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*Targeting strategies for pre-exposure prophylaxis (PrEP) among adolescent sexual minority males (ASMM) in the United States: a modeling study*.

# Parameters

All parameters are taken directly from Jenness et al. 2016 (1), unless noted below.

## **Entry and debut**

Individuals are able to enter the population at multiple ages (13-18), and to experience anal intercourse (AI) debut either upon entry into the population, or sometime thereafter. This is because our population definition consists of those who have begun to identify as gay/bisexual, ***or*** who have begun sexual activity with males. That is, an individual need not have sexually debuted to fall within our population definition.

The probability of each age at entry is given by:

|  |  |
| --- | --- |
| **Age at Entry** | **Probability** |
| 13 | 44% |
| 14 | 13% |
| 15 | 12% |
| 16 | 11% |
| 17 | 10% |
| 18 | 10% |

These numbers were derived through back-calculation from the size of the respondent pool in the Youth Risk Behavioral Surveillance System, or YRBSS (2), which began with:

|  |  |  |  |
| --- | --- | --- | --- |
| **Current age** | **Weighted # ASMM** | **Weighted # males** | **Est. % ASMM** |
| 14 | 6,648 | 141,975 | 4.7% |
| 15 | 14,789 | 310,381 | 4.8% |
| 16 | 20,566 | 309,489 | 6.6% |
| 17 | 17,957 | 280,313 | 6.4% |
| 18+ | 14,658 | 181,363 | 8.1% |

We excluded ages below 14 since the numbers of adolescent sexual minority males (ASMM) were small and the estimates highly variable. We then fit a logarithmic curve to these five numbers:

We selected a logarithmic curve over a linear one since the former recognizes that the proportion of ASMM should asymptote at some older age. We used the resulting equation to develop predicted proportions for each age (13-18) in our model. We then converted these into the proportions entering our model at each age listed above.

For debut, we then derive two parameters: one for the probability of debuting at entry (i.e. first meeting the definition of ASMM because of sexual activity) and, for those not debuting at entry, at weekly probability of debuting thereafter.

We then used the data from the same adolescents about their reported age of first anal intercourse, given their current age:

|  |  |
| --- | --- |
|  | **AI debut age** |
| **Current age** | **13** | **14** | **15** | **16** | **17** | **18** | **No AI** |
| 13 | 65% |  |  |  |  |  | 35% |
| 14 | 39% | 14% |  |  |  |  | 47% |
| 15 | 32% | 15% | 10% |  |  |  | 43% |
| 16 | 32% | 13% | 13% | 11% |  |  | 31% |
| 17 | 27% | 11% | 13% | 14% | 6% |  | 29% |
| 18 | 33% | 10% | 11% | 15% | 17% | 0% | 14% |

We used approximate Bayesian computation (ABC) to find the values of our two parameters that, when simulated with the selected population entry rates above, would come closest to generating this matrix of retrospective debut times in a population interviewed at these ages. We used the Beaumont method for sequential ABC, as implemented in the R package *EasyABC*, with uniform priors on the range (0,1) and (0, 0.002) for our two parameters, and tolerance levels 1000, 100, and 75. We used the mean of all non-rejected parameters values as our final estimate, yielding a probability of AI debut at population entry of 50.6%, and a weekly probability of debut thereafter at 0.34%.

## **Sexual networks**

We reduced the number of different relational networks being modeled from three to one. Sections 1.2.1 – 1.2.3 describe specific features and parameters pertaining to the structure of this network.

### **1.2.1 Momentary degree**

The model is expressed in terms of momentary degrees (number of ASMM partners per person at a given point in time). Based on reports from Halkitis 2013 (3), 27% of sexually active ASMM are in a male-male relationships at any given time. The 0.27 mean degree set the target mean degree for sexually active ASMM. In this model of adolescents not all members of the population are active (see section 1.1). Thus, at the population level, including the proportion of ASMM that are not sexually active, the adjusted mean degree is 0.162. In order to account for heterogeneity in sexual activity, we model five risk groups, consistent with our previously published adult model (1). For these, the propensity to form partnerships was weighted by the quintile distribution of the number of anal sex partners reported in the last year by ASMM in the American Men’s Internet Survey, or AMIS (4), The parameters for momentary degree among sexually active ASMM guiding this model are:

|  |  |
| --- | --- |
| **Quintile** | **Mean momentary degree** |
| Lowest quintile | 0.054 |
| Second quintile | 0.106 |
| Third quintile | 0.161 |
| Fourth quintile | 0.247 |
| Highest quintile | 0.782 |
| Mean | 0.270 |

### **1.2.2. Age mixing**

Age mixing within the cohort of interest was not explicitly included in the model. However, the likelihood of entering the ASMM population and the likelihood of sexual debut were both a function of age, resulting in a strong increase in sexual activity with age and ensuring that most contacts were between two males both 16-18.

### **1.2.3. Relational durations**

Following previous methods [cite to be inserted when available], we matched the median duration of ongoing relationships from source data. We examined data from AMIS (4), limiting to respondents 18 or younger led to an estimate of 14 days. Our model structure implies that relational dissolution follows a memoryless process, and thus relational durations follow a geometric distribution. Converting our median to the corresponding mean for the geometric distrubition yielded average relational durations of 20.2 days (2.89 weeks). The adopted values for momentary degree and relational durations together imply a mean number of partners per year of 4.9, qualitatively similar to the value of 4.2 found in AMIS.

## **Anal intercourse (AI) frequencies**

The baseline frequency of AI within ongoing relationships was derived from Rotheram-Borus et al. 1994 (5), who reported a mean of 3.5 acts of AI over a three month period, or 0.038 acts per day. AI frequency was one of two parameters adjusted using Approximate Bayesian Computation to fit the HIV prevalence value chosen as our calibration parameter. See section 2.

## **Condom use**

The rate of condom use was 54% based on reports of unprotected anal sex over a 6-week period among those reporting any AI in Hidalgo et al 2015 (6). This was found to be highly consistent with reports from multiple other sources (7-9). The condom use rate applied to the entire population; no fixed proportion of the population always used condoms.

## **Role**

Based on estimates from the American Men’s Internet Survey (AMIS), 14.5% of the population were exclusively insertive, 28.2% were exclusively receptive and 57.3% were versatile (both insertive and receptive). Partnering between two ASMM who were exclusively receptive or exclusively insertive was forbidden in the relational model.

## **Testing**

Sharma et al. (2) explore HIV testing among ASMM. In an additional unpublished analysis for this model, they found that 29.2% of sexually experience 18-year-old ASMM had tested for HIV at least once in their lifetime. We simulated multiple weekly testing hazards until obtaining a value that yielded this outcome. This final selection was for a constant weekly hazard for testing of 0.00238, which corresponds to a mean test interval of 2,900 days.

Rates for progression through the care cascade conditional on testing were carried over from the adult model (1), in the absence of large-scale ASMM-specific data parametrized as needed for the model. However, given the very low rate of testing in this population, treatment is not widespread, so that the exact details of treatment uptake and adherence given testing are unlikely to have a large effect on our model.

## **Contact outside the population**

Transmission of HIV from partners outside the modeled population was modeled using a weekly hazard, which varied as a function of age and risk quintile. The first component of this hazard was the probability of contact outside the explicitly modeled population:

|  |  |
| --- | --- |
| **Risk Quintile** | **Age** |
| **13** | **14** | **15** | **16** | **17** | **18** |
| **Risk q1** | .0022 | .0046 | .0068 | .0092 | .0114 | .0136 |
| **Risk q2** | .0046 | .0092 | .0136 | .0182 | .0228 | .0274 |
| **Risk q3** | .0068 | .0136 | .0206 | .0274 | .0342 | .0410 |
| **Risk q4** | .0106 | .0212 | .0318 | .0424 | .0530 | .0636 |
| **Risk q5** | .0334 | .0666 | .1000 | .1334 | .1666 | .2000 |

These were derived by first calculating the overall mean contact rate, via back-calculation from data collected from 19-24 year-old young adult MSM (YAMSM). We began by estimating a mean of 6.3 AI partners in the last year for this YAMSM population, derived from analyses of data from InvolveMENt (10) and the MAN Project (11). We then derived an estimate (6.67%) of the proportion of YAMSM aged 19-25 who report their last AI act as being with a partner aged 18 years or younger, from the Checking In study (12). We focus on this study since it was conducted online (as opposed to in-person for InvolveMENt and the MAN Project), which we suspect will reduce the quite strong desirability working against reporting adolescent partners by this age group. To reverse these rates from contacts per YAMSM to contacts per sexually debuted ASMM, we then adjust by the relative sizes of those two cohorts (7 birth-years for YAMSM aged 19-25 vs. 6 birth-years for ASMM aged 13-18), and based on the proportion of adolescent ASMM who have sexually debuted (60%). We also converted from a yearly to a weekly rate, and converted from an incidence of new relationships to the prevalence of relationship by multiplying by relationship length in weeks (2.89). Together this yields:

$$6.3 ×0.0667 ×\frac{7}{6×0.6} × \frac{1}{52}×2.89=0.0454$$

To convert from this grand mean to the age-by-risk-quintile matrix above, we assumed a linear decrease in contact rates down to 0 as age declined, and applied the same relative contact rates for the risk quintiles found in the table in Section 1.2.1 to the risk quintiles here, but fixing the grand mean.

With weekly contact rates set, we then calculate a rough initial estimate of HIV infection given contact. We set these as 10% probability of the partner being HIV+ (given estimates of HIV prevalence in the 19-25 age range from the National HIV Behavioral Surveillance (13, 14) a 46% probability of not using condoms (see Section 1.4), and a 1% chance of transmission given an act with an HIV+ partner (meant as an approximate weighted average across all condomless AI acts regardless of stage). The resulting estimates then entered into the Approximate Bayesian Computation (see Section 2).

## **Pre-Exposure Prophylaxis (PrEP)**

We adopted the same four levels of per-act transmission reduction by adherence level from Jenness et al. (1), which were in turn derived from Table 2 and Figure 2 of Grant et al. (15) These values are 0%, 31%, 81%, and 95%, for the four adherence categories. We derived our base levels of the four adherence categories among ASMM from the preliminary data reported from the ATN113 trial (16), averaged across each of the follow-up timepoints, yielding 20.9%, 24.4%, 13.1% and 41.6% of ASMM in each adherence category, from low to high. Taking a weighted average across these categories means that the *average* ASMM currently prescribed PrEP experiences a 58% reduction in HIV acquisition per act. We also considered an optimistic and a pessimistic adherence scenarios, derived from the first (4 week) and last (48 week) study visit.

For discontinuation, we also used the preliminary data from ATN113, considering that those who showed 0 adherence by week 48 could effectively be considered withdrawn from active PrEP use and discontinued. We then set a constant weekly probability of discontinuation (1.43%) such that 50% of those initiating had discontinued by Week 48.

# Model calibration

## **Selection of parameters**

Two parameters were used for model calibration: a multiplier applied to the frequency of AI and a multiplier applied to the transmission probability from an MSM outside the age range of the simulation. For the former, the only data identified were from a small study more than 20 years old (5). That study also reported the proportion of ASMM having *any* AI acts over a 3-month period as 53%, which is lower than a more recent estimate over a shorter time frame—67% having AI over the last 6 weeks (6). This more recent study did not provide a measure of AI frequency in the form we needed, but did suggest that the AI rates reported in the older study are likely underestimates. For the latter metric (transmission from outside the age range), we had no direct measure of the quantity of interest, and needed to back-calculate it from reports form young adult MSM 19-25 years old (see Section 1.7); we further assumed that this metric would be subject to a particularly high level of desirability bias.

## **Approximate Bayesian Computation (ABC) procedure**

We used Approximate Bayesian Computation, with our calibration outcome being 7% HIV prevalence among 18-year-old ASMM. Our inputs were multiplication factors on the two tuning parameters, each given a uniform prior from 1 to 10. For each of the 100 parameter combinations we conducted 16 simulations, and retained those parameter combinations that yielded epidemics with HIV prevalence among 18-year-olds between 6% and 8%. We then used two-dimensional kernel density estimation to determine a final mean value for each of our multipliers. This was implemented in the R package MASS using the kde2d algorithm.

## **Results**

The final two-dimensional kernel density plot is shown below, and the final selected values for the two multipliers were 3.6 (for frequency of AI with other ASMM) and 8.2 (for contact outside the modeled population).

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1. **Final set of parameters**

The various derivations above led to the following final set of parameters that are common to all modeled scenarios. For parameters than vary between runs, see Table 1 in the body of the manuscript.

|  |  |
| --- | --- |
| **Parameter** | **Value(s)** |
| Prob. of age at entry into ASMM population | 13: 44%14: 13%15: 12%16: 11%17: 10%18: 10% |
| Prob. of AI debut at population entry | 50.6% |
| Prob. of debut (per week) if not at population entry | 0.34% |
| Expected momentary degree (number of partnerships ongoing), in quintiles | 0.054, 0.106, 0.161, 0.247, 0.782 (grand mean = 0.270) |
| Mean relational duration | 2.89 weeks |
| Mean weekly number of AI acts within ongoing relationships | 0.96 |
| Prob. condom use per Ai act | 54% |
| Sexual role | 14.5% exclusively insertive28.2% exclusively receptive57.3% versatile |
| Weekly probably of testing for HIV | 0.00238% |

Weekly probability of acquiring HIV from MSM above modeled age range

|  |  |
| --- | --- |
| **Risk Quintile** | **Age** |
| **13** | **14** | **15** | **16** | **17** | **18** |
| **Risk q1** | 8.30E-06 | 1.74E-05 | 2.56E-05 | 3.47E-05 | 4.30E-05 | 5.13E-05 |
| **Risk q2** | 1.74E-05 | 3.47E-05 | 5.13E-05 | 6.87E-05 | 8.60E-05 | 1.03E-04 |
| **Risk q3** | 2.56E-05 | 5.13E-05 | 7.77E-05 | 1.03E-04 | 1.29E-04 | 1.55E-04 |
| **Risk q4** | 4.00E-05 | 8.00E-05 | 1.20E-04 | 1.60E-04 | 2.00E-04 | 2.40E-04 |
| **Risk q5** | 1.26E-04 | 2.51E-04 | 3.77E-04 | 5.03E-04 | 6.28E-04 | 7.54E-04 |

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