Successful Linkage to Pre-Exposure Prophylaxis for HIV Prevention Using a Multicomponent Implementation Strategy Among the Uninsured/Underinsured

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To the Editor:

PRE-EXPOSURE PROPHYLAXIS (PrEP) scale-up can contribute to reducing national HIV incidence.¹ The PrEP continuum of care provides a programmatic framework in which linking HIV-uninfected individuals to care is a crucial step for successful implementation.² Barriers to linkage to care (LTC) include lack of insurance coverage, access to care, and clinic referral relationships with community partners.³⁻⁷ States with limited public insurance options have disproportionate prescription-to-need ratios,⁸ emphasizing insurance coverage's prominent role in PrEP care.^{3,4,6} We assessed LTC rates of a multicomponent community-based implementation strategy designed to link uninsured individuals to PrEP care in Missouri.

The Washington University in St. Louis (WUSTL) Division of Infectious Diseases (ID) PrEP Program piloted a multicomponent implementation strategy to link individuals in the community to PrEP services from July 2014 to October 2015. Strategy components included a telephone hotline, PrEP education, insurance navigation, medication paperwork support, and appointment coordination.^{9,10} The hotline was disseminated to community partners, health departments, and other organizations through listservs, word of mouth and social networks, flyers, and social media. Health providers also re-

ferred individuals for LTC to the WUSTL PrEP Program. Referred individuals did not call the hotline. An ID physician contacted individuals who called or were referred within 7 days. During this initial phone call, individuals were surveyed, presented information on PrEP and medication assistance programs, notified of insurance navigation and medication paperwork support services and their contact information, and provided a clinic appointment within 4 weeks through a network of PrEP clinics.

Insurance navigation was provided by a local AIDS service organization (ASO). Navigators were notified of individuals without insurance or who requested support. Navigators contacted individuals, met them at their desired location within 1 week, discussed insurance eligibility, assisted in enrollment, and reviewed PrEP clinic locations in the context of their insurance options. Medication paperwork support was provided by an HIV specialty pharmacy. Pharmacists were notified of individuals who requested their services. Pharmacists contacted individuals and scheduled sessions to fill out paperwork.

A retrospective analysis of LTC rates was performed. The primary outcome was LTC, defined as attendance of the first PrEP clinical visit as a binary measure (yes/no). Time to LTC was measured by the number of days between the date of the call/referral and clinic attendance, with an observation period from the call/referral date to November 2015.

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Presented in part at the 2015 National HIV Prevention Conference; December 6-9, 2015, Atlanta, Georgia.

Lost to follow-up was defined as those unreachable after five phone calls. Individuals were contacted to assess PrEP initiation and 3-month retention, defined as self-reported medication use. This study was approved by the WUSTL Institutional Review Board.

Bivariate analyses were performed between the primary outcome and the covariates of age, gender, insurance type, men who have sex with men (MSM), having a current HIV-infected partner, called or referred, and navigation referral and attendance using logistic regression. Significant covariates were incorporated into the final multivariable logistic regression model to determine predictors of LTC. Odds ratios (ORs) and 95% confidence intervals (CIs) are reported. All statistical tests were two sided and the significance level was set at 0.05. Analyses were performed using STATA version 12.1 (College Station, TX).

A total of 132 individuals called the hotline ($n=81$) or were referred ($n=51$) for LTC. Follow-up occurred with 93.8% of calls (vs. 76.5% referrals, $p<0.01$). Callers reported learning about the hotline through an ASO (41.4%) or friend (26.4%). Most (86.3%) referrals were by WUSTL providers. Only 10 callers sought information (i.e., side effects and costs), whereas the remaining 105 callers/referrals requested PrEP. These individuals had a median age of 30 years [interquartile range (IQR) 26–36], 91.4% were men, 1.0% were transgender, 39.1% were black, 1.9% Latino/Hispanic, 28.6% were uninsured, 79.1% identified as MSM, 45.7% had a current HIV-infected partner, 6.7% had periconception plans with their HIV-infected partner, and were followed a median of 16.0 days (IQR 6.0–82.0) (range, 2.0–315.0).

Sixty-seven percent (70/105) of PrEP seekers were linked to care; the median time to linkage was 7.5 days (IQR 5.0–17.0) (range, 2.0–164.0). Callers (vs. referrals) were more likely to be linked (OR: 8.00, 95% CI: 3.21–19.95) and time to linkage was sooner (median 7.0 vs. 16.0 days; $p=0.03$). Individuals attended appointments at WUSTL (85.7%) or Veterans Affairs (2.9%) ID clinics, two community health centers (CHCs) (2.9%), three primary care private practices (5.7%), and an immigrant/refugee clinic (2.9%).

Most (91.4%, 64/70) received a prescription, 98.4% (63/64) self-reported initiation, and 91.8% (45/49) had 3-month retention. Reasons for not receiving a prescription included individuals declined citing their low risk (2/6), were not offered because their HIV-infected partners were undetectable (2/6) or had future periconception plans (1/6), and had incomplete laboratory testing (1/6).

Forty-three percent (13/30) of the uninsured were linked compared with 76.0% (57/75) of the insured (OR: 0.24, 95% CI: 0.10–0.59). Ninety percent (27/30) of the uninsured agreed to navigation, but 63.0% (17/27) attended and 47.0% (8/17) obtained insurance. The uninsured (vs. insured) had over twice as long time to linkage (median 19.0 vs. 7.0 days; $p=0.01$). Uninsured callers (vs. referrals) were more likely to link to care (OR: 10.50, 95% CI: 1.89–58.36). Receiving navigation (OR: 3.33, 95% CI: 0.63–17.57) and obtaining insurance (OR: 4.38, 95% CI: 0.56–33.95) were associated with LTC.

Fifty-four percent (22/41) of blacks were linked compared with 75.0% (48/64) of non-blacks (OR: 0.39, 95% CI: 0.17–0.89). Racial differences in baseline insurance coverage were apparent (33.3% of blacks vs. 66.7% of non-blacks were insured; $p=0.06$). Notably, 40.0% (10/25) of insured blacks did not link to care versus 16.0% (8/50) of insured non-blacks ($p=0.02$).

Race, insurance, caller versus referral, and identifying as MSM were significant in bivariate analyses. When adjusting for race and MSM, the insured (OR: 2.81, 95% CI: 1.03–7.68) and callers (OR: 5.12, 95% CI: 1.86–14.09) were more likely to be linked (Table 1).

Among individuals not linked ($n=35$), 48.6% missed one and 8.6% missed two appointments; 8.6% wanted to determine insurance eligibility (i.e., attend a navigation and/or future Marketplace enrollment session) in anticipation of out-of-pocket costs before scheduling an appointment during the study period. Some (17.1%) were lost to follow-up due to being unreachable (2/6) or had changed contact information during appointment coordination (4/6). Others (17.1%) changed their minds about wanting PrEP citing high costs (2/6), altered periconception plans (1/6), or changed risk

TABLE 1. MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS FOR HIV PRE-EXPOSURE PROPHYLAXIS LINKAGE TO CARE AMONG 105 INDIVIDUALS IN ST. LOUIS, MISSOURI

Characteristics	Unadjusted OR (95% CI)	p	Adjusted OR ^a (95% CI)	p
Race		0.025		0.575
Non-black	1.0		1.0	
Black	0.39 (0.17–0.89)		0.75 (0.27–2.08)	
Insurance		0.002		0.045
Uninsured	1.0		1.0	
Insured	4.14 (1.69–10.14)		2.81 (1.03–7.68)	
MSM		0.006		0.373
No	1.0		1.0	
Yes	4.01 (1.50–10.67)		1.73 (0.52–5.82)	
Contact method		<0.001		0.002
Referral	1.0		1.0	
Caller	8.00 (3.21–19.95)		5.12 (1.86–14.09)	

^aAdjusted for race, insurance, MSM, and contact method.

OR, odds ratio; 95% CI, 95% confidence interval; aOR, adjusted odds ratio; MSM, men who have sex with men.

behaviors (3/6). Missed initial appointments were because individuals forgot (4/20), were unavailable (2/20), had changing work schedules (3/20), had anticipated out-of-pocket costs beyond their budget (2/20), had unfinished insurance processing (3/20), or were unknown (i.e., individuals were unreachable) (6/20).

We demonstrated high linkage to PrEP care (66.7%) using a multicomponent implementation strategy that was tailored to meet the needs of residents with varying and dynamically changing insurance coverage in a state where public insurance eligibility is limited. This strategy built upon existing local stakeholder relationships for HIV care (e.g., navigation, pharmacy) and created new ones (e.g., clinics) to operationalize PrEP LTC.^{9,10} Our study's PrEP LTC (66.7%) was higher than that at a CHC (21.3%)⁶ or a public sexually transmitted diseases clinic (31.4%)⁷ due to differences in study settings.

Having insurance was a correlate of LTC in this study. In contrast, Flash et al. and Bhatia et al. reported that serodiscordant relationships⁶ and age,⁷ respectively, were predictors of LTC. However, similar to these studies, most of the individuals who linked to care in our study also initiated PrEP and had early retention. Furthermore, racial differences in LTC were observed in all three studies, which occurred in distinguishably different settings. Together, these findings highlight the need for implementation research surrounding culturally tailored LTC intervention development.

We observed a notable number of missed appointments and prolonged LTC due to insurance processing and PrEP appointment scheduling during which individuals were lost. A longer observation time would have identified more accurate LTC estimates in this cohort since navigation attendance and fixed Marketplace enrollment periods delayed LTC for many, especially the uninsured. Identified challenges in scheduling clinical visits included trying to coordinate individual and clinic availability in the context of dynamic work schedules, uncertainty in insurance processing times, awaiting navigation attendance, and changing telephone numbers or being unreachable during business hours. Clinic referral relationships needed strengthening at the organizational (vs. provider) level because scheduling centers required several phone calls for appointment approval with PrEP prescribing doctors and overbooking within 6 weeks. In the context of available resources, LTC interventions should incorporate evidence-based strategies such as appointment reminders and accompaniment,⁹ nontelephone communication (i.e., e-mail and text messages during evening and weekend hours), on-site insurance navigation, on-site visits with same-day prescribing, and strengths-based case management.^{11,12}

The study limitations include a small sample size, single site, few women, and limited individual characteristics on survey assessment. The hotline was affiliated with a private sector academic ID clinic, promoting selection bias.

Medicaid nonexpansion states have comparatively low PrEP utilization.⁸ Therefore, tailoring LTC strategies to overcome structural barriers unique to this context is critical.^{3,4} We demonstrated high rates of linkage to PrEP care using a multicomponent implementation strategy, which included multiple community partnerships, to address the

needs of uninsured and underinsured individuals. Study findings can inform urgently needed LTC intervention development to improve outcomes at this critical step within the PrEP continuum of care.

Acknowledgments

R.R.P. is supported by the Washington University Institute of Clinical and Translational Sciences grant UL1TR000448, subaward KL2TR000450, from the National Center for Advancing Translational Sciences of the National Institutes of Health, and NIH R25MH83620. P.A.C. is supported by NIH grants R34DA042648, R34MH110369, R21MH113431, and R21MH109360. P.A.C. and A.S.N. are supported by NIH grants R34MH109371 and R01MH114657. A.S.N. is supported by the NIH grant R25MH083620. K.H.M. is supported by the Harvard Center for AIDS Research (P30 AI06354).

Author Disclosure Statement

R.R.P. receives compensation for consulting from Gilead Sciences, Inc. and ViiV Healthcare. K.H.M. has received unrestricted research grants from Gilead Sciences and ViiV Healthcare. For the remaining authors, there are no conflicts of interest.

References

1. Smith DK, Van Handel M, Grey J. Estimates of adults with indications for HIV pre-exposure prophylaxis by jurisdiction, transmission risk group, and race/ethnicity, United States, 2015. *Ann Epidemiol* 2018. [Epub ahead of print]; DOI: 10.1016/j.annepidem.2018.05.003.
2. Nunn AS, Brinkley-Rubinstein L, Oldenburg CE, et al. Defining the HIV pre-exposure prophylaxis care continuum. *AIDS* 2017;31:731–734.
3. Patel RR, Mena L, Nunn A, et al. Impact of insurance coverage on utilization of pre-exposure prophylaxis for HIV prevention. *PLoS One* 2017;12:e0178737.
4. Marks SJ, Merchant RC, Clark MA, et al. Potential healthcare insurance and provider barriers to pre-exposure prophylaxis utilization among young men who have sex with men. *AIDS Patient Care STDs* 2017;31:470–478.
5. Doll M, Fortenberry JD, Roseland D, McAuliff K, Wilson CM, Boyer CB. Linking HIV-Negative Youth to Prevention Services in 12 U.S. Cities: Barriers and facilitators to implementing the HIV prevention continuum. *J Adolesc Health* 2018;62:424–433.
6. Flash CA, Adegboyega OO, Yu X, et al. Correlates of linkage to HIV preexposure prophylaxis among HIV-testing clients. *J Acquir Immune Defic Syndr* 2018;77:365–372.
7. Bhatia R, Modali L, Lowther M, et al. Outcomes of pre-exposure prophylaxis referrals from public STI clinics and implications for the preexposure prophylaxis continuum. *Sex Transm Dis* 2018;45:50–55.
8. Siegler AJ, Mouhanna F, Mera Giler R, et al. Distribution of Active PrEP Prescriptions and the PrEP-to-Need Ratio, US Q2 2017. Presented at: Conference on Retroviruses and Opportunistic Infections. Boston, MA. Abstract 1022LB. 2018.

9. Bradford JB, Coleman S, Cunningham W. HIV System Navigation: An emerging model to improve HIV care access. *AIDS Patient Care STDs* 2007;21:S49–S58.
10. Powell BJ, Waltz TJ, Chinman MJ, et al. A refined compilation of implementation strategies: Results from the Expert Recommendations for Implementing Change (ERIC) project. *Implement Sci* 2015;10:21.
11. Gilman B, Hidalgo J, Thomas C, Au M, Hargreaves M. Linkages to care for newly diagnosed individuals who test HIV positive in nonprimary care settings. *AIDS Patient Care STDs* 2012;26:132–140.
12. Craw JA, Gardner LI, Marks G, et al. Brief strengths-based case management promotes entry into HIV medical care:

Results of the antiretroviral treatment access study-II. *J Acquir Immune Defic Syndr* 2008;47:597–606.

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