Progression and Transmission of HIV/AIDS (PATH 2.0): A New Agent-Based Model to Estimate HIV Transmissions in the United States

Chaitra Gopalappa, PhD, Paul G. Farnham, PhD, Yao-Hsuan Chen, PhD, Stephanie L. Sansom, PhD

Background. *HIV transmission is the result of complex dynamics in the risk behaviors, partnership choices, disease stage and position along the HIV care continuum—individual characteristics that themselves can change over time. Capturing these dynamics and simulating transmissions to understand the chief sources of transmission remain important for prevention.* ***Methods.*** *The Progression and Transmission of HIV/AIDS (PATH 2.0) is an agent-based model of a sample of 10,000 people living with HIV (PLWH), who represent all men who have sex with men (MSM) and heterosexuals living with HIV in the U.S.A. Persons uninfected were modeled as populations, stratified by risk and gender. The model included detailed individual-level data from several large national surveillance databases. The outcomes focused on average annual transmission rates from 2008 through 2011 by disease stage, HIV care continuum, and sexual risk group.* ***Results.*** *The relative risk of transmission of those in the acute phase was nine-times [5th and 95th percentile simulation interval (SI): 7, 12] that of those in the non-acute phase, although, on average, those with acute infections comprised 1% of all PLWH. The relative risk of transmission was 24- to 50-times as high for those in the non-acute phase who had not achieved viral load suppression as compared with those who had. The relative risk of transmission among MSM was 3.2-times [SI: 2.7, 4.0] that of heterosexuals. Men who have sex with men and women generated 46% of sexually acquired transmissions among heterosexuals.* ***Conclusions.*** *The model results support a continued focus on early diagnosis, treatment and adherence to ART, with an emphasis on prevention efforts for MSM, a subgroup of whom appear to play a role in transmission to heterosexuals.* ***Key words:*** *HIV AND AIDS; Simulation Methods (Monte Carlo Methods;simulation; etc); Decision Analysis; Risk Communication or Risk Perception.* ***(Med Decis Making XXXX;XX:xx–xx).***

In the United States, approximately 50,000 HIV transmissions occurred per year from 2007 through 2010, as per the most recent estimates available.[1] The large majority of those transmissions were from sexual contact. A key goal of the National HIV/AIDS Strategy, released in 2015,[2] is to decrease the annual number of new transmissions by 25% by 2020 as compared with that in 2010. Understanding the key sources of transmission is important to achieving the NHAS goal. The key sources of transmission that are potential foci for HIV prevention programs include transmission by disease stage, by position in the HIV care continuum, from diagnosis to viral load suppression, and by sexual risk group.

We developed the Progression and Transmission of HIV/AIDS (PATH 2.0) from a detailed, individual-based, disease progression model. To incorporate a dynamic, HIV transmission component, we designed PATH 2.0 as an agent-based model based on a sample of 10,000 persons living with HIV (PLWH), who represented all men who have sex with men (MSM) and heterosexuals living with HIV in the U.S. We modeled the uninfected as populations, stratified by risk and gender. The model integrated detailed demographic, clinical and behavioral data from several large national databases to both inform the initial distribution of PLWH across the key subgroups and to inform the simulation of new HIV transmissions. We calibrated model inputs informing sexual

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mixing between risk groups by comparing the average proportion of all new sexual transmissions that occurred among MSM and heterosexual males and females for the years 2007 through 2009 against the average proportions over the same 3-year period, as reported by Prejean and colleagues.[3]

Our outcomes focused on average annual HIV transmission rates from 2008 through 2011 by disease stage (acute v. non-acute), the HIV care continuum, from diagnosis to viral load suppression, and by sexual risk group, men who have sex with men (MSM) and heterosexuals. We also calculated a relative transmission rate to indicate the magnitude of difference between the lowest and highest transmission rates in each category.

METHODS

HIV transmission is a result of the interactions between multiple individual behavioral, demographic, disease, and care characteristics that change over time, thus making it appropriate for modeling in an individual-level model. However, considering the very low prevalence of HIV in the US (~0.6% in 2006), individual-level models that include both the infected and the uninfected and that are representative of the US population must be very large and inclusive of a majority of people who will never be infected. Additionally, most behavioral data available to inform models, including partnership characteristics, are based on the perspective of a surveyed individual, not a partnership or a network. As a result, we developed an agent-based model of only persons infected with HIV. We initiated the model with 10,000 persons to represent the 1.1 million persons living with HIV (PLWH) in the U.S. in 2006.[4,5] PLWH in the model were categorized according to sex and age, sexual transmission risk group (heterosexual and MSM),[3,4,6,7] stage of disease (acute versus non-acute), stage in the HIV care continuum from diagnosis to viral load suppression, and, among those diagnosed, by CD4 T lymphocyte (CD4) count. We derived the demographic and clinical characteristics largely from the National HIV Surveillance System (NHSS) and Medical Monitoring Project (MMP).[8,9] We also characterized the sexual behaviors associated with transmission based on data from three national surveys: the National Survey of Family Growth (NSFG), the National Survey of Sexual Health and Behavior (NSSHB), and the National HIV Behavioral Surveillance system (NHBS).[10-20]

We simulated uninfected persons as populations stratified by risk and gender. When HIV transmissions occurred, we transitioned the newly infected into the agent-based model. We provide a discussion in the Appendix of the equivalence between our approach and that of individual-level models that explicitly include both persons who are infected and uninfected with HIV. Our framework is similar to that of Graw and colleagues, who applied this approach to simulate IDU transmissions in Latvia.[21]

Modeling Partnerships

PLWH also were assigned details about their partners, such as each partner's HIV transmission risk group and age, and the partnership, such as each partnership's duration in months (remaining length of partnership), type (main or casual), number of sex acts per month, and proportion of sex acts protected by condoms. The values for each person infected with HIV partners and partnership characteristics, including the probabilities of partnership formation, were based on surveillance data, where individuals responded to questions related to the characteristics of themselves, and each of their partners during the past year.[10-20]

We modeled MSM to have main partners only, casual partners only, or main and casual partners.[11,20] We modeled heterosexuals as having main partners only, as we did not have data on their casual partnerships. We defined casual partnerships as those in which the person infected with

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HIV had 1 to 3 sex acts with a partner in a partnership that lasted no more than 1 month. We defined main partnerships as those occurring over a period of at least 1 month, although most lasted a year or more,[10] with some average number of sex acts per month. The duration of main partnerships in months was an increasing function of age.[10] We assigned the proportion of sex acts in which condoms were used, which differed between main and casual partnerships and between heterosexuals and MSM, and, in all cases, was a decreasing function of age.[12-14,16]

We modeled 21% of the MSM population as men who have sex with men and women (MSMW), a calibrated a result close to the estimates in the literature.[11,17,20,22] While we lacked data on the proportion of MSMW partners who were female, model calibration to match the average annual proportion of all new HIV infections occurring in MSM and heterosexual males and females indicated that 80% of sexual contacts of MSMW were with female partners. Thus, our transmission analysis focused on transmissions from heterosexuals to heterosexuals, MSMW to heterosexual females, and MSM to MSM. Based on survey data, we also assumed 15% of diagnosed MSM practiced serosorting; i.e., selected a partner who was also HIV infected.[23-25]

We modeled 52% of MSM as having more than one partner at the same time, either casual or main, based on MSM-reported data regarding the possibility of their partners having other partners at the same time.[26] Drawing on survey data, we assumed 9% of heterosexuals had more than one partner at the same time.[27,28]

The duration of partnership overlap was drawn from a probability distribution of the months of concurrent partnerships based on heterosexual males and applied to MSM. We estimated the remaining duration of the concurrent partnership for those just infected with HIV using geometrically distributed random variables around an estimated mean duration.[27,28] We also estimated the probability of a gap between partnerships, based on survey data.[10]

To illustrate partnership formation and dissolution in the model, Figure 1 depicts partnerships in a hypothetical population at three time points (months in time (t) = 1, 3, and 4) of the simulation, and the events related to partnership formation or dissolution that occur during each of these months. At t = 1, the population consisted of only four persons infected with HIV, A+, B+, E+, and F+, where the positive sign indicates HIV infection. The solid oval indicates that these individuals were tracked in the agent-based model.

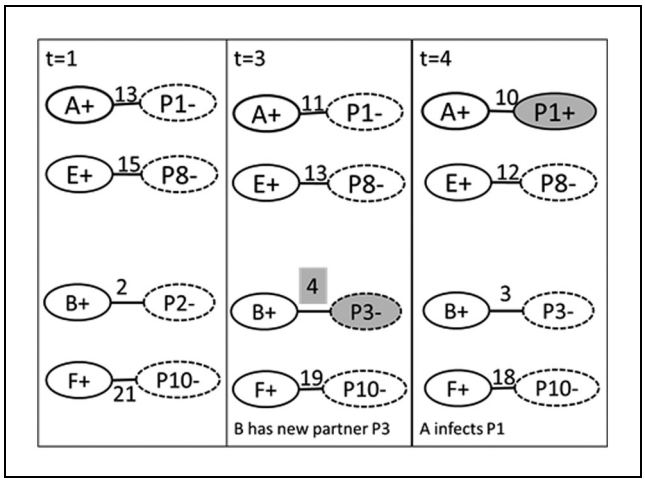

Figure 1 Schematic of simulation of partnership formation and dissolution between persons infected with HIV and their immediate partners in PATH 2.0. Solid oval: infected person, dashed oval: uninfected partner; shaded: changes; lines and numbers: partnership and remaining duration of partnership; t= time in months.

Partners of A+, B+, E+, and F+ are P1-, P2-, P8- and P10-, respectively, the negative sign indicating that the partners are not infected with HIV. The dotted oval indicates that the uninfected partners are not tracked individually but are modeled as characteristics of the partner who is infected. The lines between the ovals indicate the partnership, and the number over the lines shows the remaining duration of the partnership in months.

Time t=2 is not shown in Figure 1 because there are no changes in partnerships or HIV transmissions in that period. At t=3, the two-month partnership between B+ and P2- ends, and a new partnership between B+ and P3- begins, with a partnership duration of 4 months. P2- was not infected by the end of this partnership and cannot contribute to future infections, so we do not attempt to track this person further.

At every time unit, there is a probability of HIV transmission from person who is infected with HIV to his or her partner. When partner P1- is infected by A+ at t=4, P1+ is added as an individual to the model (depicted by the change from the dotted to a solid oval) and all attributes related to his or her current partnership with A+, including the remaining duration of the partnership, are also added as

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characteristics of P1+. Until P1+ and A+ have new partners who are HIV-negative, they will not transmit infection to others.

Simulating Transmissions

At every time unit, we used a Bernoulli process model (see Appendix)[29] to simulate HIV transmission from a person who is infected to his or her partner based on the stage of HIV disease, the partner's HIV status, and the partnership's number and type of sex acts (anal or vaginal, insertive or receptive), and degree of condom use. The probability per sex act was highest in the acute phase and lowest when the person was taking an ART regimen with viral load suppressed.[30-32]

In an individual-level model that simulates the entire population, if an uninfected person has two infected partners (a type of partnership concurrency), the model will clearly identify both the uninfected and infected partners. However, in focusing the simulation only on infected persons, when an uninfected partner becomes infected by one of two infected partners, PATH 2.0 does not automatically identify the second infected partner or change the second partner's partnership attributes to reflect that one of his previously uninfected partners is now infected. If uncorrected, this would erroneously allow for another transmission to occur. Therefore, upon determining that the newly infected person has another infected partner, the model prevents the error by matching the second infected partner's predicted age and sexual orientation to that of the infected persons already identified in the model. We provide more details in the Appendix on how the model handles partnership concurrency.

Modeling Disease Progression

We updated the disease-specific values of every person infected with HIV in the model at each time step to depict disease progression and changes in position in the HIV care continuum from diagnosis through to viral load suppression. Each person infected with HIV transitioned through the following disease stages: acute infection, asymptomatic infection, symptomatic infection/AIDS, and death. We modeled improved CD4 counts and decreased viral loads based on probabilities of the success of different regimens when persons infected with HIV initiated ART. Disease progression was modeled similar to that in a previous model[33], and further details can be found in the Appendix.

Modeling Uninfected Persons as Populations

For persons uninfected, we divided the population by sex and HIV-risk group and kept track of the size of the population over time. At the start of the simulation in year 2006, we determined the proportion of people in each risk and gender group as follows, taking MSM as an example. Let $p_{msm,t}$ be the proportion of uninfected MSM at year t. Then $p_{msm,t=2006}$ = (1 − prevalence of HIV among MSM in year 2006) × (proportion of MSM in the U.S.). At every time-unit, we updated $p_{msm,t} = p_{msm,t-1} - \frac{dp_{msm}}{dt}$, where $\frac{dp_{msm}}{dt}$ is the proportion of MSM who are newly infected, estimated in the agent-based model.

Selection of Time Unit

The time unit in PATH determined how often we estimated the probability of transmission from a person infected with HIV to his or her partner. Longer time units could result in inaccurate counts of new onward transmissions because people infected during one time period cannot infect others until the next time period when their HIV status changes from uninfected to infected. The time unit is particularly important in the case of acute infection when a newly infected person with a high transmission risk has the opportunity to quickly transmit to uninfected partners. The selection of the time-unit is especially critical in PATH because the longer the time unit, the greater the probability that an uninfected person with two infected partners will be recorded as infected by both, leading to an overestimation of the number of transmissions. Therefore, we selected a time unit that minimizes computation time with the least amount of error in the counts of the number of transmissions generated. We used a monthly time unit in the non-acute phase and a weekly unit in the acute phase to accommodate the weekly changes in transmission risk, which are substantially higher than in those in the non-acute phase. See the Appendix for more details.

Categories of HIV Transmission

We simulated transmissions generated by persons infected with HIV in the USA according to stage of disease and position in the HIV care

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continuum (diagnosed, in care, on an ART regimen, with a suppressed viral load). We also evaluated transmissions generated by persons infected with HIV by their sexual orientation/transmission risk group; i.e., heterosexuals and MSM. We further categorized transmissions within MSM by men who had sex with men only and those who had sex with men and women.

Outcome Measures

For each population in the analysis, categorized by disease stage or sexual orientation, we computed the average annual proportion of PLWH in that disease stage or sexual orientation category between 2008 and 2011. We also computed the average annual proportion of all transmissions generated by people in that category. We calculated an average, annual transmission rate per 100 person-years for persons in each category by dividing the number of transmissions generated by people in that category by the number of people infected with HIV in the category. We also provided a relative transmission risk by using the lowest transmission rate category as a reference case, and dividing higher annual transmission rates by the reference case. We ran the model 30 times to estimate an average and a range [5th and 95th percentile simulation intervals (SI)] for the proportion of transmissions generated by each category, the number of people (or acts) in each category, the annual transmission rate associated with each category, and the relative risk of transmission from one category compared to another. We chose 30 runs because each run consisted of 10,000 or more people, and the distributions for each input were applied to each person in the run. Therefore, the results of each run are based on a large sample.

Analysis Model Calibration and Validation

We additionally calibrated the model inputs for rates of diagnosis, linkage to care and prescription of ART so that the proportion of MSM and heterosexuals living with HIV in the model who were diagnosed, linked to care and in treatment matched published estimates for the years 2006 and 2008.[6,34] We validated the model by comparing the total number of simulated and independently reported sexually transmitted infections in years 2007 through 2009.[3] We also compared model outputs to independent estimates of the annual number of heterosexuals and MSM newly diagnosed with HIV from 2007 to 2011,[35,36] the median CD4 count at diagnosis among heterosexuals and MSM in 2012,[9] the number of MSM and heterosexuals living with diagnosed HIV during the years 2009 through 2011,[9] and the median number of years, assuming no treatment, from HIV seroconversion to attainment of CD4 counts of <500, <350 and <200.[37]

RESULTS

In our analysis of transmissions generated by HIV infection disease stage (acute v. non-acute) and position in the HIV care continuum, we estimated that, on average, over the 4-year period from 2008 to 2011, the proportion of all transmissions generated by those in the acute phase was 9% (5th and 95% percentile simulation intervals (SI): 7%, 11%), with the remainder by those in the non-acute phase (Table 1). The average annualized HIV transmission rate was 40 (31, 52) per 100 person-years for those in the acute disease stage and 4.1 (3.9, 4.4) for those in non-acute stage. Thus, the risk of transmission in the acute phase was 9 times (7, 12) that of the non-acute phase. Over the 4 years, 1% (1%, 1.3%) of PLWH were estimated on average to be in the acute phase.

Among those in the non-acute phase, most transmissions were from those unaware, 40% of all transmissions, (36%, 43%) and aware but not in care [38%, (35%, 41%)], compared to those on ART with viral load suppression [1% (1%, 2%)] or on ART but not virally suppressed [8%, (6%, 10%)]. The average annualized transmission rate ranged from 8.4 (7.7, 9.2) per 100 person-years for the unaware to 0.2 (0.1, 0.3) for those on ART with viral load suppression, generating a relative risk 24- to 50-times higher for those in the non-acute phase who had not achieved viral load suppression compared with those who had.

When categorizing transmissions by sexual orientation, we found heterosexuals generated 16% (13%, 18%) of all sexually transmitted infections, and MSM, (including MSMW), generated 84% (82%, 87%) (Table 2). The average annual transmission rate for heterosexual persons infected with HIV was 2.3 (1.9, 2.6) per hundred person-years and for MSM was 6.7 (6.3, 7.1), yielding a relative risk of transmission among MSM of 3.2 (2.7, 4.0) compared to heterosexuals. The simulation also showed that 71% (66%, 76%) of all transmissions were from MSM to other MSM. And, based on calibrated results that 21% of MSM were MSMW, 80% of sex acts among MSMW were with women, and 50% of

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Table 1 Average Annual HIV Transmission Outcomes from 2008 to 2011 among Heterosexuals and MSM in the United States by Stage of Disease, Care, Treatment, and Viral Load Suppression Status

Stage	Proportion of Total HIV Transmissions Generated by Heterosexuals and MSM Living in Each HIV Disease Stage (5th and 95th percentile)	Proportion of all Heterosexuals and MSM Living with HIV (5th and 95th percentile)	Transmission Rate (Number of transmissions per 100 person-years) (5th and 95th percentile)	Relative Risk (Transmission rate relative to reference transmission rate) (5th and 95th percentile)
Acute or non-acute phase				
Acute	9% (7–11%)	1% (1–1.3%)	40 (31–52)	9 (7–12)
Non-acute	91% (89–93%)	99% (98.7–99%)	4.1 (3.9–4.4)	Reference
Diagnosis and care status of non-acute phase				
ART regimen with viral load suppression	1% (1–2%)	26% (25–26%)	0.2 (0.1–0.3)	Reference
ART regimen- no viral load suppression	8% (6–10%)	9% (8.9–9.7%)	3.8(3–4.5)	24 (12–42)
Aware in care with no ART regimen	4% (3–5%)	4% (3.4–4.0%)	4.9 (3.4–6.4)	27 (13–45)
Aware not in care	38% (35–41%)	38.9% (38.8–38.9%)	4.5 (4.1–4.8)	27 (14–46)
Unaware	40% (36–43%)	21.5% (21.3–21.6%)	8.4 (7.7–9.2)	50 (26–83)

Table 2 Average Annual HIV Transmission Outcomes from 2008 to 2011 among Heterosexuals and MSM in the United States by Sexual Orientation

Transmissions From	Proportion of Transmissions Generated by Heterosexuals and MSM Living with HIV (5th and 95th percentile)	Proportion of Heterosexuals or MSM Living with HIV (5th and 95th percentile)	Transmission Rate (Transmissions per 100 person-years) (5th and 95th percentile)	Relative Risk (Transmission rate relative to reference transmission rate) (5th and 95th percentile)
Heterosexuals	16% (13–18%)	36% (35–36%)	2.3 (1.9–2.6)	Reference
MSM* (Total)	84% (82–87%)	64% (64–65%)	6.7 (6.3–7.1)	3.2 (2.7–4.0)

*Among MSM, 53.5% (5th and 95th percentiles: 53%, 54%) were estimated by the model to be men who have sex with men only and they generated 71% (66%, 76%) of all new transmissions. Also among MSM, 13% (11%, 16%) were estimated by the model to be men who have sex with men and women and they generated 10.8% (10.6%, 11.0%) of all new transmissions.

those acts were anal, the simulation further showed that 13% (11%, 16%) of all transmissions were from MSMW to females. The results indicated that MSMW generated 46% of new sexually acquired transmissions among heterosexuals (29% of all infections were acquired by heterosexuals, including 16% from other heterosexuals and 13% from MSMW).

Validation of Results

When we compared the model's simulated number of sexual transmissions in the years 2007, 2008 and 2009 against the incidences reported by Prejean and colleagues,[3] the model's median estimates in 2007 were between the median published estimate and the lower bound of the 95% confidence interval (Figure 2). The estimates for 2008 and 2009 were close to the median published estimate. The model's simulated outcomes also reasonably matched independent counts or estimates of the annual number of heterosexuals and MSM newly diagnosed with HIV from 2007 to 2011[35,36], the median CD4 count stratum at diagnosis for heterosexuals and MSM in 2012[9], the number of MSM and heterosexuals living with diagnosed HIV

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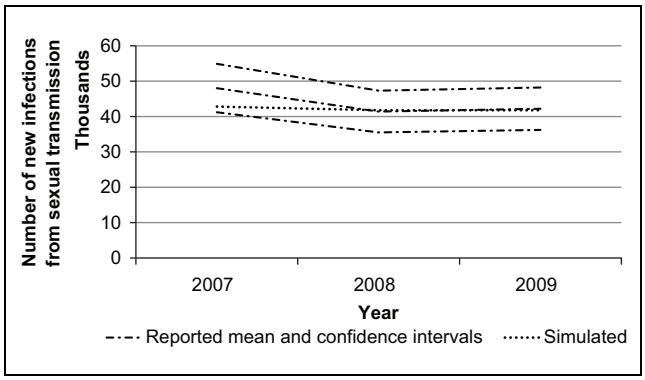

Figure 2 Comparing the simulated and reported[3] number of new HIV infections from sexual transmissions in the United States, 2007 to 2009.

during the years 2009 through 2011[9], and the median number of years, assuming no treatment, from HIV seroconversion to CD4 counts, 500, <350, and <200.[37] (Appendix, Figure S3).

DISCUSSION

We developed PATH 2.0 as an agent-based model of persons infected with HIV, with uninfected persons included as populations stratified by risk and gender. We applied PATH to simulate the distribution of HIV transmissions in the United States among subgroups of people living with HIV and to estimate transmission rates among those groups. We estimated that the relative risk of transmission of those in the acute phase was 9-times that of the non-acute phase, though, on average, the acutely infected comprised only 1% of all PLWH. The relative risk of transmission was 24- to 50-times as high for those in the non-acute phase who had not achieved viral load suppression compared with those who had. The relative risk of transmission among MSM was 3.2-times that of heterosexuals. Men who have sex with men and women generated 46% of sexually acquired transmissions among heterosexuals. These results support ongoing efforts to develop tools to diagnose HIV early in the course of infection, and to promptly notify the newly diagnosed and link them to care. They also support a continued focus on the HIV care continuum, from diagnosis to viral load suppression, and they support enhanced efforts to deliver prevention interventions to MSM and their female partners.

Our transmission rate estimates for those in the acute and non-acute phases of infection are similar to those previously reported by Pinkerton[38,39] and Prabhu and colleagues,[40] who used a different estimation procedure. Differences between their estimates and ours may be related to differences in the methods. Their static models relied on surveillance data to provide both the total number of new transmissions and the number of PLWH in each group, as well as other data on the estimates of the relative risk of transmission by disease stage and position along the HIV care continuum. The relative risks incorporated differences in sexual risk behaviors and the probability of viral load suppression by subgroup.

Skarbinski and colleagues[41] published an analysis that focused on transmission rates by stage of the HIV care continuum. Our results were similar to theirs, though we had somewhat higher transmission rates for PLWH who were in care but had not achieved viral load suppression. Our higher rates were, in part, because we did not attribute additional reductions in risk behaviors to diagnosed people in care as compared with those not in care. Overall, however, the prevention policy implications from both analyses are similar; i.e., continued focus on linkage to care, and prescription of and adherence to ART so that PLWH achieve the lowest levels of transmission associated with viral load suppression.

Skarbinski and colleagues[41] also provided transmission rates by risk group. They estimated an annual transmission risk among MSM of 4.4 per 100 person-years, and among heterosexual males and females of 3.5 and 1.6, respectively. Our estimates were 6.7 per 100 person-years for MSM and 2.3 for male and female heterosexuals combined. Skarbinski and colleagues' method included the use of a static model and the division of all PLWH by transmission subgroup, based on HIV surveillance data. They then generated the average probability of transmission from each group based on data about behaviors, disease stage and position in the HIV care continuum and multiplied that probability by the number of PLWH in the subgroup. They totaled all transmissions and estimated a multiplier that would equate their total with the published total HIV incidence estimate for 2009. They then applied the same multiplier to each subgroup so that the total modeled number of infections equaled the published incidence estimate. In contrast, PATH is a dynamic model, designed to generate over time both the PLWH transmission subgroup and the number of new transmissions from each subgroup. We calibrated the model in part by comparing the proportion of new transmissions that occurred

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among MSM and heterosexual males and females during 2007 to 2009 against published data for those years. The calibration led to refined inputs regarding the subset of MSM who have sex with women, and this appears to be one factor behind our higher estimate of MSM transmission rates.

Our estimate that 46% of transmissions in the heterosexual population were from MSMW should be considered with caution given the lack of data on the proportion of MSMW sex acts that are with women; but we believe the number is plausible based on model calibration. In one simulation, we assumed no mixing between MSM and heterosexuals. When we compared the average proportion of new HIV cases generated among heterosexual males and females and MSM to the 3-year average annual proportion reported by Prejean and colleagues,[3] we found that the model generated 22% of the new cases among heterosexual females reported in surveillance data, 68% of the cases reported for heterosexual males, and 120% of the cases reported for MSM (see Appendix, Supplemental Table S6). In a second simulation, where we assigned behavior to heterosexuals that was much riskier than reported in survey data (10 partners per year instead of 1 or 2, 50% of sex acts as anal sex instead of 2% to 11%, and 0% of all sex acts protected by condoms, instead of 1% to 79%), the model generated 58% of the new cases reported among heterosexual females, 71% of the new cases reported among heterosexual males, and 121% of the new cases reported among MSM. In a third simulation, where we used the current model assumptions (21% of MSM had sex with women, 80% of the MSMW acts were with women, and 50% of those were anal acts), the model generated 91% of the new cases reported among heterosexual females, 77% of the new cases reported among heterosexual males, and 98% of the new cases reported among MSM. Thus, the current model assumptions regarding behaviors among MSMW and female partners generated results that more closely matched independent estimates.

Our findings with respect to MSMW transmissions to heterosexual females also are corroborated to some extent by empirical data reported by Oster and colleagues.[42] Based on the use of molecular HIV surveillance data, they found that, among heterosexual women living with HIV for whom potential transmission partners were identified, 29% were linked to MSM, 21% to heterosexual men, and 12% to persons who inject drugs.

PATH 2.0 is subject to limitations, especially regarding sexual behavioral data. We modeled transmissions from MSMW to women but, given the lack of data on the proportion of women with partners who are MSMW, we could not model transmissions from women to MSMW. Behavioral data as a whole are subject to reporting bias. Additional bias could result from integrating independent surveillance systems. The model did not include sexual transmissions to or from injecting drug users, and this could have resulted in smaller or larger transmission rates for MSM and heterosexuals. In addition, our technique of building the partnerships of people infected with HIV over time, instead of using an individual-based model that included all infected and uninfected people, is subject to a small margin of error as discussed in the time unit estimation section of the Appendix.

In conclusion, this paper presents a newly developed, agent-based model that integrates several independent surveillance and behavioral databases to estimate new HIV infections as a function of individual-level sexual behavior, disease stage, and position along the HIV care continuum. The model is well validated against a number of outcomes, including HIV incidence. The model findings support a continued focus on early diagnosis, treatment and adherence to ART, with an emphasis on prevention efforts for MSM and their female partners.

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