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SUPPLEMENT ARTICLE

Ending the HIV Epidemic Among Persons Who Inject Drugs: A Cost-Effectiveness Analysis in Six US Cities

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Background. Persons who inject drugs (PWID) are at a disproportionately high risk of HIV infection. We aimed to determine the highest-valued combination implementation strategies to reduce the burden of HIV among PWID in 6 US cities.

Methods. Using a dynamic HIV transmission model calibrated for Atlanta, Baltimore, Los Angeles, Miami, New York City, and Seattle, we assessed the value of implementing combinations of evidence-based interventions at optimistic (drawn from best available evidence) or ideal (90% coverage) scale-up. We estimated reduction in HIV incidence among PWID, quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICERs) for each city (10-year implementation; 20-year horizon; 2018 $ US).

Results. Combinations that maximized health benefits contained between 6 (Atlanta and Seattle) and 12 (Miami) interventions with ICER values ranging from $94 069/QALY in Los Angeles to $146 256/QALY in Miami. These strategies reduced HIV incidence by 8.1% (credible interval [CI], 2.8%–13.2%) in Seattle and 54.4% (CI, 37.6%–73.9%) in Miami. Incidence reduction reached 16.1%–75.5% at ideal scale.

Conclusions. Evidence-based interventions targeted to PWID can deliver considerable value; however, ending the HIV epidemic among PWID will require innovative implementation strategies and supporting programs to reduce social and structural barriers to care.

Keywords. HIV; localized HIV microepidemics; interventions; cost-effectiveness; injection drug use; dynamic HIV transmission model.

In the United States, persons who inject drugs (PWID) continue to be disproportionately at risk of human immunodeficiency virus (HIV) infection. Successes in New York City, Vancouver, British Columbia, and countries such as Australia, the United Kingdom, and France have provided evidence that important reductions in HIV incidence among PWID are possible with the widespread provision of HIV care and services to prevent and reduce harms caused by substance use [1]. Domestically, the steady declines in HIV incidence among PWID has been a success story and several jurisdictions are now focused on preventing resurgence and getting new HIV infections attributed to drug injection to zero. Nonetheless, following the rise in prevalence of opioid injection, 2015 marked the first time in 2 decades that injection-related infections increased in the United States [2].

There is considerable evidence suggesting that broad implementation of prevention programs can be highly effective in reducing transmission of HIV and other blood-borne pathogens among PWID [1, 3, 4]. Nevertheless, the high prevalence of drug injection-related HIV infections among people living with HIV (18.1% in 2016) [5] and the lifetime prevalence of injection drug use in the United States (estimated to be 2.6%) [6] underscore how the public health response and short supply of these services have been (and remain) inadequate in many settings [1, 7, 8].

The US Centers for Disease Control and Prevention (CDC) have recommended a comprehensive approach to reduce the risk of HIV acquisition and transmission among PWID [9]. Long-standing recommendations include sterile syringe and needle distribution, and medication for opioid use disorders, both with robust evidence of effectiveness and cost-effectiveness [10–13]. In addition, the CDC's guidance includes expanded HIV testing and the provision of antiretroviral therapy

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(ART) for treatment and prevention, the latter of which can have large independent effects on incidence reduction among PWID [4]. Although preexposure prophylaxis (PrEP) at current prices has not been found to be cost-effective among PWID in prior US-based modelling studies [12, 14], the US Preventive Services Task Force recently recommended that PrEP be offered to all persons at high risk of HIV acquisition, including PWID [15]. Despite a consensus that combination implementation strategies are necessary to reduce HIV incidence among PWID [1, 3], determining which combination should be expanded across cities with different underlying injection drug use epidemics is necessary to deliver maximum value and produce the greatest impact.

We hypothesized that combination implementation strategies providing the greatest value would vary across cities with different epidemiological and structural conditions. Using a dynamic compartmental HIV transmission model populated and calibrated to replicate the HIV microepidemics in 6 US cities, we aimed to determine the highest-valued combination implementation strategies to reduce the burden of HIV among PWID.

METHODS

Model Description

Our analysis builds on a previously published dynamic, compartmental HIV transmission model adapted and calibrated to replicate city-level HIV microepidemics in Atlanta, Baltimore, Los Angeles, Miami, New York City, and Seattle. We selected these 6 cities because they represent nearly one-quarter of the population of persons living with HIV in the United States and the fact that they represent diverse HIV microepidemics with extensive epidemiological and structural differences in their public health responses to HIV [16]. This computer simulation model was based on a synthesis of the best available evidence on epidemiological and structural conditions for each city and has previously been described in detail elsewhere [7, 17]. The model tracked HIV-susceptible individuals through infection, diagnosis, treatment with ART, and ART discontinuation. In each city, the adult population aged 15–64 years was partitioned by sex at birth, HIV risk group (men who have sex with men [MSM], PWID, MSM who inject drugs [MSMWID], and heterosexuals), race/ethnicity (black/African American, Hispanic/Latinx, and non-Hispanic white/others) and sexual risk behavior level (high vs low risk). We incorporated region-specific ART initiation and persistence rates stratified by race/ethnicity and HIV risk group from a prior analysis of HIV Research Network data [18].

We derived estimates of the size of the PWID population by multiplying race/ethnicity-stratified total population numbers by sex-weighted, race/ethnicity-specific prevalence estimates for each city. We assumed that gender proportions of PWID were equivalent within race/ethnicity strata and used prevalence estimates from the most recent available year [7, 19]. Given the uncertainty in population sizes for MSMWID, we derived population estimates by taking the average of 2 estimated population sizes: (1) the proportion of MSM that inject drugs and (2) the proportion of male PWID that have sex with men [7, 17, 20–22]. Finally, based on the best available evidence, we assumed that 72.7% of PWID and MSMWID had an opioid use disorder [23].

HIV transmission within the model was possible between any 2 HIV-discordant individuals. The probability of HIV transmission was determined by: (1) the probability of selecting a partner living with HIV; (2) the type of risk behavior engaged in (heterosexual or homosexual activity, or sharing injection equipment); (3) the infected individual's HIV disease stage (acute or by CD4-based strata); (4) the infected individual's ART status; (5) whether the uninfected individual was on PrEP; and (6) the probability of condom use. We allowed for a combination of assortative and proportional sexual partnership mixing; assortative mixing accounted for individuals being more likely to form partnerships within a common stratum (eg, race/ethnicity, risk behavior level), while proportional mixing accounted for individuals with many partners being more likely to select a partner who also had many partners. We also assumed proportional mixing among PWID (ie, individuals who share many injections were more likely to select a partner who also shares many injections). Further details on the probability of HIV transmission in the model have previously been provided elsewhere [17].

The model also captured heterogeneity in maturation (eg, rates at which individuals age out of the model) and mortality, and the disparities in accessing health, prevention, and treatment services, including HIV testing, ART, syringe service programs (SSP), medication for opioid use disorder (MOUD), and PrEP.

Model Calibration and Validation

For each city, we calibrated the model to match HIV prevalence, new diagnoses, and deaths (2012–2015), stratified by sex, race/ethnicity, and HIV risk group (17 targets total, including prevalence among PWID and MSMWID), and validated against external incidence estimates [17]. The model was used to project microepidemic trajectories over a 20-year time horizon (2020–2040), accounting for external estimates of population growth, which incorporated demographic shifts in race/ethnic composition for each city, to serve as the basis of comparison [24]. In the projections, status quo service levels of prevention, testing, and treatment services were held at their 2015 levels (Table 1) except for PrEP, which was held at 2017 levels to account for its recent rapid growth in uptake among MSM.

Interventions

We selected 14 evidence-based interventions within 4 specific domains (Table 2): HIV prevention programs (SSP, MOUD with either methadone or buprenorphine, PrEP); HIV testing; ART engagement (ART initiation and retention); and ART

Table 1. HIV Among Persons Who Inject Drugs in 2017 and Selected HIV Treatment and Prevention Service Levels in 2015 in 6 Cities

Treatments and Services	Atlanta, GA	Baltimore, MD	Los Angeles, CA	Miami, FL	New York City, NY	Seattle, WA
Persons who inject drugs who are living with HIV, No. (% among all living with HIV)[a]						
Prevalence	3612 (11.3)	4759 (21.3)	5575 (10.8)	2425 (9.3)	13 037 (10.5)	884 (12.9
New diagnoses[b]	67 (4.1)	50 (11.4)	146 (7.5)	27 (2.3)	64 (3.0)	17 (10.8)
HIV prevention program service levels						
Estimated annual number of syringes distributed per PWID	2	20	19	6	24	196
Coverage of medication for opioid use disorder among PWID, %[c]	3.0	9.4	15.7	7.1	19.9	11.9
HIV testing levels among PWID/MSMWID[d]						
Percent receiving an HIV test in the past year	30/15	11/ 12	40/25	16/15	9/41	43/51
HIV treatment engagement among PWID/MSMWID[d]						
Percent of diagnosed initiating ART[e]	44/38	55/47	51/44	48/41	39/42	51/46
Percent discontinuing ART[e]	28/25	11/8	14/13	24/21	11/8	5/4
Percent reinitiating ART[e]	42/44	28/29	23/20	43/46	31/32	49/50

Counties included in city boundaries for Atlanta, Baltimore, Los Angeles, and Miami match those included in the definition of Ryan White EMA or TGA. New York City and Seattle boundaries are restricted to a subset of counties. Counties included in cities are: Atlanta (Barrow, Bartow, Carroll, Cherokee, Clayton, Cobb, Coweta, DeKalb, Douglas, Fayette, Forsyth, Fulton, Gwinnett, Henry, Newton, Paulding, Pickens, Rockdale, Spalding, Walton); Baltimore (Anne Arundel, Baltimore City, Baltimore County, Carroll, Harford, Howard, Queen Anne's); Los Angeles (Los Angeles county); Miami (Miami-Dade county); New York City (county and borough: New York [Manhattan], Kings [Brooklyn], Queens [Queens], Bronx [Bronx], Richmond [Staten Island]); Seattle (King county). Excluded counties for New York City compared to the Ryan White EMA definition included Westchester, Rockland, and Putnam, and excluded counties for Seattle compared to Ryan White TGA definition included Snohomish and Island.

Abbreviations: ART, antiretroviral therapy; EMA, Eligible Metropolitan Area; HIVRN, HIV Research Network; MSMWID, men who have sex with men who inject drugs; PWID, persons who inject drugs; TGA, Transitional Grant Area.

[a]Persons who inject drugs include men who have sex with men who inject drugs.

[b]New diagnoses are from 2017 in city surveillance reports, except for Los Angeles were new diagnoses are for 2016, or from the Centers for Disease Control and Prevention's Surveillance HIV Surveillance Supplemental Report.

[c]Coverage is among the 72.7% of PWID estimated to have an opioid use disorder [23].

[d]While the model runs in monthly cycles, we have converted these figures to yearly probabilities for ease of interpretation.

[e]ART initiation rates were estimated from the HIVRN data, and ART discontinuation and reinitiation rates were estimated by a continuous-time multistate Markov model based on the same HIVRN data [18].

reengagement (reinitiation and relinkage). These interventions were selected from the US CDC *Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention* and from the recently published literature [25, 26].

Although the model captured outcomes across risk groups for the entire adult population in each city, the implementation of interventions in our analysis was targeted exclusively to PWID and MSMWID (jointly referred to as PWID hereafter). Access to health services were held at status quo levels among the non-PWID population in each of the scenarios we describe below. Scale-up from status quo service levels was implemented proportionally across risk and ethnic groups over an 18-month period, entailing greater scale-up for groups receiving higher service levels at baseline, thus accounting for underlying structural barriers to health care access.

We assessed interventions individually and in all combinations (excluding any that would not practically be implemented jointly) for a total of 10 239 unique combinations. We assessed these combinations at optimistic implementation levels, where HIV testing and ART engagement and reengagement interventions were delivered at the upper bound of publicly documented evidence of scale-up [26].

Regarding the selected HIV prevention interventions, first, we defined optimistic expansion of SSP in accordance with the World Health Organization's (WHO) definition of high coverage [38] (200 syringes per PWID per year), with the exception of Seattle (Table 2). Second, we considered scaled-up access to methadone and buprenorphine individually given the different constraints on each modality in the US [39]. We defined the optimistic expansion of MOUD as 40% coverage of treatment with buprenorphine among PWID with an opioid use disorder to reach WHO guidelines on high coverage [38]. Optimistic expansion of MOUD with methadone was derived from the highest annual growth among PWID across the 6 cities [7, 26], thus reaching 40%–55% total MOUD coverage across cities. In addition to the preventive benefit of reducing the number of injections (and therefore shared injections) [37], we incorporated evidence indicating that MOUD decreases the probability of ART discontinuation [40], improves the quality of life [41], and reduces the risk of mortality [42]. Finally, given the uncertainty about PrEP uptake among PWID [43], we assumed no coverage in the status quo and that optimistic expanded access would result in 50% coverage among PWID. The methods and data sources we used to estimate the scale of delivery and the costs of implementing, delivering, and sustaining each intervention were previously described elsewhere [7, 17, 26].

Economic Analysis

We calculated incremental costs (2018 US $) and quality-adjusted life-years (QALYs) for the entire adult population in each city associated with the implementation of evidence-based interventions targeted exclusively to PWID.

Table 2. Description, Effectiveness, and Scale-up Implementation Scenarios for the Evidence-Based HIV Prevention Programs and Care Interventions Included in Analysis

	Supporting Evidence				Scale-up Implementation Scenarios[e]	
Intervention	Source, Evidence Level[a]	Study Design	Study Setting	Description and Effectiveness[b]	Optimistic, %	Ideal, %[c]
HIV prevention programs						
SSP	Aspinall et al 2014 [11], 2a	Meta-analysis	SSP	Clean injection equipment reduces the risk of parenteral HIV transmission by 58%	200 syringes/ PWID/year[f]	90
MOUD with buprenorphine	MacArthur et al 2012 [37], 2a	Meta-analysis	Primary care and OTP	Office-based MOUD reduces the number of shared injections by 54% for PWID with OUD[d]	29[g]	90[h]
MOUD with methadone	MacArthur et al 2012 [37], 2a	Meta-analysis	Primary care and OTP	Opioid treatment program-based MOUD reduces the number of shared injections by 54% for PWID with OUD[d]	Additional scale-up of 17	90[h]
Full-time PrEP	Liu et al 2016 [27], 1b	RCT substudy and cohort study	Primary care	Protective level adherence to PrEP (≥4 doses/week) reduces the risk of HIV infection by 60%[i]	50	90
HIV testing						
EMR testing offer reminder	Felsen et al 2017 [28], 2b	Pre/post	Hospital	HIV testing increases by 178% among PWID visiting the ER	13–35	14–36[d]
Nurse-initiated rapid testing	Anaya et al 2008 [29], 2b	RCT	Primary care	Nurse-initiated screening and rapid testing increases HIV testing by 73% during health care visits	34–52	56–87
MOUD integrated rapid testing	Metsch et al 2012 [30], 1b	RCT	DTP	On-site rapid testing increases HIV testing by 352% among PWID receiving MOUD	22	49
ART engagement						
Case management (ARTAS)	Gardner et al 2005 [31] 1b	RCT	HIV clinics	Contacts with a case manager increases ART initiation by 41% among PLHIV linked to care	61	77
Care coordination	Robertson et al 2018 [32], 2b	Pre/post[j]	HIV clinics	Comprehensive care coordination increases ART retention by 10% among PLHIV	12–25	34–68
Targeted care coordination	Robertson et al 2018 [32], 2b	Pre/post[j]	HIV clinics	Targeted comprehensive care coordination increases ART retention by 32% among PLHIV with CD4 < 200 cells/μL	41–48	57–66
EMR ART engagement reminder	Robbins et al 2012 [33], 1b	RCT	HIV clinics	Interactive EMR alerts reduces ART drop-out by 31% among PLHIV on ART	47–84	60–91[d]
RAPID ART initiation	Pilcher et al 2017 [34], 3b	Cohort study	HIV clinics	Multidisciplinary care and support increases immediate ART initiation by 32% among newly diagnosed PLHIV	38–71	47–90
ART reengagement						
Enhanced personal contact	Gardner et al 2014 [35], 1b	RCT	HIV clinics	Continuous contact increases ART reinitiation by 22% among PLHIV having dropped out of ART	49	62
Relinkage program	Bove et al 2015 [36], 2b	Cohort study	HIV clinics	Outreach using surveillance data increases ART reinitiation by 70% among PLHIV who are out of care	10	22

Abbreviations: ARTAS, Antiretroviral Treatment Access Study; DTP, drug treatment program; EMR, electronic medical records; ER, hospital emergency room; MOUD, medication for OUD; OTP, opiate treatment program; OUD, opioid use disorder; PLHIV, people living with HIV; PrEP, preexposure prophylaxis; Pre/post, Prospective, quasi-experimental pre/post study; PWID, people who inject drugs; RAPID: rapid ART program for individuals with an HIV diagnosis; RCT, randomized control trial; SSP, syringe service program; WHO, World Health Organization.

[a]Levels of evidence adapted from Oxford Centre for Evidence-based Medicine Levels of Evidence: 1a, systematic review of RCTs; 1b, individual high-quality RCT; 2a, systematic review of cohort studies; 2b, individual cohort study or quasi-experimental study; 3a, systematic review of case-control studies; 3b, individual case-control study; 4, case series.

[b]Interventions target the PWID adult population aged 15–64 years including men who have sex with men who inject drugs.

[c]Ideal implementation refers to 90% adoption unless otherwise noted by [d] which refers to 100% adoption of EMR.

[d]MOUD also reduces the risk of mortality, increases quality of life, and decreases the probability of ART discontinuation.

[e]Where applicable, scale-up ranges indicate evidence stratified by sex/gender and/or race/ethnicity and/or city/region.

[f]As recommended by WHO [38], except Seattle (400 syringes/PWID/year) because status quo service levels were already equivalent to this level.

[g]As recommended by WHO [38], 40% coverage among the 72.7% of PWID with an OUD [23] results in 29% coverage among all PWID.

[h]Maximum 90% coverage of both medications combined among the 72.7% of PWID with an OUD [23].

[i]Effectiveness defined as efficacy for 4 doses/week (96%; 95% confidence interval, 90%–99%) × protective level adherence (62.5%; associated with taking ≥ 4 doses/week), further details in Supplementary Materials.

[j]Study with contemporaneous surveillance registry-based comparison group.

The cost-effectiveness analysis conformed to best practice guidelines of the Second Panel on Cost-Effectiveness in Health and Medicine, and we used a health care sector perspective, including government, employer-paid, and out-of-pocket health care expenditures [44]. Interventions were sustained for a period of 10 years to match the goals of the Ending the HIV Epidemic initiative with outcomes evaluated over 20 years to capture long-term individual health benefits and second-order transmission effects (ie, prevented cases beyond those directly reached by the interventions). We adhered to best-practice guidelines for health economic evaluation and both costs and QALYs were reported using a 3% annual discount rate [44]. Model-projected outcomes also included new HIV infections averted and we reported reduction in incidence among PWID over a 10-year period.

In addition, we estimated health production functions, representing combination implementation strategies providing the greatest health benefits for a range of investment levels, incremental to the status quo. We followed methodological conventions [45] to estimate incremental cost-effectiveness ratios (ICERs) as the incremental cost per QALY gained for successive optimal combination implementation strategies along the health production function, compared to the next most costly strategy. We identified the strategy producing the greatest health benefits while still remaining cost-effective (highly cost-effective, ICER ≤ 1 × per capita gross domestic product; cost-effective, ICER > 1 to ≤ 3 × per capita gross domestic product) [44].

Sensitivity Analysis

We performed probabilistic sensitivity analysis (using the 2000 best-fitting calibrated parameter sets for each city) on individual interventions and the strategies producing the greatest health benefits while still remaining cost-effective to evaluate the extent of parameter uncertainty. Furthermore, using the selected combination for each city, we assessed the impact on incidence of an ideal implementation scenario, whereby each intervention reached 90% of its target population (Table 2).

We also conducted a scenario sensitivity analysis examining the impact of the changing opioid epidemic in 2 ways. First, we assumed a 40% increase in the PWID population with an opioid use disorder based on the projections of opioid injection prevalence from Chen et al [46]. Second, we accounted for increased mortality risk from the introduction of fentanyl into the illicit drug supply for PWID who were not receiving MOUD by adjusting mortality estimates for each city using state-level evidence of law enforcement encounters testing positive for fentanyl (full details are presented in the Supplementary Material) [47]. Finally, we considered in a separate scenario sensitivity analysis the impact of free PrEP provision (ie, zero PrEP medication costs) in response to recent announcements to this end [48].

RESULTS

Combination Implementation Strategies

Combination implementation strategies producing the greatest health benefits while remaining cost-effective were composed of between 6 (Atlanta and Seattle) and 12 (Miami) individual interventions (Figure 1 and Figure 2). Among the 5 different combinations (Baltimore and New York City had the same set of interventions), care coordination to improve ART engagement and RAPID (Rapid ART Program for Individuals with an HIV Diagnosis) were not included in any city's optimal strategy, while expanded access to MOUD (with buprenorphine and methadone) and rapid HIV testing integrated with MOUD were included across all cities. Additional scale-up of SSP was only recommended in cities with lower current syringe distribution levels (highly cost-effective in Atlanta and Los Angeles and cost-saving in Miami), and PrEP for PWID was only included in Miami's optimal strategy (full results are in the Supplementary Material).

These strategies were estimated to produce QALY gains of between 5914 (95% credible interval [CI], 3791–8312) in Seattle and 25 615 (CI, 17 729–35 736) in New York City, over the 20-year study horizon. We estimated the selected strategies could reduce HIV incidence by between 8.1% (CI, 2.8%–13.2%) in Seattle to 54.4% (37.6%–73.9%) in Miami, by 2030 (Figure 3). Implementing the selected combination strategies at near-ideal levels would result in large reductions in Atlanta, Los Angeles, and Miami (44.8%, 49.0%, and 75.5%, respectively) and Baltimore, New York City, and Seattle reaching 16.1%, 17.7%, and 19.2% reductions, respectively (Figure 3).

Effects of Individual Interventions

Expanding integrated rapid testing with receipt of MOUD was found to be cost-saving in Baltimore, Los Angeles, and Miami, and highly cost-effective in all other cities (Supplementary Table 1). Both the electronic medical records HIV testing reminder and nurse-initiated rapid HIV testing interventions were cost-saving in Baltimore and Miami, and they were either highly cost-effective or cost-effective in every other city with the exception of Seattle. Interventions designed to improve ART engagement and reengagement provided greater value within each city compared to ART initiation interventions. Among these interventions, ART relinkage provided the most value in Atlanta, Los Angeles, and Miami, targeted ART retention in Baltimore and New York City, and ART reinitiation in Seattle. Finally, the ART initiation intervention was only cost-effective in Miami and New York City.

Sensitivity Analysis

The changing opioid epidemic scenario had a profound impact on the projections and the increased mortality among PWID living with HIV resulted in 2030 status quo incidence that was now projected to be lower by 6.1% (Miami) to 19.6% (Baltimore).

As a result of the lower prevalence of PWID living with HIV, strategies producing the greatest health benefits while remaining cost-effective achieved more modest incidence reductions, ranging from 8.7% in Baltimore to 31.6% in Miami. Strategies for Baltimore, Los Angeles, New York City, and Seattle included the same set of interventions, whereas expansion of SSP in Atlanta and PrEP in Miami were no longer included despite remaining cost-effective when evaluated individually. Finally, the provision of free PrEP resulted in incidence reductions that now ranged from 33.4% in New York City to 52.2% in Los Angeles, and Miami remained unchanged at 54.4% (Figure 3; full results are in the Supplementary Material).

DISCUSSION

Results from this simulation study of 6 US cities with diverse microepidemics suggest that distinct combinations of evidence-based interventions targeted to PWID were required to produce the greatest public health impact in each setting. In no city would the combination that maximized health benefits while remaining cost-effective according to international standards completely eliminate new HIV infections among PWID. Nevertheless, optimistic expansion of targeted, locally oriented strategies could achieve greater decreases in the burden of HIV in cities with relatively higher rates of new infections, with reductions in HIV incidence among PWID by 2030 ranging from 29.4% in Atlanta to 54.4% in Miami. In addition, these combinations could prevent resurgence in cities that have maintained low levels of HIV incidence among PWID and result in incidence below 1 new HIV infection per 1000 PWID in Baltimore, New York City, and Seattle.

Opioid-related harms continue to be a major public health concern in the United States and the immediate and life-long improvements in the quality of life from expanded access to MOUD has the potential to provide considerably more health benefits (measured in QALYs) to PWID than any other intervention. Whereas there are clear similarities between New York City and Baltimore (earlier

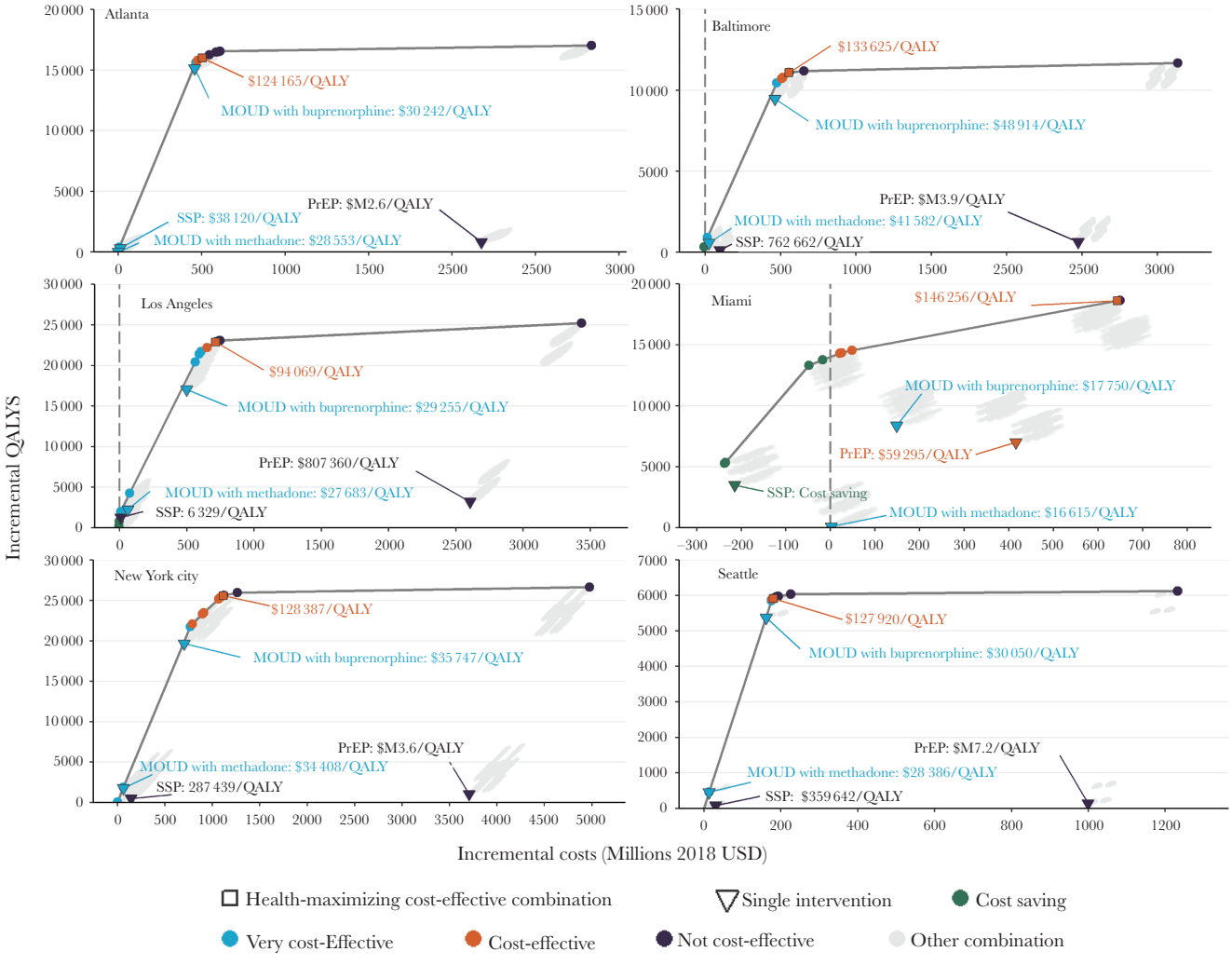

Figure 1. City-level health production functions for evidence-based prevention and care interventions targeted to persons who inject drugs and men who have sex with men who inject drugs. Abbreviations: MOUD, medication for opioid use disorder; PrEP, preexposure prophylaxis; QALY, quality-adjusted life-year; SSP, syringe service program.

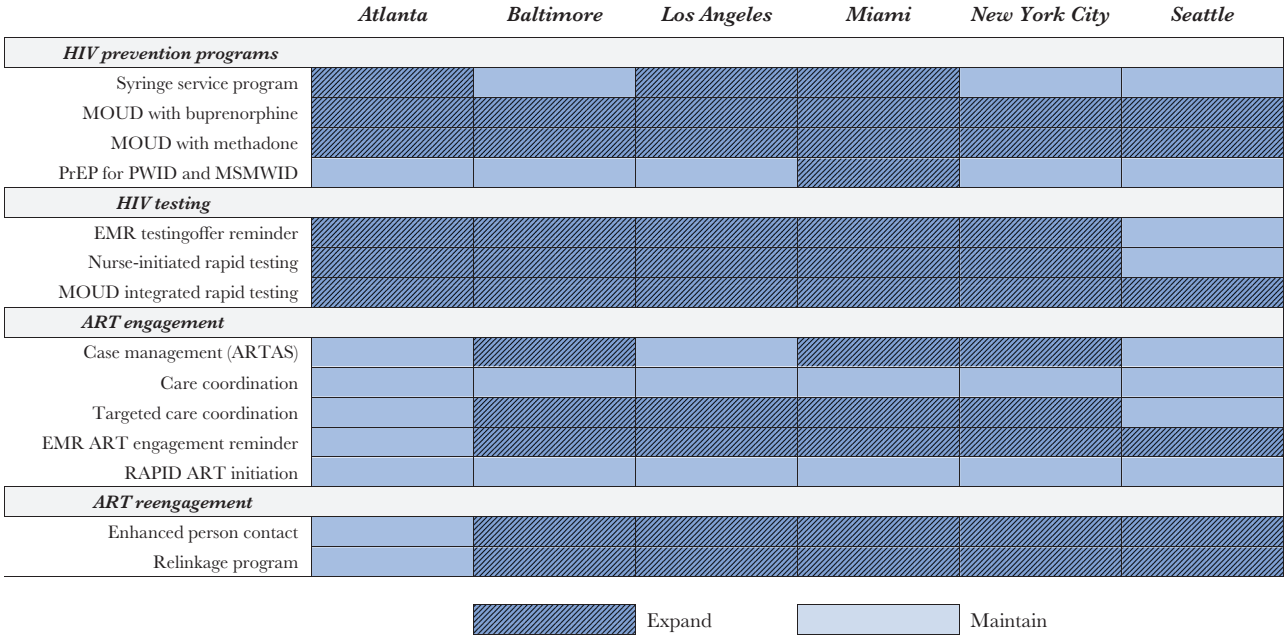

Figure 2. Interventions composing the health-maximizing cost-effective combinations. Abbreviations: ART, antiretroviral therapy; ARTAS, Antiretroviral Treatment Access Study; EMR, electronic medical records; MOUD, medication for opioid use disorder; MSMWID, men who have sex with men who inject drugs; PrEP, preexposure prophylaxis; PWID, persons who inject drugs; RAPID, Rapid ART Program for Individuals with an HIV Diagnosis.

epicenters of the epidemic among PWID driven by opioids) and cities like Miami, Los Angeles, and Seattle (featuring more injection of stimulants) our findings suggested that the substantial value provided by expanded access to MOUD was robust in the context of different settings with respect to injection drug use. With 1 in 4 American with an opioid use disorder receiving any care and less than a third of those in care receiving MOUD (or as low as 8% among PWID living with HIV) [49], access to evidence-based treatment has not kept pace with the increasing problems associated with the opioid epidemic in the United States [50, 51].

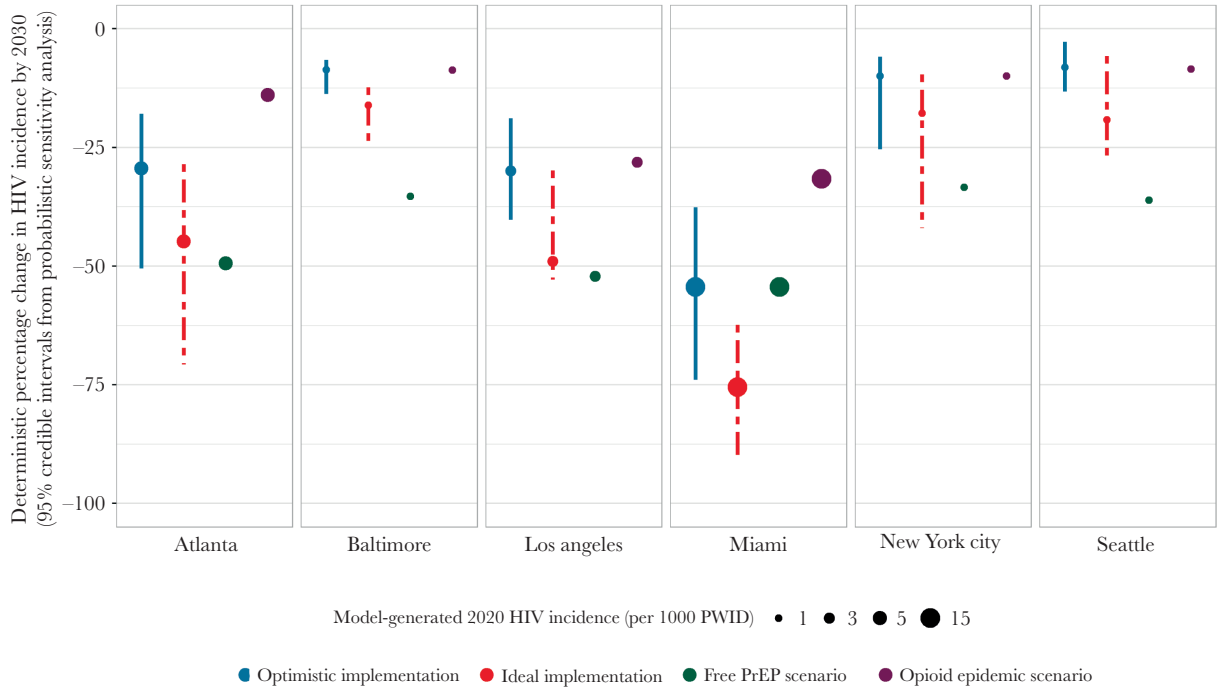

Figure 3. Projected reductions in HIV incidence among persons who inject drugs and men who have sex with men who inject drugs.

There has been a strong consensus among communities of injection drug users (and the scientific community) that the implementation of PrEP for PWID should only be considered together with widespread access to comprehensive, low-threshold HIV prevention and care [33, 52]. In agreement with prior US-based modelling studies [12, 14], our results indicate that the large incremental costs and modest additional health benefits of expanding PrEP among PWID across cities (eg, clusters on the right in Figure 1) did not provide sufficient value at current prices to be included in each distinct strategy. Miami offers an important counterexample. With an HIV epidemic featuring relatively higher transmission rates among MSM, PrEP provided a comparatively greater public health benefit than in other cities. Furthermore, the expansion of SSP services in Miami resulted in important cost-savings that offset a large portion of the PrEP expansion costs in the chosen health-maximizing strategy. Naturally, there is the potential to achieve greater reductions in HIV incidence when PWID have access to PrEP, as highlighted by our free PrEP sensitivity analysis. Potential price reductions from generics or following the recent approval of a new PrEP formulation by the US Food and Drug Administration [53] may offer opportunities to improve the cost-effectiveness of providing PrEP to PWID. Nevertheless, using PrEP remains an individual choice, with adherence greatly determining its efficacy. Access to this biomedical intervention needs to be considered in the context of criminalization of persons who use drugs and structural barriers to HIV prevention and care that could potentially diminish the effectiveness of PrEP among PWID. Additionally, it is important to emphasize in the context of recommendations to offer PrEP to all persons at high risk of HIV acquisition [15] that a large proportion of PWID living with HIV have yet to fully benefit from ART as treatment and prevention [49].

Recent trends in the diagnosis of PWID living with HIV have shown promise [54] yet ART engagement among those diagnosed has stalled [49, 54]. Sustained viral suppression is necessary for reducing HIV transmission risk [55], and as our analysis suggests, additional funding to improve ART engagement among PWID and to reengage those who have discontinued treatment may be well justified across most settings. These findings were consistent with previous studies noting poorer retention [56], lower probability of ART initiation [57], and reinitiation that varied across geographic regions [18] and lower rates of viral suppression for PWID relative to non-PWID [49]. There have been promising examples of reducing disparities in viral suppression rates [58]. Nonetheless, multidimensional public health strategies addressing stigma and broader social determinants of health such as the lack of fulfillment of basic needs (food, housing, and education) will be necessary to achieve and maintain undetectable viral loads among the most vulnerable communities, and ultimately stop the spread of HIV.

We have previously outlined limitations in the structure of the model and its evidence base [7, 17]. Our analysis had other limitations. First, our model was calibrated and validated using historical data and may not capture changing HIV outbreaks among PWID that are most likely indicative of emerging patterns of drug use, vulnerability, and injection behavior [59, 60]. Our sensitivity analysis on the changing opioid epidemic allowed us to assess the robustness of our results when accounting for both changing injection drug use prevalence and associated risks. Second, we did not explicitly account for the variation in injection frequency or sexual risk networks among subgroups using different substances [61]. Nonetheless, we accounted for average behavior among all PWID and conducted probabilistic sensitivity analysis on all relevant parameters, determining the value of different strategies at the population level. Lastly, we only captured HIV prevention benefits from SSP. Incorporating broader health benefits from HCV and overdose prevention would likely result in assessments of greater value even for well-resourced cities.

In conclusion, evidence-based interventions targeted to PWID can deliver considerable value; however, ending the HIV epidemic among PWID will require innovative implementation strategies and supporting programs to reduce social and structural barriers to care.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Author contributions. E. K. and B. N. conceptualized the study and wrote the first draft. E. K. and X. Z. conducted analyses. E. K., X. Z., and B. E. contributed to the evidence synthesis. B. E. contributed to manuscript development. B. N. secured funding for the study. All authors aided in the interpretation

of results, provided critical revisions to the manuscript, and approved the final draft.

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