Modeling the Impact of Interventions Along the HIV Continuum of Care in Newark, New Jersey

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Background. The human immunodeficiency virus (HIV) epidemic in Newark, New Jersey, is among the most severe in the United States. Prevalence ranges up to 3.3% in some groups. The aim of this study is to use a mathematical model of the epidemic in Newark to assess the impact of interventions along the continuum of care, leading to virologic suppression.

Methods. A model was constructed of HIV infection including specific care-continuum steps. The model was calibrated to HIV/AIDS cases in Newark among different populations over a 10-year period. Interventions applied to model fits were increasing proportions tested, linked and retained in care, linked and adherent to treatment, and increasing testing frequency, high-risk-group testing, and adherence. Impacts were assessed by measuring incidence and death reductions 10 years postintervention.

Results. The most effective interventions for reducing incidence were improving treatment adherence and increasing testing frequency and coverage. No single intervention reduced incidence in 2023 by >5%, and the most effective combination of interventions reduced incidence by approximately 16% (2%–24%). The most efficacious interventions for reducing deaths were increasing retention, linkage to care, testing coverage, and adherence. Increasing retention reduced deaths by approximately 27% (24%–29%); the most efficacious combination of interventions reduced deaths in 2023 by approximately 52% (46%–57%).

Conclusions. Reducing HIV deaths in Newark over a 10-year period may be a realizable goal, but reducing incidence is less likely. Our results highlight the importance of addressing leaks across the entire continuum of care and reinforcing efforts to prevention new HIV infections with additional interventions.

Keywords. HIV; care continuum; mathematical model.

More than 30 years into the human immunodeficiency virus (HIV)/AIDS epidemic, Newark, New Jersey, continues to be one of the most severely HIV/AIDS-impacted communities within the United States. Newark residents have an HIV prevalence of 2.3%, nearly 7 times that of the rest of New Jersey [1]. Moreover, the non-Hispanic black community in Newark is disproportionately affected, with an HIV prevalence of 3.3%, similar to the prevalence observed in some sub-Saharan African countries—for example, Ghana (1.8%) and Rwanda (2.9%) [2–4]. The profile of risk behaviors in Newark is complex, with high prevalence and interaction of injection drug use and risky sexual behaviors [1, 5, 6].

Prevention interventions over the last decade have not succeeded in substantially reducing HIV incidence in the United States [7]. Nevertheless, there is reason for new optimism as recent studies demonstrated that effective antiretroviral therapy (ART) of HIV-infected persons results in a 96% decrease in sexual HIV transmission [8]. This has led to intense dialogue and new initiatives to increase HIV testing coverage, improve connection/retention in care, and expand ART with maximal rates of virologic suppression. Mathematical modeling may help assess potential contributions of various interventions and identify combinations that may

Received 7 June 2013; accepted 11 September 2013; electronically published 17 October 2013.

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Clinical Infectious Diseases 2014;58(2):274–84

DOI: 10.1093/cid/cit687

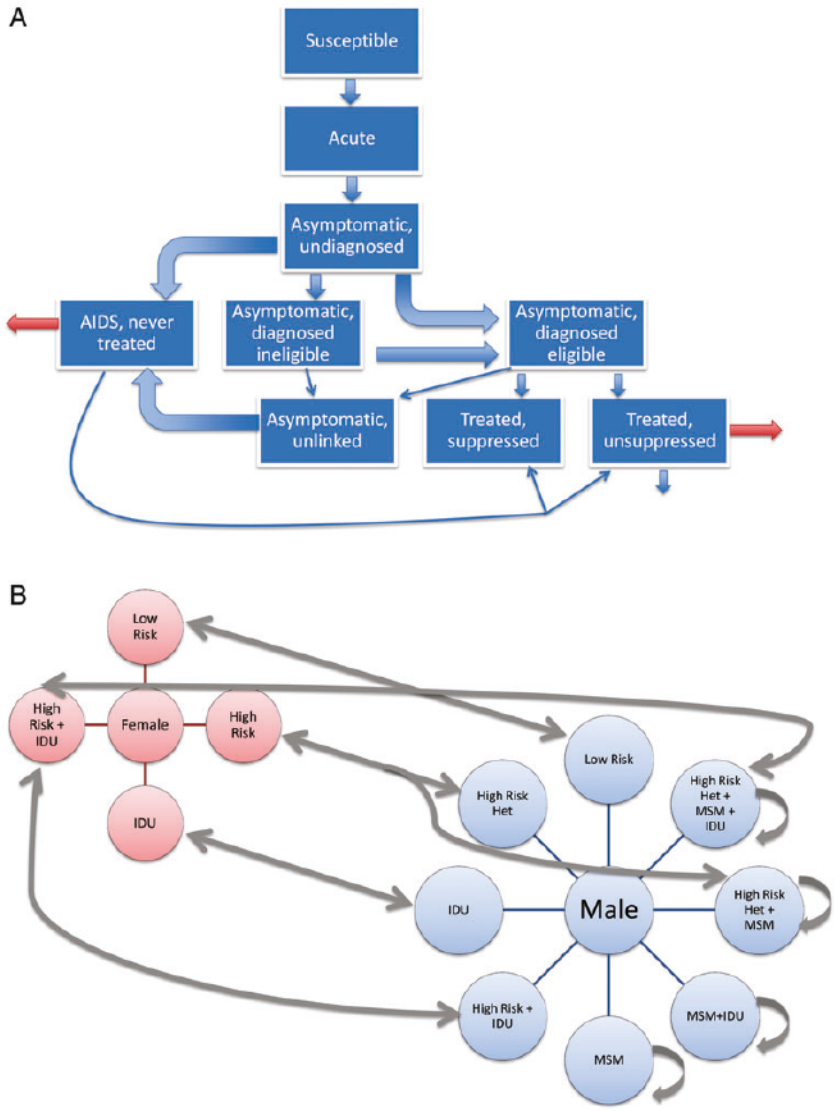

Figure 1. Graphical representation of model flow and risk group interactions. *A*, Susceptible individuals flow into the acute infection compartment via the force of infection. Acutely infected individuals flow into asymptomatic undiagnosed. Asymptomatic individuals either receive a diagnosis before progressing to AIDS or do not. Tested, ineligible individuals eventually become eligible as their CD4 counts drop, but may be lost to follow up before attaining eligibility. Tested-eligible individuals can be lost to follow-up or not linked to treatment, or be linked to treatment and then either be virologically suppressed or not suppressed. Unsuppressed individuals move into a dead-end AIDS post–antiretroviral therapy compartment. Finally, undiagnosed and unlinked individuals progress to AIDS–never treated, from which they either die or present for treatment and then either show suppression or do not. Flows are in blue arrows and excess deaths are in red. *B*, Male and female risk groups are shown with arrows indicating groups that most strongly assort. Abbreviations: ART, antiretroviral therapy; Het, heterosexual; IDU, injection drug user; MSM, men who have sex with men.

contribute most to overall epidemic control. Previous modeling work has suggested that universal test-and-treat interventions may control local HIV epidemics [9]. However, significant doubt remains, due to the difficulty of scaling up screening programs and the marked heterogeneity among HIV-infected persons with respect to disease transmission, access, and acceptance of care and ART [10]. Additionally, impact of test-and-treat strategies may differ in areas with generalized epidemics compared with concentrated microepidemics.

The HIV epidemic in the United States is a set of microepidemics—"hotspots" of infection [11]. Results of modeling for generalized HIV epidemics may not accurately inform HIV control in the United States. Modeling the impact of interventions to prevent HIV in Newark, New Jersey, is an important case study for several reasons: Newark is a well-described hotspot of HIV infection in the United States, and its epidemic is driven by multiple factors including heterosexual transmission, intravenous drug use, and unreported sexual activity among

Table 1. Prior and Posterior Parameter Ranges

Parameter Name	Description	Prior Range	Posterior Range	Source
α	Death rate when CD4 <200	0.2–2 y^{-1}	0.20–1.99 y^{-1}	[18–20]
ζ	1/duration of drug use	.025–.1667 y^{-1}	0.03–.09 y^{-1}	[21]
θ	1/duration of acute period	1.5–6 y^{-1}	1.62–5.98 y^{-1}	[19, 20]
ε	Assortativeness coefficient	.05–.95	0.05–.95	ME
$c(m,h)$	Rate of partner change in high-risk men (het)	3–10 partners/y	3.02–9.79 partners/y	[22]
$c(m,l)$	Rate of partner change in low-risk men (het)	0.01–2 partners/y	0.04–1.98 partners/y	[16, 22]
$c(hrhm:m)$	Rate of male partner change in bisexual men	1–5 partners/y	1.21–4.98 partners/y	[23], ME
$c(msm,h)$	Rate of partner change in high-risk MSM	3–10 partners/y	3.01–9.97 partners/y	[23], ME
$c(msm,l)$	Rate of partner change in high-risk MSM	.1–3 partners/y	0.14–2.92 partners/y	[22], ME
mx	Proportion of men exclusively MSM	0.03–.12	0.04–.12	[24]
η_d	Needles shared per partner	50–350 needles/partner	52.64–349.65 needles/partner	[21]
ψ_{red}	Coefficient of reduction in drug use incidence	0.001–.1	0.0025–.0951	ME
$\nu(l,l)$	Number of sex acts in a low-risk/low-risk partnership	20–150 sex acts/partner	20.09–149.95 sex acts/partner	ME
$\nu(h,h)$	Number of sex acts in a high-risk/high-risk partnership	1–30 sex acts/y	1.48–29.85 sex acts/y	ME
$\nu(l,h)$	Number of sex acts in a low-risk/high-risk partnership	1–30 sex acts/y	1.02–28.79 sex acts/y	ME
β_{mf}	Ratio of transmission probability male to female	1.5–6	1.54–5.8	[25]
β_{mm}	Ratio of transmission probability male to male	1.5–6	1.52–5.92	[25]
ω_{I0}	Ratio of infectiousness during acute phase	20–30	20.25–29.98	[19]
ϕ	Per-sex-act transmission probability	1×10^{-5}–.01/sex act	1e-4–.0032/sex act	[20]
σ_d	Per-injection transmission probability	2×10^{-5}–.05/injection	5e-4–.049/injection	[26]
pdu	Initial percent prevalence of drug use	0.5%–10%	4%–10%	[6]
$pmdu$	Initial percent prevalence of drug use among MSM	0. 5%–20%	1%–20%	[27]
prm	Proportion of MSM high risk	0.1–.95	0.19–.95	[26]
cd	Rate of change of needle-sharing partner	0.5–3 partners/y	0.51–2.97 partners/y	ME
q_{nm}	Coefficient of reduction in unprotected sex acts when aware of status	.1–.9	0.11–.88	ME

Abbreviations: het, heterosexual; ME, model estimate; MSM, men who have sex with men.

men in prisons or other settings. Furthermore, as Newark is a small city, it may be possible to implement interventions and assess validity of modeling. Results of modeling may therefore, be useful for other US hotspots. Here, we use dynamic models, linked to epidemiological data, to assess probable impact of several interventions on future HIV incidence and mortality in Newark, New Jersey. Crucially, our model explicitly includes each step in the continuum of HIV care leading to virologic suppression (ie, testing, linkage to care, retention in care, linkage to treatment, and adherence to treatment) [12].

METHODS

Model

To capture the dynamics of the Newark epidemic, a compartmental model was used (Figure 1*A*). Following others (eg, [9, 13–15]), the model includes compartments for 3 infection stages: acute, high viral load but short duration (3–6 months); asymptomatic, lower viral load with duration of 8 years; and AIDS, intermediate viral load with duration approximately 2.5 years. These stages are further stratified by awareness of infection, eligibility, and treatment status. Progression is as follows: Susceptible individuals move to acute infection, which progresses to asymptomatic–will be diagnosed before CD4 <200 cells/μL or asymptomatic–will be diagnosed after CD4 <200 cells/μL. Those who are tested and diagnosed move into the category "tested, eligible for ART" or "tested, ineligible for ART." Eligibility for ART depends on CD4 count. Before 2010, those with CD4 <350 cells/μL are eligible. From 2011 onward, all HIV-infected individuals are deemed eligible. Tested ineligible individuals become eligible as CD4 count declines. Eligible individuals move into "treated, suppressed compartment" or "treated, unsuppressed compartment" categories.

Current percentages of infected individuals passing each point in the continuum are included in the model: Tested individuals are linked to care, individuals linked to care upon testing are retained in care, and individuals retained in care are linked to ART, if eligible, with a mean delay of 3 months. Individuals linked to treatment achieve viral suppression, depending on ART adherence. Individuals who were never tested or

Table 2. Invariant Parameters

Parameter	Description	Value	Source
T_{test}	Time between infection and testing if tested before CD4 count <200 cells/μL and eligible when tested	4 y	[30–32]
z	Percent of diagnosed individuals diagnosed before CD4 <200	41%	[32]
$zratio_i$	Ratio of testing in other risk groups to heterosexual women	.68–1.1	[32]
$test_{lnk}$	Percent linked to care given tested	75%	[33–36]
ret	Percent retained in care given linked	51%	[33–36]
trt_{lnk}	Percent linked to treatment given retained in care	89%	[33–36]
x	Percent of treated who achieve viral suppression	77%	[33–36]
$xratio_i$	Ratio of adherence/suppression in other risk groups to heterosexual women	.8–1	EO
T_{treat}	Time between eligibility and treatment	.25	EO
y	Percentage of asymptomatic individuals eligible for treatment when tested (CD4 count 200–349 cells/μL)	30%	[32]
T_{elig}	Time to eligibility if tested and not eligible	2 y	[30–32]
$\omega_{I_A}, \omega_{I_{ts}}\omega_{trns}, \omega_A$	Weighting of transmission probability by stage of infection	1, .04, .9, 7	[8–19]
γ_{nm}	Rate of progression for untreated individuals from HIV to AIDS	$1/8\ y^{-1}$	[18–20]
γ_{ns}	Reduced progression rate for treated, unsuppressed individuals	$1/12\ y^{-1}$	EO
μ, μ_{IDU}	Death rates/recruitment rates (non-IDU, IDU)	$1/58\ y^{-1}$, $1/36\ y^{-1}$	[37]
$pdur, pdurf$	Percentage of IDUs who engage in risky sexual behavior (M, F)	34%, 18%	[21]
$pmdur$	Percentage of MSM IDUs who engage in risky sexual behavior	80%	ME
pr	Percentage of heterosexual men engaging in high-risk behavior	30%	[22]
prf	Percentage of heterosexual women engaging in high-risk behavior	20%	[22]
fdu	Percentage of IDUs who are female	36%	[21]
$hrhm$	Percentage of high-risk heterosexual men engaging in bisexual behavior	15%	[21], ME
$c(hrhm:f)$	Rate of female partner change in bisexual men	3 partners/y	[21], ME
T_{ART}	Year of availability of ART	1995	[1]
ψ_0	Initial incidence of injection drug use (approximated by prevalence/duration)	$pdu \times \zeta$	
$nred$	Coefficient of reduction in needle sharing per 5 years	.3	ME

Abbreviations: ART, antiretroviral therapy; EO, expert opinion; HIV, human immunodeficiency virus; IDU, injection drug user; ME, model estimate.

dropped out from the care continuum progress with infection, until presenting for care with a CD4 count of <200 cells/μL. Individuals who progress to AIDS after failing on ART die after 1–3 years.

The equations are applied to males and females comprising high- and low-risk sexual activity classes, and injection drug users (IDUs) and non-IDUs. The model takes into account heterosexual, homosexual, bisexual, and injection drug use transmission, as well as combinations of sexual and injection drug use risk behaviors. Individuals move between IDU and non-IDU groups, and sexual mixing is assortative as per a study conducted using sexually transmitted infection clinic data from Newark in the 1990s [16] (Figure 1*B*). Additionally, the model includes a bounded decline in needle sharing and drug-use incidence as injection drug use has declined in Newark [17].

Ranges for model parameters were gathered from the literature (Tables 1 and 2). Uncertainty analysis was performed, altering parameters one at a time to see what influence ranging a given parameter had on results. In this way, a subset of influential parameters, those whose variation yielded >10% average shift over all model outputs, was selected for fitting. Next, Latin-hypercube sampling was performed using the subset of influential parameters [28]. A multidimensional grid describes the model's parameter space. Latin-hypercube sampling forces each grid segment to be sampled exactly once, thus efficiently covering the whole parameter space. Model outputs from sampled parameter sets were then compared with observed counts stratified by risk group of persons living with HIV/AIDS in Newark over time. Parameter sets were accepted if they fit within prior limits of the data [28]. Sensitivity analysis was performed by calculating partial rank correlation coefficients (PRCCs) using standard methods [28]. PRCCs provide a postfitting breakdown of which parameters influence model outputs the most, thereby enabling validation of model assumptions.

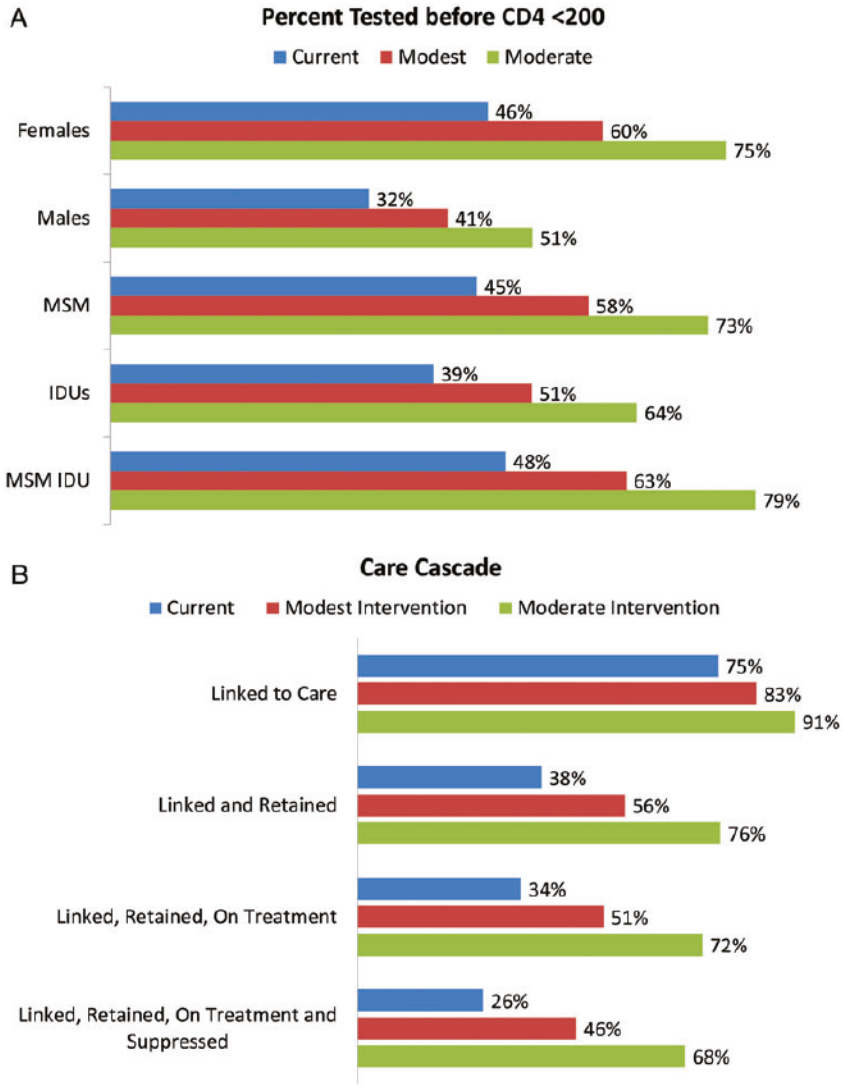

Figure 2. Testing and care-continuum interventions. *A*, Current, modest intervention, and moderate intervention levels are shown of percentages of individuals tested before reaching a CD4 count of <200, in current, modest intervention, and moderate intervention levels. *B*, Percentages of individuals achieving each step in the care continuum, in current, modest intervention, and moderate intervention levels. Abbreviations: IDU, injection drug user; MSM, men who have sex with men.

Interventions

Increasing tested and adherent proportions overall (Figure 2*A*) and in high-risk groups by 5% and 25% and increasing testing frequency were implemented. For tested HIV-infected individuals, interventions at each point in the care continuum were implemented at 3 different levels representing a modest, moderate, or optimal level of intervention (Figure 2*B*).

Data

Data used for the fitting came from Project IMPACT (Intensive Mobilization to Promote AIDS Awareness through Community-based Technologies), a New Jersey Department of Health initiative to address the HIV epidemic in New Jersey communities most affected [1, 3]. Project IMPACT data represent reported cases for Newark from 2002 to 2010 as ascertained by epidemiological surveillance.

Many parameter estimates came from National HIV Behavioral Surveillance (NHBS) data. Created in 2003 by the Centers for Disease Control and Prevention to collect behavioral information on individuals at high risk for acquiring HIV, the NHBS is conducted in rotating cycles targeting men who have sex with men (MSM), IDUs, and high-risk heterosexuals. A range of sampling techniques are used for each key population, and standardized, anonymous questionnaires on behavior, testing, and prevention are administered and HIV testing is offered [29].

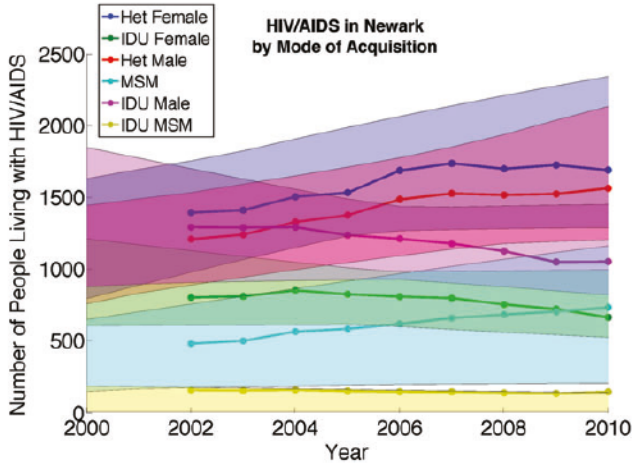

Figure 3. Model fits and data. Data from project IMPACT (solid lines with dots) are shown, overlaid with the range of model fits for each data point. The 12 risk groups in the model are aggregated into 6 shown here as follows: Het Female comprises low- and high-risk non-injection drug user (IDU) heterosexual females; IDU Female, low- and high-risk IDU heterosexual females; Het Male, low- and high-risk non-IDU heterosexual males and non-IDU bisexual males; MSM, low- and high-risk non-IDU men who have sex with men (MSM); IDU Male, low- and high-risk IDU heterosexual males and IDU bisexual males; and MSM IDU, Men who have sex with men who are also IDU. Abbreviations: Het, heterosexual; HIV, human immunodeficiency virus; IDU, injection drug user; MSM, men who have sex with men.

RESULTS

Model Fitting

The fitting process was run until 100 parameter sets were identified that produced model runs within the specified prior limits. Figure 3 shows the range of fitted runs plotted with data points by risk group (Table 1 shows prior and posterior intervals on fitted parameters). PRCCs were calculated using the posterior range of each parameter against model outputs of prevalence and incidence. Different parameters showed peak influence for incidence and each risk group's prevalence, although parameters that governed drug-use incidence and duration and contact patterns were influential on all outputs (Supplementary Table A). The amount of initial uncertainty that was reflected in the prior ranges of the influential parameters varied significantly; some parameters such as transmission probability ratios for male–female and male–male transmission and death rate at a CD4 count of <200 cells/μL had comparatively small ranges, whereas others, such as number of sex acts per low-risk/low-risk partnership, had wide ranges. While size of prior range may influence parameter sensitivity, PRCC strength can inform the relative importance of ascertaining more informative priors for these parameters for future studies. Crucially, however, in this model, the qualitative results of scenario testing are robust to the differences in parameter fits.

Interventions

To test the impact of interventions at each point in the care continuum, parameters dictating the intensity at a given point were altered in isolation and conjunction, representing a range of intervention strength. Intervention scenarios were run on all parameter sets to assess their efficacy. Parameters included proportion of individuals tested before CD4 <200 cells/μL, proportion connected to care given newly positive test, proportion retained in care given connection to care, proportion receiving ART given retention in care, proportion virally suppressing given ART (ie, proportion adherent to ART), percentage of increase in testing and viral suppression in high-risk groups, time between infection and test if tested before CD4 <200 cells/μL, and proportion eligible if tested before CD4 <200 cells/μL.

The top 4 most efficacious interventions for averting infections were run in isolation and combination on all parameter sets. According to the best parameter fit, these were, in descending order of efficacy: increasing ART adherence in high-risk groups, increasing ART adherence in all groups, reducing time between infection and testing, and increasing proportion tested before CD4 <200 cells/μL. Combinations of these interventions resulted in larger reductions in incidence than single interventions (Table 3, Figure 4*A*).

The top 4 most efficacious interventions for reducing the number of deaths were similarly run in isolation and combination on all parameter sets. According to the best parameter fit, these were, in descending order of efficacy: increasing proportion retained in care, increasing proportion linked to care, increasing testing coverage, and increasing ART adherence in all groups. Again, combinations of interventions resulted in larger numbers of deaths averted (Table 4, Figure 4*B*).

Of note, the order of efficacy of interventions varied slightly between parameter sets, but the 4 most efficacious remained the same across all parameter sets.

The 10-year impact on incidence of any individual intervention was small, but when all interventions were run together at maximum levels, incidence declined steeply (Figure 5). This highlights the importance of closing gaps throughout the care continuum. Each individual intervention can only have limited effect if the cascade is "leaky" elsewhere. Figure 5 also shows impact of secular declines in injection drug use over time. The red line shows a counterfactual scenario, that is, one without reductions in incidence of injection drug use and needles shared. The epidemic in Newark had the potential to be worse, with approximately 40% higher annual incidence.

Although no currently available individual intervention can effect a substantial reduction in incidence, combination interventions at intermediate levels can yield a reduction in incidence in 2023 of approximately 16%. Interventions may have different levels of achievability and cost, and various combinations at different levels can yield similar results. Contour plots

Table 3. Impact of Interventions on Incident Cases

Intervention	Change From Baseline Level	% Incident Cases Change in 2023 (Range)	Absolute Change in Incident Cases in 2023 (Range)	% Change in Cumulative Incident Cases 2013–2023 (Range)	Absolute Change in Cumulative Incident Cases 2013–2023 (Range)
Increase in high-risk ART adherence	25% increase	4.6 (0.8–6.4)	22 (2–43)	2.4 (0.5–3.1)	133 (13–260)
Increase in all-group ART adherence	77%–95%	3.8 (0.6–5.8)	18 (1–38)	1.9 (0.3–2.8)	108 (9–225)
Increase in testing frequency	4 y–1.5 y	2.6 (0.2–6.2)	12 (0–40)	2.3 (0.3–4.4)	127 (7–340)
Increase in HIV testing coverage	46%–75%	2.3 (0.2–4.3)	11 (1–30)	1.2 (0.1–2.3)	68 (4–197)
Increase in ART adherence: all-group and high risk	As above	8.3 (1.2–11.2)	38 (3–72)	4.2 (0.8–5.5)	235 (21–422)
Increase in ART adherence: all-group and high risk plus increase in testing coverage	As above	11.1 (1.6–14.8)	52 (4–98)	5.6 (1.1–7.3)	314 (27–565)
All top 4 interventions	As above	15.8 (2.1–24.5)	73 (5–158)	9.1 (1.6–13.7)	508 (40–1039)

Abbreviations: ART, antiretroviral therapy; HIV, human immunodeficiency virus.

show the combination levels for pairs of interventions that can achieve similar results (Supplementary Figure 2). Changing the profile of combination interventions changes the distribution of incident infection sources (Figure 6).

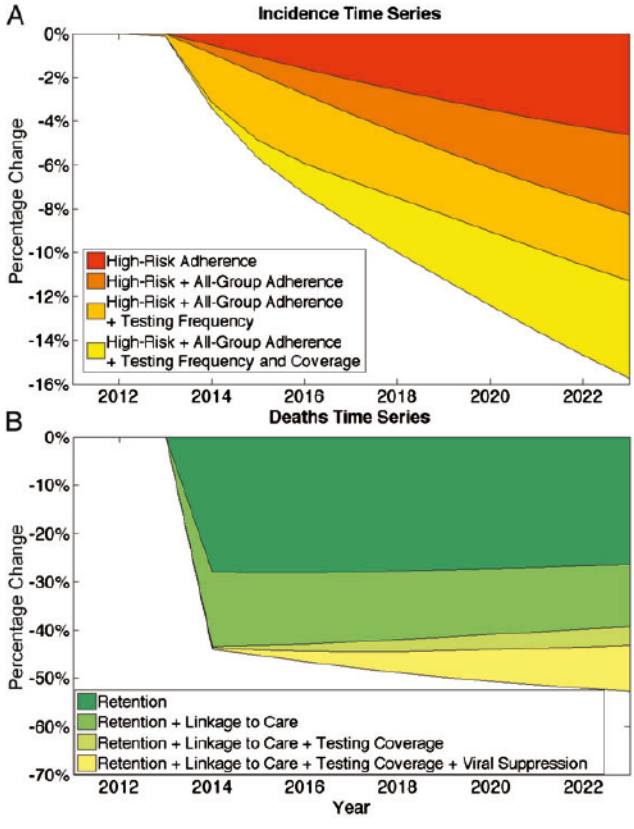

Figure 4. Incident cases and deaths time series: percentage change over time by intervention (according to best-fit parameter set). *A*, Projected change in incident cases over time under increasing combinations of the top 4 most efficacious interventions. *B*, Projected change in deaths over time under increasing combinations of the top 4 most efficacious interventions.

DISCUSSION

HIV remains highly endemic in focal areas of the United States. Despite availability of ART, HIV incidence in the United States has been relatively stable, with roughly 50 000 new infections per year [7]. Recent empirical work has shown the efficacy of treatment as prevention in a clinical trial setting among stable serodiscordant couples and confirmed that maintenance of virologic suppression is key in HIV prevention [8]. Given the recent national dialogue regarding the care continuum, in which only 33%–55% of HIV-infected persons are retained in care and 19%–26% achieve virologic suppression [33–36], our model addresses the key questions of which interventions are most likely to prove efficacious at decreasing HIV acquisition and mortality. Surprisingly, HIV incidence is estimated to decrease by just 16%, when all interventions along the continuum of care are implemented at "achievable" levels, suggesting that ART interventions cannot alone be relied upon to curb HIV transmission in hotspots and that additional prevention interventions are urgently required.

A major contributor to the modest impact of interventions is the "leaky" care continuum. Large impacts on HIV incidence are only evident when all interventions approach 100%. In Newark, as in other settings, there is a subset of individuals who either cannot or will not access care. In a study of HIV acquisition among women living in areas of the United States with high levels of poverty and HIV prevalence, 20% reported that they were unable to access needed medical care [38]. The Affordable Care Act may improve access to care, but other factors (eg, distrust of the medical establishment and stigma

Table 4. Impact of Interventions on Deaths

Intervention	Change From Baseline Level	% Deaths Change in 2023 (Range)	Absolute Change in Deaths in 2023 (Range)	% Change in Cumulative Deaths 2013–2023 (Range)	Absolute Change in Cumulative Deaths 2013–2023 (Range)
Increase in retention	51%–67%	26.4 (24–29.1)	89 (39–150)	24.7 (23–26.6)	1056 (484–1650)
Increase in Linkage to care	75%–83%	9.4 (8.6–10.3)	32 (14–53)	8.6 (8–9.2)	370 (167–578)
increase in HIV testing coverage	46%–75%	5 (3.3–6.5)	17 (5–31)	3.2 (1.7–4.2)	135 (34–275)
Increase all-group ART adherence	25% Increase	5.4 (3–6.7)	18 (5–31)	2.3 (1.1–3)	97 (23–176)
Increase in retention and linkage	As above	39.4 (36–43.5)	132 (60–224)	37.4 (34.9–40.4)	1598 (741–2496)
Increase in retention, linkage and testing coverage	As above	43.2 (39.1–47.2)	145 (63–247)	39.4 (36.6–42.3)	1687 (762–2656)

Abbreviations: ART, antiretroviral therapy; HIV, human immunodeficiency virus.

associated with HIV infection) may continue to contribute to poor care access. Nonetheless, for individuals successfully linked/retained in care, this modeling exercise estimates mortality decreases of approximately 35%. The challenges surrounding improved linkage and retention in care are particularly difficult, as improved retention requires ongoing efforts rather than single-point change. Novel strategies to link and retain individuals in care need to be created and tested. Only by combining interventions that involve linking and retention in care can further reductions in mortality be realized.

Virologic suppression is a demonstrated powerful tool for averting HIV transmission. However, maximizing adherence to ART is challenging as it involves extensive follow-up and monitoring of individuals over long periods of time. Indeed, test-and-treat interventions may have the potential to increase numbers of patients initiating ART early, but without stabilizing the back end of treatment continuation (ie, care retention and ART adherence), test-and-treat strategies cannot achieve full potential.

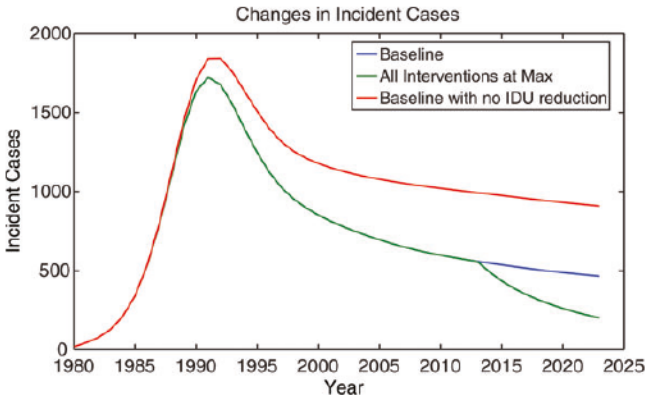

Figure 5. Pressure test of interventions. Impact on annual number of new infection incidence of maximal implementation of all interventions. By 2023, there are <200 incident cases. Abbreviation: IDU, injection drug user.

The proportion of incident cases that arise from acute infections does not decline with successive interventions (Figure 6),

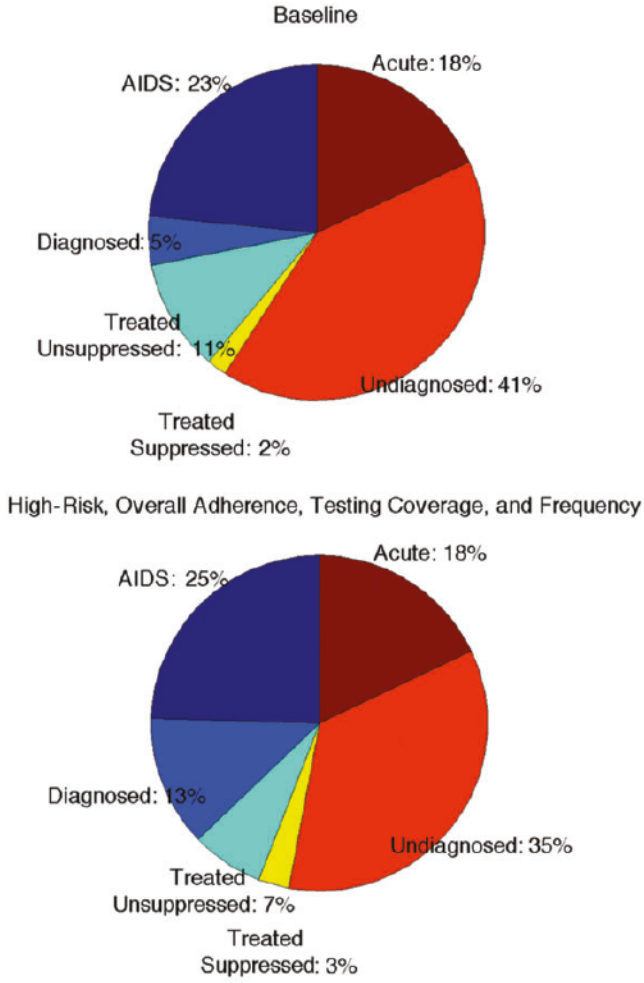

Figure 6. Pie charts designating provenance of incident cases in 2023 for baseline and top 4 most efficacious interventions at moderate level.

so HIV transmission is maintained even in the 4-intervention scale-up scenario. This result suggests that unaddressed acute infection may play a critical role in the limited efficacy of test-and-treat interventions to decrease HIV incidence at least over the short time-scales examined here; however, further exploration of this hypothesis is needed. No intervention tested in this study addresses acute infection directly, as many commonly used testing algorithms are unable to detect acute infection [39]. Implementation of newer-generation HIV tests that simultaneously assess acute and chronic infection may be critical to further decreasing HIV incidence [39, 40].

Previous modeling studies have assessed the efficacy of test-and-treat interventions in different settings. Granich et al [10] predict transition of the epidemic into an elimination phase after introduction of test-and-treat in a setting of generalized HIV infection, but their assumptions differ from those in this study in several substantive ways: immediate treatment, higher adherence rates (ie, elements of a perfect care continuum), and only heterosexual transmission. The results of the model presented here are more consistent with the predictions of Dodd et al [16], who explore the efficacy of test-and-treat in a range of epidemiological settings. Although they also test scenarios that include perfect or near-perfect care continua, they predict modest HIV incidence reductions in settings with greater variation in risky behavior, where key populations at high risk of infection and transmission drive the epidemic. Powers et al [40] also predict modest reductions in HIV prevalence in a developing world setting (even with high coverage) unless individuals with early infection are targeted [40]. Walensky et al [41], examining outcome measures in Washington, D.C., draw similar conclusions on test-and-treat impact, predicting increases in life expectancy but only a 15% reduction in HIV incidence over 5 years of overall population life-years spent with transmissible viral load [41]. Long et al [41], using a model based on 2007 US data, predict similarly modest effects of test-and-treat; incidence is reduced by 2.3% with enhanced testing, and ART averts only 10.3% of infections over 20 years [15]. Last, Sorensen et al [42], modeling an urban population based on MSM in New York City, report a greater impact on incidence, predicting roughly a 50% reduction over 20 years with intermediate levels of interventions implemented throughout the care continuum [42]. The present analysis offers a unique perspective on the Newark epidemic, but agrees broadly with some prior predictions in the literature about the impact of test-and-treat strategies in the United States.

This study adds to the literature a bespoke model for a developed-world urban setting; it takes into account differential dynamics between heterosexual, homosexual, and bisexual HIV transmission in addition to injection drug use. Although there is uncertainty around many of the model parameters, the fitting process used in this study helps quantify it. Additionally, this model incorporates all steps in the care continuum, from initial test through linkages and viral suppression.

There are inevitable simplifications in the model that may lend some uncertainty to the results. Only approximations are used for disease stage. There is no age structure, and the model does not take into account ethnic variation, which is likely an oversimplification of the transmission situation in Newark. Whereas individuals can change drug-use status, no change in sexual risk behavior over time is incorporated. Most parameters stay constant over time, and as there are multiple pathways to being treated, some individuals may suffer too short a survival penalty upon reaching this state, which may in turn slightly impact mortality estimates.

In addition, assumptions made about sexual mixing patterns were derived from a single study performed in Newark's sexually transmitted infection clinic roughly 15 years ago. As can be seen in the PRCCs (Supplementary Table B), the assortativity coefficient only comes up as influential for heterosexual prevalence measures. This result validates model assumptions: Sexual-mixing diversity should be most important in heterosexual groups because they mix with the greatest number of other groups. Sexual assortativeness does not play a role in transmission among IDUs, as IDUs are far more likely to acquire infection through drug use than sexual contact. Similarly, MSM are naturally more assortative as they only acquire infection from other MSM or the few bisexual men. Model prevalence estimates are also roughly validated by incidence predictions, although available data on incidence are limited. Although these assumptions may compromise the specific quantitative accuracy of the model predictions, the general predictions of relative efficacy of various interventions are robust.

Our model of the Newark HIV epidemic suggests that realistic implementation of current interventions will have a modest impact on decreasing HIV incidence; however, a more marked impact on mortality is possible. Our results emphasize the importance of reinforcing additional forms of HIV prevention and reducing losses of patients throughout the entire care continuum. We believe that the implications of these results are important, and may have policy applications for other US areas. It is imperative that innovative strategies to link and retain HIV-infected persons in care be developed and tested. Only by stopping care-continuum leakage will we be able to effectively decrease new HIV infections in the United States.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

Acknowledgments. The authors thank Paula Grant from the New Jersey State Department of Health, Division of HIV, STD and TB Services, for assistance with data acquisition; Steven Saunders, MS, Director, Prevention and Education, New Jersey Department of Health, Division of HIV, STD and TB Services; Barbara Bolden, PhD, Acting Director, Epidemiologic Services, New Jersey Department of Health, Division of HIV, STD and TB Services; and Professors Andrea Graham and Simon Levin from the Princeton University Department of Ecology and Evolutionary Biology for their helpful comments.

Financial support. The work was supported by a grant from the New Jersey Health Foundation (formerly University of Medicine and Dentistry Foundation). R. B. B. was supported by a Princeton University Department of Ecology and Evolutionary Biology Fellowship. B. T. G. was supported by the Bill and Melinda Gates Foundation and the RAPIDD program of the Science and Technology Directorate, US Department of Homeland Security, and the Fogarty International Center, National Institutes of Health. T. B. H. was supported by the Bill and Melinda Gates Foundation and Imperial College.

Potential conflicts of interest. S. L. H. has received research support from BMS, Gilead, Janssen Therapeutics, and Viiv-GSK, and has served as a consultant for Janssen Therapeutics, BMS, Gilead, and Merck & Co. S. L. H.'s spouse is a member of the Becton-Dickinson board of directors, and has Merck & Co. stock options. A. S. has serves as a consultant for Merck Inc. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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