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Promotion of Research on the HIV Continuum of Care in the United States: The CFAR HIV Continuum of Care/ECHPP Working Group

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Introduction

Addressing the challenges of the HIV care continuum remains a major public health priority in the United States. This is exemplified by the July 2013 Executive Order from the White House which established the HIV Care Continuum Initiative to “mobilize and coordinate Federal efforts in response to recent advances regarding how to prevent and treat HIV infection.”¹ This third and final supplemental issue developed by the CFAR HIV Continuum of Care (CoC)/Enhanced Comprehensive HIV Prevention Planning Project (ECHPP) Working Group² for the *Journal of Acquired Immune Deficiency Syndrome (JAIDS)* highlights the work of academic investigators from seven cities, four of which include co-authors from local public health departments, to conduct research on the HIV continuum of care. This supplemental issue describes the third series of studies to emerge from an initiative supported by the National Institutes of Health (NIH) Centers for AIDS Research (CFAR) Program designed to stimulate research among the CFARs around the HIV prevention and care continuum.

The present introductory article begins with a brief overview of the CFAR CoC/ECHPP Working Group; continues with synopses of NIH funding opportunities and current CDC programs that have been developed to address the continuum of care; and concludes with a synthesis of the seven articles that are included in this supplement.

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CFAR HIV Continuum of Care/ECHPP Working Group

As described previously,^{3,4} the CFAR HIV CoC/ECHPP Working Group was initiated in 2011 to support HIV research by academic investigators in collaboration with their local Departments of Health. Building upon various models of collaboration that have been established between universities and health departments for HIV surveillance and prevention (e.g. in North Carolina, San Francisco, Seattle & King County and Washington D.C.), the CoC/ECHPP WG worked to foster academic-public health partnerships throughout the CFAR network.

The NIH CFAR program first provided support for this initiative in 2011 to CFAR investigators located in nine of the twelve highest U.S. AIDS prevalence cities to conduct HIV prevention and care research in support of the CDC ECHPP initiative (“ECHPP-1”). The first HIV CoC/ECHPP WG JAIDS supplement was then published in 2013 and included studies on HIV testing, prevention, and the care continuum.^{5–13} A second round of studies (“ECHPP-2”) was funded in 2012 to further support HIV care continuum research in these same nine cities – and articles about this research were published in the second HIV CoC/ECHPP WG JAIDS supplement in 2015.^{14–23} The third and final round of projects (“ECHPP-3”) were funded in 2013 to investigators at 10 CFARs (six of which were new to the WG) to “build on existing collaborations with their local health departments and to propose pilot interventions at one or more important junctures in the treatment cascade”.²⁴

Thus through the three rounds of ECHPP funding, 16 different CFARs (there are currently 20 CFARs) have received support through this initiative. In addition, at least three CFARs (the Tennessee, Third Coast [Chicago] and DC CFARs) have now included their local or state health departments as institutional partners in their CFARs.^{25–27} It is our hope that academic-health department partnerships for HIV prevention and research that have been promoted by the CFAR HIV CoC/ECHPP Working Group will be enduring and will continue to support national efforts to bring an end to the HIV epidemic in the United States.

NIMH and NIAID research initiatives and activities to address the HIV continuum of prevention and care

It is difficult to succinctly summarize the updated activities germane to this supplemental issue because these research and service directions have become so integral to the NIH HIV/AIDS prevention and treatment agenda. Although this agenda includes the contribution of other participating NIH entities (including the Office of AIDS Research and other NIH institutes; NICHD, NIDA, NIAAA, etc.), due to space limitations, this update will only address the NIMH/NIAID shared activities because these were the primary ICs involved in the CFAR/ECHPP program. Academic, public health, and community partners in NIMH/NIAID efforts also receive substantial support from these other relevant ICs.

Three major sets of activities have been shared by the Division of AIDS Research (DAR) at NIMH and the Division of AIDS (DAIDS) at NIAID since the previous supplemental issue of JAIDS that was a product of the CFAR/ECHPP programs.⁴ First, DAR and DAIDS have articulated and formalized a process and activities for an integrated biobehavioral HIV

prevention and care agenda²⁸ that includes collaboration on priority-setting and funding opportunities in these domains. Importantly, the integrated agenda has also benefited from the co-location of the program personnel who lead these scientific areas lead by DAR and DAIDS. Below, this integrated agenda is briefly highlighted. Second, there are standing funding announcements, published in the NIH Guide in 2014 and 2015, to be re-issued in the first quarter of 2017, that outline the unique and shared research priorities within the missions of DAR and DAIDS that directly address the types of projects in this special issue – and also call for the next iterations of this work that will evolve due to the expanding effective HIV prevention and treatment tools. An exemplar but not exhaustive list of these funding opportunities are described here. Third, DAR and DAIDS have continued to broker, encourage, and fund efforts that require collaborations among scientists, clinicians, public health programs, and community partners. Notably, the CFAR program at DAIDS and DAR leadership have utilized timely solicitation and funding of supplements in order to move quickly and target research in this area in order to meet the needs of affected communities. Two such calls for supplements and funded projects in 2015–2016 are outlined to conclude this brief update.

The integrated biobehavioral HIV/AIDS research agenda – spanning basic, translational, and implementation science has been outlined by NIAID leadership²⁹ and was publicly presented by DAR/NIMH leadership at the NIAID/DAIDS AIDS Research Advisory Council (ARAC) in September 2016.³⁰ Coupled with the biomedical advances that have occurred over the past 35 years, but especially the treatment and prevention advances in treatment-as-prevention and PrEP, an extensive behavioral and social science research agenda has defined the behaviors that put individuals at risk for infection, as well as the mutable contextual factors that influence uptake and adherence to ARVs and PrEP.^{31–33} Moving forward, it will continue to be critical for behavioral and biomedical funders and executors to assure that ongoing and planned prevention/treatment trials from Phases 1–4 have the state-of-the-science in both domains, that the HIV cure agenda fosters team science which combines discoveries from biomedical, behavioral, neuroAIDS, and participatory research to advance HIV eradication, and investments are expanded in targeted implementation research on the HIV care continuum and prevention tools (e.g., PrEP) to optimize public health impact.

To meet these aims, DAR and DAIDS issued collaborative funding opportunities developed to address the HIV continuum for prevention and care, that have included solicitations such as “Advancing Structural Level Interventions Through Enhanced Understanding of Social Determinants in HIV Prevention and Care”³⁴; “Improving Delivery of HIV Prevention and Treatment through Implementation Science and Translational Research”³⁵; “Methods for Prevention Packages Program IV”³⁶; “Limited Interaction Targeted Epidemiology (LITE) to Advance HIV Prevention”³⁷; and “Improving the HIV Pre-Exposure Prophylaxis (PrEP) Cascade”.³⁸ Collectively, these highlighted funding opportunities delineate major sets of priority research directions that will continue to fuel the efforts that defined the original CFAR/ECHPP projects that were supported by NIAID, NIMH and the other CFAR participating ICs.

Finally, in addition to the above funding opportunities for multi-year large efforts to address the continuum of prevention and care, DAR and DAIDS have also used supplements to NIMH and NIAID existing grants and centers, as a means to quickly stimulate and fund innovative high-priority pilot projects. Two are highlighted here. In 2016, DAR and DAIDS partnered to solicit research applications to collaborate with the CDC-funded public health departments and community partners who had received demonstration project support to advance PrEP uptake in US cities with high HIV incidence: “HIV Pre-exposure Prophylaxis (PrEP) Implementation Science in CDC-funded Public Health Demonstration Projects (Admin Supp)”.³⁹ This effort resulted in the rapid funding of eight supplemental projects that could be conducted in concert with the CDC-funded projects. In 2015 the NIAID CFAR program solicited supplement applications for high priority innovative science to address “Advancing PrEP Delivery,” and “HIV Transmission and Microepidemics” and in 2016 funded supplements in the following topics: “Tracking HIV Transmission Phylodynamics: Leveraging Collaborations with Public Health Departments and Others to Research Methods to Analyze Phylogenetic Data in Close to Real-Time,” “Advancing PrEP Delivery among at risk Youth and Young MSM (especially minority MSM)” and “Rapid HIV Treatment Initiation: Implementation Models, Uptake, and HIV Care Continuum Outcomes.” The responses to these solicitations were robust, and a total of 24 one-year innovative projects were funded in 2015 and 2016. DAR and DAIDS – in collaboration with their other NIH IC and DHHS partners (e.g., CDC, HRSA, VMAC) – will continue to use all available mechanisms to support the integrated science in the HIV/AIDS prevention and care continuum.

Update on CDC-supported programmatic initiatives on HIV prevention and the HIV continuum of care

Since our previous summary of current CDC programs on the HIV continuum of care⁴, the rapid pace of new activities at CDC has continued and the targeted focus on HIV outcomes related to linkage to and engagement in care and viral suppression among people living with HIV has intensified. CDC has ongoing funding relationships with all state health departments in the United States, eight large-city health departments, and a handful of territorial or other special health departments to implement public health activities such as HIV surveillance and HIV programs. The CDC also directly funds over 100 community-based organizations (CBOs) through general and targeted efforts, and provides indirect support to even more CBOs through health department funding. An important recent change for health department grantees is that CDC informed them in mid-2016 that CDC was going to combine the separate funding opportunity announcements (FOAs) for surveillance and HIV prevention programs into one FOA. While surveillance and programmatic activities have become increasingly linked and interdependent as surveillance data is used for programmatic purposes at both the individual level (for patient tracking through the care continuum) and the jurisdictional level (for monitoring of outcomes along the care continuum),⁴⁰ this combined FOA represents an important structural shift that has the promise of improving public health outcomes locally and nationally. The new funding announcement will begin in January 2018.

CDC has also continued to encourage jurisdictions to have laws or regulations that support the complete reporting of all CD4 and viral load test to help monitor HIV care outcomes and to include only those states with actual complete reporting in the yearly HIV monitoring report. Over 40 states now have favorable laws or regulations requiring complete reporting, and when the monitoring report of select prevention and care outcomes was published in July 2016, 32 states and the District of Columbia had actually achieved complete reporting as defined by CDC.⁴¹ In addition, CDC has continued to provide guidance on the use of continuum of care outcomes, publishing an updated guidance in July 2016 on how to calculate the two main types of continua, the prevalence-based continuum and the diagnosis based continuum.⁴²

CDC also has implemented new demonstration projects which stand on the shoulders of earlier demonstration projects that started in 2010, 2012, and 2014 to support that National HIV/AIDS Strategy (NHAS) and CDC's high impact prevention (HIP) approach to HIV activities.⁴ In 2015, two new demonstration projects were funded. The first, Project PrIDE,⁴³ was funded by CDC to support health departments in implementing two public health strategies to reduce new HIV infections in gay, bisexual, and other men who have sex with men (MSM) and transgender persons; 1) pre-exposure prophylaxis (PrEP), a daily pill to prevent getting HIV, and 2) data to care (D2C) the use of HIV surveillance and other data to identify HIV-diagnosed persons not in care, and to link, engage, or re-engage them in HIV medical care.⁴⁴ With over \$37 million in the first year of the three year project, 12 health departments were funded to implement PrEP programs targeted particularly to MSM and transgender persons of color, and 5 of these health departments also were funded to enhance their data-to-care activities for MSM and transgender persons. As discussed above, CDC then collaborated with NIH to try to increase and strengthen the lessons learned about PrEP implementation from Project PrIDE. NIH funded an administrative supplement of up to \$175,000 per applicant that was available for CFARs, NIMH AIDS Research Centers, and other grant funded researchers working on PrEP to develop research projects around PrEP implementation in collaboration with CDC's 12 PrIDE grantees.⁴⁵ Ultimately, 8 projects were funded in 6 of the 12 Project PrIDE cities. This research project followed the example of earlier NIH-funded collaborations between researchers and health departments by requiring researchers to work with health departments and propose a collaborative project. Health departments were necessary partners with researchers, but individual health departments were not required to agree to collaborate on a research project. This NIH funding provided an opportunity for willing health departments to work with researchers to address focused and public health relevant research questions that could not be explored with CDC's non-research funding.

A second new demonstration project led by CDC, now called Project THRIVE, was funded in 2015 by the Department of Health and Human Services (HHS), Secretary's Minority AIDS Initiative Fund (SMAIF). The purpose of this FOA is to support health departments to collaborate with CBOs, healthcare clinics and providers, behavioral health providers, and social services providers to develop comprehensive models of prevention, care, behavioral health, and social services models for MSM of color living with or at risk for HIV acquisition.⁴⁶ In contrast to Project PrIDE, which focused efforts on two strategies, THRIVE requires grantees to provide 13 services for MSM of color at risk for HIV acquisition and 11

services for those who are living with HIV. The FOA also is supported by a second FOA to provide training and technical assistance to support the provision of the 24 services required as part of the demonstration project. Seven state or large-city health departments were funded for this 4-year demonstration project.

A few other CDC activities are notable due to their relevance to the continuum of care and work with health departments. First, in December 2015, CDC released the second “State HIV Prevention Progress Report” which provides data, where available, across all states and the District of Columbia for six indicators that measure outcomes across the continuum of care.⁴⁷ The third report will be published in early 2017 and will allow analysis of trends over time across states. Finally, CDC launched two important communication efforts in December 2015 at the National HIV Prevention Conference (NHPC) in Atlanta. A new HIV testing campaign, called “Doing It,” was implemented targeting all groups with tailored executions for various higher risk target populations. Part of CDC’s Act against AIDS communications efforts, the campaign was developed in close partnership with community stakeholders and with extensive formative and developmental research,⁴⁸ and health departments can use all parts of the campaign locally at no cost. At NHPC, CDC also released the beta version of a new online HIV risk reduction tool.⁴⁹ This tool represents the first broad update of CDC’s HIV prevention messages to take into account new prevention innovations such as treatment as prevention and PrEP. The tool addresses prevention for the general population as well as those at high risk of acquiring HIV and those who are already living with HIV. One of the innovations of the tool is the “know your HIV risk” calculator that allows the user to input various behaviors as well as risk and protective factors to see how various actions affect overall risk. The current tool provides multiple options for users to provide input, and CDC will use this information and other research on the tool to develop and release the next version in 2017.

Synthesis of ECHPP-3 Manuscripts

The seven manuscripts in this third supplemental issue of JAIDS are summarized in this section. The cities, CFARs, first author and Site PI(s), and Aims for each project are shown in Table 1.

Researchers from the **University of Washington CFAR and the Seattle & King County, Idaho, Alaska, Oregon, Washington, Montana and Wyoming State Health Departments** conducted case investigations to assess the status of HIV cases that were considered, according to surveillance data, to be out of care for at least one year. Of 3,866 cases with no CD4 count or viral load result for at least one year in 2012–2014, a majority were found to have moved, died, or actually be in care. The authors conclude that persons living with HIV who are classified as out of care using surveillance data may not be truly out of care, resulting in underestimates of national retention in care rates, and highlighting the potential benefit of efforts to improve local surveillance data.⁵⁰

Investigators from the **University of North Carolina CFAR and the North Carolina Department of Health and Human Services** studied the longitudinal patterns of engagement in HIV care and treatment using 10 years of HIV surveillance data in North

Carolina from 2006–2015. Five relatively distinct care patterns emerged: consistently high clinic attendance, steadily declining attendance, consistently low attendance, weak attendance initially with early improvement, and weak attendance initially with later improvement. The authors conclude that although most care trajectories are sub-optimal, there are distinct patterns of HIV care trajectories over time.⁵¹

Researchers from the **District of Columbia CFAR and the DC Department of Health** assessed the feasibility of geographically focused HIV testing to identify persons who needed to be linked to or engaged in care. Twenty census tracts with a high HIV prevalence were classified as either high or low risk areas based on viral load and in care parameters, and rapid HIV testing and surveys were conducted for 1,471 participants. The authors found that their approach was useful in identifying newly diagnosed cases of HIV and persons who were out of care, but not necessarily people residing in the targeted areas.⁵²

An investigative team from the **Johns Hopkins University CFAR and the Baltimore City Health Department** developed an animated video module to address cultural barriers to HIV testing among foreign-born Latino men, and a pilot survey was then conducted to assess HIV risk and barriers to testing in 104 men. Overall, half the men were found to have never tested for HIV; and among men who had been tested, the mean time since last test was almost 3.5 years. Importantly, watching the video significantly increased men's intention to test, and thus may be used to improve testing rates in this population.⁵³

Researchers from the **Emory CFAR** assessed individual and structural level barriers associated with poor retention and re-engagement in care among HIV clinic patients in Atlanta, Georgia. A total of 32 continuously retained patients, and 27 patients with recent gaps in care, were compared. Patients who were continuously retained were more likely to have social support and to have disclosed their HIV status to their families, whereas those with gaps in care were more likely to be younger and crack cocaine users, and to have food, housing and financial instability. The authors conclude that early assessment for predictors of poor retention could help direct interventions to high risk patients.⁵⁴

Investigators from the **Rochester CFAR** examined the feasibility and acceptability of a peer support text messaging intervention to increase retention and ART use in HIV-positive black MSM. A cellphone app enabled researchers to view relevant text messages from three trained mentors and eight mentees. The authors found that the text messaging app was feasible and acceptable, and concluded that it could be further explored as a support intervention.⁵⁵

Researchers from the **UCLA CFAR in Los Angeles** studied the use of machine learning methods to assist in the rapid identification of patterns associated with HIV using large social media datasets. They assessed various machine learning methods for their ability to detect patterns of association between tweets and HIV, and found that the logistic regression and random forest techniques were the most accurate and that logistic regression was the fastest. The authors conclude that machine learning methods techniques could support the use of social big data for HIV research.⁵⁶

Summary

In summary, the Co-Editors have greatly appreciated the opportunity to work with investigators from numerous CFARs and health departments over the past five years as part of the CFAR HIV Continuum of Care/ECHPP Working Group. We are grateful to the NIH for supporting this type of public health-oriented HIV research, and also for supporting the documentation of the results of these projects in two national meetings and a trilogy of JAIDS supplements. Moving forward, this important approach could be facilitated by other funding opportunities such as those described in this paper, so that academic-health department collaborations result in research that can directly inform real world program implementation.

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Table 1

ECHPP-3 Manuscripts: Project State/City, CFAR, First Author and Project Aims

State/City	CFAR	First Author	Project Aims
Washington, Oregon, Idaho, Alaska, Montana and Wyoming	University of Washington	Dombrowski	• To determine the status of HIV cases that appear to be “out-of-care” according to surveillance data through case investigations
North Carolina	University of North Carolina	Powers	• To study the longitudinal patterns of HIV care using surveillance data
District of Columbia	District of Columbia	Castel	• To assess the feasibility of geographically focused HIV testing to identify persons in need of linkage to and engagement in care
Baltimore	Johns Hopkins University	Dolwick Grieb	• To evaluate a video intervention designed to address barriers to testing in foreign-born Latino men
Atlanta	Emory University	Colasanti	• To identify individual-level and structural barriers to poor retention in care in HIV clinic patients
Rochester	University of Rochester	Senn	• To examine the feasibility of a text message intervention for retention and ARV adherence in HIV+ black MSM
Los Angeles	University of California Los Angeles	Young	• To study machine learning methods that identify patterns of association with HIV in large social media datasets