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A New Method for Estimating the Incidence of Infectious Diseases

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Ambitious World Health Organization targets for disease elimination require monitoring of epidemics using routine health data in settings of decreasing and low incidence. We evaluated 2 methods commonly applied to routine testing results to estimate incidence rates that assume a uniform probability of infection between consecutive negative and positive tests based on 1) the midpoint of this interval and 2) a randomly selected point in this interval. We compared these with an approximation of the Poisson binomial distribution, which assigns partial incidence to time periods based on the uniform probability of occurrence in these intervals. We assessed bias, variance, and convergence of estimates using simulations of Weibull-distributed failure times with systematically varied baseline incidence and varying trend. We considered results for quarterly, half-yearly, and yearly incidence estimation frequencies. We applied the methods to assess human immunodeficiency virus (HIV) incidence in HIV-negative patients from the Treatment With Antiretrovirals and Their Impact on Positive and Negative Men (TAIPAN) Study, an Australian study of HIV incidence in men who have sex with men, between 2012 and 2018. The Poisson binomial method had reduced bias and variance at low levels of incidence and for increased estimation frequency, with increased consistency of estimation. Application of methods to real-world assessment of HIV incidence found decreased variance in Poisson binomial model estimates, with observed incidence declining to levels where simulation results had indicated bias in midpoint and random-point methods.

disease incidence rates; longitudinal data; Poisson binomial distribution; routine diagnostic testing

Abbreviations: ACCESS, Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of Sexually Transmissible Infections and Blood Borne Viruses; HIV, human immunodeficiency virus; MSM, men who have sex with men; PrEP, preexposure prophylaxis; PY, person-years; TAIPAN, Treatment With Antiretrovirals and Their Impact on Positive and Negative Men.

Recent advances in the treatment and prevention of many infectious diseases have led to ambitious World Health Organization targets which include ending the global human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (1, 2) and tuberculosis (3, 4) epidemics, interrupting malaria (5) and measles (6) transmission, eliminating mother-to-child-transmission of HIV (7) and syphilis (7), and eliminating hepatitis B and C virus infections as a public health threat (8, 9). In low-incidence settings, ambitious target incidence thresholds have been set as low as <0.1 case per 100,000 population (10, 11). This has created increased programmatic interest in more frequently measured incidence estimates. Australia has set an ambitious goal of virtually eliminating HIV transmission by 2022, with HIV preexposure prophylaxis (PrEP) being one of the key strategies (11). This requires frequent evaluation of incidence to assess the response and make necessary adjustments to PrEP and/or other strategies implemented as required (12). However, more frequent incidence estimation and reporting, such as at quarterly intervals for PrEP, leads to smaller increments in incident case numbers compared with annual reporting time frames, which presents analytical challenges and necessitates a review of current methodologies.

The gold standard method of measuring disease incidence requires repeat testing at prespecified frequent and regular intervals, typically in the context of clinical trials or prospective cohort studies (12). However, such studies are very costly and thus have not been widely adopted, especially for population-level surveillance and assessment (13). Many high-income countries rely on passive notification of diagnoses (otherwise known as case reporting) to assess trends in disease epidemiology, but these data do not reflect trends in incidence because they include both recent and established infections (2) and do not account for changes in diagnostic testing frequency (14).

Instead, the World Health Organization/Joint United Nations Programme on HIV/AIDS has recommended greater use of routinely collected health-facility data to evaluate epidemics. The World Health Organization is actively developing health statistics and information systems toolkits designed to optimize the analysis and use of routine data available through health-management information systems, including those for HIV, hepatitis, malaria, tuberculosis, and neglected tropical diseases (12, 15). This is becoming increasingly feasible as more low- and middle-income countries adopt electronic data-management systems comparable to those used in high-income countries, making input data more accessible for public health surveillance (16–19). Applications of such systems to disease incidence measurement and surveillance have been reported for at-risk populations, including female sex workers, people who inject drugs, and men who have sex with men (MSM) in both high- and low- to middle-income countries (19–24).

Therefore, we assessed the robustness of widely used incidence estimation methods (the midpoint method and the random-point method) based on routinely collected HIV testing data with unknown dates of infection and compared them with a new method which uses Poisson binomial distribution assumptions about the timing of infection. We hypothesized that the number of incident cases would get smaller the more incidence was measured, leading to increases in the variance around estimates for all of the methods but less so for the Poisson binomial method than the others. We first assessed the different methodologies using generalized simulated populations with systematically varied levels and trends in disease incidence to compare variance, bias, and consistency. We then applied these methodologies to a real-world HIV-negative cohort in Australia to assess HIV incidence among MSM over a period of expanded HIV prevention program coverage and newly introduced prevention methods, such as "treatment as prevention" and PrEP. This setting provided an example of the emerging challenges associated with accurate and timely incidence estimation in settings of decreasing numbers of detectable cases (25).

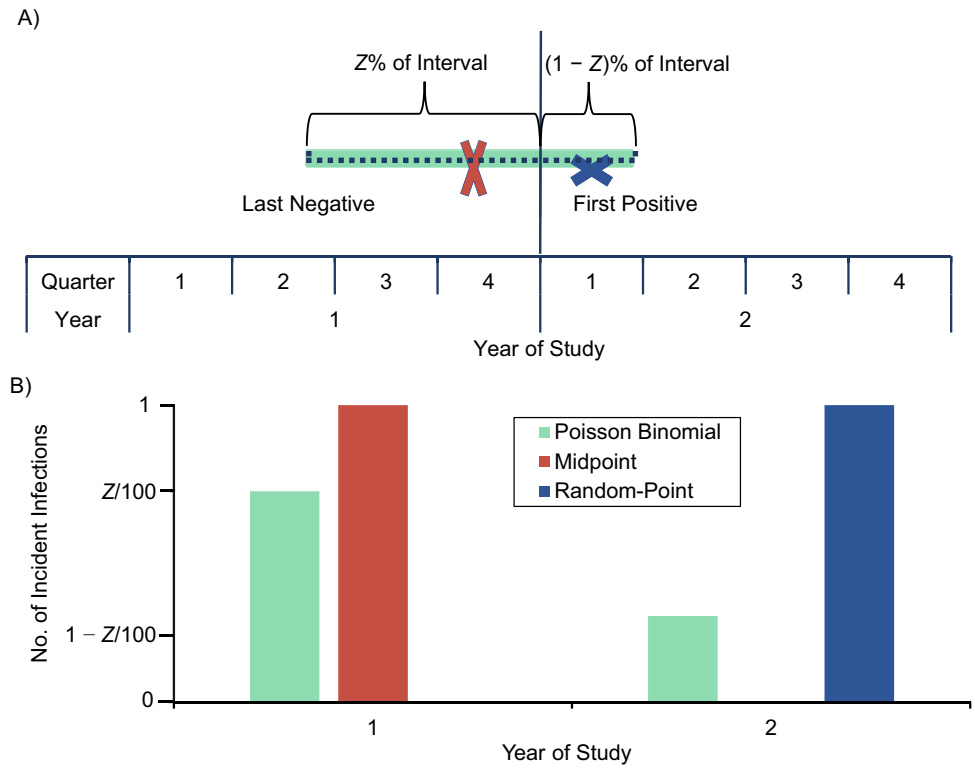

Figure 1. Illustration of 3 different methods of estimating the date of incident human immunodeficiency virus (HIV) infection between consecutive negative and positive HIV antibody tests. Panel A shows a testing interval between the last negative and the first positive HIV test (dotted lines) for a patient recorded over years 1 and 2 of a study. The red X represents dates of infection assigned by the midpoint method. The blue X represents dates of infection assigned by the random-point method. The green shaded area represents the period of infection assigned by the Poisson binomial method. Panel B shows the number of incident infections for yearly units of time based on the dates of infection.

METHODS

We applied 3 different methods to estimate the date of incident infection between consecutive negative and positive HIV antibody tests (Figure 1):

1. Midpoint method: We assumed that infections occurred at the midpoints (expected value for the uniform distribution) of negative–positive testing intervals.
2. Random-point method: We assumed that infections occurred at random points that were uniformly distributed within negative–positive testing intervals.
3. Poisson binomial method: We assumed equal probabilities of infection at each time point within negative–positive testing intervals (equal to the probability density function of the uniform distribution). This method assigns partial incidence to different follow-up periods in instances where negative–positive test intervals fall across multiple follow-up periods. The distribution of the total number of new infections at any given time point was then approximated using a Poisson distribution, with expected incident case numbers equal to the sum of individual probabilities of seroconversion. For a large sample size but a small and not necessarily equal incidence probability, the total number of incident cases is well approximated by a Poisson distribution by the law of small numbers (26). Time at risk in subintervals between negative and positive tests was reduced by 50% to reflect the expected time of failure for each interval. Where results are presented, we developed 95% confidence intervals for estimates based on the incomplete gamma function (27).

Study data

Simulated populations. Using the Stata 15.1 (StataCorp LLC, College Station, Texas) "survsim.ado" program, we simulated survival times in populations with incident infection using assumed Weibull distributions of estimated positive test times for a population size of 10,000 over 6 years of follow-up. A quasinormal distribution of test interval durations was assumed for intervals between the last negative test and the first positive test, with an average interval duration of 0.5 years ($\sigma^2 = 0.25$), but with minimum interval length restricted to positive durations. Analysis time was restricted to the last 5 years of follow-up, with left-censoring applied to the first year of follow-up to reduce effects of incomplete follow-up associated with negative test dates occurring prior to the start of the analysis.

Decreasing and constant incidence rate scenarios were simulated through variation of the Weibull shape parameter ($\eta = 0.5$, $\eta = 1.0$), while different baseline incidence levels were simulated through variation of the Weibull scale parameter ($\rho = 0.001$, $\rho = 0.010$, and $\rho = 0.100$). Scenarios were simulated using different incidence estimation frequencies: 4 times per year (quarterly), twice per year (half-yearly), and once per year (yearly).

The effect of testing frequency (quarterly, half-yearly, and yearly) on incidence estimates was estimated for constant, low-incidence-rate scenarios ($\eta = 1$, $\rho = 0.001$).

A real-world HIV-negative population: TAIPAN Study data. We used data from the Treatment With Antiretrovirals and Their Impact on Positive and Negative Men (TAIPAN) Study, an Australian study of HIV incidence in MSM, to examine the utility of models applied to real-world data. TAIPAN is a retrospective, longitudinal, open-cohort study created using routine HIV testing data (28). Inclusion in the cohort was based on having more than 1 HIV test recorded within the participating network of clinical services during the study period (January 1, 2011–June 30, 2019), with the first test being HIV-negative. MSM status was based on recorded sexual behavior or on records of male patients that indicated testing for a rectal sexually transmissible infection (29). The date of study entry was the date of the first negative HIV test during the study period, based on screening using fourth-generation HIV immunoassays. The date of study exit was set as the date of the last negative test (if there were no positive tests) or the first positive test during the study period. Incident cases were assigned to the time period between the last negative HIV test and the first positive HIV test.

Data were extracted from 52 clinics (comprised of primary health-care, sexual health, and hospital clinics) in the 2 most populous states in Australia—New South Wales and Victoria, where an estimated two-thirds (64%) of MSM reside and where over 60% of national annual HIV diagnoses are reported (30, 31). The clinics were participating in a sentinel surveillance program called the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of Sexually Transmissible Infections and Blood Borne Viruses (ACCESS) (32). These data are recorded in health-management information systems as part of routine care and are extracted and transferred regularly to research institutes via GRHANITE data extraction software (GRHANITE Health Informatics Unit, University of Melbourne, Melbourne, Victoria, Australia), which creates an anonymized unique identifier for everyone (33). The anonymized unique identifier allows individuals' medical records from multiple clinics and laboratories to be reliably linked (33, 34). The analysis was conducted using data from the period January 1, 2011–June 30, 2019 to estimate HIV incidence throughout the period from January 1, 2012, to December 31, 2018—encompassing a period before and during the scale-up of coverage of treatment as prevention (from 2012) and, more recently, PrEP (from 2016) in Australia (35–38).

Ethics approval

Ethics approval for the ACCESS program was granted by the human research ethics committees of St. Vincent's Hospital, Sydney (Sydney, New South Wales, Australia); the University of New South Wales (Sydney, New South Wales, Australia); and the Alfred Hospital (Melbourne, Victoria, Australia). Site-specific assessment approvals were obtained from local research governance offices as required.

Statistical analysis

Simulations were conducted using systematically varied estimation frequencies and the trend and incidence levels

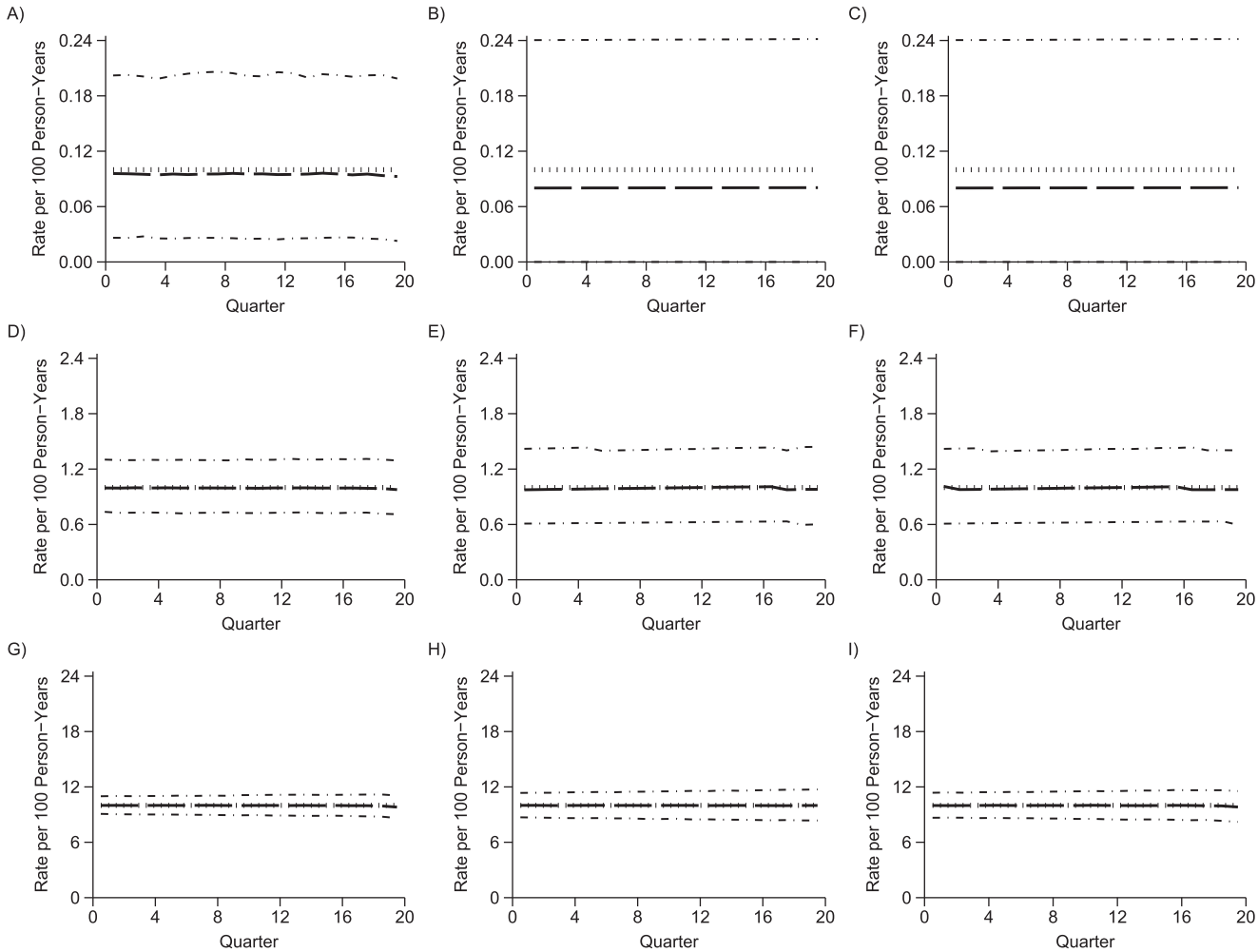

Figure 2. Estimated incidence of human immunodeficiency virus seroconversion per 100 person-years (PY) for constant simulated incidence and quarterly units of time, by simulated baseline incidence rate and method of estimation, for 1,000 simulations. A) Simulated baseline incidence of 0.10 cases/100 PY and the Poisson binomial method of estimation; B) simulated baseline incidence of 0.10 cases/100 PY and the midpoint method of estimation; C) simulated baseline incidence of 0.10 cases/100 PY and the random-point method of estimation; D) simulated baseline incidence of 1 case/100 PY and the Poisson binomial method of estimation; E) simulated baseline incidence of 1 case/100 PY and the midpoint method of estimation; F) simulated baseline incidence of 1 case/100 PY and the random-point method of estimation; G) simulated baseline incidence of 10 cases/100 PY and the Poisson binomial method of estimation; and H) simulated baseline incidence of 10 cases/100 PY and the midpoint method of estimation; I) simulated baseline incidence of 10 cases/100 PY and the random-point method of estimation. Bold dashed lines represent the incidence estimate for each specified method of estimation, and the dotted-dashed lines represent the 95% confidence intervals. The short-dashed line represents the incidence rate used as the basis for the simulations.

described above; and incidence rates were then calculated as numbers of cases per 100 person-years (PY) for the 3 methods. Monte Carlo simulation of incidence rates (median and 95% confidence interval) for the respective methods was conducted using the Stata "simulate.ado" program based on 10,000 repetitions per model. Relevant Stata code is provided in Web Appendices 1 and 2 (available online at https://doi.org/10.1093/aje/kwab014).

For real-world data, we compared estimates for the 3 methods with sampling (10,000 repetitions) from simulated uniformly distributed failure times across testing intervals for 2012–2018 based on follow-up testing censored at June 30, 2019. This allowed estimates to more closely approximate a true uniformly distributed set of failure times based on extended follow-up as compared with model estimates.

RESULTS

Simulation disease incidence

Constant incidence rate. For simulated incidence rates that were constant over time, estimates showed higher variance when estimation frequency was higher or incidence rates were lower (Figure 2, Web Figures 1 and 2). Variance

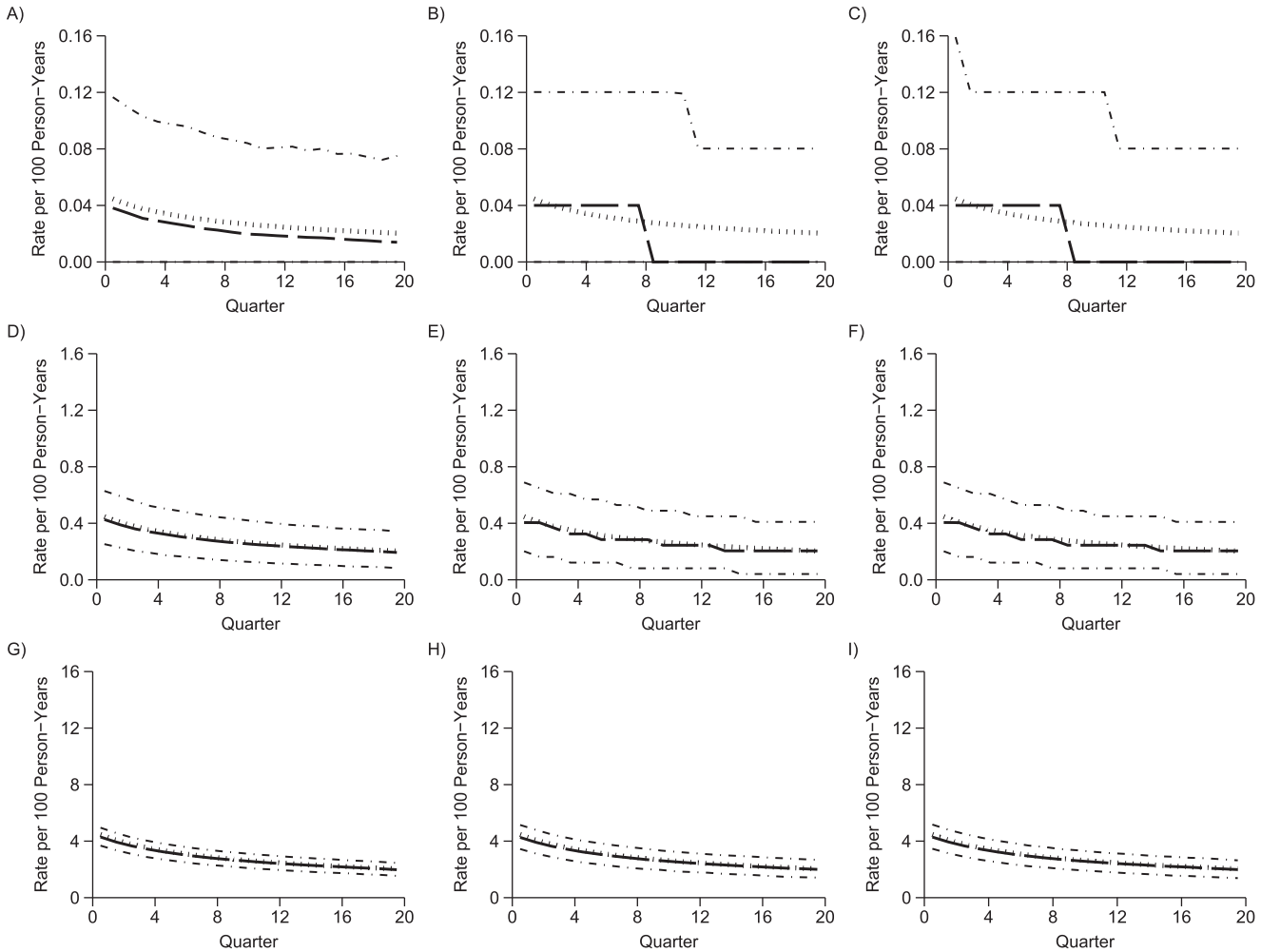

Figure 3. Estimated incidence of human immunodeficiency virus seroconversion per 100 person-years (PY) for decreasing simulated incidence and quarterly units of time, by simulated baseline incidence rate and method of estimation, for 1,000 simulations. A) Simulated baseline incidence of 0.10 cases/100 PY and the Poisson binomial method of estimation; B) simulated baseline incidence of 0.10 cases/100 PY and the midpoint method of estimation; C) simulated baseline incidence of 0.10 cases/100 PY and the random-point method of estimation; D) simulated baseline incidence of 1 case/100 PY and the Poisson binomial method of estimation; E) simulated baseline incidence of 1 case/100 PY and the midpoint method of estimation; F) simulated baseline incidence of 1 case/100 PY and the random-point method of estimation; G) simulated baseline incidence of 10 cases/100 PY and the Poisson binomial method of estimation; and H) simulated baseline incidence of 10 cases/100 PY and the midpoint method of estimation; I) simulated baseline incidence of 10 cases/100 PY and the random-point method of estimation. Bold dashed lines represent the incidence estimate for each specified method of estimation, and the dotted-dashed lines represent the 95% confidence intervals. The short-dashed line represents the incidence rate used as the basis for the simulations.

in the Poisson binomial model was lower than that observed in midpoint and random-point models for half-yearly and quarterly estimation frequency and for lower incidence rates. Models showed consistency with simulated distributions, except at the lowest incidence rates and quarterly estimation frequencies, where the midpoint method and random-point method showed negative bias leading to underestimation of incidence, while the Poisson binomial method more closely approximated simulated incidence.

Decreasing incidence rate. For simulated incidence rates that were decreasing over time, estimates showed higher variance when estimation frequency was higher or incidence rates were lower, with lower variance in the Poisson binomial model than in other models (Figure 3, Web Figures 3 and 4). At low rates the midpoint and random-point models showed some departure from simulated rates, while the Poisson binomial method was relatively consistent for all methods, although at the lowest levels of incidence and higher estimation frequencies there was an indication of negative bias.

Testing frequency. For simulated variation in testing frequency, estimates were constant across different testing rates. The Poisson binomial-method estimates showed increased variance at increased testing frequencies, and bounds

Table 1. Characteristics of the TAIPAN Study Population, New South Wales and Victoria, Australia, 2012–2018

Characteristic	HIV Seroconversion Status								
	Remained HIV-Negative (*n* = 45,719)			Seroconverted (*n* = 885)			Total (*n* = 46,604)		
	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)
Age at study entry[a], years	32 (26–43)			32 (26-42)			32 (26-43)		
Age group at study entry, years									
<30	18,470	40		339	38		18,809	40	
30–34	7,691	17		155	18		7,846	17	
35–44	9,679	21		217	25		9,896	21	
≥45	9,879	22		174	20		10,053	22	
Interval between HIV tests, days[a]									
Between negative and negative tests	104 (71–216)			117 (71–216)			105 (71–217)		
Between negative and positive tests	N/A			227 (109–566)			N/A		
No. of HIV tests taken per year[b]									
2011			1.49 (0.85)			1.73 (1.05)			1.50 (0.86)
2012			1.58 (0.92)			1.74 (1.00)			1.58 (0.93)
2013			1.60 (0.97)			1.81 (1.08)			1.61 (0.98)
2014			1.68 (1.04)			1.84 (1.14)			1.68 (1.05)
2015			1.79 (1.15)			1.75 (1.01)			1.79 (1.15)
2016			2.19 (1.48)			1.71 (1.22)			2.18 (1.48)
2017			2.43 (1.52)			1.53 (0.98)			2.43 (1.51)
2018			2.49 (1.47)			1.50 (0.91)			2.48 (1.47)
All years			2.04 (1.35)			1.74 (1.07)			2.04 (1.34)

Abbreviations: HIV, human immunodeficiency virus; N/A, not applicable; SD, standard deviation; TAIPAN, Treatment With Antiretrovirals and Their Impact on Positive and Negative Men.

[a] Values are expressed as median (interquartile range).

[b] Sequences of repeat tests with maximum separation between consecutive tests of 7 days were considered to be 1 testing event and allocated to the first test date in a given sequence.

on estimates tended toward those of the midpoint and random-point methods at higher testing frequencies (Web Figure 5).

Real-world HIV incidence: TAIPAN Study data

Population characteristics. HIV incidence estimates in the TAIPAN Study were based on 46,604 MSM and included 885 incident cases of HIV infection (1.90% of patients) over the course of the analysis period (2012–2018 inclusive). The median time between repeat tests was 105 days (interquartile range, 71–217), with longer time between repeat tests for participants who subsequently became HIV-positive (227 days (interquartile range, 109–566)). Participants were tested a mean of 2.04 times per year (standard deviation, 1.34), increasing from 1.50 times per year in 2011 to 2.48 times per year in 2018. This increase was less evident in participants who subsequently became HIV-positive, with a change from 1.73 times per year to 1.50 times per year (Table 1).

HIV incidence estimates. Estimated incidence rates trended downwards across the 7-year duration of the study, from over 1 case per 100 PY to close to 0.10 cases per 100 PY (Figure 4, Web Tables 1–3). There was increased variance in the estimates associated with the midpoint and random-point methods as compared with the Poisson binomial method,

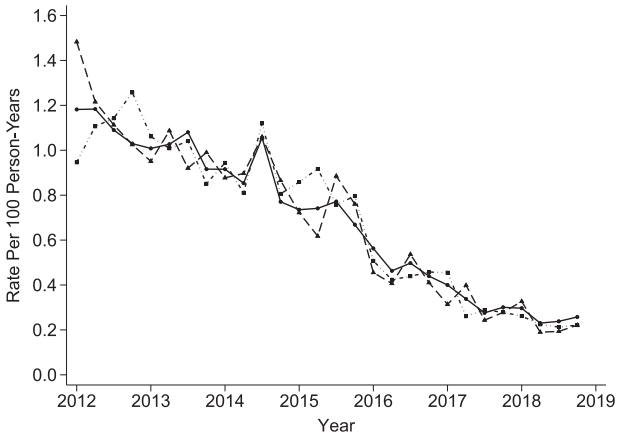

Figure 4. Estimated incidence rates of human immunodeficiency virus seroconversion per 100 person-years, by method, based on quarterly units of time with 6 months of extra follow-up, TAIPAN Study, 2012–2018. The solid line with circular markers represents the Poisson binomial method of estimation; the dotted-dashed line with square markers represents the midpoint method; and the long-dashed line with triangular markers represents the random-point method. Markers are shown at quarter 1 of each year. TAIPAN, Treatment With Antiretrovirals and Their Impact on Positive and Negative Men.

and this increased as estimation frequency increased (Web Tables 1–3). For quarterly estimation frequencies, the range in incidence rates over the interval 2012–2018 for the Poisson binomial method was 1.18–0.23 cases per 100 PY; for the midpoint method, it was 1.26–0.22 cases per 100 PY; and for the random-point method, it was 1.48–0.19 cases per 100 PY (Figure 4, Web Tables 1–3).

DISCUSSION

In settings where disease incidence is low and decreasing, we found that repeated testing methods (midpoint, random-point, and the new Poisson binomial method) produced similar annual estimates of HIV incidence in MSM. However, the Poisson binomial method more closely approximated a uniform distribution of disease transmission which was more robust to increases in incidence estimation frequency, with more continuous distributions of risk and lower variance and bias than the other repeat testing methods evaluated. This method is therefore likely to be more useful in evaluating epidemics where transmission is low and decreasing, or when reporting frequency increases, such as quarterly. The programatic monitoring of progress toward World Health Organization disease elimination targets, including those for global epidemics such as HIV and hepatitis C virus, is therefore likely to benefit from application of this method.

Methods compared in this paper all assigned the date of incidence based on an assumed uniform distribution across the interval between the last negative test and the first positive test. However, the midpoint and random-point methods allocate incident cases to a single point of time (respectively the midpoint or a random point in negative–positive testing intervals), which does not reflect uncertainty about the precise incidence date. Instead the Poisson binomial method allocates time-weighted proportions of incident cases to more than 1 unit of time when testing intervals overlap multiple time periods. While all methods were found to be accurate when incidence rates or time units were increased, the Poisson binomial method was more robust when numbers of incident cases were low and/or when there was more frequent estimation. This reflects an advantageous property of the Poisson binomial distribution in a setting of decreasing disease incidence. In particular, for small and nonidentical incidence rates, it is closely approximated by the Poisson distribution (39). Another useful property of the Poisson binomial method is that this approximation has maximum and calculable bounds on error which allow the quality of estimates to be easily quantified (40).

The application of estimation methods to a real-world cohort study monitoring testing for HIV showed similar broad trends via all methods but with less variance between consecutive time periods for the Poisson binomial method, especially when estimation frequency increased. We presented data for quarterly time intervals, which reflects commonly used HIV testing intervals for PrEP. There was more frequent testing in more recent periods for this cohort associated with increased availability of PrEP, which requires quarterly HIV testing. Since 2016, PrEP has been available in Australia through state government-funded PrEP demonstration programs and, since 2018, nationally via the pharmaceutical benefits scheme. From 2016 to 2018, the self-reported prevalence of PrEP use in Australia increased from 4.6% to 20.9% (41). This trend was associated with reduced differences between estimates derived via the 3 different methods when incidence rates had fallen to around 0.3 cases per 100 PY. Nevertheless, results from the Poisson binomial distribution suggested clearer trends for this method than for other methods. As rates fall further, we expect differences between methods to become more apparent, as reflected by simulations using baseline rates of 0.1 cases per 100 PY, where the Poisson binomial method more closely approximated simulated distributions but other methods showed a negative bias associated with low numbers of incident cases.

There are some limitations of the method. First, it is possible that the Poisson binomial model may produce underdispersed estimates as reflected by comparison with the midpoint and random-point methods. However, low-incidence settings mean that the Poisson mean and variance are closely aligned, and we observed a low rate of error using simulated distributions of risk. Second, our study did not make any assumptions about the distribution of seroconversion other than its lying with equal probability at any point between consecutive negative and positive tests. In instances of long duration between tests, this may lead to substantial inaccuracy in probabilities associated with individual cases. It is also possible that patients might be more likely to take an HIV test following high-risk events upon recognizing symptoms of primary HIV infection, which would skew the distribution of seroconversions on the interval between tests. In such cases, adaptation of the methods discussed in this

paper to incorporate distributions other than the uniform distribution may be more appropriate, although we did not investigate that here. However, considering the relatively high testing frequency in our real-world male HIV cohort (over 2 tests per year), it is likely that any such influence would be limited.

In summary, we found that estimates of incidence calculated using the repeat testing methods based on the Poisson binomial distribution were accurate and superior to those estimated by the midpoint method and the random-point method. This was mainly attributable to increased robustness at high estimation frequency and to low case numbers. Given widespread uptake of routine health-management information systems data in program monitoring, the method seems well suited to evaluation of the incidence of diseases associated with elimination goals, such as those for HIV PrEP programs or for implementation of treatment with direct-acting hepatitis C virus antiviral agents.

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REFERENCES

1. World Health Organization. *Global Health Sector Strategy on HIV 2016–2021: Towards Ending AIDS*. Geneva, Switzerland: World Health Organization; 2016. https://apps.who.int/iris/bitstream/handle/10665/246178/WHO-HIV-2016.05-eng.pdf. Accessed August 15, 2020.
2. Joint United Nations Programme on HIV/AIDS. *Understanding Fast-Track: Accelerating Action to End the AIDS Epidemic by 2030*. Geneva, Switzerland: Joint United Nations Programme on HIV/AIDS; 2015. https://www.unaids.org/sites/default/files/media_asset/201506_JC2743_Understanding_FastTrack_en.pdf. Accessed August 15, 2020.
3. World Health Organization. *Implementing the End TB Strategy: the Essentials*. Geneva, Switzerland: World Health Organization; 2015. https://apps.who.int/iris/bitstream/handle/10665/206499/9789241509930_eng.pdf. Accessed August 15, 2020.
4. World Health Organization Executive Board. *Global Strategy and Targets for Tuberculosis Prevention, Care and Control After 2015*. Geneva, Switzerland: World Health Organization; 2014. https://apps.who.int/iris/bitstream/handle/10665/172989/B134_CONF4Rev1-en.pdf. Accessed August 15, 2020.
5. World Health Organization. *A Framework for Malaria Elimination*. Geneva, Switzerland: World Health Organization; 2017. https://apps.who.int/iris/bitstream/handle/10665/254761/9789241511988-eng.pdf. Accessed October 20, 2020.
6. World Health Organization. *Global Measles and Rubella: Strategic Plan 2012–2020*. Geneva, Switzerland: World Health Organization; 2012. https://apps.who.int/iris/bitstream/handle/10665/44855/9789241503396_eng.pdf?sequence=1&isAllowed=y. Accessed April 26, 2020.
7. World Health Organization. *Global Guidance on Criteria and Processes for Validation: Elimination of Mother-to-Child Transmission of HIV and Syphilis*. 2nd ed. Geneva, Switzerland: World Health Organization; 2017. https://www.who.int/reproductivehealth/publications/emtct-hiv-syphilis/en/. Accessed August 15, 2020.
8. World Health Organization. *Global Health Sector Strategy on Viral Hepatitis 2016–2021: Towards Ending Viral Hepatitis*. Geneva, Switzerland: World Health Organization; 2016. https://apps.who.int/iris/bitstream/handle/10665/246177/WHO-HIV-2016.06-eng.pdf. Accessed October 20, 2020.
9. World Health Organization. *Technical Considerations and Case Definitions to Improve Surveillance for Viral Hepatitis*. Geneva, Switzerland: World Health Organization; 2016. https://apps.who.int/iris/bitstream/handle/10665/204501/9789241549547_eng.pdf. Accessed October 20, 2020.
10. World Health Organization. *Towards TB Elimination: An Action Framework for Low-Incidence Countries*. Geneva,

Switzerland: World Health Organization; 2014. https://apps.who.int/iris/bitstream/handle/10665/132231/9789241507707_eng.pdf. Accessed October 20, 2020.
11. Australian Government Department of Health. *Eighth National HIV Strategy 2018–2022*. Canberra, ACT, Australia: Commonwealth of Australia; 2018. https://www1.health.gov.au/internet/main/publishing.nsf/Content/ohp-bbvs-1/$File/HIV-Eight-Nat-Strategy-2018-22.pdf. Accessed August 25, 2020.
12. WHO Working Group on HIV Incidence Measurement and Data Use. *WHO Working Group on HIV Incidence Measurement and Data Use: 3–4 March 2018, Boston, MA, USA*. (Meeting report). Boston, MA: WHO Working Group on HIV Incidence Measurement and Data Use; 2018. https://www.who.int/diagnostics_laboratory/links/180622_boston_meeting_report.pdf?ua=1. Accessed June 30, 2019.
13. Kassanjee R, De Angelis D, Farah M, et al. Cross-sectional HIV incidence surveillance: a benchmarking of approaches for estimating the 'mean duration of recent infection'. *Stat Commun Infect Dis*. 2017;9(1):20160002.
14. Feigin A, El-Hayek C, Hellard M, et al. Increases in newly acquired HIV infections in Victoria, Australia: epidemiological evidence of successful prevention? *Sex Health*. 2013;10(2):166–170.
15. World Health Organization. Analysis and use of health facility data. Geneva, Switzerland: World Health Organization; 2019. https://www.who.int/healthinfo/tools_data_analysis_routine_facility/en/. Accessed November 20, 2019.
16. Joint United Nations Programme on HIV/AIDS. *Indicators for Monitoring the 2016 Political Declaration on Ending AIDS—Global AIDS Monitoring 2019*. Geneva, Switzerland: Joint United Nations Programme on HIV/AIDS; 2018. http://www.unaids.org/en/resources/documents/2018/Global-AIDS-Monitoring. Accessed March 11, 2019.
17. World Health Organization. *Consolidated Strategic Information Guidelines for HIV in the Health Sector*. Geneva, Switzerland: World Health Organization; 2015. https://apps.who.int/iris/bitstream/handle/10665/164716/9789241508759_eng.pdf. Accessed August 15, 2020.
18. Holmes C, Pillay Y, Mwango A, et al. Health systems implications of the 2013 WHO consolidated antiretroviral guidelines and strategies for successful implementation. *AIDS*. 2014;28(suppl 2):S231–S239.
19. Groseclose SL, Buckeridge DL. Public health surveillance systems: recent advances in their use and evaluation. *Annu Rev Public Health*. 2017;38(1):57–79.
20. van Griensven F, Holtz TH, Thienkrua W, et al. Temporal trends in HIV-1 incidence and risk behaviours in men who have sex with men in Bangkok, Thailand, 2006–13: an observational study. *Lancet HIV*. 2015;2(2):e64–e70.
21. Guy RJ, Spelman T, Stoove M, et al. Risk factors for HIV seroconversion in men who have sex with men in Victoria, Australia: results from a sentinel surveillance system. *Sex Health*. 2011;8(3):319–329.
22. Bernstein KT, Marcus JL, Nieri G, et al. Rectal gonorrhea and chlamydia reinfection is associated with increased risk of HIV seroconversion. *J Acquir Immune Defic Syndr*. 2010;53(4):537–543.
23. The Kirby Institute, University of New South Wales. *Annual Surveillance Report on HIV, Viral Hepatitis and STIs in Australia 2017*. Sydney, NSW, Australia: The Kirby Institute; 2017. https://kirby.unsw.edu.au/report/annual-surveillance-report-hiv-viral-hepatitis-and-stis-australia-2017. Accessed November 10, 2020.
24. Kwon JA, Iversen J, Maher L, et al. The impact of needle and syringe programs on HIV and HCV transmissions in injecting drug users in Australia: a model-based analysis. *J Acquir Immune Defic Syndr*. 2009;51(4):462–469.
25. Grulich AE, Guy R, Amin J, et al. Population-level effectiveness of rapid, targeted, high-coverage roll-out of HIV pre-exposure prophylaxis in men who have sex with men: the EPIC-NSW prospective cohort study. *Lancet HIV*. 2018;5(11):e629–e637.
26. Chen SX, Liu JS. Statistical applications of the Poisson-binomial and conditional Bernoulli distributions. *Stat Sin*. 1997;7(4):875–892.
27. Scholz F. Confidence bounds & intervals for parameters relating to the binomial, negative binomial, Poisson and hypergeometric distributions with applications to rare events. Seattle, WA: University of Washington; 2019. http://faculty.washington.edu/fscholz/DATAFILES498B2008/ConfidenceBounds.pdf. Accessed December 15, 2019.
28. Callander D, Stoové M, Carr A, et al. A longitudinal cohort study of HIV 'treatment as prevention' in gay, bisexual and other men who have sex with men: the Treatment with Antiretrovirals and Their Impact on Positive and Negative Men (TAIPAN) Study protocol. *BMC Infect Dis*. 2016;16(1):Article 752.
29. Wilkinson A, El-Hayek C, Fairley CK, et al. Incidence and risk factors associated with chlamydia in men who have sex with men: a cohort analysis of Victorian Primary Care Network for Sentinel Surveillance data. *Sex Transm Infect*. 2012;88(5):319–324.
30. Prestage G, Ferris J, Grierson J, et al. Homosexual men in Australia: population, distribution and HIV prevalence. *Sex Health*. 2008;5(2):97–102.
31. The Kirby Institute, University of New South Wales. *HIV, Viral Hepatitis and Sexually Transmissible Infections in Australia: Annual Surveillance Report 2018*. Sydney, NSW, Australia: The Kirby Institute; 2018. https://kirby.unsw.edu.au/report/hiv-viral-hepatitis-and-sexually-transmissible-infections-australia-annual-surveillance. Accessed November 10, 2020.
32. Guy R, Lim MS, Wang YH, et al. A new surveillance system for monitoring HIV infection in Victoria, Australia. *Sex Health*. 2007;4(3):195–199.
33. Callander D, Moreira C, El-Hayek C, et al. Monitoring the control of sexually transmissible infections and blood-borne viruses: protocol for the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance (ACCESS). *JMIR Res Protoc*. 2018;7(11):e11028.
34. Boyle DI, Kong FYS. A systematic mechanism for the collection and interpretation of display format pathology test results from Australian primary care records. *Electron J Health Inform*. 2011;6(2):e18.
35. Zablotska IB, Selvey C, Guy R, et al. Expanded HIV pre-exposure prophylaxis (PrEP) implementation in communities in New South Wales, Australia (EPIC-NSW): design of an open label, single arm implementation trial. *BMC Public Health*. 2018;18(1):Article 210.
36. Holt M, Lea T, Mao L, et al. Community-level changes in condom use and uptake of HIV pre-exposure prophylaxis by gay and bisexual men in Melbourne and Sydney, Australia: results of repeated behavioural surveillance in 2013–17. *Lancet HIV*. 2018;5(8):e448–e456.
37. New South Wales Ministry of Health. *NSW HIV Strategy 2012–2015: Quarter 3 2015 Data Report*. Sydney, NSW, Australia: New South Wales Ministry of Health; 2015. https://www.health.nsw.gov.au/endinghiv/Publications/q3-2015-hiv-data-report.pdf. Accessed November 10, 2020.

38. New South Wales Ministry of Health. *NSW HIV Strategy 2016–2020 Quarter 1 2018 Data Report*. Sydney, NSW, Australia: New South Wales Ministry of Health; 2018. https://www.health.nsw.gov.au/endinghiv/Publications/q1-hiv-2018-hiv-data-report.pdf. Accessed November 10, 2020.
39. Le Cam L. An approximation theorem for the Poisson binomial distribution. *Pac J Math*. 1960;10(4):1181–1197.
40. Barbour AD, Holst L, Janson S. *Poisson Approximation*. 1st ed. Oxford, United Kingdom: Clarendon Press; 1992.
41. Bavinton BR, Grulich AE, Broady T, et al. Increases in HIV testing frequency in Australian gay and bisexual men are concentrated among PrEP users: an analysis of Australian behavioural surveillance data, 2013–2018. *AIDS Behav*. 2020;24(9):2691–2702.