. doi: 10.1097/QAI.0b013e318246538f.
- ^x Yang C, McNulty A, Diallo K, Zhang J, et al. Development and application of a broadly sensitive dried-blood-spot-based genotyping assay for global surveillance of HIV-1 drug resistance. *J Clin Microbiol.* 2010 Sep;48(9):3158-64. doi: 10.1128/JCM.00564-10. Epub 2010 Jul 21.
- ^{xi} Schmitz ME(1), Agolory S, Junghee M, et al; for VL-DBS Study Group. Field evaluation of Dried Blood Spots for HIV-1 viral load monitoring in adults and children receiving antiretroviral treatment in Kenya: Implications for scale-up in resource-limited settings. *J Acquir Immune Defic Syndr.* 2016 Dec 17. doi: 10.1097/QAI.0000000000001275.[Epub ahead of print
- ^{xii} Centers for Disease Control and Prevention (CDC). Voluntary medical male circumcision – southern and eastern Africa, 2010–2012. *MMWR Morb Mortal Wkly Rep.* 2013 Nov 29;62(47):953-7.
- ^{xiii} Centers for Disease Control and Prevention (CDC). Impact of an innovative approach to prevent mother-to-child transmission of HIV--Malawi, July 2011–September 2012. *MMWR Morb Mortal Wkly Rep.* 2013 Mar 1;62(8):148-51.
- ^{xiv} Centers for Disease Control and Prevention (CDC), Botswana Ministry of Health, Harvard TH Chan School of Public Health. Botswana Combination Prevention Project. In: *ClinicalTrials.gov* [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2016 Dec 21]. Available from: <https://clinicaltrials.gov/ct2/show/NCT01965470>. NLM Identifier: NCT01965470
- ^{xv} Auld AF, Agolory SG, Shiraishi RW, et al. Antiretroviral therapy enrollment characteristics and outcomes among HIV-infected adolescents and young adults compared with older adults--seven African countries,2004-2013. *MMWR Morb Mortal Wkly Rep.* 2014 Nov 28;63(47):1097-103.
- ^{xvi} Auld AF, Shiraishi RW, Mbofana F, et al. Lower Levels of Antiretroviral Therapy Enrollment Among Men with HIV Compared with Women - 12 Countries, 2002-2013. *MMWR Morb Mortal Wkly Rep.* 2015 Nov 27;64(46):1281-6. doi: 10.15585/mmwr.mm6446a2.
- ^{xvii} Torres-Rueda S, Wambura M, Weiss HA et al. Cost and Cost-Effectiveness of a Demand Creation Intervention to Increase Uptake of Voluntary Medical Male Circumcision in Tanzania: Spending More to Spend Less. *J Acquir Immune Defic Syndr.* 2018 Jul 1;78(3):291-299. doi: 10.1097/QAI.0000000000001682.
- ^{xviii} Greene SA, McGrath CJ, Lehman DA et al. Increased Cervical Human Immunodeficiency Virus (HIV) RNA Shedding Among HIV-Infected Women Randomized to Loop Electrosurgical Excision Procedure Compared to Cryotherapy for Cervical Intraepithelial Neoplasia 2/3. *Clin Infect Dis.* 2018 May 17;66(11):1778-1784. doi: 10.1093/cid/cix1096.
- ^{xix} Williams D, Mackellar D, Dlamini M, et al. Rapid ART initiation and index client testing outcomes of Commlink, a community-based, HIV testing, mobile HIV care, and peer-delivered, linkage case management program - Swaziland, 2017 AIDS 2018, 22nd International AIDS Conference, 23-27 July 2018, Amsterdam, Abstract book (THAC0401), 712-13.
- ^{xx} Makhema MJ, Wirth K, Pretorius Holme M, et al. Impact of prevention and treatment interventions on population HIV incidence: Primary results of the community-randomized Ya Tsie Botswana prevention project. *AIDS 2018, 22nd International AIDS Conference, 23-27 July 2018, Amsterdam, Abstract book (WEAX0105LB), 1079-1080.*