Supplemental Digital Content

I. Study Populations and Informed Consent

A. Inclusion criteria

Inclusion criteria for each study are as follows:
Sabes: Age ≥18 years, assignment of male sex at birth, self-report of a cisgender male or transgender woman sexual partner in the previous 12 months, lack of awareness of HIV status, and elevated risk for HIV based on previously described criteria, such as sex work, having an HIV-positive sex partner, or having a sexually transmitted disease in the past six months.
Feminas: Age ≥18 years, assignment of male sex at birth, identifying as a transgender woman or on the trans-feminine continuum (e.g., trans, travesti, transgender, or transsexual), and being unaware of their HIV status, or HIV positive but not engaged in HIV care.
Microepidemics: Age ≥18 years, assignment of male sex at birth, being unaware of their HIV status, and willing to undergo HIV point-of-care testing and pre- and post-test counseling.

B. Removing duplicate data

All studies included in analyses were overseen by Asociación Civil Impacta Salud y Educación (IMPACTA). IMPACTA maintains a central secure tracking system of participants in all studies, in which participants are assigned a code that is linked to their national identification number. While the data we used was de-identified and we used study-specific participant ID numbers for all analyses, we were provided this code to verify any repeat participants. This allowed us to include only one sample from each person even if they were enrolled in multiple studies.

C. Defining early infection

Early infection was defined as incident infection during study follow up of initially HIV-uninfected participants. The number of participants categorized as early versus late infection are shown below in sTable1. In Sabes, early infections were identified within 3 months of HIV acquisition based on prior negative HIV test (testing was conducted monthly) and HIV RNA testing. Participants with early infection were either seronegative but HIV RNA+ or seropositive for HIV; all had an HIV-negative test within the past 3 months. In Feminas, HIV serology testing was performed every three months, with three incident infections diagnosed during study follow up. Participants who were HIV seropositive at the screening visit for Sabes or Feminas who did not have a documented prior HIV-negative test were classified as presumed prevalent, which we defined as samples collected >6 months after presumed HIV acquisition or for which no data were available about date of HIV acquisition. Microepidemics used cross-sectional data collection and therefore all participants from Microepidemics were labeled as presumed prevalent.

sTable 1. Source and types of data used in molecular epidemiology analysis

	Sabes	Feminas	Microepidemics
Number of participants in study	3,336	216	568
Number included in this analysis	367	40	63
Dates of data collection	7/2013 – 9/2015	10/2016 – 3/2018	1/2017 – 6/2017
HIV diagnosis			
Early	302	3	0
Presumed prevalent	65	37	63
Demographic group			
Cisgender men who reported sex with transgender women (MSTW)	14	0	11
Cisgender men who have sex with men (MSM)	268	0	35
Transgender women	82	40	17
Epidemiologic data available	Yes (baseline)	Yes (baseline)	No

D. Informed Consent

Sabes and Microepidemics explicitly obtained informed consent for the use of samples for HIV phylogenetic analyses. Feminas sought informed consent for the use of samples for future research. The exact language, as it appeared in the consent forms, is provided in sTable 2.

sTable 2. Language related to future use of samples that was included in consent forms

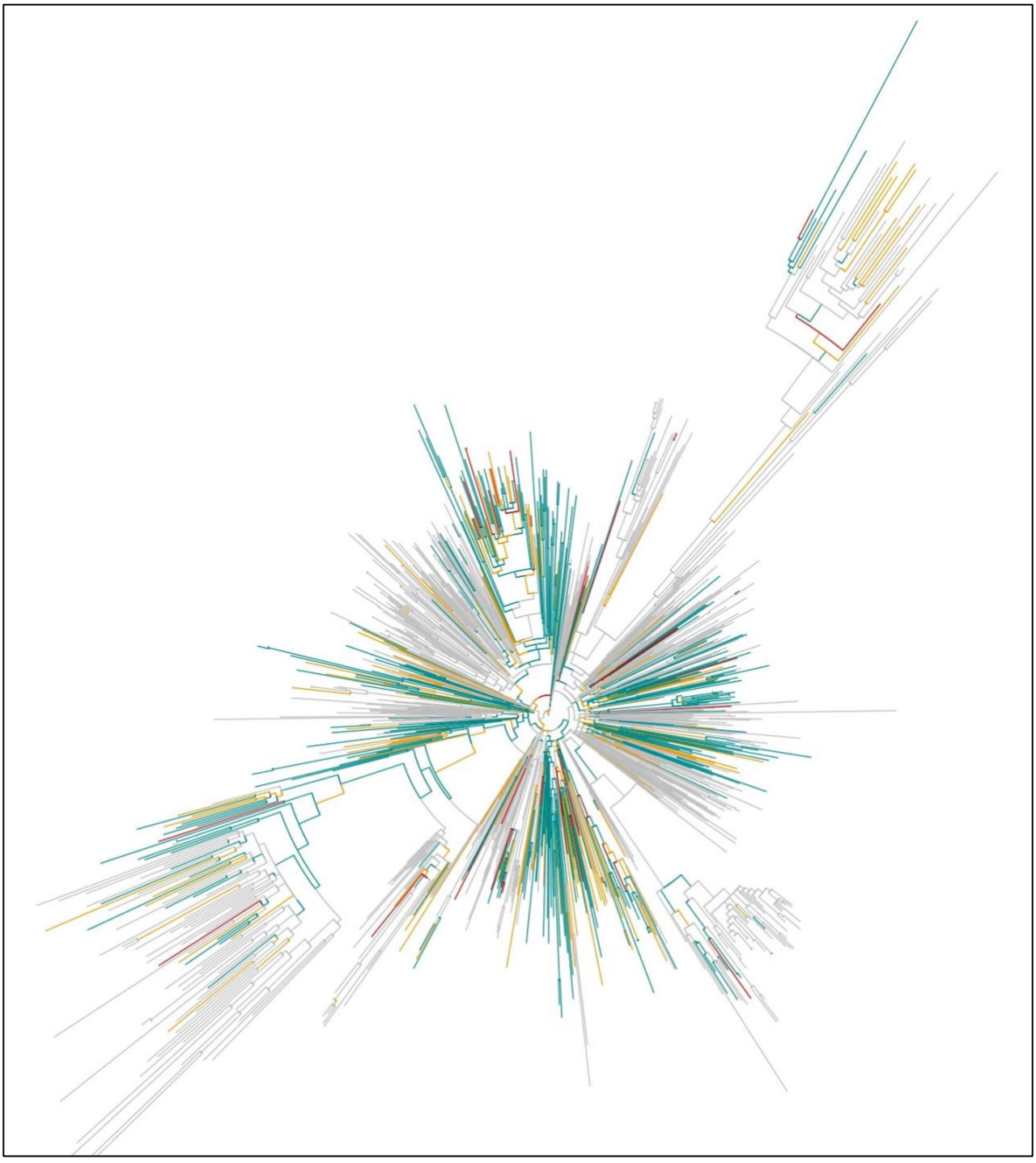
Sabes	Samples for Phylogenetic Analysis of HIV: If you agree, left over blood from the sample collected for HIV testing will be saved and stored. If HIV is detected, this sample will be used for detailed studies of HIV (phylogenetic analysis). Samples for sequencing will be processed from all HIV+ persons who are identified shortly after the infection occurs. The results of this analysis will be posted on a shared database. The data will not have any of your personal identification and only researchers will be able to look at it.
Microepidemics	We cannot predict exactly how your samples and information will be used if you decide to donate them. Any study that uses these samples or information will be reviewed by an institutional review board (IRB)/Ethics Committee at the research institution that requests the samples or information. This Board will make sure that the proposed study protects your privacy and your rights. The studies may include genetic tests. Your genes are passed down from your mother and father. The researchers will not examine all your genes, only those related to immunologic system and HIV related illness. The researchers will not disclose the results of tests performed on your samples to you, to this clinic, or to your doctor. The results will not register in your medical history. Any other studies using your samples and information will not represent any personal benefit. They will not be necessary for your medical care. Rather, the studies will be done to help to the community through new scientific discovery. If your tests results are positive, part of the specimens will be analyzed in the laboratory to know how different is the virus in your body in comparison with the virus of other people who acquired HIV recently. This analysis is called 'phylogenetic analysis'.
Feminas	You have qualified and have voluntarily agreed to participate in a free program of hormonal therapy for feminization to which you would go monthly, regardless of your diagnosis of HIV infection, in order to know if this strategy in conjunction with a health mentor program, it can increase the effectiveness of diagnosing, testing, treating and maintaining transwomen in HIV health care. While you are participating in the study, blood samples will be drawn and tested for your health. We ask that you give us your permission to store some of the blood that is not used in these tests, so that it can be used in the future in tests that will evaluate the health of transgender women. This format contains information so that you can decide to authorize us to store your samples for future use. The decision to allow researchers to store your blood samples for future testing is entirely voluntary. What you decide will not affect your participation in the main study or the care you receive here. If you do not wish to authorize your samples to be stored and analyzed in the future, the samples will be destroyed at the end of the study. There is no time limit for storing your samples. You can change your mind about the storage and authorization of the use of your samples at any time. If that happens, let us know and all your stored samples will be destroyed. Once they are destroyed, we will let you know. The stored samples may be shared with researchers in the United States and in other countries. We will not sell your stored blood samples or pay you for them. We will not share any information that makes it possible for researchers to identify you. We will share information without identification, which may include characteristics such as your age, use of hormones, race, health status, including your HIV status. If you decide to authorize storage of your samples, we cannot predict exactly how your samples will be used. Any study that uses those samples and the information you provide will be reviewed by an Institutional Review Board / Ethics Committee at the research institution requiring the samples and information. That Board or Committee will ensure that the proposed study protects your privacy and your rights. You, this clinic, or the study doctor will not have access to the results of future tests on your stored blood samples. They will not be recorded in your medical record either. The tests performed on your stored blood samples will not impact your personal benefit or be necessary for your medical care. Those analyzes will be done to help your community through new scientific discoveries.

II. Molecular Epidemiology Sensitivity Analysis

A. Methods

In primary analyses, pairwise genetic distances were calculated using the TN93 model, and cluster membership was defined using a relatively conservative genetic distance threshold of 1·5%. To examine if genetic distance thresholds affected the results of these analyses, sensitivity analyses were conducted using pairwise genetic distance with a less conservative genetic distance threshold of 3% to define cluster membership.

sFigure 1. Phylogenetic tree. This phylogeny includes data from three study populations (Sabes, Feminas, and Microepidemics) and South American pol sequences from the Los Alamos National Database. Colors indicate group (Blue: MSM; Yellow: transgender women; Red: MSTW; Gray: Los Alamos sequences, group unknown).



B. Results

Using pairwise genetic distance, 302 of 470 (65%) study participants were found in clusters (of ≥2 participants) using a genetic distance threshold of 0·03 substitutions per site. Three participants were dropped from analysis due to being only found in clusters with reference sequences in the Los Alamos National Laboratory (LANL) HIV Sequence Database. The 467 remaining participants were found in 59 clusters with between 2 and 48 participants. In this analysis, the likelihood of appearing in a cluster did differ somewhat between the groups. We found 70% of MSM appearing in clusters, compared to 55% of transgender women and 52% of MSTW. Compared to MSM, transgender women were 21% less likely to appear in a cluster (PR=0·79, 95% CI=0·66-0·93) and MSTW were 26% less likely, however the difference in cluster membership between MSM and MSTW was not statistically significant (PR=0·74, 95% CI=0·51-1·09) (sTable 3).

Using a genetic distance threshold of 3%, we found that having an early HIV diagnosis (≤6 months after HIV infection) was associated with an 18% increase in likelihood of appearing in a cluster (PR=1·18, 95% CI=1·01-1·37) compared to prevalent diagnoses (>6 months after HIV infection or no data available on previous testing). In analyzing possible demographic or behavioral predictors of being found in a cluster, age 35 years or older was associated with reduced likelihood of being found in a cluster (PR=0·60, 95% CI=0·42-0·87) compared to age <25 years.

In this sensitivity analysis, 72% of clustered transgender women were found in a cluster with MSM and 71% of clustered MSM were found in a cluster with transgender women. Clusters containing both transgender women and MSM accounted for 42% of all clusters found in this analysis. Among MSM and transgender women, in-group clustering was more common than between-group clustering; 80% of transgender women clustered with transgender women and 95% of MSM clustered with MSM. We had a limited sample of MSTW who were found in clusters (n=13), but this group was more likely to cluster with transgender women (77%) and MSM (77%) than with each other (15%). In the analysis of predictors of all cisgender men (both MSM and MSTW) clustering with transgender women, when using a genetic distance of 3% bisexual identity was significantly associated with clustering with TW compared to gay identity (PR=1·22, 95% CI=1·01-1·47) (sTable 4). No other characteristics were predictive of clustering with transgender women in this analysis.

C. Interpretation

Varying the threshold to define cluster membership did not change the inference from this analysis. While we found some variability in statistical significance of correlates in these analyses compared to the primary analysis, this is likely due to a difference in power to detect associations. In sensitivity analyses, we found that transgender women were less likely to be found in a cluster (PR=0·79, 95% CI=0·66-0·93) and that those with early diagnosis (<6 months) were more likely to be found in a cluster (PR=1·18, 95% CI=1·01-1·37).

Under less conservative cluster membership thresholds, predictors of all cisgender men (MSTW and MSM) clustering with transgender women remained similar to the primary analysis. Results from the primary analysis suggested that bisexual cisgender men were more likely to cluster with transgender women, but this finding was not statistically significant. However, this association was statistically significant when a genetic distance threshold of 3% was used (PR=1·22, 95% CI=1·01-1·47). When observing clustering of transgender women and MSM with each other, results found in sensitivity analyses did not change the inference. While the prevalence of clustering changed as we used a wider definition of clustering, we still observed patterns of in-group clustering with some cluster overlap between MSM and transgender women. The patterns observed in the primary analysis are likely more meaningful than those observed in this sensitivity analysis, because primary analyses captured more genetically similar links, and therefore are more likely to infer recent transmission between identified sequences or through intermediaries not identified.

sTable 3. Predictors of being found in a cluster at cluster size ≥2 using TN93 3%

Characteristic[a]	N	Clustered n (%)	PR	95% CI	p-value
Diagnosis year	467	302 (64·7)	0·98	(0·93, 1·03)	0·385
Study					
Sabes	365	241 (66·0)	1		
Feminas	39	23 (59·0)	0·89	(0·68, 1·17)	0·416
Microepidemics	63	38 (60·3)	0·91	(0·74, 1·13)	0·407
Group					
MSM	304	213 (70·1)	1		
TW	138	76 (55·1)	0·79	(0·66, 0·93)	0·005
MSTW	25	13 (52·0)	0·74	(0·51, 1·09)	0·128
HIV Diagnosis					
Prevalent	164	95 (57·9)	1		
Early (<6 months)	303	207 (68·3)	1·18	(1·01, 1·37)	0·033
City[b]					
Lima	342	225 (65·8)	1		
Callao	56	35 (62·5)	0·95	(0·76, 1·18)	0·643
Age category[c]:					
<25	196	141 (71·9)	1		
25-34	154	99 (64·3)	0·89	(0·77, 1·03)	0·133
≥35	39	17 (43·6)	0·61	(0·42, 0·88)	0·008
Any post-secondary school[d]					
No	157	97 (61·8)	1		
Yes	246	166 (67·5)	1·09	(0·94, 1·27)	0·251
Sexual Orientation[e]					
Gay	195	141 (72·3)	1		
Bisexual	90	59 (65·6)	0·91	(0·76, 1·09)	0·268
Heterosexual	10	8 (80·0)	1·11	(0·80, 1·53)	0·539
Housing status[f]					
Own place/alone	87	57 (65·5)	1		
With sexual partner	44	27 (61·4)	0·94	(0·71, 1·24)	0·647
With parent or family	224	149 (66·5)	1·02	(0·85, 1·21)	0·868
With friend	30	18 (60·0)	0·92	(0·66, 1·27)	0·601
Sexual role[g]					
Insertive	52	36 (69·2)	1		
Receptive	162	100 (61·7)	0·89	(0·72, 1·11)	0·303
Versatile	185	124 (67·0)	0·97	(0·79, 1·19)	0·760
Sex Worker[h]					
No	309	206 (66·7)	1		
Yes	79	45 (57·0)	0·85	(0·69, 1·05)	0·137
Gender of partners reported[i]					
Cisgender man	232	149 (64·2)	0·99	(0·86, 1·13)	0·842
Transgender woman	16	7 (43·8)	0·67	(0·38, 1·17)	0·159

Cisgender woman	6	3 (50·0)	0·77	(0·35, 1·72)	0·526
Reported partnership type[i]					
Stable/spouse	151	100 (66·2)	1·02	(0·88, 1·18)	0·774
Casual	66	37 (56·1)	0·83	(0·67, 1·05)	0·118
One time/anonymous	103	64 (62·1)	0·94	(0·79, 1·11)	0·442
Sold/client[j]	18	9 (50·0)	0·76	(0·47, 1·21)	0·243
Purchased[j]	9	5 (55·6)	0·85	(0·47, 1·53)	0·583

[a]Year of diagnosis, study, group, and HIV diagnosis (early vs prevalent) are reported for all three studies. All other data is reported from Sabes and Feminas.
[b]City data missing for n=5 Feminas participants and n=1 Sabes participant.
[c]Age data missing for n=1 Feminas participant and n=14 Sabes participants.
[d]Education data missing for n=1 Feminas participant. Education defined as any post-secondary or vocational training
[e]Sexual orientation data was not collected among TW in the Sabes study (n=82). In Feminas, n=27 TW identified their sexual orientation as transgender and are counted as missing for this analysis.
[f]Housing status data missing for n=5 Feminas participants and n=14 Sabes participants
[g]Sex role data missing for n=5 Feminas participants
[h]Sex worker data missing for n=15 Feminas participants and n=2 Sabes participants.
[i]Partnership data reported from the last three sexual partners, beginning with the most recent.
[j]Purchasing and selling sex defined as exchange goods, services, a place to sleep, or money for sex. Sold/client refers to encounters in which the participant acquired goods, services, or money, while purchased refers to encounters in which the participant gave goods, services, or money.
PR: prevalence ratio; CI: Confidence Interval; MSM: men who have sex with men; TW: transgender women; MSTW: partners of transgender women

sTable 4. Correlates of clustering with TW among all cisgender men (MSM and MSTW) using TN93 3% (n=226)

Characteristics	N	No TW in cluster[a]		PR	95% CI	P-value
		n	(%)			
MSTW						
No	213	142	(66·7)	1		
Yes	13	10	(76·9)	1·15	(0·84, 1·58)	0·371
Sexual Orientation						
Gay	136	87	(64·0)	1		
Bisexual	59	46	(78·0)	1·22	(1·01, 1·47)	0·037
Heterosexual	5	2	(40·0)	0·63	(0·21, 1·85)	0·396
HIV diagnosis						
Presumed prevalent	41	29	(70·7)	1		
Early (<6 months)	185	123	(66·5)	0·94	(0·75, 1·17)	0·585
Age category						
<25	109	72	(66·1)	1		
≥25	117	80	(68·4)	1·04	(0·86, 1·24)	0·711
Any post-secondary[b] education						
No	59	44	(74·6)	1		
Yes	141	91	(64·5)	0·87	(0·71, 1·05)	0·143
Sexual role						
Insertive	35	23	(65·7)	1		
Receptive	55	37	(67·3)	1·02	(0·76, 1·39)	0·879
Versatile	110	75	(68·2)	1·04	(0·79, 1·36)	0·790
Purchased sex[c] (6 months)						
No	174	118	(67·8)	1		
Yes	24	16	(66·7)	0·98	(0·73, 1·33)	0·912
Sold sex[c] (6 months)						
No	162	107	(66·1)	1		
Yes	36	27	(75·0)	1·14	(0·91, 1·41)	0·256

[a]Data on reporting a TW partner and HIV diagnosis are from both Sabes (n= 129) and Microepidemics (n= 15) participants. All other variables include cisgender men from the Sabes study. TW found in the cluster could be from Sabes, Feminas, or Microepidemics.
[b]Post secondary education defined as any school after secondary school, or vocational training.
[c]Purchasing and selling sex defined as exchange goods, services, a place to sleep, or money for sex. Data on purchased and sold sex missing for n=2 Sabes participants.
TW: transgender women; PR: prevalence ratio; CI: confidence interval.

III. Structured Coalescent Modeling

Source code is available at https://github.com/dianatordoff/LimaCoalescent.

A. Model Specification

Three demographic groups were included in epidemic model—transgender women (TW), MSTW, and MSM—as well a source compartment. The source compartment represents the regional reservoir of HIV and is used to estimate the rate of imported lineages to Lima. The source sequences were represented by LANL reference genomes from other Latin and South American countries. Due to the relatively small sample size and limited data on the stage of infection at sampling, our model only includes one stage of infection and is estimated for all HIV subtypes. Using a system of ordinary differential equations (ODEs), we modeled transmission between groups as:

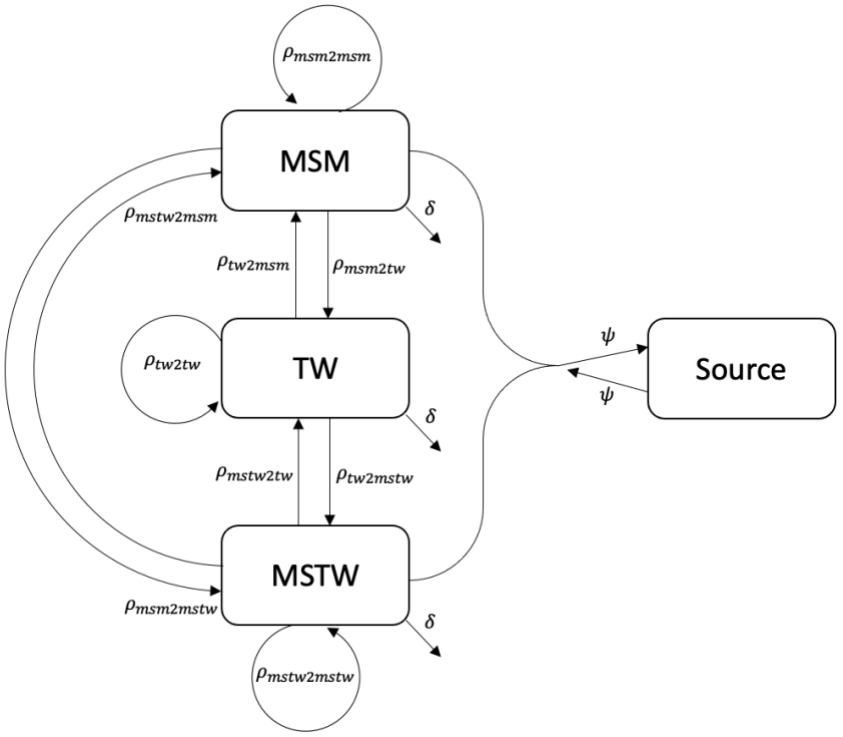
$$\frac{d\,I_{tw}}{dt} = \rho_{msm2tw}\lambda\, I_{msm} + \rho_{mstw2tw}\nu\, I_{mstw} + \rho_{tw2tw}\mu\, I_{tw} - \delta I_{tw}$$
$$\frac{d\,I_{mstw}}{dt} = \rho_{msm2mstw}\lambda\, I_{msm} + \rho_{mstw2mstw}\nu\, I_{mstw} + \rho_{tw2mstw}\mu\, I_{tw} - \delta I_{mstw}$$
$$\frac{d\,I_{msm}}{dt} = \rho_{msm2msm}\lambda\, I_{msm} + \rho_{mstw2msm}\nu\, I_{mstw} + \rho_{tw2msm}\mu\, I_{tw} - \delta I_{msm}$$

Where μ, ν, and λ are the HIV transmission rates per person-year for transgender women, MSTW and MSM, respectively. The proportion of overall infections between demographic groups is parameterized by the proportion of transmissions from transgender women to MSM (ρ_{tw2msm}), MSTW ($\rho_{tw2mstw}$), and to other transgender women (ρ_{tw2tw}); the proportion of transmissions from MSTW to MSM ($\rho_{mstw2msm}$), other MSTW ($\rho_{mstw2mstw}$), and transgender women ($\rho_{mstw2tw}$); and the proportion of transmissions from MSM to other MSM ($\rho_{msm2msm}$), MSTW ($\rho_{msm2mstw}$), and transgender women (ρ_{msm2tw}). We constrained the proportion of transmissions to equal unity, such that:

$$\rho_{msm2msm} = 1 - \rho_{msm2tw} - \rho_{msm2tw}$$
$$\rho_{tw2tw} = 1 - \rho_{tw2msm} - \rho_{tw2mstw}$$
$$\rho_{mstw2mstw} = 1 - \rho_{mstw2msm} - \rho_{mstw2tw}$$

Therefore, we do not explicitly estimate within group transmission probabilities (i.e. $\rho_{msm2msm}$, ρ_{tw2tw}, and $\rho_{mstw2mstw}$). We chose this parameterization because our research question was primarily concerned with between-group transmission patterns.

sFigure 2. Model Schematic



Using methods similar to those described by Nascimento et al, we modelled a global reservoir of HIV as having a constant effective population size using two parameters: the importation rate ($\boldsymbol{\psi}$) and the effective population size of the source compartment (N_e).[1] We assume that migration of infections from the source population to transgender women, MSTW, and MSM compartments is bidirectional and equal in magnitude. Because these migrations do not impact the size of the infected compartments, these terms are omitted from the ODEs above. Lastly, we do not model the number of susceptible individuals through time and thus do not use mass-action terms in our system of ODEs. Thus, our model does not include the common assumption that incidence is proportional to the number of individuals within each demographic group.

The structured coalescent modeling approach decomposes epidemic models into births $F(t)$ (e.g. new infection or transmission events), migrations $G(t)$ (e.g. progression through different strata, included disease progression) and deaths $\eta(t)$, expressed as matrices[2]:

$$F(t) = \begin{vmatrix} \rho_{msm2tw}\lambda\, I_{msm} & \rho_{mstw2tw}\nu\, I_{mstw} & \rho_{tw2tw}\mu\, I_{tw} & 0 \\ \rho_{msm2mstw}\lambda\, I_{msm} & \rho_{mstw2mstw}\nu\, I_{mstw} & \rho_{tw2mstw}\mu\, I_{tw} & 0 \\ \rho_{msm2msm}\lambda\, I_{msm} & \rho_{mstw2msm}\nu\, I_{mstw} & \rho_{tw2msm}\mu\, I_{tw} & 0 \\ 0 & 0 & 0 & \frac{1}{2}\frac{{I_{src}}^2}{Ne} \end{vmatrix}$$

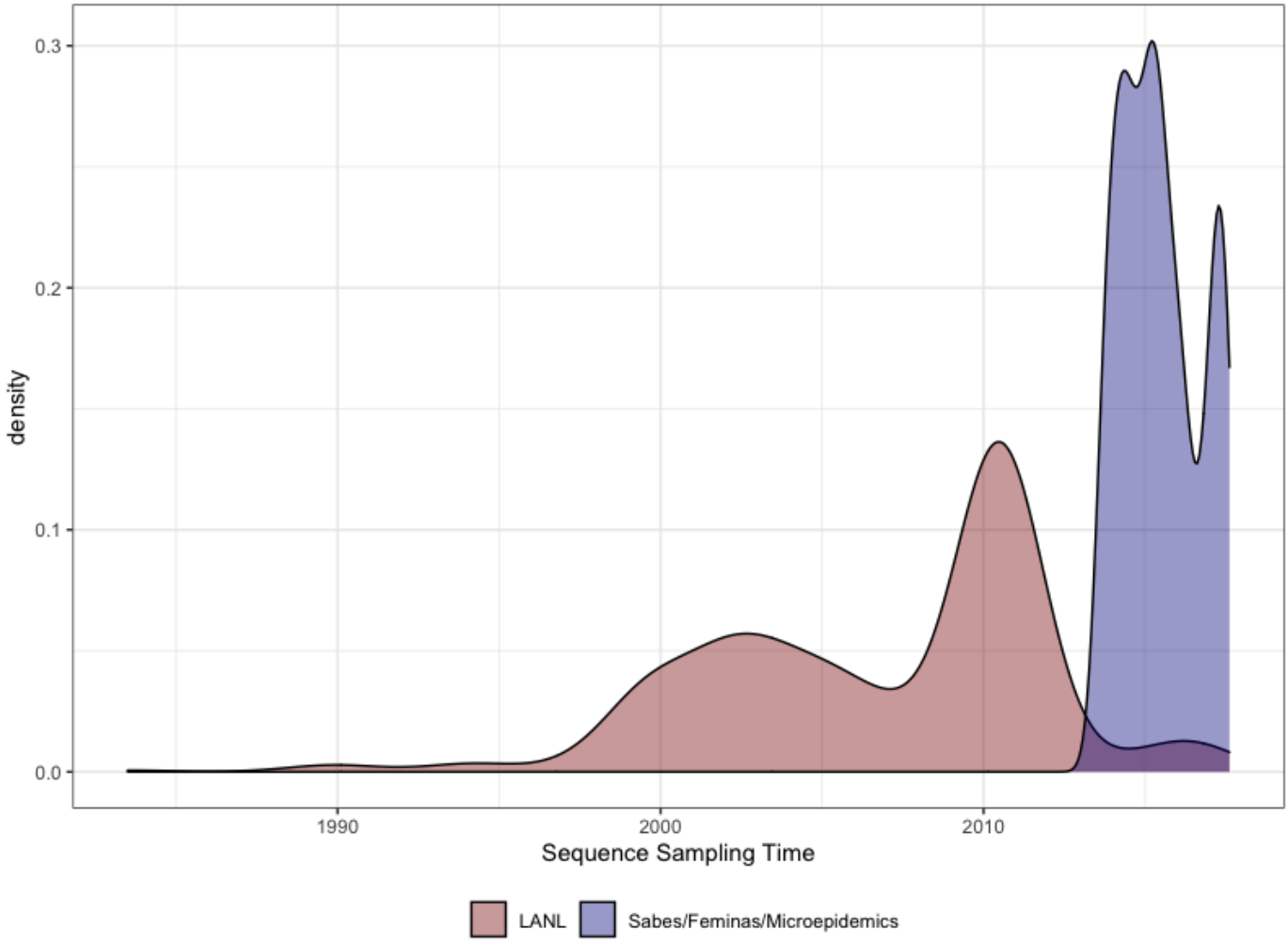
$$G(t) = \begin{vmatrix} 0 & 0 & 0 & \psi\, I_{tw} \\ 0 & 0 & 0 & \psi\, I_{mstw} \\ 0 & 0 & 0 & \psi\, I_{msm} \\ \psi\, I_{tw} & \psi\, I_{mstw} & \psi\, I_{msm} & 0 \end{vmatrix}$$

$$\eta(t) = \begin{vmatrix} \delta\, I_{tw} \\ \delta\, I_{mstw} \\ \delta\, I_{msm} \\ \frac{1}{2}\,\frac{{I_{src}}^2}{Ne} \end{vmatrix}$$

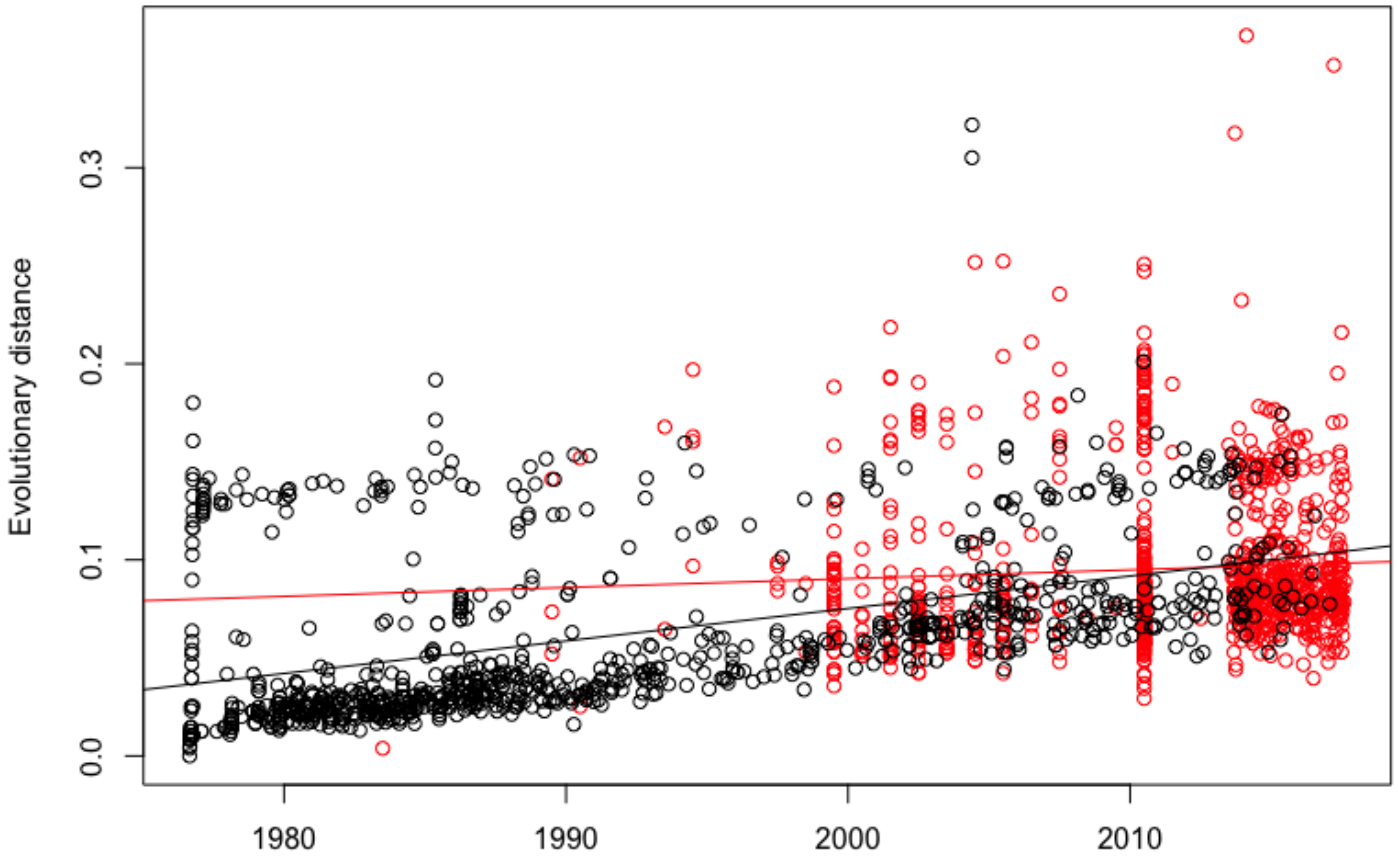
B. Time-Calibrated Phylogeny

We estimates a time calibrated phylogeny using the date of sequence sampling and the *treedater* algorithm assuming a strict molecular clock.[3] The estimated date of MRCA was 1976 and the mean substitution rate was 0.0019.

sFigure 3. Distribution of sequencing sampling times



sFigure 4. Root to Tip Regression from *treedater*. Red circles indicate the date of sampling for all included HIV sequence, including sequences obtained from the study as well as LANL. Black circles represent the estimated date of the internal nodes of the phylogeny. The red and black lines represent the least squares regression for the sample and internal nodes, respectively.



C. Bayesian Model Fitting

We fit the mathematical model to the time-calibrated phylogeny using a Bayesian approach using the *BayesianTools* package in R. Model parameters were estimated using a differential evolution Markov Chain Monte Carlo (MCMC) *zs* sampler using 100,000 iterations. We used the *phydynR* package in R to calculate the likelihood of a parameter set given a time-calibrated phylogeny and the model compartment to which each sampled sequence belonged. We report the maximum aposteriori value (MAP)—or mode—and the 95% credible interval of the resulting posterior distribution of each model parameter.

D. Parameters

sTable 5. Fixed Parameters

Parameter	Value	Comment
TW population size	5e4	~0·5% of Lima Population [4]
MSTW population size	5e4	Assumed to be same size as TW population
MSM population size	5e5	~5% Lima Population [5]
Source Size	1e7	
HIV prevalence among MSM	0·206	Prevalence observed in Sabes study
HIV prevalence among TW	0·197	Prevalence observed in Sabes study
HIV prevalence among MSTW	0·081	Prevalence observed in Sabes study

E. Prior Distributions and Sensitivity Analyses

Prior distributions were used to constrain the parameters. Our primary analysis used informative priors, and we conducted additional sensitivity analyses using non-informative priors. We obtained similar results using both sets of prior distributions. Informative priors were determined based on a review of the literature on HIV incidence and self-reported partnership patterns among TW, MSTW, and MSM. Most data on partnerships among TW, MSTW, and MSM are from studies conducted in San Francisco (n=7), Lima (n=4), southern California (n=2), and national US studies (n=2); the remaining data came from a study conducted in Atlanta and Baltimore (n=1), and a study conducted in several countries across Latin America (n=1).

sTable 6. Literature Review for Informative Priors

HIV Incidence Estimates

Parameter	Description of Prior Data	Range of estimates	Study Level Estimate (95% CI)	Reference
λ	HIV incidence among MSM in Peru	2·3-5·1 per 100 person-years	4·0 (3·9–4·1) per 100 person-years	6
			3·5 (2·3–4·7) per 100 person-years	7
			4·0 (2·9–5·1) per 100 person-years	8
μ	HIV incidence among TW in Peru	2·1- 5·1 per 100 person years	2·3 (2·1–2·5) per 100 person-years	6
			4·0 (2·9–5·1) per 100 person-years	8

Proportions of Sexual Mixing

Parameter	Description of Prior Data	Pooled Estimate (%, 95% CI)	Study Level Estimate (%, 95% CI)			Reference
			Numerator	Denominator	Proportion (95% CI)	
$\rho_{msm2msm}$	Proportion of partnerships among cisgender MSM that are with cisgender men	90·4% (89·3-91·5%)	1455	1526	95·3% (94·3-96·4%)	9
			1085	1285	97·7% (96·8-98·5%)	10
ρ_{msm2tw}	Proportion of cisgender MSM or gay/bisexual identified cisgender men who reported having a TW partner	2·6% (2·3-2·8%)	199[a]	967	20·6% (18·0-23·1%)	11
			14	392	3·6% (1·7-5·4%)	12
			100	11552	0·9% (0·7-1·0%)	13
			44	244	18·0% (13·2-22·9%)	14
			12	1285	0·9% (0·4-1·5%)	10
ρ_{tw2msm}	Proportion of TW who reported partnering with a cisgender man who identified as gay	12·5% (10·6-14·4%)	80	464	17·2% (13·8-20·7%)	15
			44	376	11·7% (8·5-15·0%)	16
			25	349	7·2% (4·5-9·9%)	10
ρ_{tw2tw}	Proportion of TW who reported having a TW partner	11.5% (10.4-12.6%)	26	123	21·1% (13·9-28·4%)	17
			13	575	2·3% (1·0-3·5%)	18
			210	464	45·3% (40·7-49·8%)	15
			2	142	1·4% (0·0-3·3%)	9
			97	1167	8·3% (6·7-9·9%)	19
			9	376	2·4% (0·8-3·9%)	16
			12	349	3·4% (1·5-5·4%)	10
$\rho_{tw2mstw}$	Proportion of TW who reported having a partnership with a hetero- or bisexual cisgender man, or proportion of partnerships among TW with cisgender men	86·2% (84·9-87·4%)	293	464	63·1% (58·8-67·5%)	15
			537	575	93·4% (91·4-95·4%)	18
			138	142	97·2% (94·5-99·9%)	9
			1070	1167	91·7% (90·1-93·3%)	19
			291	379	77·4% (73·2-81·6%)	16
			321	349	92·0% (89·1-94·8%)	10
$\rho_{mstw2msm}$	Proportion of MSTW who reported partnering with cisgender men, or who self-identified as gay or bisexual	28·1% (24·6-31·7%)	21	174	12·1% (7·2-16·9%)	20
			8	19	42·1% (19·9-64·3%)	21
			68	185	36·8% (29·8-43·7%)	22
			23	46	50·0% (35·6-64·4%)	23
			28	146	19·2% (12·8-25·6%)	9
			23	43	53·5% (38·6-68·4%)	24
			6	16	37·5% (13·8-61·2%)	25
$\rho_{mstw2tw}$	Proportion of partnerships among MSTW that are with TW	65·5% (58·3-72·7%)	94	146	64·4% (56·6-72·2%)	9
			16	22	72·7% (54·1-91·3%)	25

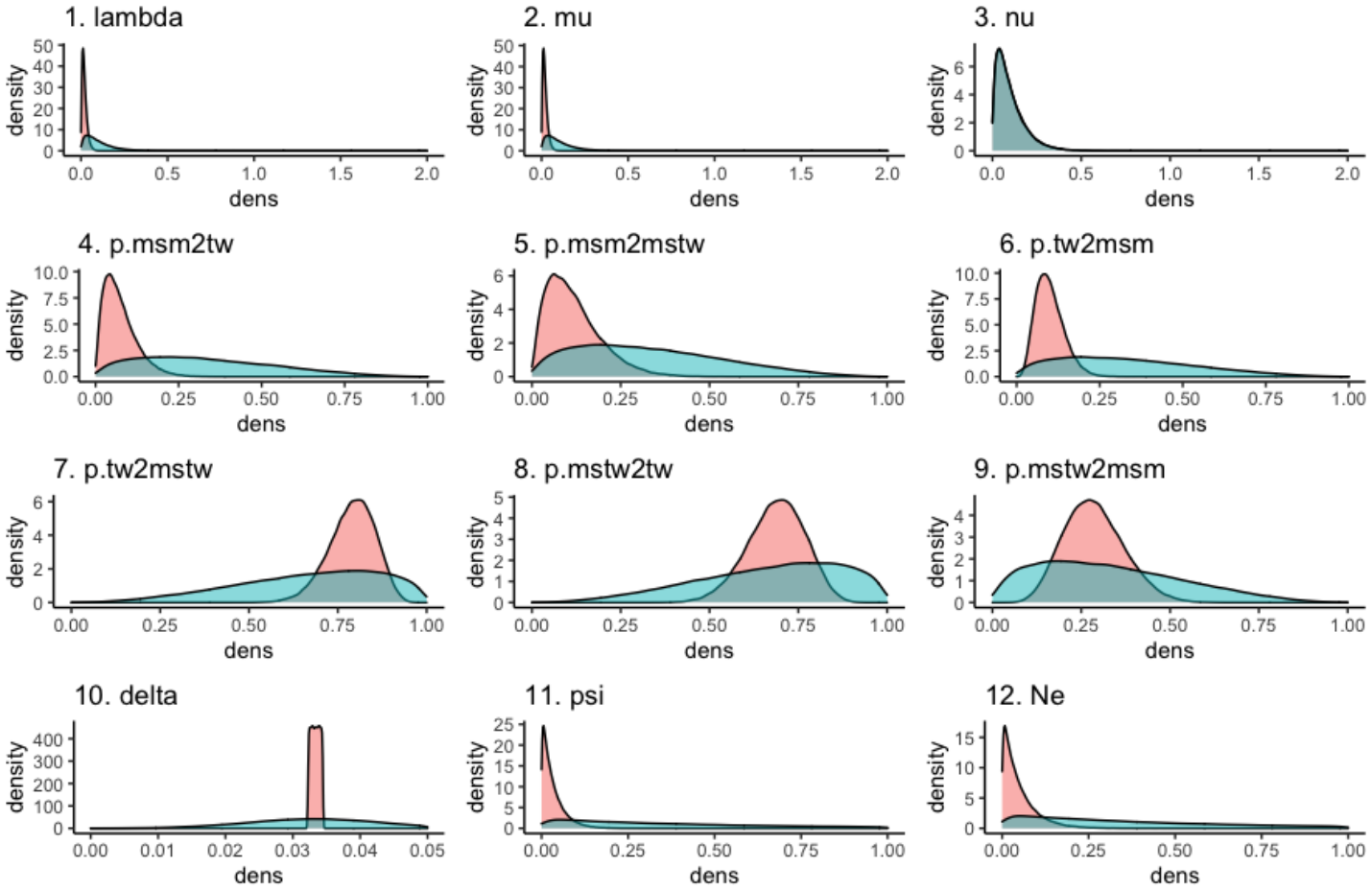
[a] *72.8% of the 273 gay and bisexual men who reported having any transgender partner who specifically reported partnering with transgender women*

There are no published data on HIV incidence among MSTW (ν), so we use an uninformative prior for these parameters in the both the primary and sensitivity analyses. Lastly, we chose informative priors for δ, ψ, and N_e based on prior implementations of this phylodynamic model.[1]

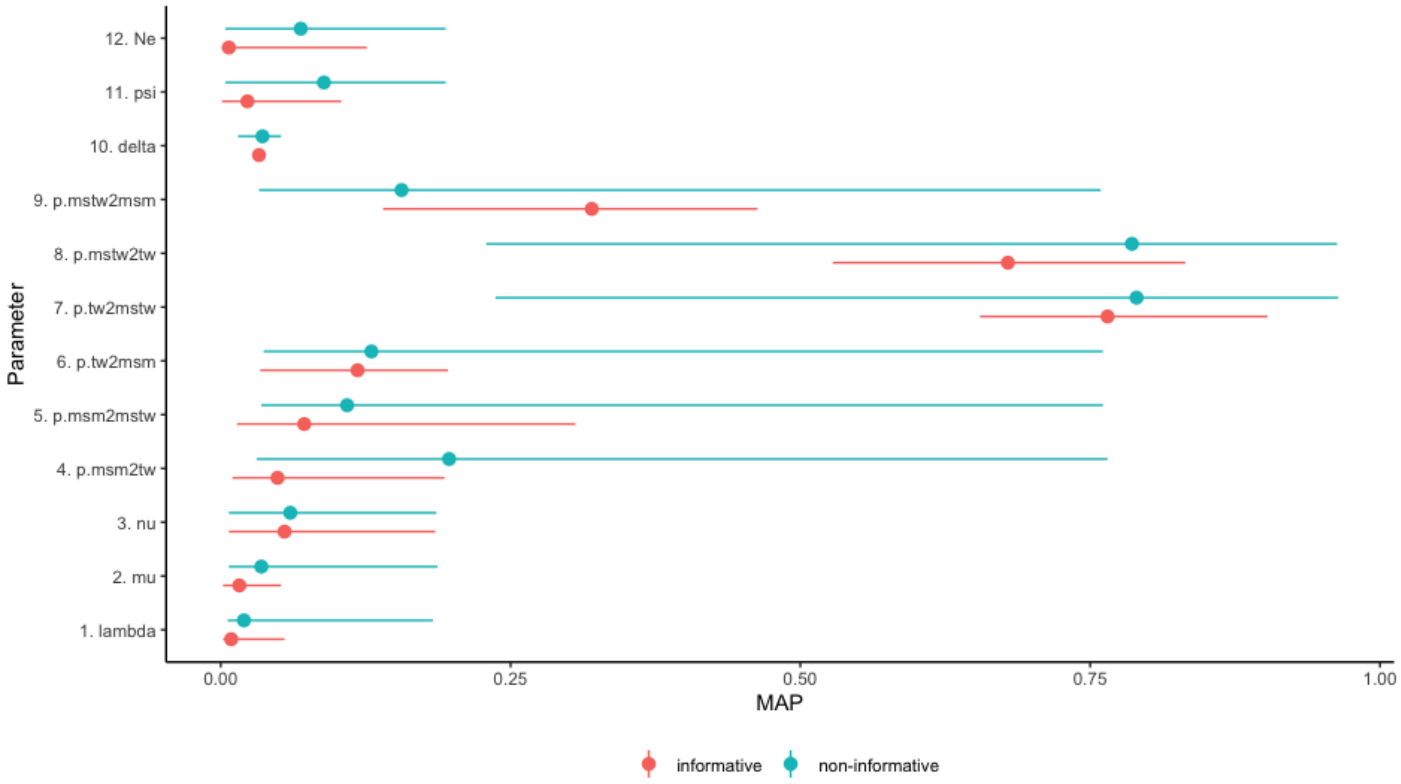
sTable 7. Prior distributions, PSRF, Estimates for Primary and Sensitivity Analyses

#	Parameter	Informative Prior (Primary Analysis)			Non-informative Prior (Sensitivity Analysis)		
		Prior	PSRF	MAP (95% CI)	Prior	PSRF	MAP (95% CI)
1	λ	$gamma(\alpha = 2, \beta = 100)$	1·012	0·009 (0·002, 0·055)	$gamma(\alpha = 1.\cdot 5, \beta = 15)$	1·003	0·020 (0·006, 0·183)
2	μ	$gamma(\alpha = 2, \beta = 100)$	1·020	0·016 (0·002, 0·052)	$gamma(\alpha = 1.\cdot 5, \beta = 15)$	1·002	0·035 (0·007, 0·187)
3	ν	$gamma(\alpha = 1 \cdot 5, \beta = 15)$	1·002	0·055 (0·007, 0·185)	$gamma(\alpha = 1.\cdot 5, \beta = 15)$	1·001	0·060 (0·007, 0·186)
4	ρ_{msm2tw}	$beta(\alpha = 2, \beta = 25)$	1·004	0·049 (0·010, 0·193)	$beta(\alpha = 1 \cdot 5, \beta = 3)$	1·001	0·109 (0·035, 0·761)
5	$\rho_{msm2mstw}$	$beta(\alpha = 2, \beta = 15)$	1·009	0·072 (0·014, 0·306)	$beta(\alpha = 1 \cdot 5, \beta = 3)$	1·002	0·130 (0·037, 0·761)
6	ρ_{tw2msm}	$beta(\alpha = 5, \beta = 45)$	1·005	0·118 (0·034, 0·196)	$beta(\alpha = 1 \cdot 5, \beta = 3)$	1·002	0·790 (0·237, 0·964)
7	$\rho_{tw2mstw}$	$beta(\alpha = 30, \beta = 8)$	1·001	0·765 (0·655, 0·903)	$beta(\alpha = 3, \beta = 1 \cdot 5)$	1·000	0·156 (0·033, 0·759)
8	$\rho_{mstw2tw}$	$beta(\alpha = 22, \beta = 10)$	1·014	0.679 (0.528, 0.832)	$beta(\alpha = 3, \beta = 1 \cdot 5)$	1·007	0·036 (0·015, 0·052)
9	$\rho_{mstw2msm}$	$beta(\alpha = 8, \beta = 20)$	1·003	0·320 (0·140, 0·463)	$beta(\alpha = 1 \cdot 5, \beta = 3)$	1·003	0·089 (0·004, 0·194)
10	δ	$unif\left(\frac{1}{31}, \frac{1}{29}\right)$	1·012	0·033 (0·031, 0·034)	$norm\left(\mu = \frac{1}{30}, \sigma = \frac{1}{100}\right)$	1·003	0·020 (0·006, 0·183)
11	ψ	exp $(\lambda = 30)$	1·020	0·023 (0·001, 0·104)	exp $(\lambda = 2)$	1·002	0·035 (0·007, 0·187)
12	N_e	exp $(\lambda = 20)$	1·002	0·007 (0·001, 0·126)	exp $(\lambda = 2)$	1·001	0·060 (0·007, 0·186)

sFigure 5. Informative and non-informative prior distributions



sFigure 6. Comparing Maximum Aposteriori Value (MAP) and 95% Credible Interval Estimates for Informative and Non-informative Priors



F. Model Convergence and Trace Plots

Model convergence was evaluated based on the effective sample size (ESS), Gelman-Rubin's diagnostic for convergence using potential scale reduction factors (PSRF) and examining trace plots. Phylogenetic MCMC analyses are characterized by a high level of autocorrelation; In general, MCMC is significantly less efficient at exploring the parameter space for phylogenetic tree topologies.[26] Thus, phylogenetics often use a more pragmatic approach to evaluating MCMC; an ESS above 200 as considered to be a threshold that suggests the posterior distribution has been sufficiently sampled, and additional metrics (such as PSRF) can be used evaluate convergence and model fit for phylogenetic MCMC analyses.[27] For the primary analysis, the ESS was 1,084, all PSRFs were well below 1·200 (see sTable 7), and trace plots, which are all suggestive of model convergence.

IV. Summary of Mathematical Models including Transgender Women

To date, only six mathematical models of HIV transmission have included transgender women, including four set in Lima, Peru.

sTable 8. Overview of Mathematical Models of HIV that include transgender women

Author/Citation	Geographic Location	Demographic Groups Included
Gomez et al. 2012[28]	Lima, Peru	Men who mostly have sex with women, men who mostly have sex with men, cisgender women sex workers, and transgender women.
Poteat et al. 2015[29]	Lima, Peru and San Francisco, CA	Transgender women sex workers not in a stable relationship, transgender women sex workers in a stable relationship, cisgender male clients, cisgender male stable partners
Melesse et al. 2018[30]	Pakistan	Cisgender women sex workers, people who inject drugs, and *hijra*/transgender/male sex workers aggregated as one group
Dimitrov et al. 2019[5]	Lima, Peru	Men who have sex with men (MSM) and transgender women aggregated as one population. Model is calibrated to data on cisgender MSM only
Bórquez et at. 2019[31]	Lima, Peru	Transgender women sex workers not in a stable relationship, transgender women sex workers in a stable relationship, cisgender male clients, cisgender male stable partners [note: model adapted from Poteat et al. (2015)]
Bórquez et at. 2020[32]	Lima, Peru	Gay/homosexual self-identified MSM, heterosexual/bisexual self-identified MSM, male sex workers, and transgender women [note: model adapted from Gomez et at. (2012)]

V. References

1. Nascimento FF, Baral S, Geidelberg L, et al. Phylodynamic analysis of HIV-1 subtypes B, C and CRF 02_AG in Senegal. Epidemics. 2019 Nov;100376.

2. Volz EM. Complex Population Dynamics and the Coalescent Under Neutrality. Genetics. 2012 Jan;190(1):187–201.

3. Volz EM, Frost SDW. Scalable relaxed clock phylogenetic dating. Virus Evolution. 2017 Jul 1;3(2).

4. Meerwijk EL, Sevelius JM. Transgender Population Size in the United States: a Meta-Regression of Population-Based Probability Samples. Am J Public Health. 2017;107(2):216.

5. Dimitrov D, Wood D, Ulrich A, et al. Projected effectiveness of HIV detection during early infection and rapid ART initiation among MSM and transgender women in Peru: A modeling study. Infectious Disease Modelling. 2019;4:73–82.

6. Castillo R, Konda KA, Leon SR, Silva-Santisteban A, Salazar X, Klausner JD, et al. Human Immunodeficiency Virus (HIV) and Sexually Transmitted Infection (STI) incidence and associated risk factors among high-risk MSM and male-to-female transgender women in Lima, Peru. JAIDS. 2015;69(5):567.

7. Sanchez J, Lama JR, Peinado J, Paredes A, Lucchetti A, Russell K, et al. High HIV and Ulcerative Sexually Transmitted Infection Incidence Estimates among Men who Have Sex with Men in Peru: Awaiting for an Effective Preventive Intervention. JAIDS. 2009;51(Suppl 1):S47.

8. Janes H, Brown MD, Glidden D V., Mayer KH, Buchbinder SP, McMahan VM, et al. Evaluating the impact of policies recommending PrEP to subpopulations of men and transgender women who have sex with men based on demographic and behavioral risk factors. PLoS One. 2019.

9. Long JE, Ulrich A, White E, Dasgupta S, Cabello R, Sanchez H, et al. Characterizing Men Who Have Sex with Transgender Women in Lima, Peru: Sexual Behavior and Partnership Profiles. AIDS & Behavior. 2019.

10. Ayer A, Perez-Brumer A, Segura E, Chavez-Gomez S, Fernandez R, Arroyo C, et al. Let's Talk About Sex: The Impact of Partnership Contexts on Communication About HIV Serostatus and Condom Use Among Men Who Have Sex with Men (MSM) and Transgender Women (TW) in Lima, Peru. AIDS & Behavior. 202;25(7):2139–53.

11. Hall GC, Young A, Krakauer C, Watson CC, Cummings V, Mayer K, et al. Sexual risk behaviors among black men who have sex with men who also report having sex with transgender partners: Analysis of HIV prevention trials network (HPTN) 061 study. AIDS Educ Prev. 2017;29(5):418–31.

12. Hassan A, Wertheim JO, Blumenthal JS, Ellorin E, Dube MP, Corado K, et al. Characteristics of a cohort of high-risk men who have sex with men on pre-exposure prophylaxis reporting transgender sexual partners. Medicine. 2019;98(50):e18232.

13. Reisner S, Perez-Brumer A, Oldenburg C, Gamarel K, Malone J, Leung K, et al. Characterizing HIV risk among cisgender men in Latin America who report transgender women as sexual partners: HIV risk in Latin America men. Int Journal of STD & AIDS. 2019;30(4):378–85.

14. Bockting W, Miner M, Rosser B. Latino men's sexual behavior with transgender persons. Arch Sex Behav. 2007;36(6):778–86.

15. Prescott MR, Santos GM, Arayasirikul S, Wilson E. Partnership-level correlates of sexual risk taking within the sexual partnerships of young transwomen in San Francisco, California. Sex Transm Infect. 2020 Feb 1;96(1):58–61.

16. Satcher M, Segura E, Silva-Santisteban A, Sanchez J, Lama J, Clark J. Partner-Level Factors Associated with Insertive and Receptive Condomless Anal Intercourse Among Transgender Women in Lima, Peru. AIDS & Behavior. 2017;21(8):2439–51.

17. Wilson EC, Chen Y-H, Raad N, Raymond HF, Dowling T, McFarland W. Who are the sexual partners of transgender individuals? Differences in demographic characteristics and risk behaviours of San Francisco HIV testing clients with transgender sexual partners compared with overall testers. Sex Health. 2014;11(4):319.

18. Wilson EC, Santos GM, Raymond HF. Sexual mixing and the risk environment of sexually active transgender women: Data from a respondent-driven sampling study of HIV risk among transwomen in San Francisco, 2010. BMC Infect Dis. 2014 Aug 6;14(1).

19. Murphy E, Segura E, Lake J, L, Huerta L, Perez-Brumer A, Mayer K, et al. Intimate Partner Violence Against Transgender Women: Prevalence and Correlates in Lima, Peru (2016-2018). AIDS & Behavior. 2020;24(6):1743–51.

20. Operario D, Nemoto T, Iwamoto M, Moore T. Risk for HIV and unprotected sexual behavior in male primary partners of transgender women. Arch Sex Behav. 2011 Dec;40(6):1255–61.

21. Poteat T, Cooney E, Malik M, Restar A, Dangerfield DT, White J. HIV Prevention Among Cisgender Men Who have Sex with Transgender Women. AIDS & Behavior. 2021.

22. Gamarel KE, Sevelius JM, Reisner SL, Richardson RL, Darbes LA, Nemoto T, et al. Relationship Stigma and HIV Risk Behavior Among Cisgender Men Partnered with Transgender Women: The Moderating Role of Sexual Identity. Arch Sex Behav. 2020 Jan 1;49(1):175–84.

23. Operario D, Burton J, Underhill K, Sevelius J. Men who have sex with transgender women: challenges to category-based HIV prevention. AIDS & Behavior. 2008;12(1):18–26.

24. Coan DL, Schrager W, Packer T. The Role of Male Sexual Partners in HIV Infection Among Male-to-Female Transgendered Individuals. International Journal of Transgenderism. 2008;8(2–3):21–30.

25. Reback C, Larkins S. HIV risk behaviors among a sample of heterosexually identified men who occasionally have sex with another male and/or a transwoman. J Sex Res. 2013;50(2):151–63.

26. Lanfear R, Hua X, Warren DL. Estimating the Effective Sample Size of Tree Topologies from Bayesian Phylogenetic Analyses. Genome Biol. Evol. 2016; 8(8): 2319–2332.

27. Nascimento FF, dos Reis M, Yang Z. A biologist's guide to Bayesian phylogenetic analysis. Nat Ecol Evol. 2017; 1(10): 1446–1454.

28. Gomez GB, Borquez A, Caceres CF, et al. The Potential Impact of Pre-Exposure Prophylaxis for HIV Prevention among Men Who Have Sex with Men and Transwomen in Lima, Peru: A Mathematical Modelling Study. Salomon JA, editor. PLoS Medicine. 2012 Oct 9;9(10):e1001323.

29. Poteat T, Wirtz AL, Radix A, et al. HIV risk and preventive interventions in transgender women sex workers. The Lancet. 2015 Jan 17;385(9964):274–86.

30. Melesse DY, Shafer LA, Emmanuel F, et al. Heterogeneity in geographical trends of HIV epidemics among key populations in Pakistan: a mathematical modeling study of survey data. Journal of Global Health. 2018 Jun;8(1):010412.

31. Bórquez A, Guanira JV, Revill P, et al. The impact and cost-effectiveness of combined HIV prevention scenarios among transgender women sex-workers in Lima, Peru: a mathematical modelling study. The Lancet Public Health. 2019 Mar 1;4(3):e127–36.

32. Bórquez A, Rich K, Farrell M, et al. Integrating HIV pre-exposure prophylaxis and harm reduction among men who have sex with men and transgender women to address intersecting harms associated with stimulant use: a modelling study. Journal of the International AIDS Society. 2020 Jun 19;23(S1):e25495.