Clinical Infectious Diseases

MAJOR ARTICLE

Potential Effects of the Coronavirus Disease 2019 (COVID-19) Pandemic on Human Immunodeficiency Virus (HIV) Transmission: A Modeling Study in 32 US Cities

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Background. The degree to which the 2019 novel coronavirus disease (COVID-19) pandemic will affect the US human immunodeficiency virus (HIV) epidemic is unclear.

Methods. We used the Johns Hopkins Epidemiologic and Economic Model to project HIV infections from 2020 to 2025 in 32 US metropolitan statistical areas (MSAs). We sampled a range of effects of the pandemic on sexual transmission (0–50% reduction), viral suppression among people with HIV (0–40% reduction), HIV testing (0–50% reduction), and pre-exposure prophylaxis use (0–30% reduction), and indexed reductions over time to Google Community Mobility Reports.

Results. Simulations projected reported diagnoses would drop in 2020 and rebound in 2021 or 2022, regardless of underlying incidence. If sexual transmission normalized by July 2021 and HIV care normalized by January 2022, we projected 1161 (1%) more infections from 2020 to 2025 across all 32 cities than if COVID-19 had not occurred. Among "optimistic" simulations in which sexual transmission was sharply reduced and viral suppression was maintained we projected 8% lower incidence (95% credible interval: 14% lower to no change). Among "pessimistic" simulations where sexual transmission was largely unchanged but viral suppression fell, we projected 11% higher incidence (1–21% higher). MSA-specific projections are available at www.jheem.org?covid.

Conclusions. The effects of COVID-19 on HIV transmission remain uncertain and differ between cities. Reported diagnoses of HIV in 2020–2021 are likely to correlate poorly with underlying incidence. Minimizing disruptions to HIV care is critical to mitigating negative effects of the COVID-19 pandemic on HIV transmission.

Keywords. HIV; COVID-19; dynamic HIV transmission model; infectious disease transmission.

Human immunodeficiency virus (HIV) imposes substantial burdens in the United States, with 36 398 new infections in 2019 and greater than 1 million prevalent cases [1]. The 2019 novel coronavirus disease (COVID-19) pandemic has caused major disruptions, including to HIV care [2]. The degree to which the pandemic will impact HIV transmission is unclear.

The COVID-19 pandemic and attendant disruptions in services affect HIV incidence in several ways. Social distancing and restrictions may reduce sexual encounters [3–7]. Attempts to minimize time outside the home and a shift towards telemedicine may have led to reduced testing, less use of pre-exposure prophylaxis (PrEP), and/or disruptions in the HIV care continuum [4, 8–17]. Moreover, the HIV epidemic is driven by local heterogeneities, and COVID-19 is likely to impact different local epidemics in different ways [13, 18].

Mathematical models of infectious disease can facilitate examination of potential epidemic trajectories [19, 20]. Existing models have explored the potential impact of COVID-19 on HIV transmission in the United States, but not across a wide and representative range of cities [21–23]. We used the Johns Hopkins Epidemiologic and Economic Model (JHEEM), a dynamic transmission model of HIV, to explore the potential impacts of the COVID-19 pandemic on HIV epidemics in 32 US cities [24]. We evaluated the effect that pandemic-induced disruptions to HIV testing, viral suppression among persons with HIV (PWH), and PrEP use, plus alterations to behaviors that promote sexual transmission, might have on future incidence and diagnoses of HIV.

METHODS

Model Structure

The JHEEM is a dynamic, compartmental model of HIV transmission stratified by age, race/ethnicity, sex/sexual behavior,

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and current/prior intravenous drug use. The JHEEM is calibrated at the local level to 32 separate individual metropolitan statistical areas (MSAs), which encompass the 50 high-burden counties plus Washington, DC, identified in the Ending the HIV Epidemic Initiative [25]. It represents the adult population according to HIV infection status (uninfected; acute HIV, the first 2.9 months after infection [26]; or chronic HIV), awareness of infection, and PrEP status (Figure 1). The model is represented as a set of differential equations (detailed in the Supplementary Material), solved using the *odeintr* package in R, version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria) [27, 28].

Model Calibration

The calibration process has been previously detailed [24]. Briefly, we fit the model using Adaptive Metropolis Sampling—a Bayesian process running 400 000 simulations in each MSA to identify model parameter values that reproduce the observed HIV epidemic [29]. Model calibration reproduces 10 targets (Supplementary Table 1), including reported diagnoses and prevalence, plus local levels of viral suppression among PWH, HIV testing, and use of PrEP. One hundred thirty-one parameters govern subgroups' risks of HIV infection, frequency of HIV testing, PrEP use, and viral suppression (Supplementary Tables 2–7). This process yields 1000 simulations that best represent the HIV epidemic in each city. We projected each simulation forward to 2025 under different scenarios representing the impact of the COVID-19 pandemic.

Effects of the COVID-19 Pandemic

We represented the effects of the COVID-19 pandemic and lockdowns on HIV epidemiology via reductions in 4 parameters:

1. The rate of sexual transmission of HIV, a product of the average number of partners and the average number of unprotected encounters per partner per time
2. The rate of HIV testing
3. The proportion of serostatus-aware PWH who are virally suppressed
4. The proportion of the HIV-uninfected population at risk for HIV acquisition who are enrolled in a PrEP program

We framed reductions as time-varying multipliers relative to what each parameter would have been absent the pandemic. For example, if the reduction in testing was 25% in April 2020, then for each of the 135 strata of age/race/sex/drug use, the rate

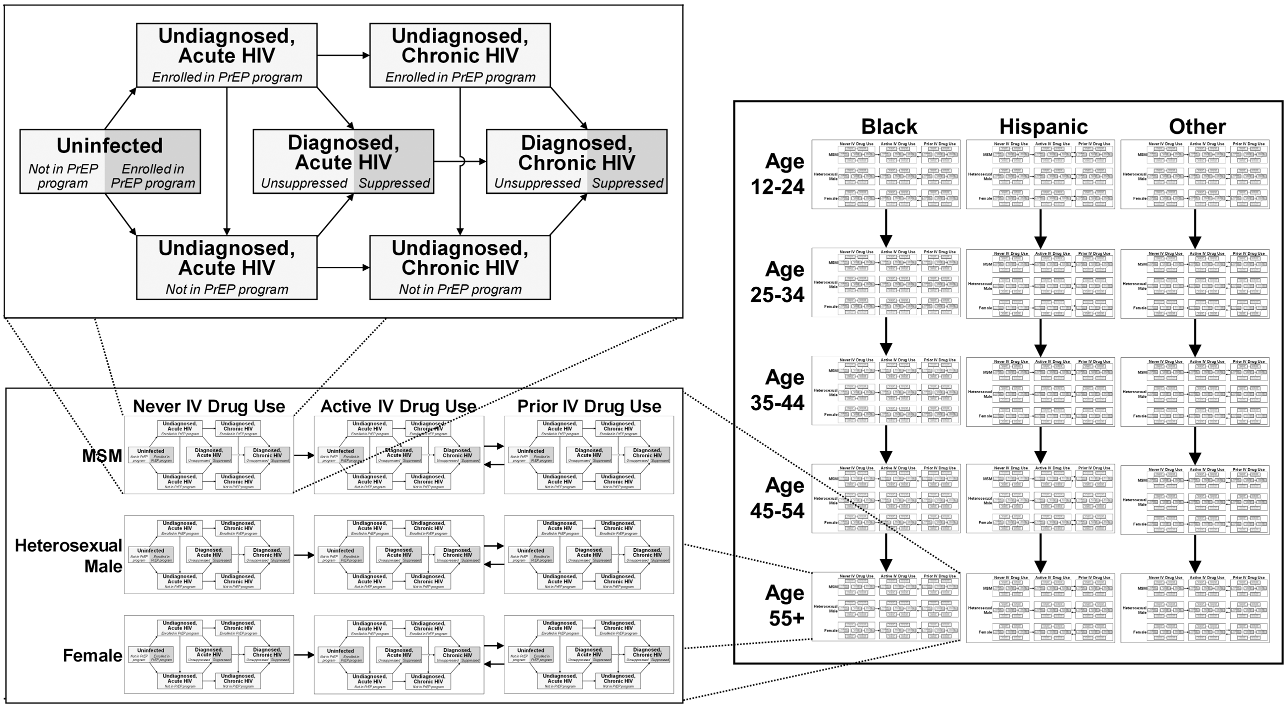

Figure 1. Model structure. The upper left panel shows model populations (compartments) representing HIV disease and continuum of care. Each uninfected population has a proportion who are enrolled in a PrEP program. As individuals become infected, they first enter the acute HIV phase, where transmissibility is high, before progressing to chronic HIV. People who become infected with HIV while enrolled in a PrEP program are diagnosed at an average rate of once every 3 months. Persons with HIV (PWH) who are unaware of their diagnosis and not in a PrEP program are diagnosed according to testing rates that depend on their age, race/ethnicity, sex/sexual behavior, IDU status, location, and calendar year. All populations of PWH who are aware of their diagnosis have a proportion who are virally suppressed and do not transmit HIV. Each population is further stratified by sex/sexual behavior and IDU status (top right), and by age and race/ethnicity (bottom). Abbreviations: HIV, human immunodeficiency virus; IDU, intravenous drug use; MSM, men who have sex with men; PrEP, pre-exposure prophylaxis.

of testing during pandemic-induced disruptions was calculated to be three-quarters of what it otherwise would have been at that time.

We varied reductions over time in relationship to changes in Google Community Mobility Reports [30]. For 5 categories of mobility data—workplace, groceries and pharmacies, transit, retail, and residential—we calculated the average change from baseline in each city for each month after March 2020, and divided by the maximal change (in April 2020). We averaged the 5 values, yielding a proportion change in mobility for each month, ranging from zero (no change from baseline) to 1 (maximal change), as detailed in Supplementary Figures 1 and 2.

We ran simulations under 2 scenarios with different timelines over which pandemic effects took place. In both scenarios, disruptions began on 1 March 2020; sexual transmission remained reduced, proportional to changes in mobility, until 8 March 2021 (when the Centers for Disease Control and Prevention [CDC] announced guidance for fully vaccinated individuals, including that they did not need to socially distance or wear masks indoors [31]); after 8 March 2021, the effect on sexual transmission was attenuated (diverging from mobility trends), returning to normal by 4 July 2021 [32]. In a "Rapid Resumption of Care" scenario, we assumed that HIV testing, viral suppression, and PrEP use followed the same timeline. In a "Prolonged Barriers to Care" scenario—which we used for our primary analysis—we assumed that normalization of HIV testing, viral suppression, and PrEP use was delayed by 6 months relative to normalization of sexual activity (ie, HIV services began to normalize on 8 September 2021, and did not fully normalize until 4 January 2022).

For each of the 32 MSAs, we conducted 1000 simulations under each scenario. For each simulation, we randomly sampled values of 4 parameters, representing the maximal effect of COVID-19, from uniform distributions:

1. Reduction in sexual transmission: 0 to 50% [3–7]
2. Reduction in viral suppression: 0 to 40% [9–12]
3. Reduction in HIV testing rate: 0 to 50% [4, 13, 14]
4. Reduction in PrEP usage (among those at risk): 0 to 30% [4, 15–17]

We based these ranges on published studies that characterized changes pre-pandemic to during the pandemic (most studies dated from early in the pandemic); we selected ranges broad enough to include the largest published estimates as well as no change. Indexing these effects to mobility data meant that the full reduction applied only in April 2020, and was less in subsequent months depending on how much local mobility trends approached pre-pandemic levels. As it is unclear how closely geographic mobility correlates with health-related behaviors, we randomly sampled a fifth parameter: the correlation between the reduction in HIV parameters and the change in mobility data, ranging from zero (the pandemic's effects have no correlation with mobility) to 1 (the pandemic's effects correlate perfectly with the monthly average change in mobility), as illustrated in Supplementary Figure 3.

Outcomes

Our primary outcome was the change in the projected number of incident infections from 2020 to 2025 compared with projections if the COVID-19 pandemic had not occurred:

$$\frac{\begin{array}{c}\mathit{infections}\ (2020\ \mathit{to}\ 2025)\ \mathit{in\ COVID\ scenario}\\ -\mathit{infections}\ (2020\ \mathit{to}\ 2025)\ \mathit{absent\ COVID}\end{array}}{\mathit{infections}\ (2020\ \mathit{to}\ 2025)\ \mathit{absent\ COVID}} \times 100\%$$

We also evaluated the projected annual incidence, reported diagnoses, and prevalence of HIV. For each outcome, we calculated the mean and 95% credible interval (CrI) as the 2.5th and 97.5th quantiles from 1000 simulations.

Sensitivity Analyses

We conducted probabilistic sensitivity analyses to estimate the influence of COVID-19–related reductions in sexual transmission, viral suppression, HIV testing, and PrEP use on HIV incidence. We calculated the Spearman correlation coefficient between each of the 4 COVID-19 parameters and our primary outcome across all 32 cities. We also compared the outcome in the 20% of simulations with a low value of each parameter to the 20% of simulations with a high value—both for each individual parameters and for 2-way combinations of influential parameters [20].

Web Tool

We developed an interactive, publicly available web tool at www.jheem.org?covid to visualize projected HIV incidence, prevalence, reported diagnoses, and mortality under each COVID-19 scenario and under user-customizable scenarios in each of the 32 MSAs.

RESULTS

Absent the COVID-19 pandemic, if pre-2020 trends in sexual behavior and healthcare utilization had continued, simulations projected 103 553 (95% CrI: 92 299–115 613) incident infections across all 32 MSAs from 2020 to 2025 (Figure 2 and Supplementary Figure 4). The "Prolonged Barriers to Care" scenario (in which sexual transmission returned to normal by 4 July 2021, but HIV testing, PrEP use, and viral suppression did not normalize until 4 January 2022) projected an average of 1161 more infections (1% more) than if COVID-19 had not occurred. The CrIs were wide, ranging from 11 872 (11%) fewer to 17 785 (17%) more cases. Projections depended strongly on the pandemic's effect on sexual transmission (Spearman correlation, −0.82), and the reduction in viral suppression (Spearman correlation, 0.48; see Figure 3 and Supplementary Figure 5). In

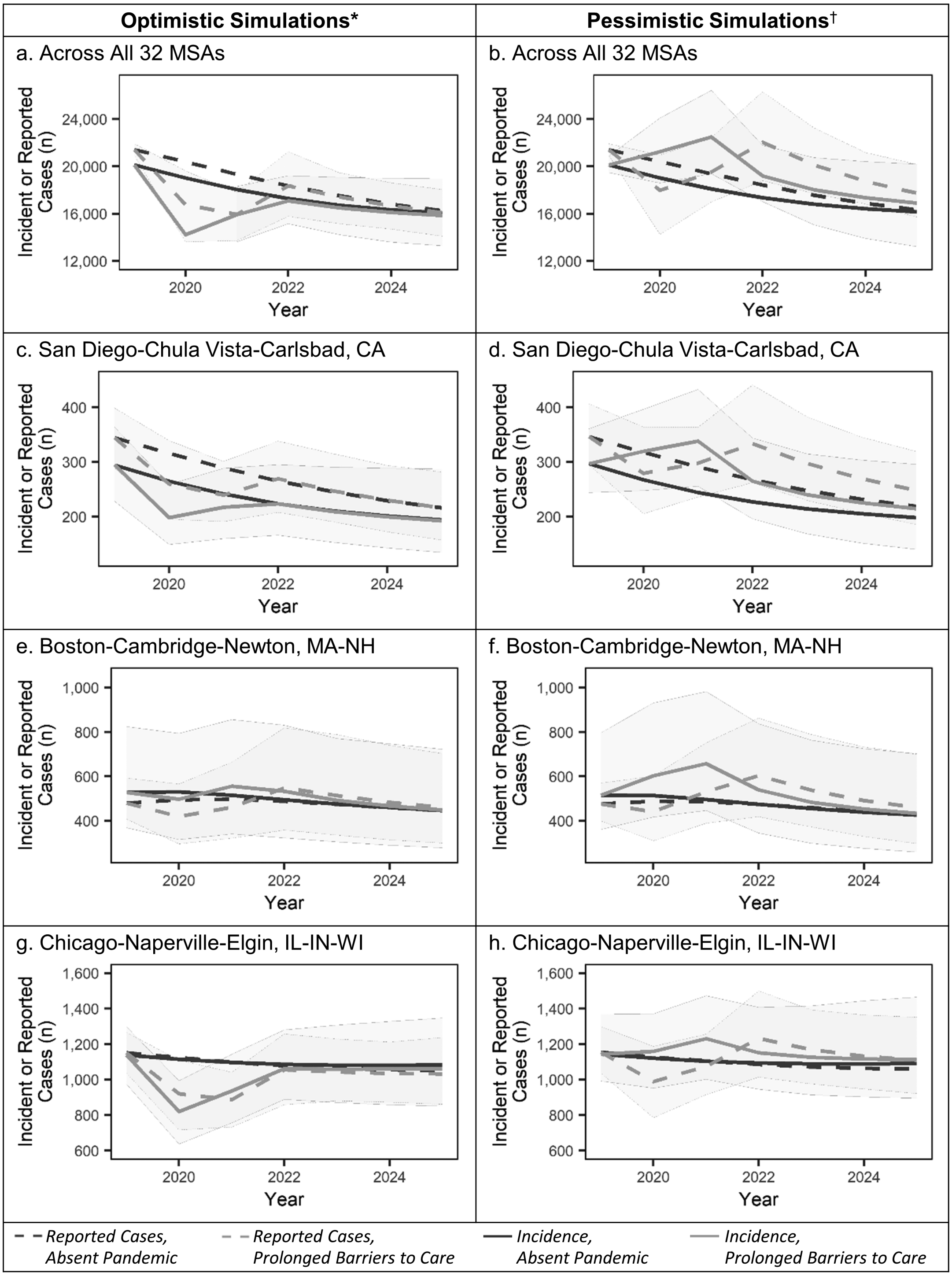

Figure 2. Projected incidence (solid lines) and reported diagnoses (dashed lines), according to potential effects of the COVID-19 pandemic on sexual transmission and viral suppression. *Optimistic simulations (panels *a*, *c*, *e*, and *g*) assume large (>30%) maximal reductions in sexual transmission and small (<20%) maximal reductions in viral suppression. †Pessimistic simulations (panels *b*, *d*, *f*, and *h*) assume small (<20%) reductions in sexual transmission and large (>20%) reductions in viral suppression. All simulations assume sexual transmission normalized by 4 July 2021; HIV testing, viral suppression, and PrEP use do not normalize until 4 January 2022 (the "Prolonged Barriers to Care" scenario). Gray lines indicate the mean projection taking into account the COVID-19 pandemic. The shaded ribbons indicate the 95% credible interval. Black lines illustrate projections if the COVID-19 pandemic had never occurred. Abbreviations: COVID-19, coronavirus disease 2019; HIV, human immunodeficiency virus; MSA, metropolitan statistical area; PrEP, pre-exposure prophylaxis.

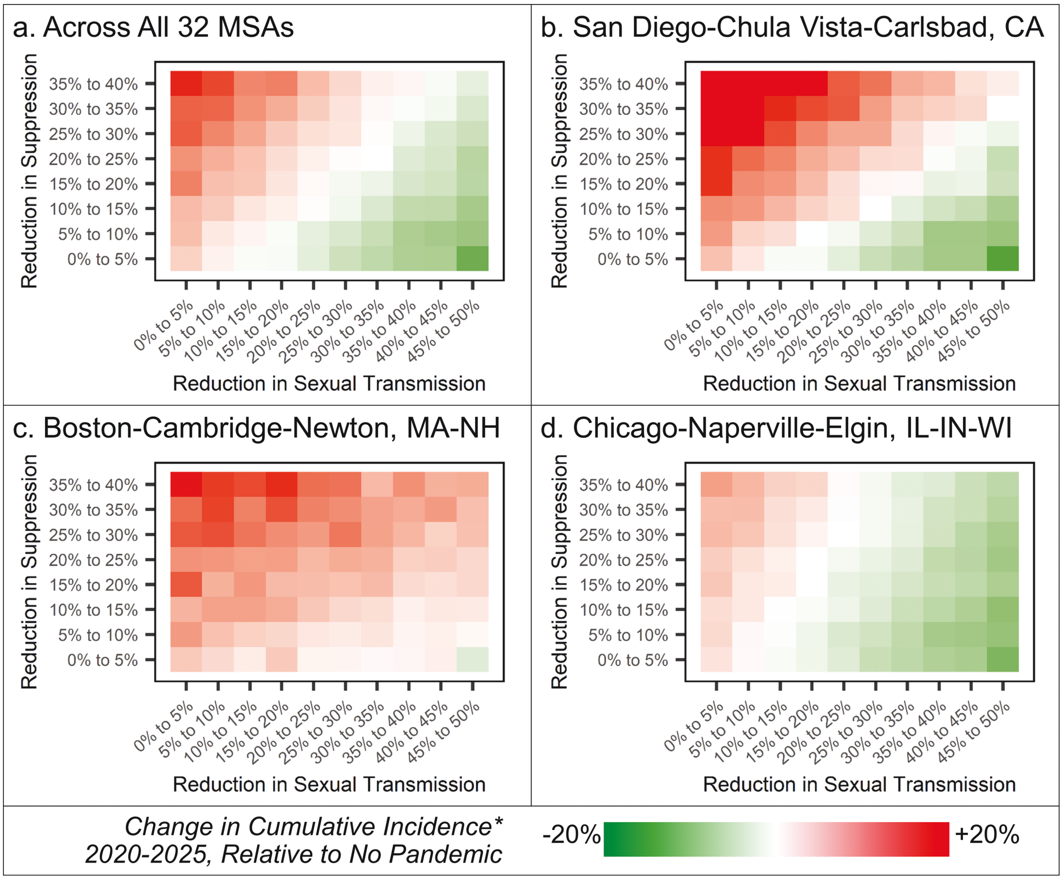

Figure 3. *a–d*, Impact of reductions in sexual transmission and viral suppression on cumulative HIV incidence 2020–2025. Each cell is shaded according to the average change in cumulative incidence from 2020–2025 for simulations whose parameters fall within the corresponding ranges. *The change in cumulative incidence is calculated as the cumulative projected incident infections from 2020–2025 under the COVID-19 scenario minus the cumulative incident infections if COVID-19 had not occurred, divided by the cumulative incident infections if COVID-19 had not occurred. Projections are from the Prolonged Barriers to Care scenario (sexual transmission normalized by 4 July 2021; HIV testing, viral suppression, and PrEP use do not normalize until 4 January 2022). Abbreviations: COVID-19, coronavirus disease 2019; HIV, human immunodeficiency virus; MSA, metropolitan statistical area; PrEP, pre-exposure prophylaxis.

"optimistic" simulations in which sexual transmission was reduced by more than 30% at the start of the pandemic and viral suppression was reduced by less than 20%, we projected an 8% decrease (95% CrI: 14% reduction to no change) in cumulative HIV incidence (2020–2025) versus if the COVID-19 pandemic had not occurred (Figure 2). In "pessimistic" simulations—if sexual transmission levels were largely maintained (<20% maximal reduction) but viral suppression fell by more than 20% at the pandemic's outset—HIV incidence was projected to be 11% greater (95% CrI: 1% to 21% greater).

The "Rapid Resumption of Care" scenario (in which HIV testing, PrEP use, and viral suppression all returned to normal by 4 July 2021 along with sexual transmission) resulted in an average of 3089 fewer infections than the "Prolonged Barriers to Care" scenario (95% CrI: 171 to 6838 fewer infections; Figure 4 and Supplementary Figure 4).

Across all 32 MSAs, more than 99% of simulations under both COVID-19 scenarios projected a decline in reported diagnoses in 2020 (mean: 19% reduction from 2019; 95% CrI: 3% to 36%) (Figure 2), before rebounding in either 2021 (61% of simulations) or 2022 (an additional 20% of simulations). The change in reported diagnoses did not correlate closely with projected incidence, especially in "pessimistic" simulations (Figure 2). "Pessimistic" simulations from the "Prolonged Barriers to Care" scenario projected a 16% average decrease in reported diagnoses from 2019 but a 5% increase in incidence. By 2022, incidence was decreasing by 14% from 2021 but reported diagnoses were up by 13%.

Both scenarios projected 2025 prevalence across all 32 MSAs to be no more than 0.5% different, on average (95% CrI: 9% less to 9% more), than if the pandemic had not occurred. The number of PWH with acute HIV peaked at 11% more in 2022 in the Prolonged Barriers to Care scenario than absent the pandemic (95% CrI: 11% less to 45% more) and was down to 2% greater by 2025. In the "Prolonged Barriers to Care" scenario, the projected proportion of new diagnoses who were acutely infected was 9% in 2020 and 2021 among "optimistic" simulations (decreased sexual transmission and maintained viral suppression)

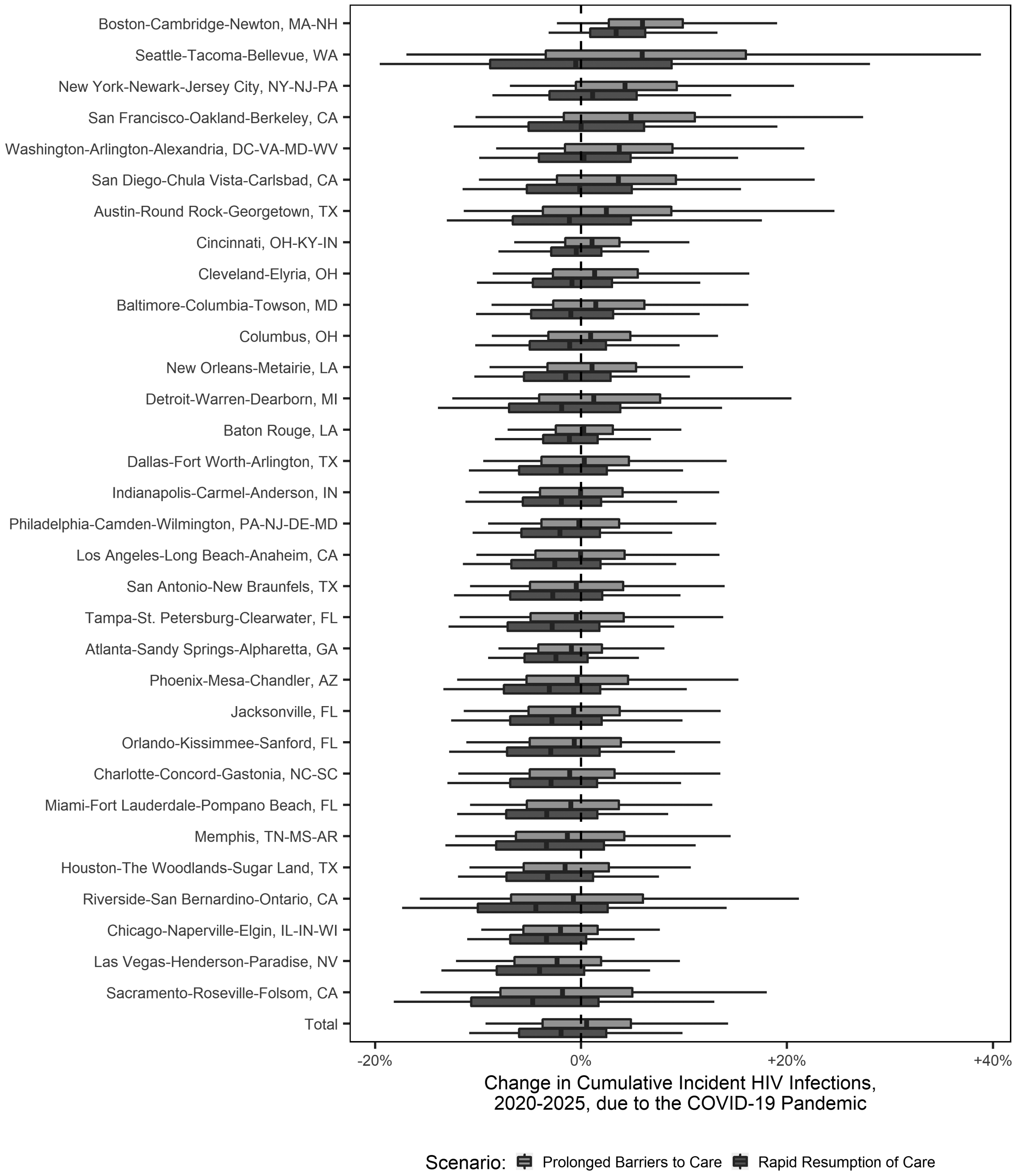

Figure 4. Change in cumulative projected incidence 2020–2025, under Prolonged Barriers to Care and Rapid Resumption of Care scenarios vs no pandemic, by metropolitan statistical area. Light gray = Prolonged Barriers to Care scenario (sexual transmission normalized by 4 July 2021; HIV testing, viral suppression, and PrEP use do not normalize until 4 January 2022); Dark gray = Rapid Resumption of Care scenario (sexual transmission, HIV testing, viral suppression, and PrEP use all normalize by 4 July 2021). The dark vertical lines represent the median across 1000 simulations of the change in cumulative incident HIV infections from 2020–2025, calculated as the projected incident infections from 2020–2025 under the COVID-19 scenario minus the incident infections if COVID-19 had not occurred, divided by the cumulative incident infections if COVID-19 had not occurred. The boxes denote the interquartile range, and the whiskers denote the 95% credible interval. Abbreviations: COVID-19, coronavirus disease 2019; HIV, human immunodeficiency virus; PrEP, pre-exposure prophylaxis.

compared to 12% in 2020 and 11% in 2019 among “pessimistic” simulations (maintained sexual transmission and decreased viral suppression); by 2022, all simulations projected that 10% of new diagnoses were among acutely infected individuals.

Projections of cumulative incidence from 2020 to 2025 varied substantially by city, ranging from 5% fewer infections than if the pandemic had not occurred (95% CrI: 24% fewer to 19% more) in Sacramento-Roseville-Folsom, California, under the Rapid Resumption of Care scenario to 9% more (21% fewer to 75% more) in Seattle-Tacoma-Bellevue, Washington, in the Prolonged Barriers to Care scenario (Figure 4). Some cities were more affected by changes in sexual transmission, while others were more susceptible to disruptions in viral suppression among PWH (Figure 3). Cities with higher levels of pre-pandemic suppression had a greater rise in incidence for a given degree of continuum disruptions than cities with lower suppression at baseline (Supplementary Figure 6). Detailed projections for all 32 MSAs are available in Supplementary Tables 8–25 and at www.jheem.org?covid.

DISCUSSION

We present a detailed model of HIV, calibrated to 32 US MSAs, that explores the impact of the COVID-19 pandemic on HIV transmission. Our simulations indicate that potential effects of COVID-19 on the US HIV epidemic span a wide range of possibilities: in "optimistic" simulations where sexual transmission decreased and access to healthcare was largely maintained, we projected 7754 (8%) fewer infections than if the pandemic had not occurred (95% CrI: 14% fewer infections to no change), while "pessimistic" simulations—if sexual transmission did not change greatly and the HIV continuum of care was significantly disrupted—projected 11 323 (11%) more infections (95% CrI: 1% to 21% more). Metropolitan statistical area–level projections showed differing susceptibility to the pandemic's effects, with average estimates ranging from 5% fewer infections in Sacramento, California, to 13% more in Seattle, Washington. Interactive, city-level projections are available at www.jheem.org?covid.

Our simulations also suggest that reported diagnoses are likely to fall in 2020–2021 and subsequently rebound, whereas incidence may either rise or fall. Similarly, most simulations projected a subsequent rebound in diagnoses 1 to 2 years later, even if incidence was decreasing, reflecting diagnoses from a "reservoir" of undiagnosed cases built up during the height of the pandemic. Our results thus demonstrate that trends in HIV diagnoses in the years during and immediately following the COVID-19 pandemic cannot be used to infer its impacts on underlying incidence.

In light of these uncertainties, it will be critical to look beyond standard HIV reporting outcomes to understand the trajectory of the HIV epidemic in the years during and after the COVID-19 pandemic. Changes in reporting of other sexually transmitted infections (STIs)—particularly symptomatic STIs (gonorrhea and primary and secondary syphilis)—may provide an approximation of changes in sexual transmission [33]. As HIV diagnosis is often made several years after infection [34], reductions in the volume of HIV tests (which decreased by 17.5% in March to October 2020 compared with March–October 2019) [13] are likely to reflect a decrease in screening rather than a decreased need for tests, and give a sense for diagnostic delays.

The effects of the COVID-19 pandemic on the HIV continuum of care and viral suppression will be challenging to discern. The onset of the pandemic precipitated an abrupt shift towards telemedicine; while many sites have reported positive effects on engagement, ongoing evaluation of how this engagement translates to retention, adherence, and maintenance of viral suppression over the medium to long term is necessary [35, 36]. Individual clinics have reported a range of effects on the proportion of viral loads that are suppressed (ranging from no change to 31% decrease [8–10]). Complicating these data, the volume of viral load tests performed in PWH dropped substantially (up to 50% during the early phases of the pandemic) [13, 14, 37], and further studies will be needed to determine if this indicates lower rates of suppression or maintained suppression in the face of decreased monitoring.

A few other models have explored the local effects of the COVID-19 pandemic on HIV. Zang et al [21] projected a 16.5% decrease in incidence across 6 US cities if risk behaviors decreased by 50% but HIV care remained unchanged, compared with a 9% increase if risk behaviors stayed the same but access to care decreased by 50%. Jenness et al [22] projected minimal effects on HIV incidence when the pandemic's effects on transmission behaviors and HIV care were similar. Mitchell et al [23] projected smaller changes to cumulative incidence among men who have sex with men in Baltimore: a 3% decrease for a 25% reduction in sexual partnerships and a 1.5% increase for a 10% reduction in viral suppression. The results from Zang and Jenness are similar to ours, and all 3 studies illustrate the opposing effects of interruptions to HIV care versus alterations of transmission behaviors. Our study expands the previous results by making projections for 32 US cities and indexing the pandemic's effects to local mobility data—highlighting that some cities are more vulnerable to negative impacts of the pandemic. We also project the trajectory of reported diagnoses and how it is likely to diverge from incidence in the coming years.

Our study has some limitations. First, the effects of COVID-19 on HIV care and transmission remain unclear; we based our estimates on studies largely done during the early phases of the pandemic in specific risk groups and extrapolated through 2020 and 2021. We incorporated uncertainty around this extrapolation by (1) sampling a broad range of possible effects and (2) indexing to mobility data. However, if the early pandemic's effects differ systematically from the late pandemic beyond what is suggested by mobility, the true impact on HIV incidence may skew to the lower or higher end of our projections. Second, our single parameter for "decrease in sexual transmission" collapses the number and types of sexual partnerships and encounters per partnership into 1 effect. However, the pandemic may have had different effects on long-term compared with casual partnerships. Our parameter models an average effect across all sexual encounters in a population but may under- or overestimate the effects in subgroups where partnerships skew heavily towards either casual or long-term relationships. Third, our model collapses the HIV continuum of care into suppressed compared with unsuppressed and is thus unable to project the pandemic's effects on continuum engagement. Fourth, we assumed that the effects of the COVID-19 pandemic are uniform across all strata of age, race, sex, and HIV risk factors. In reality, COVID-19 is likely to have a disproportionate effect on HIV control in disadvantaged subgroups [36]; our projections may understate the impacts of COVID-19 if its effects are heavily concentrated in a small subgroup. Last, we do not explicitly incorporate potential effects of the rise of variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). If variants impair access to healthcare at the end of 2021 and early 2022 without greatly impacting sexual transmission, our "Prolonged Barriers to Care" scenario may be accurate, but if the effects of the Delta or other variants persist throughout 2022, then our projections will understate the total impact of the COVID-19 pandemic. Our web tool can address some of these limitations by allowing users to generate projections with different effects or time frames as further data become available.

In summary, this analysis illustrates that the effects of the COVID-19 pandemic on the HIV epidemic in the United States remain uncertain and that cities are differentially susceptible to its effects. The pandemic is also likely to alter the relationship between reported diagnoses and underlying incidence in the coming years, further complicating our ability to understand its impact on HIV transmission. Close attention to data on other STIs and the volume of HIV testing may help to separate incidence trends from pandemic-related delays in diagnosis. Minimizing disruptions to the HIV continuum of care will be critical to mitigating negative effects of the COVID-19 pandemic on HIV transmission.

Supplementary Data

Supplementary materials are available at *Clinical 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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