Ending the HIV epidemic in the USA: an economic modelling study in six cities

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Summary

Background The HIV epidemic in the USA is a collection of diverse local microepidemics. We aimed to identify optimal combination implementation strategies of evidence-based interventions to reach 90% reduction of incidence in 10 years, in six US cities that comprise 24·1% of people living with HIV in the USA.

Methods In this economic modelling study, we used a dynamic HIV transmission model calibrated with the best available evidence on epidemiological and structural conditions for six US cities: Atlanta (GA), Baltimore (MD), Los Angeles (CA), Miami (FL), New York City (NY), and Seattle (WA). We assessed 23 040 combinations of 16 evidence-based interventions (ie, HIV prevention, testing, treatment, engagement, and re-engagement) to identify combination strategies providing the greatest health benefit while remaining cost-effective. Main outcomes included averted HIV infections, quality-adjusted life-years (QALYs), total cost (in 2018 US$), and incremental cost-effectiveness ratio (ICER; from the health-care sector perspective, 3% annual discount rate). Interventions were implemented at previously documented and ideal (90% coverage or adoption) scale-up, and sustained from 2020 to 2030, with outcomes evaluated until 2040.

Findings Optimal combination strategies providing health benefit and cost-effectiveness contained between nine (Seattle) and 13 (Miami) individual interventions. If implemented at previously documented scale-up, these strategies could reduce incidence by between 30·7% (95% credible interval 19·1–43·7; Seattle) and 50·1% (41·5–58·0; New York City) by 2030, at ICERs ranging from cost-saving in Atlanta, Baltimore, and Miami, to $95 416 per QALY in Seattle. Incidence reductions reached between 39·5% (26·3–53·8) in Seattle and 83·6% (70·8–87·0) in Baltimore at ideal implementation. Total costs of implementing strategies across the cities at previously documented scale-up reached $559 million per year in 2024; however, costs were offset by long-term reductions in new infections and delayed disease progression, with Atlanta, Baltimore, and Miami projecting cost savings over the 20 year study period.

Interpretation Evidence-based interventions can deliver substantial public health and economic value; however, complementary strategies to overcome social and structural barriers to HIV care will be required to reach national targets of the ending the HIV epidemic initiative by 2030.

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Introduction

Concerted efforts and substantial investments in HIV prevention and care in the USA have resulted in a 69% reduction in mortality and a 48% reduction in new diagnoses since the mid-1990s.[1,2] Nonetheless, 38 000 new cases were diagnosed in 2017, a reduction of only 7% from 2012. In 2017, adolescent and adult males accounted for 81% of new diagnoses,[2] and 67% of all new diagnoses were attributed to male-to-male sexual contact.[2] Overall, 1·1 million people in the USA are currently living with HIV infection, including an estimated 15% who are unaware of their status.

Ethnic, racial, and sexual minorities have not benefited from advances in treatment and prevention of HIV/AIDS in the USA.[3] Of new infections reported in US men in 2017, 56% were in black and Hispanic men who have sex with men (MSM), a group representing less than 1% of the US population.[3] If current rates of HIV infection persist, 41% of black MSM and 22% of Hispanic MSM in the US will be diagnosed with HIV during their lifetimes.[4] Black and Hispanic women are also disproportionately affected,[3] with lifetime risk of HIV diagnosis nearly 17 times higher in black women and four times higher in Hispanic women than in white women.[4] Furthermore, 2015 was the first time in 20 years that infections attributed to drug injection increased.[5]

Rather than a homogeneous national epidemic, the US HIV epidemic is a collection of diverse local micro-epidemics, concentrated primarily in the southern, so-called hotspot counties[5] and large urban centres with fundamental differences in health system infrastructure, funding, and HIV-related laws and policies between the regions.[6] Health literacy deficits, stigma, and challenges in navigating the complex US health system further

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Research in context

Evidence before this study

We did a search of PubMed for articles published in English from database inception up to June 30, 2019, with the terms ("HIV") AND ("incidence" OR "end HIV epidemic") AND ("USA") AND (("combination") OR ("local*" OR "focus*" OR "target")) AND ("model*" OR "cost-effectiveness"). We identified no papers on a multicity dynamic HIV transmission model applied in the USA. We broadened our search to include non-US-based studies and identified a study modelling the effects of geographically focused HIV interventions compared with national interventions in Kenya. Other studies in the USA had modelled combination strategies for HIV among specific HIV risk groups, or for the general epidemic at a national level; however, none followed the unique approach undertaken in Kenya, which was a defining feature of the current study. A geographically focused approach was found to be more cost-effective in Kenya, and studies in the USA evaluating combination strategies found that selected intervention bundles were cost-effective and could avert more new HIV infections than single interventions. One national-level modelling study in the USA concluded that reaching the new ending the HIV epidemic targets would require resources and implementation of HIV interventions at unprecedented levels.

Added value of this study

We identified combination implementation strategies of evidence-based interventions that provide the greatest value in reaching the new ending the HIV epidemic targets in six US cities. Interventions were implemented at previously documented and ideal levels of implementation or scale-up, and sustained from 2020 to 2030. In no city did we find that targets could be approached without implementation of interventions at scales of delivery not previously recorded. Despite requiring higher amounts of funding than what has been proposed in the ending the HIV epidemic initiative, the strategies we identified would be cost-effective, and cost-saving in some settings.

Implications of all the available evidence

Within our six US cities, implementing combinations of evidence-based interventions can provide good public health and economic value, and can approach the targets of the ending the HIV epidemic initiative in some settings. Meeting national targets would also reduce racial HIV-related disparities and inequities in health-care access. Complementary strategies to overcome social and structural barriers to HIV care will be required to bridge the implementation gap.

undermine epidemic responses.[7,8] These issues have resulted in disparate rates of new HIV diagnoses;[6] for instance, in 2017, Miami had 49 new diagnoses per 100 000 residents annually, representing the highest rate among US cities, while Seattle had ten new diagnoses per 100 000, ranking 75th overall.

On Feb 5, 2019, at the State of the Union Address, the US President Donald Trump announced an intention to end the US HIV epidemic by reducing new infections by 75% within 5 years and by 90% within 10 years. This announcement marked a departure from the 2015 National HIV/AIDS Strategy, which called for 90-90-90 goals (90% of people with HIV diagnosed, 90% of those diagnosed treated with antiretroviral therapy, and 90% of those treated achieving viral suppression) to be reached by 2020. The US Department of Health and Human Services proposed initially to target 48 counties plus Washington, DC, San Juan (Puerto Rico), and seven southern states, which comprise approximately 50% of new diagnoses in the USA.[9] New funding allocations have been proposed alongside parallel cuts to existing social safety net programmes. Affected programmes include those that provide access to affordable medical insurance and reasonably priced drugs, with the cuts threatening to undermine benefits of the 2019 strategy in states with uneven access to health care, as medications are foundational to many combination HIV prevention strategies. Furthermore, as a result of limitations at each stage of implementation, previously documented scale-ups of delivery of evidence-based interventions have been shown to have limited population effects.[10]

For more on the **US ending the HIV epidemic initiative** see https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview

A data-driven public health approach, embracing evidence-based interventions and engaging communities in ways that mitigate stigma and discrimination, has been proposed as a means of reaching the ambitious 2019 targets.[3,5] Focusing resources on those at greatest risk of infection and mortality has long been a central theme in guidance issued by the President's Emergency Fund for AIDS Research, WHO, and UNAIDS, with data-driven programming informed by a so-called know your epidemic assessment framework.[11] Simulation models can quantify the potential public health and economic effects of multiple health interventions over the long term within specific geographical regions, accounting for synergistic effects of different interventions and local context.[12] Model-based cost-effectiveness analyses, guided by national and international practice standards[13,14] and supported with the best available data, can ensure that the ending the HIV epidemic strategy is executed efficiently and on the principle of health equity. This approach can also weigh opportunity costs against competing priorities elsewhere in the health sector.[15]

In this report, we aimed to identify combinations of evidence-based interventions with the highest value in terms of reducing the public health burden of HIV/AIDS in disparate geographical regions. In the context of the ambitious goals of the national strategy to end the HIV epidemic, we focus on six US cities comprising 24·1% of all people living with HIV in the USA.

Methods

Study design

In this economic modelling study, we used a computer simulation model based on our previous synthesis of the best available data on city-level HIV microepidemics[16] and evidence-based interventions to diagnose, treat, and prevent HIV.[10] We simulated HIV microepidemics in Atlanta (GA), Baltimore (MD), Los Angeles (CA), Miami (FL), New York City (NY), and Seattle (WA), capturing current availability of prevention, testing, and treatment services.[17] These cities were selected to show the breadth of differences in local demographics, structural features, and available services to address the HIV/AIDS epidemic in the USA. We assessed alternative strategies by defining a set of optimal strategies that provide the greatest value across a range of investment levels, termed the health production function. The health-maximising strategy that was also cost-effective was determined by calculating the incremental cost-effectiveness ratio (ICER), defined as the additional cost of a specific combination implementation strategy divided by its additional health benefit, as compared with the next most costly strategy in the health production function. The numerator represented the total increment in health-care costs (in 2018 US$) for the adult population (aged 15–64 years) in a given city, and the denominator represented the total gain in quality-adjusted life-years (QALYs) for this group. ICERs were categorised as cost-saving (greater health benefits and lower costs versus comparator), cost-effective (ICER ≤$100 000 per QALY gained), or not cost-effective (ICER >$100 000 per QALY gained).

Model description

We adapted and calibrated our previous dynamic compartmental HIV transmission model[16,18] to replicate city-level HIV microepidemics in each of our US cities (table 1). Administrative regions (counties) were the main unit of analysis because they correspond to both the lowest level of resource allocation decisions and, in many cases, the finest resolution of available input data. Of the cities above, three are contained within a single county each (Los Angeles, Miami, and Seattle), and three span multiple counties (Atlanta, Baltimore, and New York City), with full details on city boundary selection described previously.[16]

For each city, the model tracked individuals susceptible to HIV over the course of infection, diagnosis, and treatment with antiretroviral therapy (ART; accounting for ART dropout). In each city, the adult population was partitioned by biological sex (male or female), HIV risk group (MSM, people who inject drugs, MSM who inject drugs, and heterosexual individuals), race and ethnicity (black or African American, Hispanic or Latino, and non-Hispanic white or other) and sexual risk behaviours (high risk *vs* low risk). The model captured heterogeneity in the risk of HIV transmission, maturation, and mortality, and the disparities in accessing health, prevention, and treatment services, including HIV testing, ART, syringe service programmes, medication for opioid use disorder, and targeted pre-exposure prophylaxis (PrEP) for MSM at high risk of infection.

The model was populated with 1667 parameters, 1517 (91%) of which were city-specific and 150 (9%) of which were common for all cities. We used a mixed-method evidence synthesis strategy to populate model parameters in six categories: (1) initial HIV-negative and HIV-infected populations; (2) parameters used to calculate the probability of HIV transmission; (3) screening, diagnosis, treatment, and HIV disease progression; (4) HIV prevention programmes; (5) the costs of medical care; and (6) health utility weights. We synthesised evidence from 11 primary database analyses, 59 peer-reviewed publications, and 24 public health and surveillance reports to generate the parameters needed to populate the model for each city.[16] Parameters ranked as best-quality to moderate-quality evidence, based on clasifications of the Oxford Centre for Evidence-based Medicine—Levels of Evidence, comprised 58 (39%) of the common parameters, and ranged from 56% (848 parameters in Baltimore) to 60% (909 in New York City) of the city-specific parameters in each city. We calibrated the model to match the the total number of diagnosed cases (11 calibration targets), new diagnoses (3 targets), and deaths (3 targets) across race and ethnicity groups and HIV risk groups (17 calibration targets in total) and validated against external incidence estimates (overall and among MSM) from 2012–15 for each city.[18] The projected model outcomes showed a good fit to calibration targets according to an overall goodness of fit metric (defined as the weighted sum of the goodness of fit of the individual calibration targets), and model-derived incidence estimates for the years 2012–2015 corresponded with externally estimated uncertainty ranges, showing good external validity.[18] Our calibration and validation process[18] has been documented in detail previously. With our model we projected HIV microepidemic trajectories, accounting for official population growth estimates and demographic shifts for each city up to 2040 (table 1), to serve as the so-called status quo scenario for comparison.[17]

For the **Oxford Centre for Evidence-based Medicine—Levels of Evidence** see https://www.cebm.net/2009/06/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/

Evidence-based interventions

Into our model, we incorporated 16 evidence-based interventions with established efficacy or effectiveness data and promising scalability according to three pillars of the ending the HIV epidemic strategy: protect (via HIV prevention programmes such as syringe service programmes, medication for opioid use disorder, and targeted PrEP); diagnose (via HIV testing); and treat (via ART initiation and retention and ART re-initiation; table 2). These interventions were selected from the US Centers for Disease Control and Prevention compendium of evidence-based interventions and best practices for HIV prevention and from the published literature,[10]

For the **US Centers for Disease Control and Prevention compendium** see https://www.cdc.gov/hiv/research/interventionresearch/compendium/index.html

	Atlanta, GA	Baltimore, MD	Los Angeles, CA	Miami, FL	New York City, NY	Seattle, WA
Total adult population in 2016*	3 812 143	1 874 601	6 964 983	1 821 311	5 865 683	1 503 497
Projected adult population in 2040 (% growth)	5 224 254 (37%)	1 859 757 (–1%)	6 853 768 (–2%)	2 113 048 (16%)	6 046 493 (3%)	1 733 640 (15%)
Adult population in 2016 by race and ethnicity (% of total)*						
Black or African American	1 336 469 (35%)	553 665 (30%)	568 815 (8%)	296 354 (16%)	1 304 687 (22%)	95 550 (6%)
Hispanic or Latino	391 265 (10%)	102 495 (5%)	3 385 948 (49%)	1 246 583 (68%)	1 703 286 (29%)	137 818 (9%)
Non-Hispanic white or other	2 084 409 (55%)	1 218 441 (65%)	3 010 220 (43%)	278 374 (15%)	2 857 710 (49%)	1 270 129 (84%)
Projected adult population in 2040 by race and ethnicity (% of total)						
Black or African American	1 800 171 (34%)	650 255 (35%)	460 413 (7%)	295 396 (14%)	1 312 629 (22%)	131 365 (8%)
Hispanic or Latino	1 037 139 (20%)	154 281 (8%)	3 609 531 (53%)	1 600 165 (76%)	1 995 693 (33%)	274 266 (16%)
Non-Hispanic white or other	2 386 944 (46%)	1 055 221 (57%)	2 783 824 (41%)	217 487 (10%)	2 738 171 (45%)	1 328 009 (77%)
People living with HIV†						
Prevalence in 2016 (n per 100 000)	31 961 (670)	16 931 (718)	48 100 (564)	26 128 (1120)	117 260 (959)	7768 (312)
New diagnoses in 2017 (n per 100 000)	1618 (33)	441 (19)	1720 (20)	1150 (49)	2608 (21)	248 (10)
National rank‡	2	25	27§	1	21§	75§

Percentages do not always equal 100% due to rounding. Metropolitan statistical areas might differ from our city boundaries. Counties containing the city boundaries of Atlanta, Baltimore, Los Angeles, and Miami match those included in the definition of Ryan White Eligible Metropolitan Area or Transitional Grant Area; the New York City and Seattle boundaries were restricted to a subset of counties within the Ryan White definitions. Counties containing each city are listed in parentheses: Atlanta (Barrow, Bartow, Carroll, Cherokee, Clayton, Cobb, Coweta, DeKalb, Douglas, Fayette, Forsyth, Fulton, Gwinnett, Henry, Newton, Paulding, Pickens, Rockdale, Spalding, and Walton); Baltimore (Anne Arundel, Baltimore City, Baltimore County, Carroll, Harford, Howard, and Queen Anne's); Los Angeles (Los Angeles County); Miami (Miami-Dade County); New York City (New York [Manhattan borough], Kings [Brooklyn borough], Queens [Queens borough], Bronx [Bronx borough], and Richmond [Staten Island borough]); and Seattle (King County). Excluded counties for New York City compared with the Ryan White Eligible Metropolitan Area definition were Westchester, Rockland, and Putnam, and excluded counties for Seattle compared with the Ryan White Transitional Grant Area definition were Snohomish and Island. *Data sourced from the United States Census Bureau. †Data sourced from the HIV Surveillance Supplemental Report (2017) of the Centers for Disease Control and Prevention.[2] ‡Ranking based on rate of new diagnoses. §Ranking was for the metropolitan statistical area and might not reflect city boundaries as defined.

***Table 1:* Demographic and HIV-related characteristics of the adult populations (15–64 years) in the focal US cities**

For the **United States Census 2010–19 data** see https://www.census.gov/data/tables/time-series/demo/popest/2010s-national-detail.html

For more on the **RE-AIM framework** see http://www.re-aim.org/

with evidence for efficacy and scale-up based on the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework for health interventions.

Initially, we estimated ranges on the costs and level of scale-up according to publicly available evidence,[10] which constituted the previously documented level of implementation. We have documented our methods for estimating the effectiveness, scale, and costs of each individual intervention in a separate manuscript.[10] Scale-up from existing service levels was implemented proportionally across risk and ethnic groups, implying an increased scale-up of delivery after implementation for groups receiving high service levels at baseline. Based on real-world evidence, the scenarios were designed to represent an estimate of the expected level of scale-up that can be achieved within current social and structural constraints on access to care.

We assessed all combinations of the 16 interventions (excluding combinations that would not practically be implemented jointly, such as two HIV testing interventions delivered in primary care) for a total of 23 040 unique combinations including the status quo scenario. We then reassessed these combinations in an ideal implementation scenario in which we assumed each intervention would achieve 90% coverage (protect programmes) or 90% adoption (for diagnose and treat interventions) within the target population of each intervention.

Cost-effectiveness analysis

We estimated health production functions that represented combination implementation strategies providing the greatest health benefits for a range of investment levels incremental to the status quo at both previously documented and ideal scale-up. Combination strategies were sustained for a period of 10 years (2020–30) to match the goals of the ending the HIV epidemic initiative[5] and with outcomes evaluated over 20 years (2020–40) to capture long-term individual health benefits and second-order transmission effects (ie, prevented cases beyond those directly reached by the interventions).

Model-projected outcomes included QALYs, total costs (in 2018 US$), and new HIV infections. Costs were disaggregated by type, as those for ART, PrEP, and medication for opioid use disorder, other medical costs, and other intervention costs. The cost-effectiveness analysis conformed to best practice guidelines of the Second Panel on Cost-Effectiveness in Health and Medicine, and was done from the health-care sector perspective, including government, employer-paid, and out-of-pocket health-care expenditures.[14] Both costs and QALYs were reported with a 3% annual discount rate.[13] We followed conventional incremental cost-effectiveness analysis rules[22] to estimate ICERs as the incremental cost per QALY gained for successive optimal combination implementation strategies along the health

	Effectiveness and target population*	Effectiveness evidence level†	Coverage: previous implementation	Coverage: ideal implementation‡
Protect: HIV prevention programmes				
Syringe service programme	Clean injection equipment reduces parenteral HIV transmission by 58% among people who inject drugs	2a	Additional scale-up from status quo of 11%	90%
MOUD with buprenorphine	Office-based MOUD for people who inject drugs reduces the number of injections per individual by 54%	2a	Additional scale-up from status quo of 14%	90%
MOUD with methadone	MOUD within an opioid treatment programme for people who inject drugs reduces the number of injections per individual by 54%	2a	Additional scale-up from status quo of 12%	90%
Targeted PrEP for high-risk MSM	PrEP reduces the risk of HIV infection by 60%§ among high-risk MSM and MSM who inject drugs¶	1b	Additional scale-up from status quo of 68%	90%
Diagnose: HIV testing||				
Opt-out testing in the emergency room	Routine HIV testing increases by 28% among individuals visiting the emergency room	1b	3–6%**	10–26%**
Opt-out testing in primary care	Routine HIV testing increases by 28% during primary care visits	1b	25–40%**	53–85%
Electronic medical records testing offer reminder	HIV testing increases by 178% among individuals visiting the emergency room	2b	11–29%**	10–26%**
Nurse-initiated rapid testing	HIV testing increases by 73% during health-care visits††	2b	25–40%**	53–85%**
MOUD-integrated rapid testing	On-site HIV testing increases by 352% among people who inject drugs receiving MOUD	1b	17%	49%
Treat: ART engagement and re-engagement||				
Case management (ARTAS)	ART initiation increases by 41% among people living with HIV linked to care	1b	57%	77%
Care coordination	ART retention increases by 10% among people living with HIV	2b	10–20%‡‡	34–68%‡‡
Targeted care coordination	ART retention increases by 32% among people living with HIV with CD4 cell count of <200 cells per μL	2b	30–46%§§	41–63%§§
Electronic medical records ART engagement reminder	ART dropout is reduced by 31% among people living with HIV on ART	1b	42–78%‡‡	54–82%‡‡
Initiation of Rapid ART Program for Individuals with an HIV Diagnosis	Immediate ART initiation increases by 32% among newly diagnosed people living with HIV	3b	30–61%§§	41–84%§§
Enhanced personal contact with patients	ART re-initiation increases by 22% among people living with HIV who have discontinued ART	1b	45%	62%
Relinkage with care programme	ART re-initiation increases by 70% among people living with HIV who are out of care	2b	8%	22%

All data sources and calculations have been reported previously.[10] MOUD=medication for opioid use disorder. PrEP=pre-exposure prophylaxis. MSM=men who have sex with men. ART=antiretroviral therapy. ARTAS=Anti-Retroviral Treatment and Access to Services. *Interventions target the general adult population (15–64 years) unless noted otherwise. †Adapted from the Oxford Centre for Evidence-based Medicine—Levels of Evidence: 1a, systematic review of randomised controlled trials; 1b, individual high-quality RCT; 2a, systematic review of cohort studies; 2b, individual cohort study or quasiexperimental study; 3a, systematic review of case-control studies; 3b, individual case-control study; 4, case series; 5, expert opinion. ‡Ideal implementation defined as 90% adoption. §Effectiveness calculated as efficacy for four doses per week (96% [95% CI 90–99])[19] multiplied by protective-level adherence (≥4 doses per week; 63%).[20] ¶Assuming 25% of MSM are at high risk of infection and indicated for PrEP in accordance with the Centers for Disease Control and Prevention guidelines.[21] ||Coverage defined as the product of reach and adoption. **Scale ranges indicate evidence stratified by sex or gender, race or ethnicity, and region. ††With either a physician or health-care professional. ‡‡Scale ranges indicate coverage levels across cities. §§Scale ranges indicate evidence stratified by sex or gender, HIV risk group, and region.

Table 2: **Selected evidence-based interventions, their effectiveness, and previously documented scale-up of delivery based on the Reach, Effectiveness, Adoption, Implementation, and Maintenance framework**

production function, compared with the next most costly strategy. We identified the strategy producing the greatest health benefits while remaining cost-effective. Although no explicit threshold exists in the USA, we defined cost-effective interventions as those with an ICER below $100 000 per QALY, consistent with efforts in 2016 to approximate the threshold according to the opportunity costs of displacing existing services.[23]

We did probabilistic sensitivity analysis on optimal strategies and other strategies producing the most proximal value to quantify decision uncertainty in the recommended strategy (appendix p 3). We also did deterministic sensitivity analyses (appendix pp 3–4). In one scenario we considered the potential effects of the donation of PrEP medications to the USA from Gilead, first reported in 2019,[24] by setting medication costs to zero

See Online for appendix

but maintaining associated implementation and monitoring costs across our focal cities. In another scenario, we examined changes in the epidemiology of injection drug use, accounting for increased prevalence from the escalation of opioid prescribing, and increased mortality risk resulting from the influx of fentanyl in the illicit drug supply (appendix pp 3–4). We projected the effect of these changes by adjusting model parameters to increase entry into injection drug use over time, and increase mortality for people who inject drugs not receiving medication for opioid use disorder (appendix pp 3–4, 17)

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Results from the first step of our analysis, which was to calculate city-level health production functions at previously documented scale-up, showed production functions with the expected form (figure 1A). For each city, substantial gains in health were coupled with small increments in cost at low overall total costs, corresponding to steep rises at the start of the curve. The production functions then showed diminishing returns, whereby greater health effects were possible, but at much greater cost.

When assessed at previously documented scale-up, strategies producing the greatest health benefits while remaining cost-effective included between nine (Seattle) and 13 (Miami) individual interventions (figure 1B). Opt-out testing in emergency departments and primary care settings, and non-targeted care coordination to improve ART retention were not included in the optimal strategy for any city, whereas expanded access to medication for opioid use disorder (with buprenorphine and methadone), offer reminders for testing of electronic medical records, nurse-initiated rapid HIV testing, medication for opioid use disorder-integrated rapid testing, and six ART engagement or re-engagement interventions (except care coordination, which would conflict with targeted care coordination) were included across all cities. Additional scale-up of syringe service programmes was only recommended in cities with insufficient syringe distribution (Atlanta, Los Angeles, and Miami), similar to targeted PrEP for high-risk MSM, which was included only in the optimal strategies for Atlanta, Baltimore, Los Angeles, and Miami.

At previously documented scale-up, these optimal combination strategies were estimated to produce QALY gains of between 2046 (95% credible interval [CrI] 1496–2656) in Seattle and 23 591 (17 930–31 118) in Los Angeles, over the 20 year time horizon. ICERs ranged from cost-saving in Atlanta, Baltimore, and Miami, to $95 416 per QALY in Seattle (figure 1A). Furthermore, at previously documented scale-up, we estimated the selected combination strategies could reduce HIV incidence by between 30·7% (19·1–43·7; Seattle) and 50·1% (41·5–58·0; New York City) by 2030 (figure 2), with a weighted average of 37·9% (95% CrI 27·5–46·0) across cities.

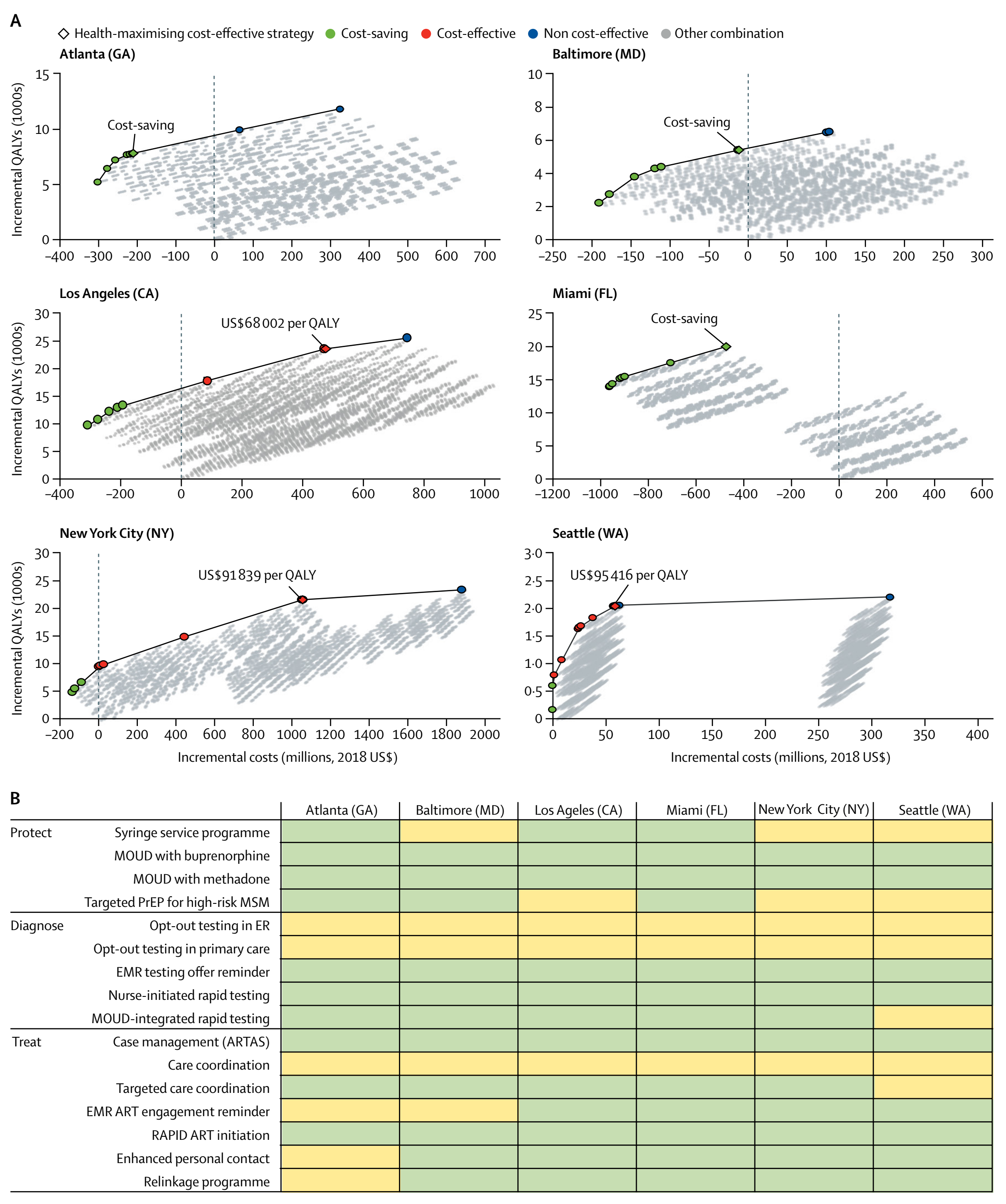
The costliest combination strategy in the health production function was not optimal according to our cost-effectiveness decision rules for any city (figure 1 and appendix pp 5–16). Furthermore, only in Seattle did the absolute costliest strategy produce greater health benefits than the optimal strategy. In that case, health gains were minimal (168 additional QALYs over 2020–40, 8·2% greater than the optimal strategy) and came at high incremental cost ($260 million; appendix p 15). In Miami, the costliest combination strategy was estimated to produce just 30·1% of the health benefits (13 955 less QALYs) estimated for the optimal strategy, at an incremental cost of $0·99 billion (figure 1).

Implementing the optimal combination strategies at previously documented scale-up would entail savings at 2018 value of $474 million (95% CrI 214–895) in Miami, to incremental expenditures of $1·06 billion (0·56–1·51) in New York City over the 20 year time horizon. These expenditures would peak in 2023–25, with a peak annual overall annual expenditure of $559 million in 2024 (comprising an additional $15 million in Seattle, to $179 million in New York City; figure 3A). Overall costs over the 10 year implementation period would total $3·51 billion at 2018 value, with 63% of these costs attributable to expanding access to ART medications (figure 3B).

Implementing the combination strategies at ideal implementation levels would result in a weighted average incidence reduction of 63·5% across cities. Atlanta, Baltimore, and Miami would approach national incidence reduction targets: 74·4% (95% CrI 67·0–80·7), 83·6% (70·8–87·0), and 78·3% (51·5%-86·9%), respectively), whereas Los Angeles, New York City, and Seattle would reach reductions of 41·5% (30·5–56·1), 58·1% (48·1–66·9), and 39·5% (26·3–53·8).

The results of probabilistic sensitivity analyses showed that the selected strategies had a high probability of providing the greatest health gains, compared with competing strategies providing the next closest value, with probabilities ranging from 35·7% (Seattle) to 94·9% (Baltimore; appendix pp 19–20).

When incorporating potential changes in injection drug use initiation and mortality rates to capture the opioid syndemic, we found the optimal set of interventions maintained the same composition in each city, but were estimated to increase QALY gains, which were between 2267 in Seattle and 24 199 in Los Angeles. The strategies also elicited savings of $475 million in Miami, to incremental expenditures of $1·08 billion in New York City, over the 20 year time horizon (appendix pp 24–25). Alternatively, if PrEP medication costs were



		Atlanta (GA)	Baltimore (MD)	Los Ageles (CA)	Miami (FL)	New York City (NY)	Seattle (WA)
Protect	Syringe service programme	🟩	🟨	🟩	🟩	🟨	🟨
	MOUD with buprenorphine	🟩	🟩	🟩	🟩	🟩	🟩
	MOUD with methadone	🟩	🟩	🟩	🟩	🟩	🟩
	Targeted PrEP for high-risk MSM	🟩	🟩	🟨	🟩	🟨	🟨
Diagnose	Opt-out testing in ER	🟨	🟨	🟨	🟨	🟨	🟨
	Opt-out testing in primary care	🟨	🟨	🟨	🟨	🟨	🟨
	EMR testing offer reminder	🟩	🟩	🟩	🟩	🟩	🟩
	Nurse-initiated rapid testing	🟩	🟩	🟩	🟩	🟩	🟩
	MOUD-integrated rapid testing	🟩	🟩	🟩	🟩	🟩	🟨
Treat	Case management (ARTAS)	🟩	🟩	🟩	🟩	🟩	🟩
	Care coordination	🟨	🟨	🟨	🟨	🟨	🟨
	Targeted care coordination	🟩	🟩	🟩	🟩	🟩	🟨
	EMR ART engagement reminder	🟨	🟨	🟩	🟩	🟩	🟩
	RAPID ART initiation	🟩	🟩	🟩	🟩	🟩	🟩
	Enhanced personal contact	🟨	🟩	🟩	🟩	🟩	🟩
	Relinkage programme	🟨	🟩	🟩	🟩	🟩	🟩

***Figure 1:* City-level health production functions and composition of the optimal combination implementation strategies**

(A) Production functions comprise the optimal combinations of interventions for different investment levels. All costs and benefits were in 2018 US$ value and accrued over a 20 year time horizon, with interventions implemented for a 10 year period. Health production functions were created by plotting the cost and effects of all combinations of interventions, with each curve showing the maximum possible health benefits (number of QALYs gained, 2020–40) at a given cost, for each city. The incremental cost-effectiveness of each strategy along the curve was compared with the next most costly strategy on the health production function. The appendix (p 2) provides full details. (B) Optimal combination implementation strategies represent interventions delivered at previously documented scale-up. Shading indicates whether an intervention was selected for a given city: green indicates an intervention that should be implemented or scaled up; yellow indicates an intervention that should not be implemented or increased from existing service levels. QALY=quality-adjusted life year. MOUD=medication for opioid use disorder. PrEP=pre-exposure prophylaxis. MSM=men who have sex with men. ER=emergency room. EMR=electronic medical records. ARTAS=Anti-Retroviral Treatment and Access to Services. ART=antiretroviral therapy. RAPID=Rapid ART Program for Individuals with an HIV Diagnosis.

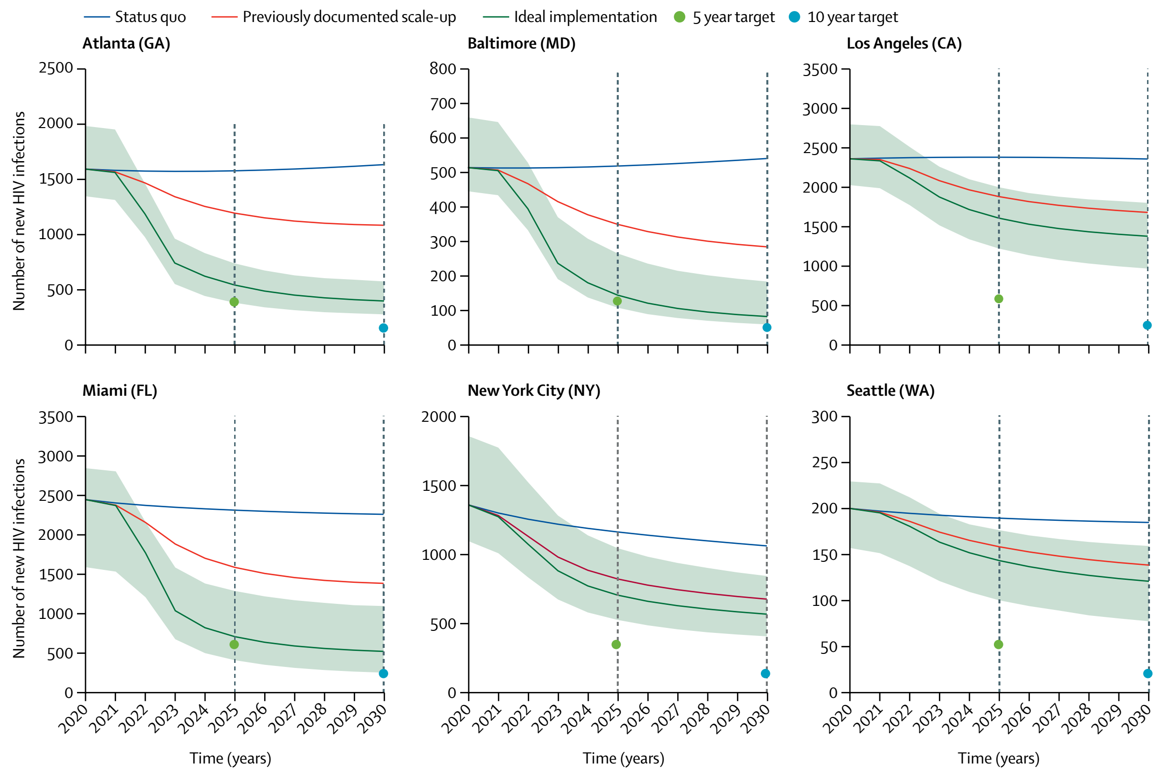


Figure 2: Projected reductions in HIV incidence

The targets at 5 years and 10 years correspond with 75% and 90% reductions in the number of new HIV infections in each city in 2025 and 2030, compared with 2020. The projections for 2020–30 were constructed by holding all health services at the 2015 levels except for pre-exposure prophylaxis, which was held at 2017 levels to account for rapid increase in use over this extended period,[17] while accounting for externally reported population growth and demographic shifts in each city. Further details regarding the construction of the status quo scenarios can be found in a previous study.[25] The shaded band surrounding the ideal implementation estimates represents the 95% credible interval for the optimal combination scenario, derived from probabilistic sensitivity analysis. Other credible intervals have been suppressed for clarity (reported previously for status quo estimates[17] and provided in the appendix [p 19] for previously documented scale-up estimates).

eliminated, PrEP would be included in the optimal set of interventions for all cities, with QALY gains of 1993 in Seattle and 23 442 in New York City, with incremental costs of $15 million and $869 million, where additional PrEP scale-up was not recommended at baseline PrEP costs (appendix pp 21–22). With free PrEP, incidence would be reduced further by the resulting optimal strategies, reaching a 69·1% reduction by 2030 in New York City and a 49·1% reduction in Seattle at ideal levels of implementation (appendix p 23).

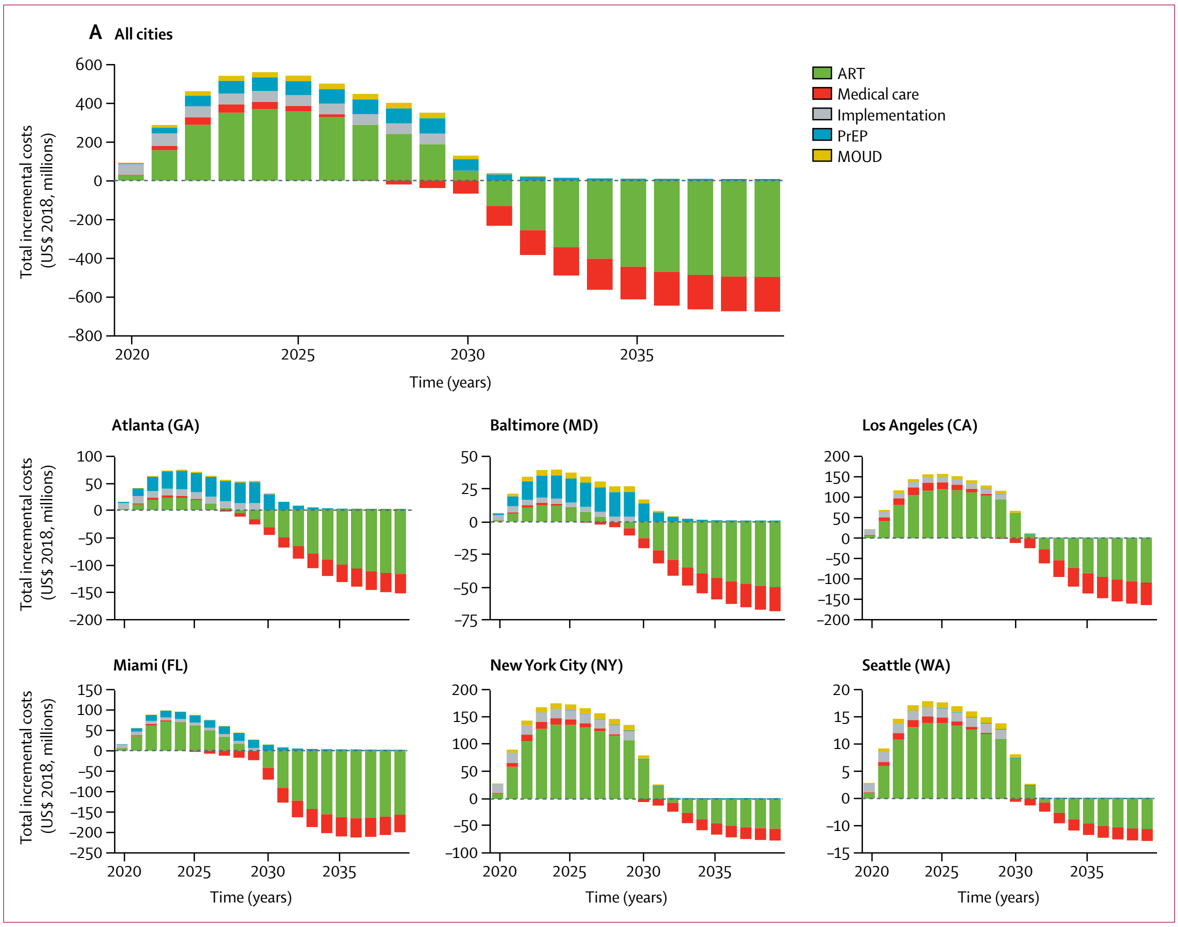
Discussion

In this simulation study of six US cities with substantial HIV disease burdens, each city required distinct combination implementation strategies to address their heterogeneous microepidemics. In all cities, the targets for ending the HIV epidemic were only approached by implementing interventions at scales of delivewry that have not previously been recorded. Nonetheless, we found city-specific combination strategies implemented at previously documented scale-up could reduce incidence by between 30·7–50·1% (with a weighted average of 37·9% across cities), at an overall estimated cost of $3·51 billion by 2030. This investment would be front-loaded, peaking at an annual expenditure of $559 million in 2024, equating to 2·7% of all federal domestic expenditures on the care and prevention of HIV/AIDS in 2018,[26] with the timing of positive incremental costs varying by city and cost component. Our conservative annual incremental spending projections for the focal cities at previously documented implementation would thus require 1·9 times the proposed allotment of the US national budget ($291 million in fiscal year 2020) to the ending the HIV epidemic initiative, not accounting for potential budget cuts to existing services, which could make this discrepancy considerably larger. These investments would nonetheless provide long-term value in each setting, with upfront investments offset by downstream reductions in health-care costs as a result of averted infections and delayed disease progression. At previously documented scale-up, these health-care gains outweighed the costs of implementing and delivering health services in some settings, resulting in net cost savings in Atlanta, Baltimore and, most notably, Miami, where the highest rate of new HIV diagnoses in the USA was reported in 2017.[25]

The combination implementation strategies we assessed and recommended should not be considered exhaustive. The ending the HIV epidemic plan explicitly defines identification and rapid responses to clusters and outbreaks of new HIV infections as one of the four pillars of HIV prevention, and both HIV partner services and the testing of high-risk populations are long-standing core components of HIV prevention that could be expanded in some areas. If sufficient scale can be reached, partner services, in particular, might be effective.[27,28] Other interventions with a more limited evidence base include testing in non-health-care settings,[29] particularly self-testing;[30,31] PrEP for people who inject drugs[32] and heterosexuals at high risk of infection;[33] testing in correctional settings[34] and transitional care support,[35] linkage to care programmes,[36] and low-barrier care delivery;[37] and e-health solutions to improve ART persistence.[38,39] Furthermore, we focused on evidence-based interventions, while remaining agnostic about the capacity or specific circumstances of public health departments. As new evidence on demographics, service delivery, and intervention effectiveness and scale of delivery emerges, the current modelling platform could assess the incremental value and fit of innovative interventions within a combination implementation strategy to maximise health.

In this study, we only considered costs of delivering interventions that directly affect HIV-related outcomes. People who are most likely to be living with or acquire HIV are frequently living in poverty, without stable housing or reliable health insurance, hindering access to care.[3] The limited scale-up of delivery for interventions incorporated in this study[10] reflects these realities. To bridge the implementation gap, interventions will need to be augmented with efforts to reduce stigma (particularly for syringe service programmes given the potential for HIV outbreaks among people who inject drugs),[40,41] improve health literacy, and address capacity constraints in health-care delivery and other social and structural barriers to health-care access.

To combat stigma, the U=U (undetectable equals untransmittable) concept, which acknowledges that people living with HIV who are treated effectively cannot transmit HIV to their partners, will need to be embraced in health-care settings and by the most affected communities.[42] A systematic review of health literacy



(Figure 3 continues on next page)

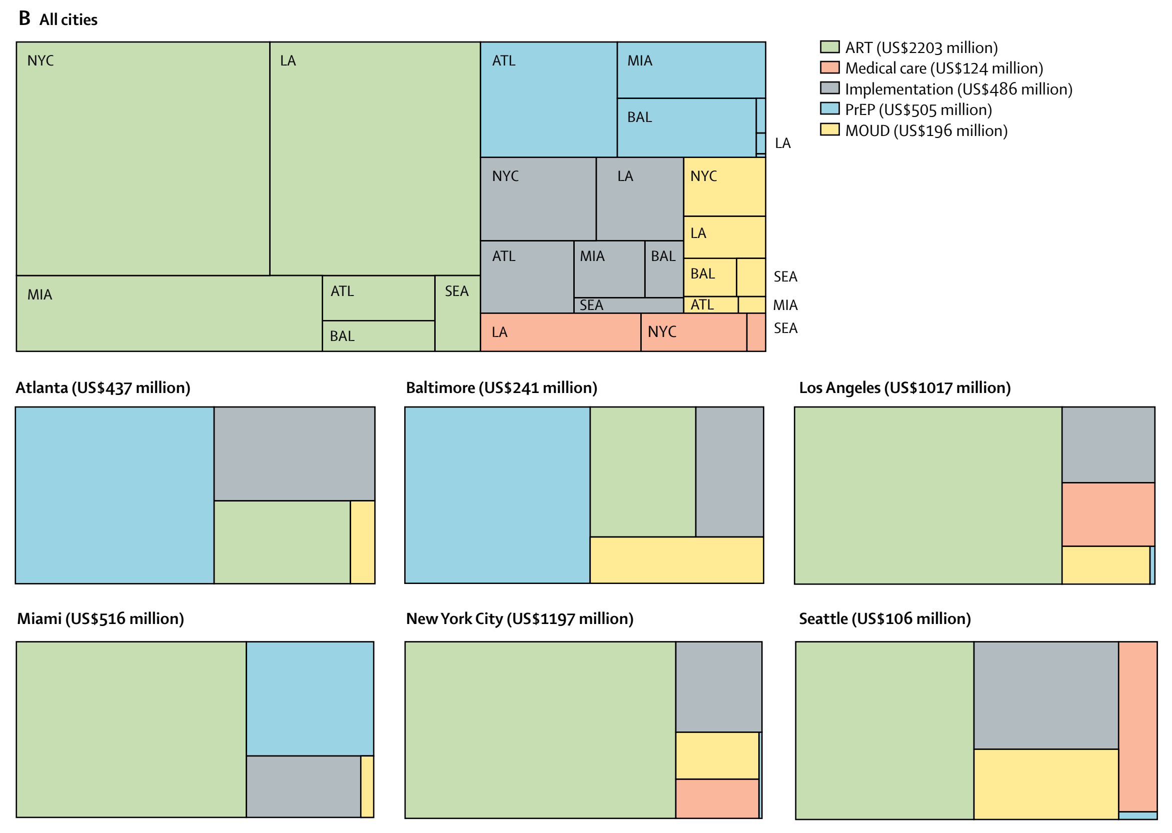


Figure 3: **Incremental costs versus status quo of implementing optimal combination implementation strategies at previously documented scale-up**
Annual incremental costs between 2020–40 (A) and total incremental costs over the 10 year sustainment period (B). Costs are shown incrementally for each year, relative to projected status quo spending in a given year. Over 20 years, the effect on medical care costs of the optimal combination implementation strategies in Atlanta, Baltimore, and Miami was cost-saving and offset medical care costs in other cities. Total discounted costs are presented at 2018 value with a 3% annual discount rate. ART=Antiretroviral therapy. PrEP=pre-exposure prophylaxis. MOUD=medication for opioid use disorder.

interventions suggested that future interventions should evaluate approaches to increase motivation, deliver information in formats other than writing, and utilise patient advocates.[43] Peer navigation reduces stigma and increases access to services in Africa,[3] and is acceptable to HIV-negative MSM for establishing linkage to PrEP.[44,45] Ending the HIV epidemic in southern US cities will require substantial efforts to overcome constraints in health-care access, including lower ratios of primary care providers to populations[46] and higher proportions of people living in poverty than in other US regions.

For **AIDSVu mapping of HIV in the southern USA** see https://aidsvu.org/local-data/united-states/south/

More than half of Americans diagnosed with HIV (>500 000) receive services through the Ryan White HIV/AIDS Program, which reports achieving viral suppression in 85·9% of its clients with ART, exceeding the national average of 59·8%. Notably, the Ryan White HIV/AIDS Program has substantially increased the rate of viral suppression among key populations, including women, black or African American individuals, and people with unstable housing, by funding grants for supportive services targeted to the needs of local populations of patients, and by developing care provider networks to further enhance quality of care.[47] These successes, and the best practices that produced them, will need to be expanded to approach the new national targets. Removing social safety programmes will undermine the strategy of the US Government, and any policy that substantially increases the number of uninsured people would lead to increased difficulty in accessing care and make achieving zero new cases nearly impossible.[48]

The ending the HIV epidemic initiative also recognises the need for a dedicated HIV workforce, or reallocation of existing human resources to ensure implementation of the plans to end the HIV epidemic. Our recommended combination implementation strategies would require substantial staffing to ensure adequate implementation, particularly for the labour-intensive interventions such as case management for ART initiation and retention.[49,50] As such, our cost estimates should be considered conservative, assuming both constant returns to scale and constant effort levels to reach and retain progressively more marginalised and hard-to-reach populations. These prerequisites further emphasise the need for scarce human and financial resources to be delivered to the right places and the right people at the right time.[51]

To reach national targets would be a staggering victory over racial HIV-related disparities and inequities in health-care access in the USA. In particular, these goals are simply not attainable without large reductions in new infections among black and Hispanic MSM. At our ideal implementation, incidence in 2030 in Miami among black MSM would be reduced by 78·8% and among Hispanic MSM by 84·7% (data not shown), nearly eliminating disparities relative to white MSM. A previous meta-analysis showed that HIV-related disparities in US black MSM, relative to MSM of other ethnicities, reflect disparities in HIV clinical care access and use, and structural (eg, unemployment and incarceration) and sexual partner characteristics, rather than sexual or substance use risk behaviours.[52] Structural factors affecting availability and choice of sexual partners (eg, low income, unemployment, incarceration, and poor education) are also associated with isolation in neighbourhoods with high HIV prevalence and community viral load.[52] Importantly, we imposed proportional scale-up of interventions across ethnic groups. An intervention approach focused on black and Hispanic populations could provide even greater value than our proposed combination strategies, as shown by modelling studies considering past national targets.[53]

We previously outlined limitations in the structure of the model,[18] the evidence base on which it was built,[16] and uncertainty in the previously documented scale-up of delivery and the attributable costs of implementation, delivery, and sustainment for each intervention.[10] We note that the status quo scenario should be considered a reflection of the expected trajectory of the HIV epidemic in each city, conditional on data available up to 2015. As we were unable to capture more recent advances in service delivery, we felt our status quo scenario represented the most objective course of action and the most relevant comparator for the interventions considered. The model can be recalibrated as new evidence emerges and otherwise tailored to local capacity constraints. Otherwise, we assumed PrEP could be perfectly targeted to individuals at high risk of infection, potentially making our results more favourable compared with routinely implemented PrEP. We also used a 20 year time horizon for our analyses; longer time horizons could have favoured strategies averting more HIV-related deaths, although costs and health effects in future years would be discounted. To this end, a value of information analysis, focusing on the uncertainty surrounding recommended strategies, can identify the highest-valued targets for increased data collection.[15] Furthermore, precise targeting of interventions, improved retention and adherence, and reduced medication costs, could substantially increase the cost-effectiveness of these interventions. In addition to high-quality surveillance data, improved data collection is required to evaluate existing interventions, and identify promising but less-studied interventions than those addressed in our scenarios.[54] Our modelling platform is generalisable and updatable as new evidence is generated over the spatiotemporal course of the epidemic, and on emerging interventions. Furthermore, cost-effectiveness is only one consideration in developing disease control priorities among many, such as equity, ethics, and political factors, which might be weighted differently depending on circumstances.

Our projections suggest that implementing combinations of evidence-based interventions can provide public health and economic value and approach national incidence reduction targets in some settings; however, complementary strategies to overcome social and structural barriers to HIV care will be required for these strategies to bridge the implementation gap.

Contributors

BN conceptualised the study and wrote the first draft of the Article. EK and BE helped to synthesise evidence and develop the manuscript. EK and XZ assisted with analyses. XZ, EK, BE, JEM, CNB, CdR, JCD, DJF, MG, BDLM, SHM, LRM, AP, BRS, SS, SAS, and BN helped to interpret results and critically revise the manuscript. BN secured funding for the study. All authors approved the final draft.

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Declaration of interests

CNB reports grants from the US National Institute on Drug Abuse (NIDA), during the conduct of the study. CdR reports grants from the US National Insitutes of Health (NIH; NIDA and the National Institute of Allergy and Infectious Diseases), during the conduct of the study. JCD and MG report grants to the University of Washington from Hologic outside of the submitted work. BDLM reports grants from Simon Fraser University, during the conduct of the study; and grants from NIH, outside the submitted work. SHM reports personal fees from Gilead Sciences, outside the submitted work. BRS reports grants from NIDA, during the conduct of the study. SS reports grants from the US National Institute of Mental Health Center for HIV Identification Prevention and Treatment Services, outside the submitted work. All other authors declare no competing interests.

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