Published in final edited form as:
Lancet HIV. 2018 October ; 5(10): e569–e577. doi:10.1016/S2352-3018(18)30176-0.

Dynamics of the HIV Outbreak and Response in Scott County, Indiana, 2011-2015: A Modeling Study

Gregg S. Gonsalves, PhD and
Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, CT, USA

Yale Law School, New Haven, CT, USA

Forrest W. Crawford, PhD
Biostatistics, Yale School of Public Health, New Haven, CT, USA

Ecology and Evolutionary Biology, Yale University, New Haven, CT, USA

Operations Program, Yale School of Management, New Haven, CT, USA

Summary

Background: In November 2014, a cluster of HIV infections was detected among people who inject drugs in Scott County, Indiana, with a total of 215 HIV infections eventually attributed to the outbreak. This study examines whether earlier implementation of a public health response would have diminished the scale of the outbreak.

Methods: We derived weekly case data from the outbreak and on the uptake of HIV testing, treatment and prevention services from publicly available reports on the outbreak from CDC and researchers in Indiana. We computed upper and lower bounds for cumulative HIV incidence by digitally extracting data from published images from a CDC study using a Bio-Rad avidity incidence testing to estimate the recency of each transmission event. Using this publicly available information, we constructed a generalization of the susceptible-infectious-removed model to capture the transmission dynamics of the HIV outbreak. We computed nonparametric interval estimates of the number of undiagnosed HIV infections, the case-finding rate per undiagnosed HIV infection, and model-based bounds for the HIV transmission rate throughout the epidemic. This allowed us to assess the potential impact of earlier implementation of a response to the outbreak.

Findings: The upper bound for undiagnosed HIV infections in Scott County peaked around January 10, 2015 at 126 undiagnosed cases, over two months before Governor Pence declared a public health emergency on March 26, 2015. Applying the observed case-finding rate scale-up to earlier intervention times suggests that an earlier public health response could have substantially reduced the total number of HIV infections. Initiation of a response in January 2013 would have

Corresponding author: Gregg S. Gonsalves, Yale School of Public Health, 60 College Street, New Haven, CT, 06510; gregg.gonsalves@yale.edu; phone: +1-203-606-9149.
Authors' contributions
GSG conceived the study and wrote the majority of the manuscript; FWC wrote the supplement, analytical software, and web application. GSG had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests
The authors state that they have no conflict of interest.

suppressed the total number of infections to fewer than 56, representing at least 127 infections averted, while an intervention in April 2011 could have reduced the number of infections to fewer than ten, representing at least 173 infections averted.

Interpretation: Early and robust surveillance efforts and case finding alone could blunt nascent epidemics. Ensuring access to HIV services and harm reduction interventions could further reduce the likelihood of outbreaks, and more substantially mitigate their severity and scope.

Funding: This study was funded by the National Institutes of Mental Health, the National Institute on Drug Abuse, the National Institutes of Health Big Data to Knowledge (BD2K) and the NIH Director's New Innovator Award programs.

Research in Context

Evidence before this study

Peters et al provided the initial report of the Indiana HIV Outbreak Investigation Team, outlining the outbreak and investigation, providing the time series of HIV diagnoses in Scott County, IN during 2014–2015, along with a contact tracing network and a reconstruction of the phylogenetic tree of sampled HIV gene sequences. In a subsequent study, Campbell et al analyzed recency assay results to infer dates of individual infection, and thereby bounds on cumulative HIV incidence during the outbreak. We searched the English language scientific literature using Google Scholar and the general literature using Lexis-Nexis from December 2014 through July 2018 to identify claims about the response to the outbreak using the following search terms alone and in combination: "Scott County"; HIV; outbreak; prevention; timing. Commentaries, newspaper articles, and editorial contributions have suggested that the outbreak could have been avoided with earlier introduction of harm reduction and HIV services (Strathdee and Beyrer; Rich and Adashi), while some public health officials (Adams) expressed skepticism. Claims about what would have happened in Scott County under different intervention circumstances have not previously been evaluated using the available incidence and diagnosis data.

Added value of this study

By analyzing publicly available epidemiological data collected during the outbreak response by CDC investigators, this study provides the first quantitative evidence that the number of undiagnosed HIV infections had already fallen substantially by the time a public health emergency was declared and SEP implemented. Using a generalization of a canonical mathematical model of infectious disease transmission, we show that HIV incidence over the course of the actual outbreak could have been dramatically reduced by earlier scale-up of case-finding.

Implications of all the available evidence

The CDC has declared 220 counties across the United States at risk for outbreaks of HIV and HCV associated with injecting drug use (Van Handel et al). The public policy response to the outbreak in Scott County IN from 2014–2015 offers a case study in management of an emerging epidemic. The deployment of HIV and harm reduction services in counties and other locales at risk for new outbreaks could avoid their emergence altogether or lessen their epidemiological impact.

Introduction

Scott County, Indiana was the site of an explosive outbreak of HIV infection in 2014–2015 among people who inject drugs (PWID).[1] On November 18, 2014, the first HIV case in Scott County attributed to this outbreak was diagnosed. An investigation by Indiana State Deparment of Health (ISDH) began on January 23, 2015, by which time 17 new HIV cases had been recorded.[1] Two months later, on March 23, 2015 a team of CDC investigators arrived in Scott County. On March 26, 2015, Indiana declared a public health emergency, allowing a temporary SEP to be established in the county. An HIV testing clinic opened on March 31, 2015.[1] SEP is known to reduce HIV transmission among PWID, and does not encourage drug use.[2] After consultations with ISDH, CDC and local law enforcement, Indiana Governor Mike Pence announced Executive Order (EO) 15–05 on April 4, 2015 declaring a public health emergency, authorizing Scott County to set up a temporary SEP for 30 days.[3] Implementation of SEP in Scott County may have been further delayed by conflicts with police officers who initially confiscated syringes.[4] On May 5, 2015, Governor Pence signed a bill allowing Indiana counties to apply to establish SEP if they could establish that a public health emergency existed.[5] These exchanges were to be temporary and did not receive state support.[3] The same day, Governor Pence signed a bill that upgraded possession of a syringe (with intent to commit a controlled substance offense) from a misdemeanor to felony charge, subject to imprisonment of up to two and a half years, to go into effect July 1, 2015.[6] By March 2017, a total of 215 HIV cases had been attributed to the outbreak.[7]

Although Governor Pence eventually authorized state officials to establish programs to prevent new HIV infections and treat those with the disease, questions about the timing and scale of the response remain.[3,8,9] Researchers have suggested that the public health response to the Scott County outbreak was not implemented in time to avert a severe epidemic, and that the majority of infections occurred prior to the declaration of a public health emergency and establishment of the response to control the outbreak in late March 2015.[10,11] Criticism of the official response, and policy prescriptions for future outbreaks, are predicated on counterfactual claims about what would have happened in Scott County, had public health intervention campaign been implemented earlier.[8,9] Campbell et al suggest that “Had an SSP [syringe service program] been in place prior to recognition of the outbreak, the explosive phase of the outbreak may have been blunted”[10]; Rich et al make the stronger assertion that “what happened in Indiana was predictable and avoidable”.[9] In a recent article, researchers from ISDH, Indiana University, the Scott County Health Department and CDC suggest that “proactive establishment of SSPs in nonurban communities with PWID might help to prevent future outbreaks of HIV”.[12] In response to claims that the outbreak would have been prevented had a SEP been implemented earlier, Jerome Adams, Indiana State Health Commissioner at the time, pointed to evidence that many cities with active SEP also have high HIV prevalence: “My colleagues and I will never know — though HIV infection remains rampant in many urban areas that have needle-exchange programs”.[13]

Would an earlier public health response, implemented before November 2014, have reduced the size of the outbreak in Scott County? Answering this question requires insight into the outbreak dynamics that would have occurred if—contrary to fact—a public health response had been implemented earlier. In this paper, we use two types of data—published time series of HIV diagnoses in Scott County and associated estimated HIV infection dates based on recency assay results—to reconstruct the dynamics of the Scott County HIV outbreak and the public health response, from 2011 to 2015. We seek to determine whether earlier implementation of a public health response like that actually enacted would have diminished the scale of the outbreak. We focus this analysis on earlier implementation of HIV case-finding; there are no publicly available data on the effects of other interventions deployed during the outbreak. Because SEP and other harm reduction interventions are known to reduce HIV transmission, our results may be interpreted as providing a lower bound on the impact of a hypothetical earlier comprehensive response to the outbreak.[2] Though our analysis is focused on the Scott County outbreak, understanding the dynamics of the outbreak and response in Indiana may permit policymakers to mitigate future outbreaks among PWID in other locations. The CDC has declared 220 counties across the United States at risk for outbreaks of HIV and HCV associated with injecting drug use.[14] Furthermore, recent outbreaks of HIV among PWID have been documented in Romania, Hungary, Greece, Israel, Ireland and Scotland.[15]

Methods

Data Sources

We obtained weekly case data from the 2014–2015 outbreak from a report by the Indiana HIV Outbreak Team.[1] We derived data on the uptake of HIV testing, treatment and prevention services from the Indiana Outbreak Team and a subsequent review of the outbreak.[1,16] Cases related to the outbreak were laboratory-confirmed infections diagnosed after October 1, 2014 in residents of Scott County, Indiana or their syringe-sharing or sexual partners, through November 1, 2015. In separate work, CDC investigators subjected serum and plasma samples from the individuals infected in the outbreak to Bio-Rad avidity incidence (BRAI) testing to estimate the recency of each transmission event.[10] The BRAI test is an enzyme-linked immunosorbent assay modified to permit measurement of antibody avidity.[17] Researchers used historical data on the relationship between avidity result post-diagnosis and dates of confirmed negative HIV test results to develop estimated dates of infection for the individuals in the outbreak.[10] We estimated upper and lower bounds for cumulative HIV incidence by digitally extracting data from published images.[10,18]

Mathematical Model

We constructed a generalization of the classical susceptible-infectious-removed (SIR) model to capture the transmission dynamics of the HIV outbreak in the community of PWID in southeastern Indiana.[19] Consider a PWID population of size N in which each individual can be classified into one of four categories. At time t, let $S(t)$ be the number of susceptible (HIV-negative) PWID, $I_{udx}(t)$ the number of HIV+ but undiagnosed individuals, $I_{dx}(t)$ the number of HIV+ diagnosed individuals, and $R(t)$ the number of removed individuals who are

HIV+ diagnosed and virally suppressed or no longer engaging in epidemiologic contact sufficient to transmit HIV infection. The population is closed so that $S(t) + I_{udx}(t) + I_{dx}(t) + R(t) = N$ for every t. Susceptible individuals become infected with a rate equal to product of the transmission rate β and the number of infectious individuals in the population, $\beta\left(I_{udx}(t) + I_{dx}(t)\right)$. Infectious individuals are diagnosed with rate $\gamma(t)$, and HIV+ diagnosed individuals are "removed" with rate ρ from the pool of infectious individuals. In this context, removal may indicate viral suppression following initiation of anti-retroviral therapy (ART), or cessation of epidemiologic contact (e.g. sharing needles, unsafe sex) sufficient to transmit HIV infection. Provision of clean injection equipment by SEP to HIV+ individuals is one mechanism by which a transition from I_{dx} to R may occur.[12] The dynamic model is described by the system of ordinary differential equations

$$\frac{dS}{dt} = -\beta S(t)\left(I_{udx}(t) + I_{dx}(t)\right)$$

$$\frac{dI_{udx}}{dt} = \beta S(t)\left(I_{udx}(t) + I_{dx}(t)\right) - \gamma(t) I_{udx}(t)$$

$$\frac{dI_{dx}}{dt} = \gamma(t) I_{udx}(t) - \rho I_{dx}(t)$$

$$\frac{dR}{dt} = \rho I_{dx}(t)$$

for $\beta > 0$, $\rho > 0$, and a possibly time-varying non-negative function $\gamma(t)$.

Reconstructing outbreak dynamics

We computed nonparametric interval estimates of the number of undiagnosed HIV infections, the case-finding rate per undiagnosed HIV infection, and model-based bounds for the HIV transmission rate throughout the epidemic. Using the time series of cumulative HIV diagnoses, we reconstructed the cumulative diagnoses curve $D(t)$. From the inferred infection dates based on recency assay results we obtained lower and upper bounds $\underline{C}(t)$ and $\bar{C}(t)$ for the cumulative HIV incidence $C(t)$.[10] Recency assays are still in the developmental phase. While their use in calculating incidence estimates has been refined, questions still remain about their accuracy.[17] In the Appendix (pages 8–9), we analyze the sensitivity of results to increasing uncertainty in infection times by scaling the incidence bounds.

Limited information is available on the number of individuals N (i.e. population of PWID and their sexual partners) during the outbreak. However, the CDC investigation reported a network of $N = 536$ individuals infected or at risk during the outbreak.[1] In the following analysis, we assume $N = 536$ is fixed, and analyze the sensitivity of results to different values of N in the Appendix (pages 5–6). Likewise, the rate of removal or viral suppression is not known with certainty; we set $\rho = 0{\cdot}024$ removals per diagnosed individual per day for the analyses presented below. In the Appendix (pages 5–7), we explain this choice of ρ and analyze the sensitivity of results to different choices of ρ.

The number of undiagnosed HIV infections at time t is the cumulative number of infections by time t minus the number of diagnosed infections, $I_{udx}(t) = C(t) - D(t)$, and the number of susceptible individuals at time t is $S(t) = N - C(t)$. We obtain lower and upper bounds for $I_{udx}(t)$ and $S(t)$ from the equivalences

$$\underline{I}_{udx}(t) = \underline{C}(t) - D(t)$$

$$\bar{I}_{udx}(t) = \bar{C}(t) - D(t)$$

$$\underline{S}(t) = N - \bar{C}(t)$$

$$\bar{S}(t) = N - \underline{C}(t)$$

We reconstructed the time-varying case-finding rate $\gamma(t)$ by considering the rate of diagnoses as a function of the number of undiagnosed infections, $\gamma(t)dt = dD(t)/I_{udx}(t)$. We calculated lower and upper bounds for $\gamma(t)$ as $\underline{\gamma}(t)dt = dD(t)/\bar{I}_{udx}(t)$ and $\bar{\gamma}(t)dt = dD(t)/\underline{I}_{udx}(t)$. Lower and upper bounds for the overall transmission rate β were computed by dividing the number of infections by the cumulative transmission risk, $\beta = (C(t) - C(0))/\int_0^t S(u)\left(I_{udx}(u) + I_{dx}(u)\right)du$. We constructed a continuous interpolation of these data on a daily timescale by fitting a cubic smoothing spline. This allowed us to compute bounds for cumulative HIV incidence, cumulative diagnoses curve, and bounds for the number of HIV+ undiagnosed individuals (Figure 1). Additional model details are provided in the Appendix (pages 1–3).

Evaluation of counterfactual intervention scenarios

Let t_s denote the date of the first HIV diagnosis in Scott County, November 8, 2014, and let t_e be a later date at which a target case-finding scale-up rate was achieved. For a hypothetical earlier date $t_s^* < t_s$, define the counterfactual case-finding rate $\gamma^*(t)$ as

$$\gamma^*(t) = \begin{cases} \gamma(t) & if \quad t < t_s^* \\ \gamma\left(t_s - t_s^* + t\right) & if \quad t_s^* \le t < t_s^* - t_s + t_e \\ \gamma\left(t_e\right) & if \quad t_s^* - t_s + t_e \le t \end{cases}$$

Define $\underline{\gamma}^*(t)$ and $\bar{\gamma}^*(t)$ by substituting $\underline{\gamma}(t)$ and $\bar{\gamma}(t)$ respectively for $\gamma(t)$ above. The resulting case-finding rate is equal to the true case-finding rate during the actual outbreak response, shifted to the earlier starting date t_s^*, and set equal to a desired target case-finding rate thereafter. Under the mathematical model specification, the model output with $\underline{\gamma}^*(t)$ or $\bar{\gamma}^*(t)$ in place of $\underline{\gamma}(t)$ or $\bar{\gamma}(t)$ respectively delivers the dynamics that would have occurred if, contrary to fact, the public health response had been implemented at the earlier date t_s^*, including the reconstructed bounds for the case-finding rate in the actual response, and a counterfactual case-finding rate under intervention on January 1, 2013 (Figure 2).

Because changes in the transmission or removal rates cannot be estimated directly from publicly available data, we conceptualize the public health response as an intervention on $\gamma(t)$ alone, and not on the HIV transmission rate β, or removal/suppression rate ρ. This approach gives conservative projections of HIV incidence under counterfactual intervention scenarios because it does not make assumptions about possible reduction in transmission or increases in the rate of viral suppression. However, because an intervention on the HIV transmission rate β, such as SEP, is of particular interest, we analyze the sensitivity of results to reduction of β in the Appendix (pages 8–9).

We selected two counterfactual values of t_s^* for the beginning of diagnostic scale-up to explore in this study, which reflect two potential opportunities that could have been available for intervening to prevent an HIV outbreak in Indiana: 1) April 3, 2011, just after an HCV outbreak in several counties in the state in 2010–2011,[20,21] and around the estimated time of the first HIV infection; and 2) January 1, 2013, around the time of the closure of the sole local HIV testing facility in Scott County.[3,8] We examine the total number of HIV infections that might have occurred if an earlier case-finding response had been implemented with the same scope and scale as the actual disease control effort initiated in 2015.

Data Sharing

We developed a web-based application for interactive evaluation of counterfactual response scenarios for the Scott County outbreak, using the R statistical language (R 3.4.4) and the "shiny" web development framework (Shiny 1.1.0).[22,23] The application was used to calculate the outbreak dynamics described below and permits choice of hypothetical earlier dates for scale-up of case-finding. The application is available at https://forrestcrawford.shinyapps.io/indiana-hiv. The source code is freely available for download and modification under the MIT license at https://github.com/fcrawford/indiana-hiv.

Role of the funding source

The funders had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

Results

The upper bound for undiagnosed HIV infections in Scott County peaked around January 10, 2015, with between 77 and 126 undiagnosed cases, and subsequently decreased rapidly; there were between 27 and 74 undiagnosed cases on March 26, 2015, when Governor Pence declared a public health emergency (Figure 1). These dynamics indicate that, as Campbell et al assert, the outbreak had substantially declined by the time public health response measures were implemented.[12] These bounds are nonparametric and can be computed directly from available data; validity of the bounds does not depend on model assumptions, nor does it require knowledge of the size N of the PWID risk population. The case-finding rate per undiagnosed HIV infection $\gamma(t)$ varied dramatically over the course of the outbreak, with the peak case-finding rate occurring midway through the outbreak, and declining rapidly in the Spring and Summer of 2015 (Figure 2).

We reconstructed upper and lower bounds for the transmission rate β as a function of the product of the number of susceptible HIV- and undiagnosed HIV+ individuals, for fixed population size N. We likewise computed bounds for the number of susceptible HIV- individuals, the number of undiagnosed HIV+ individuals, and the number of diagnosed HIV+ individuals. Beginning on the date of the first HIV diagnosis, we used the model to estimate upper and lower bounds for the number of susceptible HIV-negative, undiagnosed HIV+, and diagnosed HIV+ individuals up to August 2015. The model projections starting on November 18, 2014 for the $N = 536$ PWID and their partners identified in a contact-tracing investigation during the outbreak closely match the actual epidemiological dynamics for the outbreak (Figure 3).[1] The transmission rate for the assumed population size of $N = 536$ varies from 4×10^{-6} to 3×10^{-5} infections per susceptible-infectious pair per day. The Appendix (pages 4–5) shows that these bounds are similar to estimates computed using published data from the Scott County outbreak and other studies of HIV risk for injection drug users. The reconstructed case-finding rate ranged between zero and 0·035 diagnosed cases per undiagnosed HIV infection per day during the response.

In a counterfactual scenario of intervention on January 1, 2013, cumulative HIV incidence by August 2015 is projected to be between 0 and 56 people, compared to an estimated 183–184 infections, representing at least 127 infections averted (Figure 4). When the scale-up of case-finding starts at the beginning of April 2011 (not shown), cumulative HIV incidence in August 2015 is projected to be between 0 and ten people, representing at least 173 infections averted.

We examined projected bounds for cumulative HIV cases (by August 2015), as a function of the date of case-finding scale-up. Earlier intervention times produce lower projected cumulative HIV incidence (Figure 5). In the Appendix (page 5–9) we present a sensitivity analysis to assess the dependence of model-based results to the total HIV risk population size N, uncertainty in cumulative incidence bounds, removal rate, and a possible effect of intervention on β.

Discussion

The analyses presented in this paper—applying the observed case-finding patterns during the actual response to hypothetical earlier intervention times under simple epidemic model—lend support to claims that the HIV epidemic in Scott County might have been prevented or mitigated with an earlier response. The infection recency data from the CDC show that the initial infections that gave rise to the Scott County outbreak were not detected for several years. Even after these first infections spread into an epidemic in 2014, it took months for an outbreak to be recognized, and a year for a response to be initiated in earnest.[1,12] Our analyses show that the SEP initiative started after the peak in undiagnosed HIV infections.[1,12]

Warning signs that an HIV outbreak could occur in the region were well-known at the time. Rising rates of prescription drug abuse and overdoses in Indiana have been documented since 2004 though the establishment of new opioid agonist therapy programs were forbidden under a state ban.[24,25] Local experts recommended as early as 2008 that SEP programs be established to prevent infectious disease outbreaks associated with injection drug use.[26–28] Even after an outbreak of HCV occurred among PWID in Indiana in 2010–2011, these recommendations remained unheeded.[20,21] In addition, the sole HIV testing provider in southeastern Indiana closed in 2013 due to state funding cuts, which may have delayed the diagnosis of the initial case of HIV infection in Scott County.[3,8]

There are several potential limitations to our analyses. First, the epidemic model with time-varying removal rate may not capture the complex dynamics of a real-life HIV outbreak among PWID. Simple models, however, can often capture the essential epidemiological features of an outbreak and additional complexity requires information about the parameters of an outbreak that may not be available in the early stages of an epidemic.[29] In addition, complex models may be mathematically intractable, difficult to validate, or challenging to understand.[30] The mathematical model used to compute counterfactual outbreak trajectories uses a combination of available data and variable parameters informed by prior studies. The framework employed here is designed to rely on credible assumptions and to be robust to imperfect knowledge of HIV incidence over the course of the outbreak.

Second, the model-based evaluations of earlier intervention dates require that the total size of the PWID population N is known. In reality, the true risk population in Scott County may have consisted of PWID only, PWID and their injecting and sexual partners, or a broader group of people. Because the incidence rate β is estimated conditional on N, and model dynamics depend on N and β, projections under counterfactual intervention scenarios are relatively insensitive to the choice of N. A sensitivity analysis, presented in the Appendix (pages 5–9), shows these results.

Third, our construction of the Scott County outbreak dynamics assumes that some HIV+ diagnosed individuals could have contributed to transmission of infection to HIV-individuals, but diagnosed individuals were "removed" from the pool of infectious people with rate ρ. Empirical research supports this assumption: HIV diagnosis can reduce transmission risk behaviors, including needle sharing and unprotected sex.[31] Furthermore, antiretroviral therapy (ART) following HIV diagnosis reduces viral load and can thereby diminish the risk of transmission to susceptible needle-sharing or sexual partners.[32,33] If PWID in Scott County did not change their behavior following HIV diagnosis, or if ART initiation/adherence did not occur rapidly, projections could underestimate HIV incidence under counterfactual earlier intervention scenarios.

Fourth, we have not modeled the effect of interventions such as education or SEP on the transmission rate β. We have evaluated the impact of reductions in β in a sensitivity analysis presented in the Appendix (pages 4–5). Unlike the case-finding rate $\gamma(t)$, we cannot attribute changes in the reconstructed transmission rate during the outbreak response to any particular feature of the response (e.g. SEP) with certainty. We have also not modeled intervention-related changes in the effects of SEP on the removal rate ρ for HIV+ diagnosed individuals. Although SEP and other harm reduction interventions can contribute to the cessation of infectious contact, thus increasing ρ (and γ), no data on behavior change from the Scott County outbreak were publicly available. For this reason, projected HIV incidence in these scenarios may be conservative: since SEP can reduce HIV transmission among PWID and does not encourage drug use, implementation of SEP alongside case-finding (i.e. reducing β, increasing ρ) would likely reduce projected cumulative HIV incidence to levels even lower than we have suggested.[2]

Finally, reconstruction of epidemic dynamics using a deterministic mathematical model requires smoothing of the observed trajectories of infections and diagnoses. While the smoothed projections adhere closely to observed trajectories under the actual intervention, this smoothing operation may obscure salient dynamics at finer timescales.

Despite these caveats, the conservative nature of our approach—using actual data on diagnoses, nonparametric bounds for cumulative incidence, and not assuming an effect of SEP on the transmission rate—suggests that had the interventions deployed in Scott County in 2014–2015 been available earlier, the outbreak might have been substantially blunted. While the model presented here is specific to the events in Scott County, our findings may have broader implications. Recent HIV outbreaks among PWID in Europe, and the ongoing risk of similar outbreaks in the US, highlight the public health implications of this examination.[14,15] Future HIV outbreaks could be minimized if HIV testing and treatment are available in places vulnerable to the transmission of blood borne infections among PWID.[14] SEP and use of opioid agonist therapy are critical HIV prevention tools that could offer the chance to prevent new outbreaks among PWID in the first place.[8]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We are grateful to Ellsworth M. Campbell, William M. Switzer, A. David Paltiel, Edward H. Kaplan, Paul D. Cleary, Olga Morozova, Lauretta E. Grau, Alexander Bazazi, and Jeff Hoover.

GSG was funded by the National Institutes of Mental Health (R01MH105203), the National Institute on Drug Abuse (R01 DA015612). FWC was funded by NIH grant 1DP2 HD091799–01.

References

1. Peters PJ, Pontones P, Hoover KW, et al. HIV Infection Linked to Injection Use of Oxymorphone in Indiana, 2014–2015. N Engl J Med 2016; 375: 229–239. [PubMed: 27468059]
2. Fernandes RM, Cary M, Duarte G, et al. Effectiveness of needle and syringe Programmes in people who inject drugs - An overview of systematic reviews. BMC Public Health 2017; 17: 309. [PubMed: 28399843]
3. Golding NJ. The Needle and the Damage Done: Indiana's Response to the 2015 HIV Epidemic and the Need to Change State and Federal Policies Regarding Needle Exchanges and Intravenous Drug Users. Ind Health Rev 2017; 14: 173–266.
4. Ernst A Are local Indiana authorities sabotaging efforts to halt HIV outbreak? Al Jazeera Am. 2015; published online April 18. http://america.aljazeera.com/watch/shows/america-tonight/articles/2015/4/18/indiana-hiv-needles.html (accessed Nov 22, 2017).
5. Assembly IG. Senate Bill 461 - Health matters. Indiana Gen. Assem https://iga.in.gov/legislative/2015/bills/senate/461 (accessed Nov 13, 2017).
6. Legend drug injection devices; violation. 2015 http://iga.in.gov/static-documents/4/b/a/9/4ba9c579/2015%20ACTS.pdf.
7. Brooks JT. Emerging epidemics: will they derail progress? Rural HIV-HCV related epidemics in the US In: IAS Conference on HIV Pathogenesis, Treatment & Prevention. Paris, France, 2017 https://www.iasociety.org/Web/WebContent/File/2_D_0950-1015_John_T_Brooks.pdf.
8. Strathdee SA, Beyrer C. Threading the Needle — How to Stop the HIV Outbreak in Rural Indiana. N Engl J Med 2015; 373: 397–9. [PubMed: 26106947]
9. Rich JD, Adashi EY. Ideological anachronism involving needle and syringe exchange programs: Lessons from the indiana hiv outbreak. JAMA 2015; 314: 23–4. [PubMed: 26000661]
10. Campbell EM, Jia H, Shankar A, et al. Detailed Transmission Network Analysis of a Large Opiate-Driven Outbreak of HIV Infection in the United States. J Infect Dis 2017.
11. Volkow N The Major HIV Outbreak in Indiana Was Preventable. Noras Blog. 2015; published online May 11. https://www.drugabuse.gov/about-nida/noras-blog/2015/05/major-hiv-outbreak-in-indiana-was-preventable (accessed Nov 18, 2017).
12. Patel MR, Foote C, Duwve J, et al. Reduction of Injection-Related Risk Behaviors After Emergency Implementation of a Syringe Services Program During an HIV Outbreak. JAIDS J Acquir Immune Defic Syndr 2018; 77: 373–382. [PubMed: 29271829]
13. Adams J HIV Outbreak in Indiana. N Engl J Med 2015; 373: 1379–1380.
14. Van MH, Rose CE, Hallisey EJ, et al. County-Level Vulnerability Assessment for Rapid Dissemination of HIV or HCV Infections Among Persons Who Inject Drugs, United States. J Acquir Immune Defic Syndr 1999 2016; 73: 323–331.
15. United Nations Office on Drugs and Crime. Systematic Literature Review on HIV and Stimulant Drugs Use (A) Part 4/5 NPS and HIV Risk and Transmission. Vienna: UNODC, 2017.
16. Janowicz DM. HIV Transmission and Injection Drug Use: Lessons From the Indiana Outbreak. Top Antivir Med 2016; 24: 90–2. [PubMed: 27841978]
17. Murphy G, Pilcher CD, Keating SM, et al. Moving towards a reliable HIV incidence test–current status, resources available, future directions and challenges ahead. Epidemiol Infect 2017; 145: 925–941. [PubMed: 28004622]
18. Marin F, Rohatgi A, Charlot S. WebPlotDigitizer, a polyvalent and free software to extract spectra from old astronomical publications: application to ultraviolet spectropolarimetry. ArXiv Prepr ArXiv170802025 2017.

19. Anderson RM, May RM, Anderson B. Infectious diseases of humans: dynamics and control. Wiley Online Library, 1992.
20. McFarlane T, Gross B, Dusynski T. Emergence of acute hepatitis C in young Indiana residents who inject drugs. Indiana State Department of Health, Epidemiology Resource Center, 2013 http://208.40.244.65/isdh/files/HCV_Cluster_Investigation_-Final(2).pdf (accessed Aug 9, 2016).
21. Sczesny S Increase in Reported Acute Hepatitis C Virus (HCV) Infections in Indiana. Indiana State Department of Health, 2011 http://www.in.gov/isdh/files/Epi_V19_N01_2011_Jan_Feb(1).pdf.
22. Team RC. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2017 2017.
23. Chang W, Cheng J, Allaire J, Xie Y, McPherson J. Shiny: web application framework for R. R Package Version 011 2015; 1: 106.
24. Greene M, Wright ER, Mullins S. Fatal Drug Overdoses: A Growing Concern in Indiana. Indianapolis, Indiana: Center for Health Policy, Indiana University School of Public and Environmental Affairs, 2008 https://archives.iupui.edu//handle/2450/776.
25. Williams M, Greene M, Wright E. Opioid Treatment Programs in Indiana. Indianapolis, Indiana: Center for Health Policy, Indiana University School of Public and Environmental Affairs, 2013 https://archives.iupui.edu/handle/2450/6872.
26. Indiana Viral Hepatitis Advisory Council. Indiana Strategic Plan for the Prevention, Care, and Elimination of Viral Hepatitis. Indiana State Department of Health, 2008 https://www.in.gov/isdh/files/Indiana_Strategic_Plan_for_Viral_Hepatitis.pdf.
27. Indiana State Department of Health. HIV Prevention Planning Group Meeting Minutes. Indiana State Department of Health, 2009 http://in.gov/isdh/24528.htm.
28. Greene M, Aiypkhanova A, Aladejebi O, Wright E. Injection Drug Use in Indiana. Indianapolis, Indiana: Center for Health Policy, Indiana University School of Public and Environmental Affairs, 2010 https://archives.iupui.edu/handle/2450/5360.
29. Chowell G, Sattenspiel L, Bansal S, Viboud C. Mathematical models to characterize early epidemic growth: A Review. Phys Life Rev 2016; 18: 66–97. [PubMed: 27451336]
30. Kitching RP, Thrusfield MV, Taylor NM. Use and abuse of mathematical models: an illustration from the 2001 foot and mouth disease epidemic in the United Kingdom. Rev Sci Tech-Off Int Epizoot 2006; 25: 293.
31. Zakher B, Blazina I, Chou R. Association between knowledge of HIV-positive status or use of antiretroviral therapy and high-risk transmission behaviors: systematic review. AIDS Care 2014; 26: 514–521. [PubMed: 24007512]
32. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011; 365: 493–505. [PubMed: 21767103]
33. Des Jarlais DC, Arasteh K, McKnight C, et al. Providing ART to HIV seropositive persons who use drugs: progress in New York City, prospects for “ending the epidemic”. AIDS Behav 2016; 20: 353–362. [PubMed: 25731661]

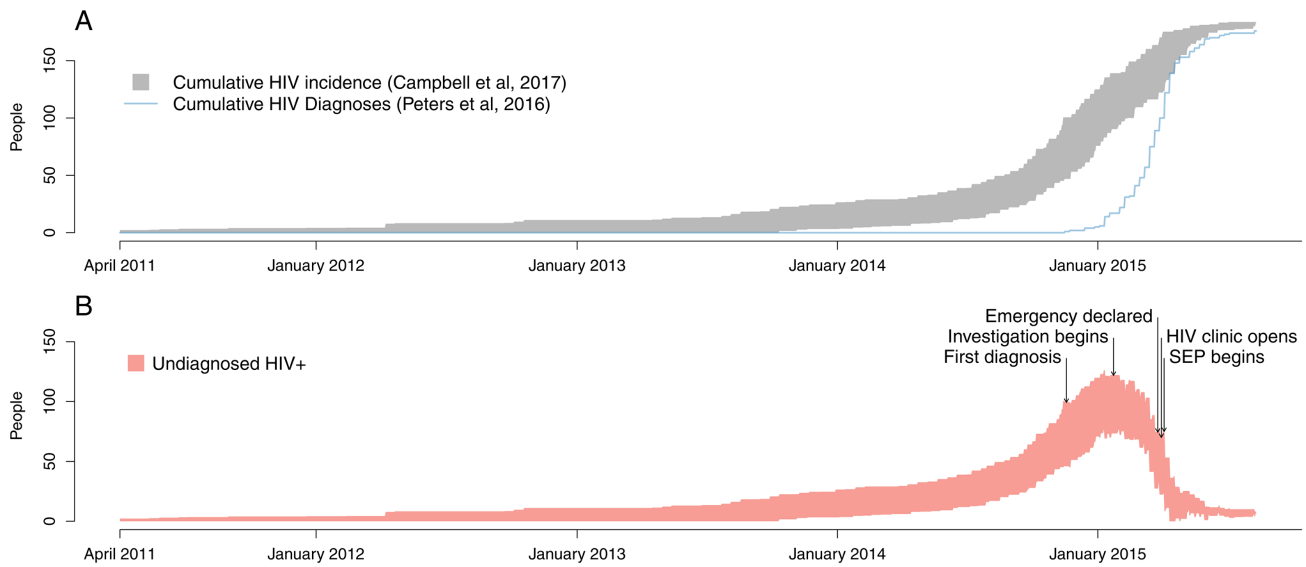

Figure 1. Raw and reconstructed data from the HIV outbreak in Scott County, Indiana from April 2011 to October 2015.

(A) Bounds for cumulative HIV incidence (grey) and cumulative diagnoses (blue).[1,19] (B) Reconstructed undiagnosed HIV infections (red) with important events from the public health response indicated.

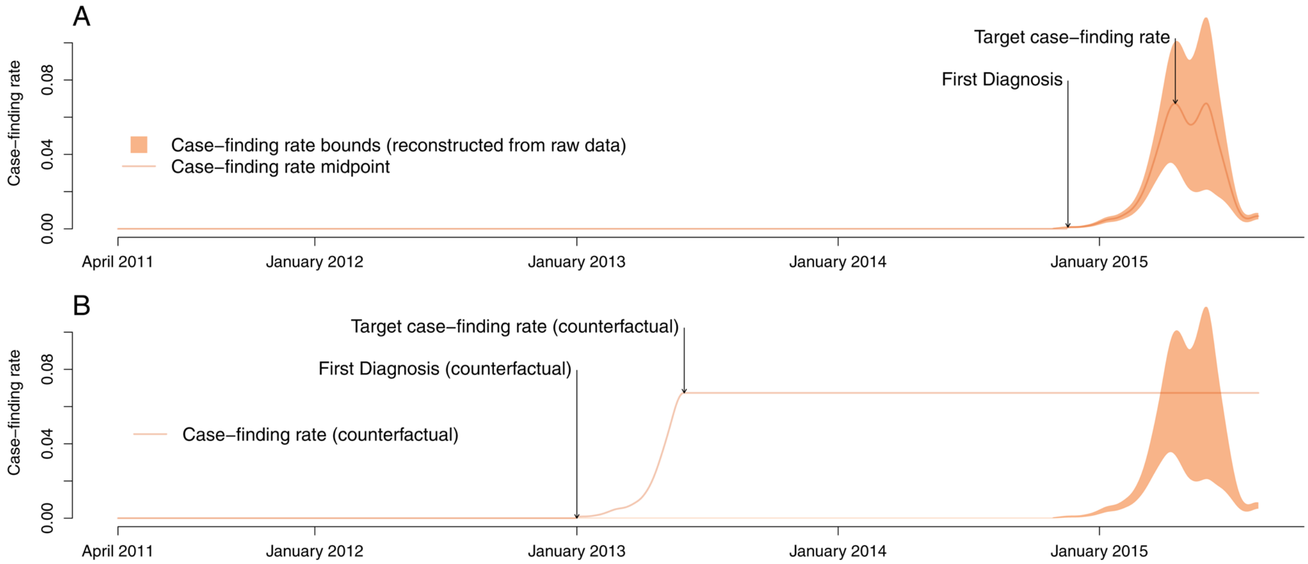

Figure 2: Illustration of actual and counterfactual case-finding rates.

(A) Bounds for the case-finding rate (orange) in the actual outbreak and the midpoint of these bounds, with the date of the first HIV diagnosis and target case-finding rate indicated. (B) Counterfactual case-finding rate (orange line) replicates the observed case-finding pattern up to the target rate, translated back in time to January 2013.

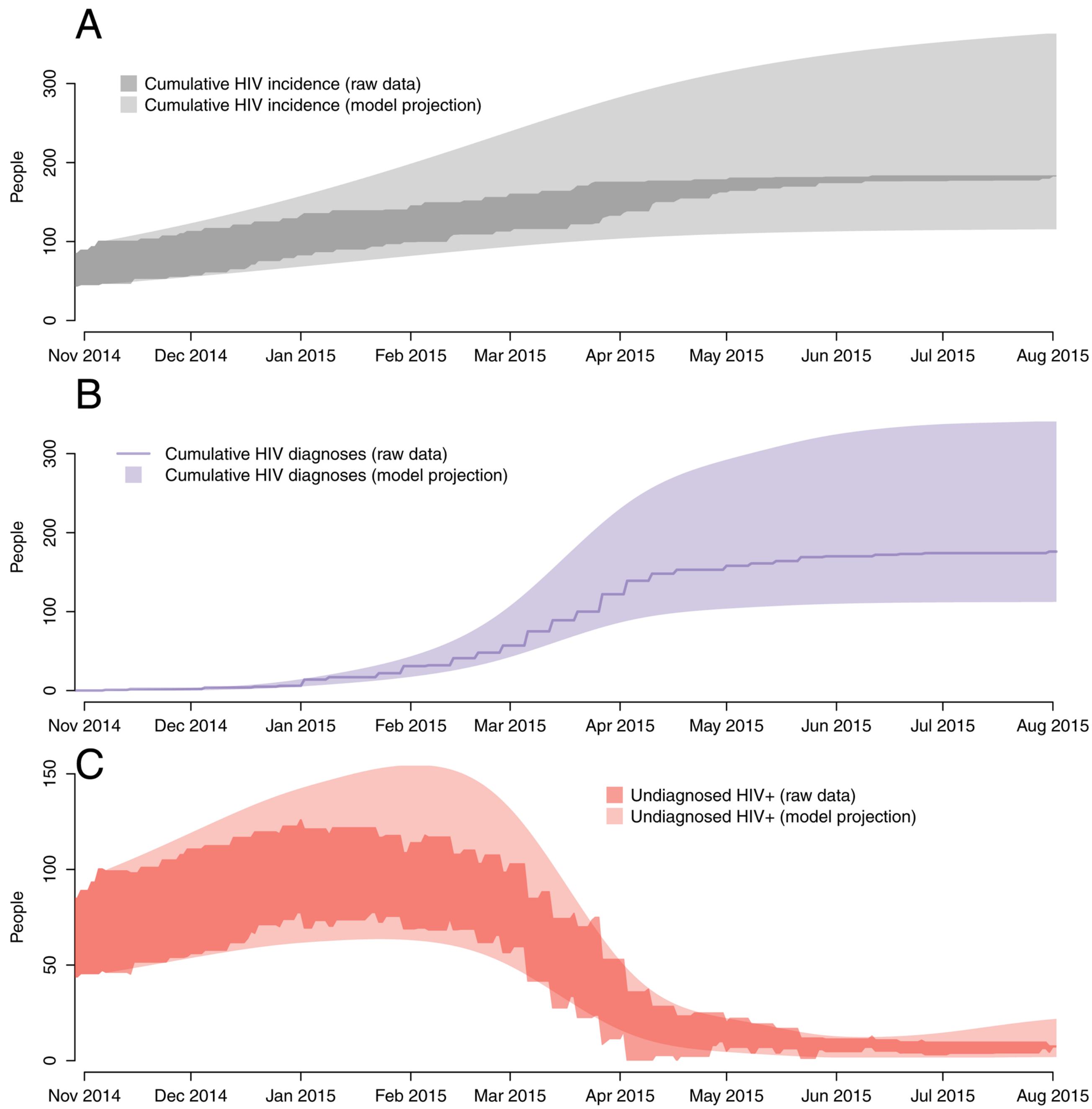

Figure 3: Comparison of raw data and outbreak model projections for the HIV outbreak in Scott County, Indiana, 2011–2015.

(A) Cumulative HIV incidence. (B) Cumulative HIV diagnoses. (C) Undiagnosed HIV infections.

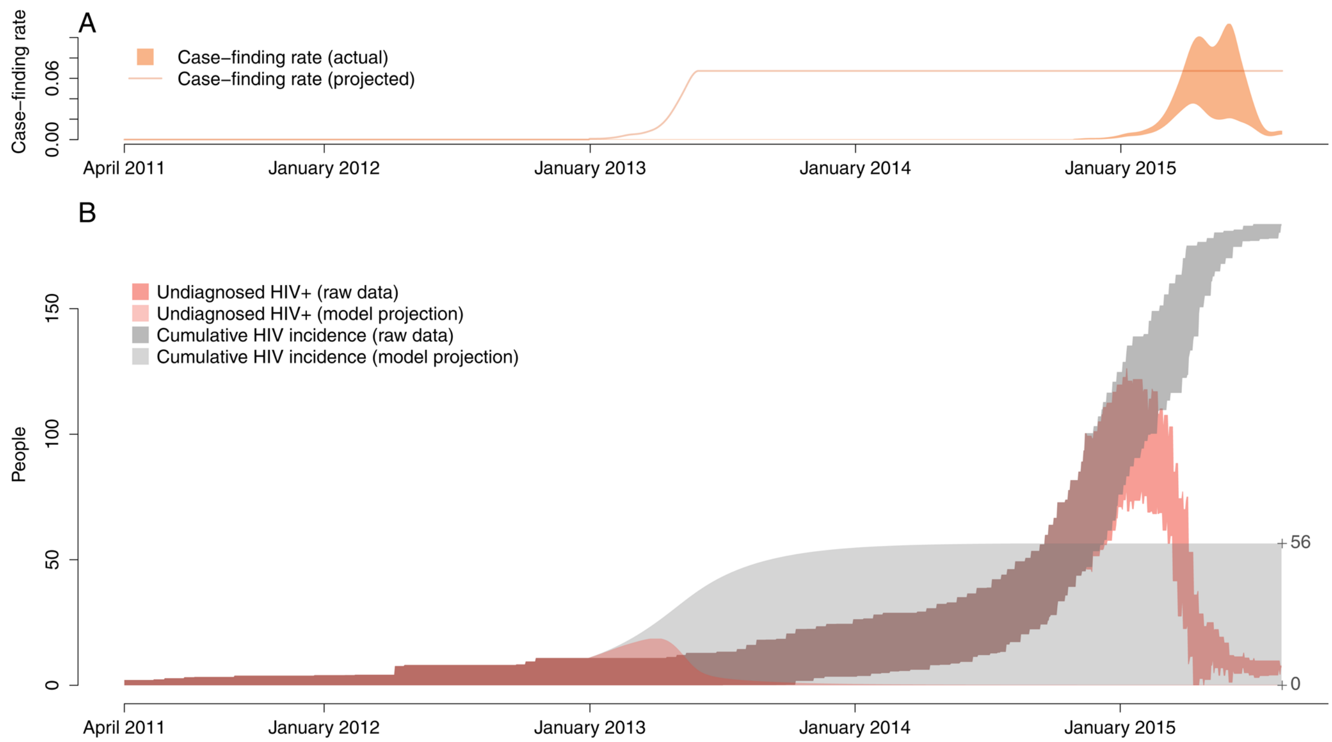

Figure 4. Evaluation of projected outbreak dynamics under a counterfactual intervention date of January 1, 2013.

(A) Counterfactual case-finding rate. (B) Cumulative HIV incidence (gray) and undiagnosed HIV infections (red) in the actual outbreak and under earlier intervention. In this scenario, cumulative HIV incidence by August 2015 is projected to be at most 56 people, compared to the actual number 183–184.

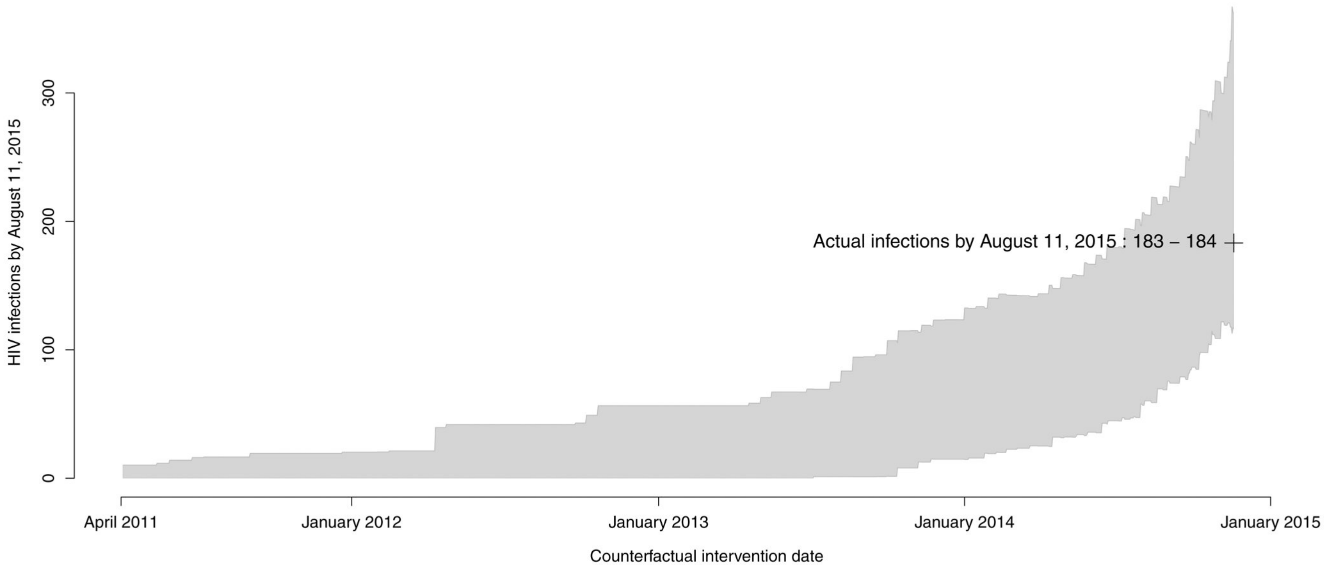

Figure 5. Projected bounds for cumulative HIV cases by August 2015, as a function of earlier counterfactual intervention dates.

Earlier intervention reduces cumuative HIV incidence.