Dynamics of the HIV outbreak and response in Scott County, IN, USA, 2011–15: a modelling study

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Summary

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

Methods In this modelling study, we derived weekly case data from the HIV outbreak in Scott County, IN, and on the uptake of HIV testing, treatment, and prevention services from publicly available reports from the US Centers for Disease Control and Prevention (CDC) and researchers from Indiana. Our primary objective was to determine if an earlier response to the outbreak could have had an effect on the number of people infected. We computed upper and lower bounds for cumulative HIV incidence by digitally extracting data from published images from a CDC study using Bio-Rad avidity incidence testing to estimate the recency of each transmission event. We constructed a generalisation of the susceptible-infectious-removed model to capture the transmission dynamics of the HIV outbreak. We computed non-parametric interval estimates of the number of individuals with an undiagnosed HIV infection, the case-finding rate per undiagnosed HIV infection, and model-based bounds for the HIV transmission rate throughout the epidemic. We used these models to assess the potential effect if the same intervention had begun at two key timepoints earlier than the actual date of the initiation of efforts to control the outbreak.

Findings The upper bound for undiagnosed HIV infections in Scott County peaked at 126 around Jan 10, 2015, over 2 months before the Governor of Indiana 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 (estimated to have been 183–184 infections by Aug 11, 2015). Initiation of a response on Jan 1, 2013, could have suppressed the number of infections to 56 or fewer, averting at least 127 infections; whereas an intervention on April 1, 2011, could have reduced the number of infections to ten or fewer, averting at least 173 infections.

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

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Introduction

Scott County, IN, USA, was the site of a severe outbreak of HIV infection in 2014–15 among people who inject drugs (PWID).[1] On Nov 18, 2014, the first case of HIV infection in Scott County attributed to this outbreak was diagnosed.[1] An investigation by the Indiana State Department of Health began on Jan 23, 2015, by which time 17 new cases of HIV infection had been recorded.[1] On March 23, 2015, a team of US Centers for Disease Control and Prevention (CDC) investigators arrived in Scott County. On March 26, 2015, Indiana Governor Mike Pence declared a public health emergency in Scott County, allowing a temporary syringe-exchange programme to be established. An HIV-testing clinic opened on March 31, 2015.[1] Syringe-exchange programmes reduce HIV transmission among PWID, and do not encourage drug use.[2] On April 4, 2015, after consultations between the Governor and the Indiana State Department of Health, CDC, and local law enforcement, and a week after Executive Order 15-05 declared a public health emergency, Scott County established a temporary syringe-exchange programme for 30 days.[3] However, implementation of the programme in Scott County was delayed by conflicts between police officers, PWID, and those distributing needles, with police officers initially confiscating syringes.[4] On May 5, 2015, Governor Pence signed a bill that allowed counties in Indiana to apply for permission to establish syringe-exchange programmes, if they could show that a public health emergency existed.[5] These exchange programmes were to be temporary and did not receive financial state support.[3] On the same day, Governor Pence also signed a bill that upgraded possession of a syringe with intent to commit an offence with a controlled substance from a misdemeanour to a felony charge, subject to imprisonment for up to 2·5 years, to go

Research in context

Evidence before this study

An initial report by the Indiana HIV Outbreak Investigation Team outlined the outbreak and investigation, provided the time series of HIV diagnoses in Scott County, IN, USA, during 2014–15, along with a contact-tracing network and a reconstruction of the phylogenetic tree of sampled HIV gene sequences. In a subsequent study, recency assay results were analysed to infer the dates of individual infections, and thereby bounds on cumulative HIV incidence during the outbreak were calculated. We searched Google Scholar and the general literature using the Lexis Nexis database for publications in English from Dec 1, 2014, to July 1, 2018, using the following terms alone and in combination: "Scott County", "HIV", "outbreak", "prevention", and "timing". Commentaries, newspaper articles, and editorial contributions have suggested that the outbreak could have been avoided with earlier introduction of harm reduction and HIV prevention and treatment services, whereas some public health officials expressed scepticism. To our knowledge, claims about what would have happened in Scott County under different intervention circumstances have not been evaluated by use of the available incidence and diagnosis data.

Added value of this study

By analysing publicly available epidemiological data collected during the outbreak response by US Centers for Disease Control and Prevention (CDC) investigators, this study provides, to our knowledge, 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 syringe-exchange programmes implemented. Using a generalisation of a canonical mathematical model of infectious disease transmission, we show that HIV incidence over the course of the actual outbreak could have been substantially reduced by earlier scale up of case finding.

Implications of all the available evidence

The CDC has declared 220 counties across the USA at risk for outbreaks of HIV and hepatitis C associated with injecting drug use. The public policy response to the outbreak in Scott County from 2014 to 2015 offers a case study in management of an emerging epidemic. The deployment of HIV and harm-reduction services in US counties and other locations at risk for new outbreaks could avoid their emergence or lessen their epidemiological effect. Understanding the dynamics of the outbreak and response in Indiana might allow policy makers to mitigate future outbreaks among PWID in other locations.

into effect on July 1, 2015.[6] By March 2, 2017, 215 new cases of HIV infection had been attributed to the outbreak.[7]

Although Governor Pence eventually authorised state officials to establish programmes to prevent new HIV infections and treat infected individuals on March 26, 2015, questions remain about the timing and scale of the response.[3,8,9] Researchers[10,11] have suggested that the public health response to the Scott County outbreak was not implemented early enough to avert a severe epidemic, and that most infections occurred before the declaration of a public health emergency and response to control the outbreak in late March, 2015. 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 the campaign for the public health intervention been implemented earlier.[8,9] Campbell and colleagues[10] suggest that "Had an SSP [syringe-service programme] been in place prior to recognition of the outbreak, the explosive phase of the outbreak may have been blunted". Rich and Adashi[9] make the stronger assertion that "what happened in Indiana was predictable and avoidable". Researchers from the Indiana State Department of Health, Indiana University, Scott County Health Department, and the 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 syringe-exchange programme been implemented earlier, Jerome Adams, Indiana State Health Commissioner during this period, highlighted evidence that many cities with active syringe-exchange programmes also have a high prevalence of HIV.[13]

Would a public health response that was implemented before November, 2014, have reduced the scale of the outbreak in Scott County? Answering this question requires insight into the dynamics of the outbreak if the public health response had been implemented earlier than in reality (ie, counterfactual scenarios). In this study, we used 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 aimed to determine whether earlier implementation of a public health response similar to the response that was actually enacted would have diminished the scale of the outbreak. We focus our analysis on earlier implementation of HIV case finding; no data are publicly available on the effects of other interventions deployed during the outbreak.

Methods

Data sources

In this modelling study, we obtained weekly case data on the 2014–15 outbreak in Scott County from a report by the Indiana HIV Outbreak Team,[1] which collected data from cases reported between Nov 18, 2014, and Nov 1, 2015. 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.[1,14] Cases determined as associated with the outbreak were laboratory-confirmed infections diagnosed after Oct 1, 2014, in residents of Scott County or their syringe-sharing or sexual partners, until Nov 1, 2015. In separate work, CDC investigators tested serum and plasma samples from the individuals infected in the outbreak with a Bio-Rad avidity incidence (BRAI) test to estimate how recent each transmission event was.[10] The ELISA-based BRAI test is modified to permit measurement of antibody avidity.[15] Researchers used historical data on the association between avidity results after diagnosis and dates of confirmed negative HIV test results to estimate dates of infection for individuals in the outbreak.[10] We estimated upper and lower bounds for cumulative HIV incidence by digitally extracting data from published images.[10,16]

Mathematical model

We constructed a generalisation of the classic susceptible-infectious-removed (SIR) model to capture the transmission dynamics of the HIV outbreak in the community of PWID in Scott County.[17] We considered a PWID population of size N in which each individual can be classified into one of four categories. At time t, $S(t)$ is the number of susceptible (HIV-negative) PWID, $I_{udx}(t)$ is the number of HIV-positive but undiagnosed individuals, $I_{dx}(t)$ is the number of HIV-positive individuals who are diagnosed, and $R(t)$ is the number of removed individuals who are diagnosed as HIV positive and virally suppressed or who no longer engage in epidemiological contact sufficient to transmit HIV infection. The population is closed, so $S(t)+I_{udx}(t)+I_{dx}(t)+R(t)=N$ for every t. Susceptible individuals become infected at a rate equal to the product of the transmission rate β and the number of infectious individuals in the population, $\beta(I_{udx}(t)+I_{dx}(t))$. Infectious individuals are diagnosed at rate $\gamma(t)$, and individuals diagnosed as HIV positive are removed at rate ρ from the pool of infectious individuals. In this context, removal could indicate viral suppression after initiation of antiretroviral therapy (ART), or cessation of epidemiological contact (eg, sharing needles, unsafe sex) sufficient to transmit HIV infection. Provision of clean injection equipment via syringe-exchange programmes to individuals who are HIV positive is one mechanism by which a transition from I_{dx} to R could occur.[12] The dynamic model is described by the following system of ordinary differential equations:

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

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

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

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

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

Reconstructing outbreak dynamics

We computed non-parametric interval estimates of the number of individuals with an undiagnosed HIV infection, 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 the CDC recency assay results, we obtained a lower bound $\underline{C}(t)$ and an upper bound $\overline{C}(t)$ for the cumulative HIV incidence, $C(t)$.[10] Recency assays are still in the developmental phase; hence, although their use in calculating incidence estimates has been refined, their accuracy is questionable.[15] In the appendix (pp 8–9), we analyse the sensitivity of results to increasing uncertainty in infection times by scaling the incidence bounds.

See Online appendix

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

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 obtained lower and upper bounds for $I_{udx}(t)$ and $S(t)$ from the equivalences

$$\underline{I}_{udx}(t) = \underline{C}(t) - D(t),$$
$$\overline{I}_{udx}(t) = \overline{C}(t) - D(t),$$
$$\underline{S}(t) = N - \overline{C}(t), \text{ and}$$
$$\overline{S}(t) = N - \underline{C}(t)$$

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 $\underline{\gamma}(t)dt = dD(t)/\overline{I}_{udx}(t)$ and $\overline{\gamma}(t)dt = dD(t)/\underline{I}_{udx}(t)$. Lower and upper bounds for the overall transmission rate β were computed by dividing the number of infections by the cumulative transmission risk

$$\beta = \frac{C(t) - C(0)}{\int_0^t S(u)(I_{udx}(u) + I_{dx}(u))du}$$

We constructed a continuous interpolation of these data on a daily timescale by fitting a cubic smoothing spline. This fitting allowed us to compute bounds for cumulative HIV incidence, cumulative diagnoses curve, and bounds for the number of undiagnosed individuals who were HIV positive. Additional model details are provided in the appendix (pp 1–3).

Evaluation of counterfactual intervention scenarios

We investigated alternative scenarios in which the intervention was started at earlier timepoints. In this model, t_s denotes the date of the first HIV diagnosis in Scott County, Nov 18, 2014, and t_e is a later date at which a target case-finding scale-up rate was achieved. For a hypothetical earlier date, $t_s^*<t_s$ we defined the counterfactual case-finding rate $\gamma^*(t)$ using the following equation:

For **interactive web application on dynamics of the HIV outbreak and response in Scott County** see https://forrestcrawford.shinyapps.io/indiana-hiv

For **source code** see https://github.com/fcrawford/indiana-hiv

$$\gamma^*(t) = \begin{cases} \gamma(t) & \text{if } t<t_s^* \\ \gamma(t_s - t_s^* + t) & \text{if } t_s^* \leq t < t_s^* - t_s + t_e \\ \gamma(t_e) & \text{if } t_s^* - t_s + t_e \leq t \end{cases}$$

Using this equation, we defined $\underline{\gamma}^*(t)$ by substituting $\underline{\gamma}(t)$ for $\gamma(t)$, and $\overline{\gamma}^*(t)$ by substituting $\overline{\gamma}(t)$ for $\gamma(t)$. 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 $\underline{\gamma}^*(t)$ in place of $\underline{\gamma}(t)$ or $\overline{\gamma}^*(t)$ in place of $\overline{\gamma}(t)$ gives the dynamics that would have occurred if the public health response had been implemented at the earlier date of t_s^*, including the reconstructed bounds for the case-finding rate in the actual response, and a counterfactual case-finding rate under an intervention starting on a given date.

Because changes in transmission or removal rates cannot be estimated directly from publicly available data, we conceptualised the public health response as an intervention on the case-finding rate $\gamma(t)$ alone, and not on the HIV transmission rate β, or removal or suppression rate ρ. This approach gave us conservative projections of HIV incidence under counterfactual intervention scenarios because the model 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 syringe-exchange programmes, is of particular interest, we analysed the sensitivity of results to reduction of β (appendix pp 8–9).

We selected two counterfactual starting dates, t_s^*, for the initiation of the intervention that reflect two potential opportunities that could have been available for intervening to prevent the HIV outbreak in Indiana. First, we chose April 1, 2011, just after a hepatitis C virus (HCV) outbreak in several counties in the state in 2010–11,[18,19] and around the estimated time of the first HIV infection. Second, we chose Jan 1, 2013, around the time of the closure of the only local HIV-testing facility in Scott County.[3,8] We examined the total number of HIV infections that might have occurred if a case-finding response had been implemented on these dates, and with the same scope and scale as the actual disease control effort initiated in 2015.

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).[20] We used the application to calculate the outbreak dynamics described in this Article and the application permits choice of hypothetical earlier dates for scale-up of case finding. The application is available online. The source code is freely available for download and modification under the Massachusetts Institute of Technology (MIT) license.

Role of the funding source

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

Results

We used weekly case data from between Nov 18, 2014, and Nov 1, 2015, covering the time around the Scott County 2014–15 HIV outbreak, to estimate that the upper bound for undiagnosed HIV infections in Scott County peaked around Jan 10, 2015, with between 77 and 126 undiagnosed cases, and subsequently decreased rapidly (figure 1). 27–74 individuals with HIV were undiagnosed on March 26, 2015, when Governor Pence declared the public health emergency (figure 1). These dynamics indicate that, as Campbell and colleagues assert,[10] the outbreak had substantially declined by the time public health response measures were implemented. These bounds are non-parametric and can be computed directly from available data. The validity of the bounds does not depend on model assumptions, nor does it require knowledge of the size N of the population of PWID at risk. The case-finding rate per undiagnosed HIV infection varied substantially over the course of the outbreak, with the peak case-finding rate occurring midway through the outbreak in April, 2015, and declining rapidly in the spring and summer of 2015 (figure 2).

Beginning on the date of the first HIV diagnosis (Nov 18, 2014) and up to Aug 23, 2015, we estimated upper and lower bounds for the number of individuals who were HIV negative and susceptible to infection, HIV positive and undiagnosed, and diagnosed as HIV positive (figure 3). For the population of 536 PWID and their partners, our model projections starting on Nov 18, 2014, match the actual epidemiological

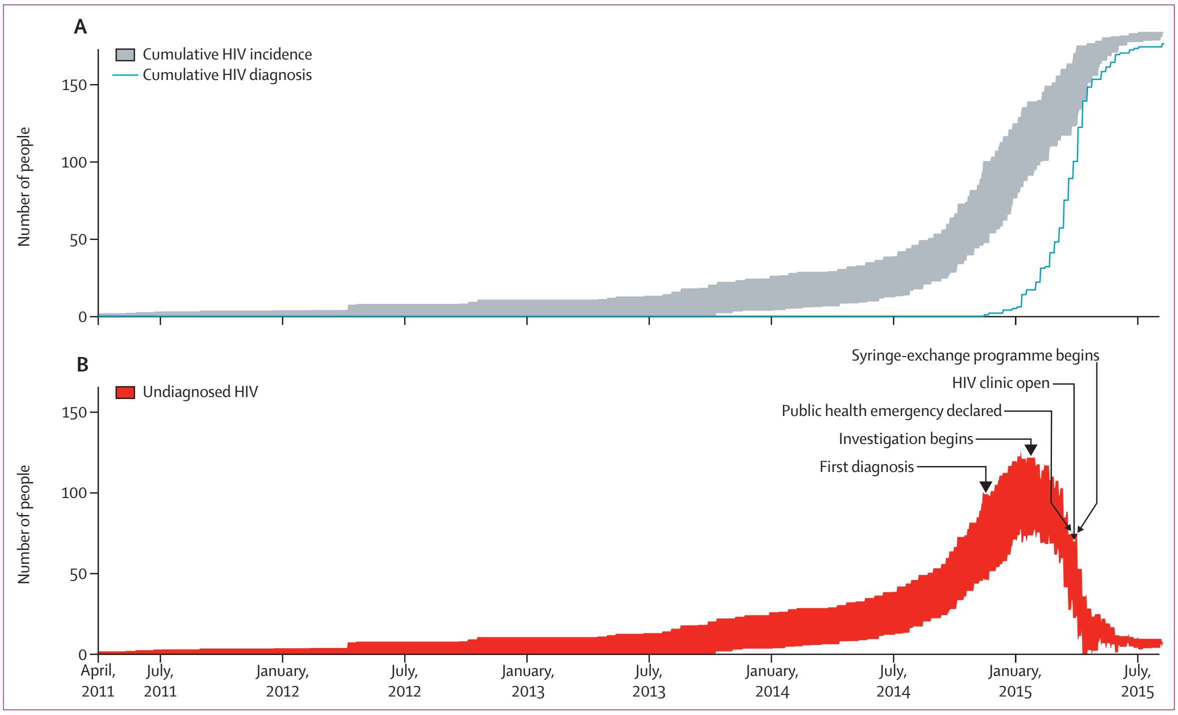

Figure 1: **Raw and reconstructed data from the HIV outbreak in Scott County, IN, USA, from April, 2011, to August, 2015**
(A) Bounds for cumulative HIV incidence, calculated by Campbell and colleagues,[10] and cumulative HIV diagnoses, calculated by Peters and colleagues.[1] (B) Reconstructed undiagnosed HIV infections with important events from the public health response shown.

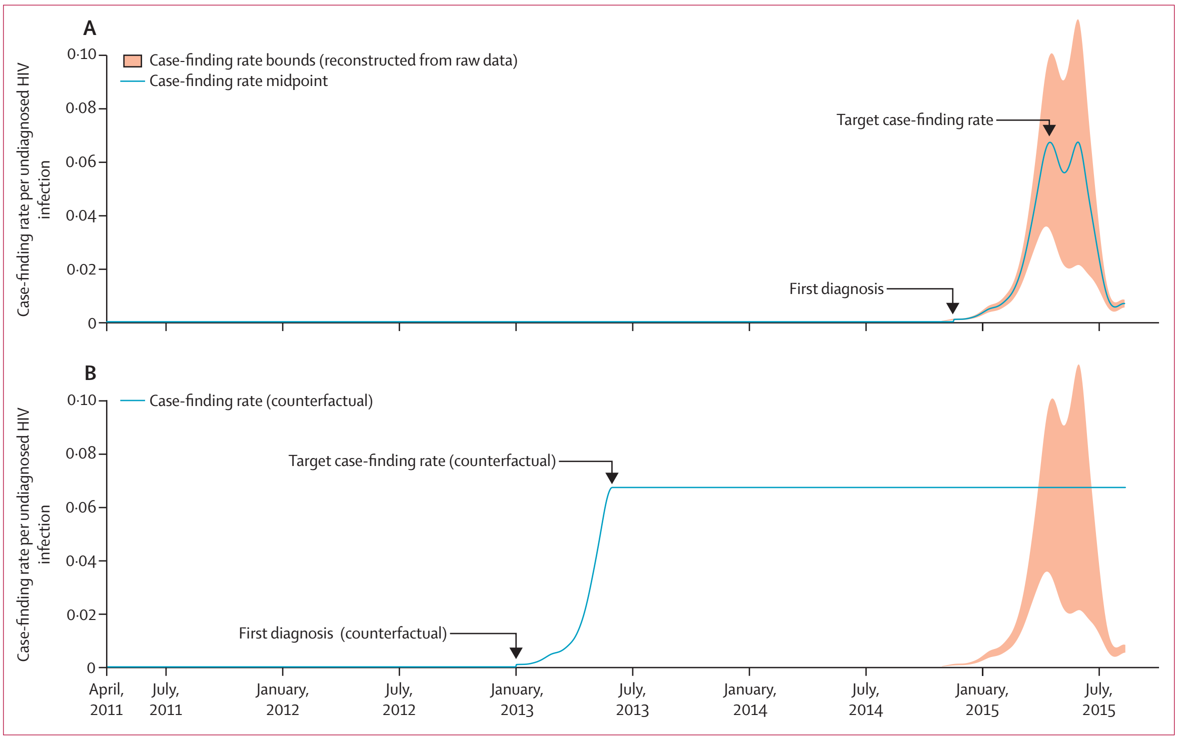

Figure 2: **Actual and counterfactual case-finding rates and dynamics during the HIV outbreak, from April, 2011, to August, 2015**
(A) Upper and lower bounds for the case-finding rate per undiagnosed HIV infection in the actual outbreak and the midpoint of these bounds, with the timepoint at which the target case-finding rate occurred indicated. (B) Counterfactual case-finding rate replicates the observed case-finding rate up to the target rate, translated back to if the intervention had started on Jan 1, 2013.

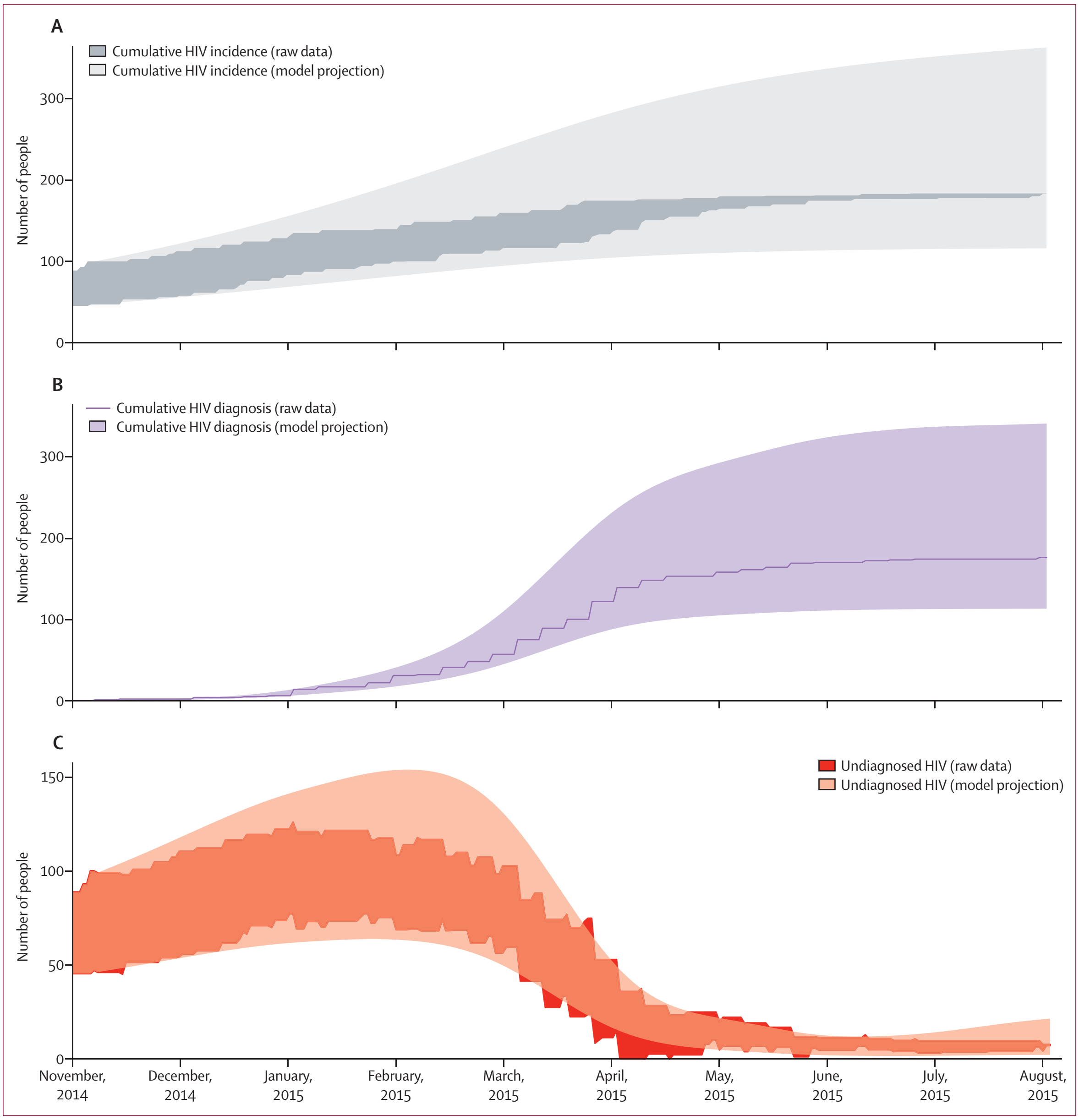

Figure 3: **Comparison of raw data and outbreak model projections for the HIV outbreak in Scott County, IN, USA, 2011–15**
(A) Cumulative HIV incidence. (B) Cumulative HIV diagnoses. (C) Undiagnosed HIV infections.

dynamics for the outbreak.[1] The transmission rate for the assumed population size 536 varies from 4×10^{-6} to 3×10^{-5} infections per susceptible–infectious pair per day. These bounds are similar to estimates we computed using published data from the Scott County outbreak[1] and other studies of HIV risk for injection drug users (appendix pp 4–5). The reconstructed case-finding rate ranged from 0 to 0·035 diagnosed cases per undiagnosed HIV infection per day during the response.

In the first counterfactual scenario, when the scale-up of case finding starts on April 1, 2011 (appendix p 4), cumulative HIV incidence on Aug 11, 2015, is projected to be between zero and ten people, compared with the estimated actual incidence of 183–184 infections, indicating at least 173 infections averted. In the second counterfactual scenario of the intervention starting on Jan 1, 2013, cumulative HIV incidence by Aug 11, 2015, is projected to be between zero and 56 people, indicating at least 127 infections that potentially could have been averted (figure 4).

We examined projected bounds for cumulative HIV cases (by Aug 11, 2015), as a function of the date of case-finding scale-up. Interventions that started earlier

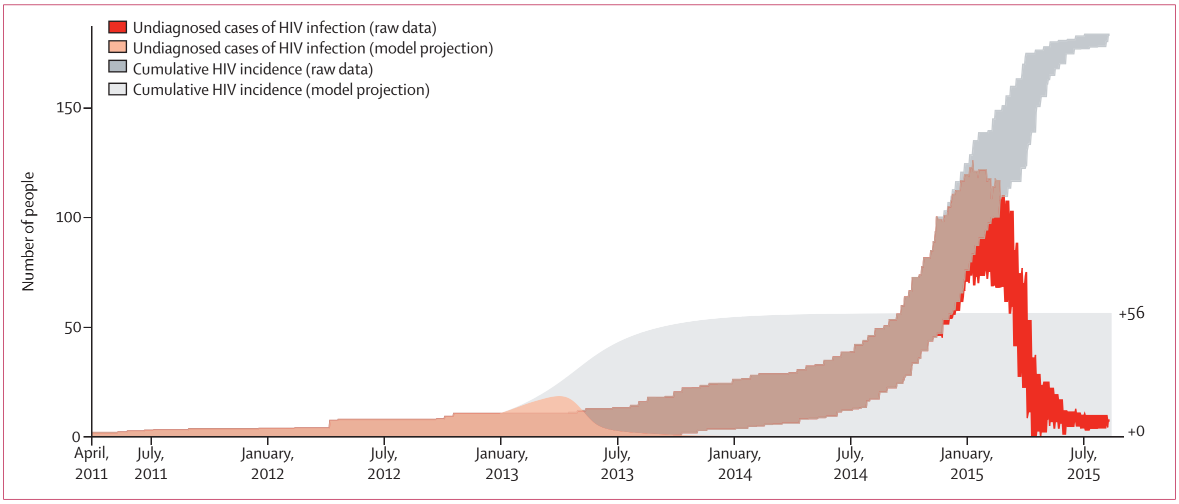

Figure 4: **Evaluation of projected outbreak dynamics under a counterfactual intervention date of Jan 1, 2013**
Cumulative HIV incidence and undiagnosed HIV infections in the actual outbreak and under our model projection with intervention on Jan 1, 2013. In this scenario, cumulative HIV incidence by August, 2015, is projected to be at most 56 people, compared with the actual number of 183–184.

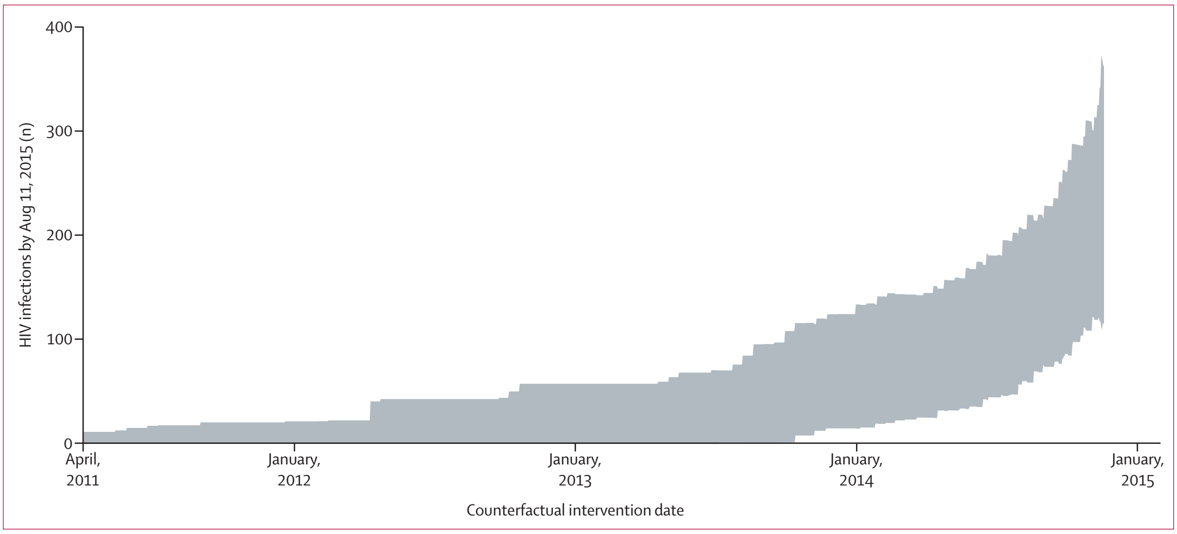

Figure 5: **Projected bounds for cumulative HIV cases by Aug 11, 2015, as a function of earlier counterfactual intervention dates**
The actual number of infections by Aug 11, 2015, in the real-life outbreak was 183–184.

produced lower projected cumulative HIV incidence than interventions that started later in the timeline (figure 5). Our sensitivity analysis showed that in both early intervention scenarios, projected cumulative HIV incidence is largely invariant to assumed population size N. For a range of plausible values of the removal rate (ρ), both early intervention scenarios show dramatic reduction in cumulative HIV incidence (appendix pp 5–9).

Discussion

Our findings in this modelling study support claims that the HIV epidemic in Scott County, IN, USA, 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 outbreak were not detected for several years. Even after these first infections spread into an epidemic in 2014, the outbreak was not recognised for months, and a year passed before a response was initiated in earnest in early 2015.[1,12] Our analyses show that the syringe-exchange programmes started after the peak in undiagnosed HIV infections.[1,12]

Warning signs that an HIV outbreak could occur in the region existed. Increasing prescription-drug abuse and overdoses in Indiana have been documented since 2004, although new opioid-agonist therapy programmes were forbidden under a state ban.[21,22] Local experts recommended in 2008 that syringe-exchange programmes be established to prevent outbreaks of infectious diseases associated with injection drug use.[23–25]

Even after an outbreak of HCV among PWID in Indiana in 2010–11, these recommendations remained unheeded.[18,19] Additionally, the only HIV testing provider in southeastern Indiana closed in 2013 because of state funding cuts, which could have delayed the diagnosis of the initial case of HIV infection in Scott County.[3,8]

Because syringe-exchange programmes and other harm-reduction interventions are known to reduce HIV transmission, our results could be interpreted as providing a lower bound on the effect of a hypothetical earlier comprehensive response to the outbreak.[2] Although our analysis is focused on the Scott County outbreak, understanding the dynamics of the outbreak and response in Indiana might allow policy makers to mitigate future outbreaks among PWID in other locations. The CDC has declared 220 counties across the USA at risk of outbreaks of HIV and HCV infection associated with injecting drug use.[26] Furthermore, since 2011, outbreaks of HIV among PWID have been documented in Romania, Hungary, Greece, Israel, Ireland, and Scotland, and our findings could help policy makers in these countries in tackling these outbreaks.[27]

Our analyses have several potential limitations. First, the epidemic model with time-varying removal rate might 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 might not be available in the early stages of the epidemic.[28] Additionally, complex models might be mathematically intractable, difficult to validate, or challenging to understand.[29] The mathematical model we used to compute trajectories of counterfactual outbreaks uses a combination of available data and variable parameters informed by previous studies. The framework we used here is designed to rely on credible assumptions and be robust to incomplete knowledge of HIV incidence during the outbreak.

Second, the model-based evaluations of earlier intervention dates require that the total size of the PWID population is known. In reality, the true at-risk population in Scott County could have consisted of PWID only, PWID and their injecting and sexual partners, or a broader group of people. However, because the incidence rate β is estimated conditionally on the size of the population N, and model dynamics depend on N and β, projections under counterfactual intervention scenarios are relatively insensitive to the choice of N, as shown in our sensitivity analysis.

Third, our construction of the dynamics of the Scott County outbreak assumes that some individuals who were diagnosed as HIV positive could have contributed to transmission of infection, but diagnosed individuals were removed from the pool of infectious people at rate ρ. Empirical research supports this assumption, because HIV diagnosis can reduce transmission-risk behaviours, including needle sharing and unprotected sex.[30] Furthermore, ART following HIV diagnosis reduces viral load and can thereby diminish the risk of transmission to susceptible needle-sharing or sexual partners.[31,32] If PWID in Scott County did not change their behaviour following HIV diagnosis, or if ART initiation or adherence did not occur rapidly, projections could underestimate HIV incidence under counterfactual scenarios.

Fourth, we have not modelled the effect of interventions such as education or syringe-exchange programmes on the transmission rate β. We evaluated the effect of reductions in β in a sensitivity analysis and, 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 (eg, syringe-exchange programmes) with certainty. We have also not modelled intervention-related changes in the effect of syringe-exchange programmes on removal rate ρ for individuals diagnosed as HIV positive. Although syringe-exchange programmes and other harm-reduction interventions can contribute to cessation of infectious contact, thus increasing ρ (and γ), no data on behaviour change from the Scott County outbreak were publicly available. For this reason, projected HIV incidence in these scenarios might be conservative because syringe-exchange programmes can reduce HIV transmission among PWID and do not encourage drug use. Implementation of syringe-exchange programmes alongside case finding (ie, reducing β, increasing ρ) would probably reduce projected cumulative HIV incidence to even lower than we have suggested.[2]

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

Despite these caveats, the conservative nature of our approach, using actual data on diagnoses, non-parametric bounds for cumulative incidence, and not assuming an effect of syringe-exchange programmes on the transmission rate, suggests that had the interventions deployed in Scott County in 2014–15 been available earlier, the outbreak might have been substantially blunted. Although the model presented here is specific to the events in Scott County, our findings could have broader implications for other HIV outbreaks. HIV outbreaks among PWID in Europe, and the ongoing risk of similar outbreaks in the USA, highlight the public health implications of this examination.[26,27] Future HIV outbreaks could be minimised if HIV testing and treatment are available in places vulnerable to the transmission of blood-borne infections among PWID.[26] Syringe-exchange programmes and use of opioid-agonist therapy are crucial HIV prevention tools that could offer the chance to prevent new outbreaks among PWID.[8]

Contributors
GSG conceived the study and wrote most of the manuscript. FWC wrote the appendix, analytical software, and web application.

Declaration of interests
We declare no competing interests.

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