Contribution of HIV disease and care stages to HIV transmission among Baltimore MSM: a modelling study for HPTN 078

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1. BACKGROUND

- Men who have sex with men (MSM) in the United States (US) are disproportionately affected by HIV
- The annual number of new HIV diagnoses in the US attributed to male-to-male sexual contact has remained constant over the last decade (Centers for Disease Control and Prevention (CDC))
- Baltimore (Maryland) is one of the US cities with the highest HIV prevalence among its MSM population, 30% in 2014 (CDC National HIV Behavioural Surveillance - NHBS)*
- Around half of HIV+ MSM from Baltimore were virally suppressed in 2017 (Maryland Department of Health data for Baltimore City)**

* http://www.cdc.gov/hiv/library/reports/surveillance/#panel2
** https://phpa.health.maryland.gov/OIDEOR/CHSE/Pages/statistics.aspx

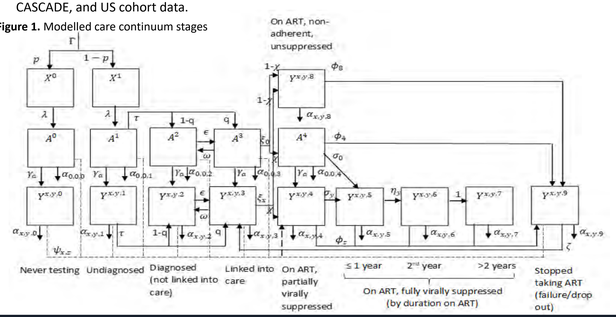
OBJECTIVE

Evaluate the contribution of subgroups of individuals in different stages of HIV disease and the HIV care continuum to new HIV infections among MSM in Baltimore over the past 30 years

2. METHODS: MATHEMATICAL MODEL OF HIV TRANSMISSION

- Mathematical model of HIV transmission among Baltimore MSM compartmented by age, race, CD4 level, set-point viral load, and care continuum stage: HIV testing, diagnosis, linkage to care, antiretroviral therapy (ART) use and adherence, and partial and full viral suppression (Figure 1).
- Demography and sexual activity parameters based on NHBS data for Baltimore MSM
- HIV progression/mortality, and ART initiation/dropout parametrised using Netherlands ATHENA, European CASCADE, and US cohort data.

Figure 1. Modelled care continuum stages



3. METHODS: ESTIMATING THE PROPORTION OF INFECTIONS CONTRIBUTED BY DIFFERENT GROUPS

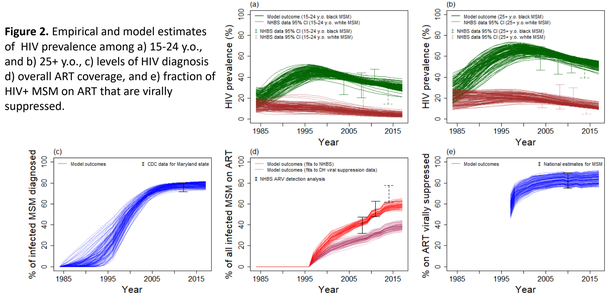
MODEL FITTING

The size and HIV prevalence of demographic groups were fitted in a Bayesian framework to Baltimore-specific surveillance data (CDC NHBS, Figure 2a-b).

The model was also fitted to proportion of MSM that were diagnosed, enrolled into HIV care, on ART, and virally suppressed over time, using Baltimore/Maryland/US MSM data (Figure 2c-e).

118 simulations matched the empirical data.

Figure 2. Empirical and model estimates of HIV prevalence among a) 15-24 y.o., and b) 25+ y.o., c) levels of HIV diagnosis d) overall ART coverage, and e) fraction of HIV+ MSM on ART that are virally suppressed.



INFECTIONS CONTRIBUTED BY DIFFERENT GROUPS

These 118 fitted simulations were used to estimate:

- The number and fraction of HIV+ MSM belonging to each group each year and over 10-year periods
- The Population Attributable Fraction (PAF) = fraction of HIV infections attributable to MSM in different disease stage and care continuum groups over 10-year periods. PAF obtained using counterfactual scenarios assuming the group could not transmit HIV-during that period: $PAF_{t_0-t} = \frac{Cl_{t_0-t}(risk) - Cl_{t_0-t}(no\ risk)}{Cl_{t_0-t}(risk)}$, with $Cl_{t_0-t}(risk)$ being the estimated cumulative number of incident HIV infections over the period [t_0, t], and $Cl_{t_0-t}(no\ risk)$ being calculated under the counterfactual scenario
- The per-capita HIV transmission rate (per 100 infected person-years) from a group was obtained by dividing the total number of excess infections over that period by the cumulative number of person-years lived in that group:

$$HIV\ transmission\ rate_{t_0-t} = 100 \times \frac{Cl_{t_0-t}(risk) - Cl_{t_0-t}(no\ risk)}{\int_{t_0}^{t} \#\ infected\ (risk)}$$

- We report median estimates across the 118 fitted simulations, and 95% uncertainty intervals (UI) (2.5th and 97.5th percentiles)

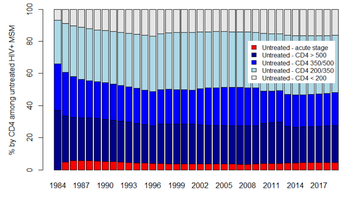
4. RESULTS: CONTRIBUTION OF HIV+ MSM WITHIN DIFFERENT HIV DISEASE AND CARE CONTINUUM STAGES

CONTRIBUTION OF UNTREATED HIV+ MSM IN DIFFERENT HIV DISEASE STAGES

The estimated fraction of untreated HIV+ MSM within the different disease stages remained fairly constant over time (Figure 3): ageing of the HIV epidemic was balanced by historical higher ART initiation rates among those with low CD4.

The model suggests that the contribution of untreated HIV+ MSM in the different disease stages has remained constant over time (Figure 4).

Figure 3. Estimated fractions of untreated HIV+ MSM in different CD4 count stages



We estimated that over the past 10 years:

- Untreated MSM (diagnosed or not) contributed to 88% (79-94%) of new HIV infections (Table 1)
- MSM in the acute stage were the most efficient HIV transmitters (rate of 54 per 100 infected person-years) and contributed to 20% (8-35%) of transmissions, while representing only 2% (1-4%) of HIV+ MSM (Table 1)
- Untreated MSM with CD4 < 200 cells/µl (AIDS stage, 8% of HIV+ MSM) transmitted HIV at 5 times the rate of those with CD4 ≥ 200 cells/µl (31 vs 7/100 infected person-years), and contributed to 40% of transmissions

Figure 4. Estimated contribution of untreated HIV+ MSM in different HIV infection stages to HIV incidence over 10-year periods

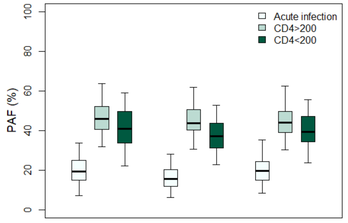


Table 1. Estimated population size, PAF and per-capita contribution to HIV incidence over 2008-2017

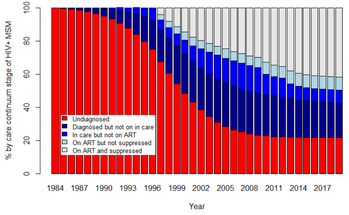
	Fraction among all HIV+ MSM (%)	PAF (%)	HIV transmission rate (per 100 infected person-years)
HIV infection CD4 stage			
Untreated acute infection	2.4% (1.2-3.5)	19.7% (8.3-35.2)	54.4 (31.1-85.2)
Untreated with CD4 ≥200	41.9% (35.4-57.3)	43.9% (30.1-62.6)	6.5 (4.4-9.3)
Untreated with CD4 <200	8.4% (5.2-14.7)	39.5% (23.7-55.7)	31.1 (20.3-44.3)
HIV care continuum stage			
Undiagnosed	21.9% (19.6-26.3)	41.3% (30.6-53.8)	12.1 (9.6-15.5)
Diagnosed	78.1% (73.7-80.4)	80.3% (71.3-87.0)	7.0 (5.2-8.7)
Untreated (not on ART)	50.6% (43.7-70.3)	88.4% (79.0-94.2)	10.3 (8.7-11.9)
Treated (on ART)	49.4% (29.7-56.3)	14.2% (7.2-28.0)	2.4 (1.3-3.4)
Diagnosed and untreated	29.7% (21.8-46.1)	63.8% (43.7-74.4)	12.1 (10.2-14.5)
Diagnosed but not in care	22.8% (11.7-33.8)	45.9% (24.6-56.3)	12.6 (10.2-15.7)
In care but not on ART	10.6% (5.6-17.0)	17.8% (9.5-25.0)	10.5 (8.4-13.2)

HIV TRANSMISSIONS FROM MSM WITHIN DIFFERENT CARE CONTINUUM STAGES

The model PAF for undiagnosed MSM declined over time, from 90% over 1988-1997 to 41% over 2008-2017, when undiagnosed MSM represented 87% and 22% of all HIV+ MSM, respectively (Figures 5, 6a, Table 1).

The PAF for diagnosed MSM increased from 13% over 1988-1997 to 80% over 2008-2017, despite diagnosed MSM transmitting less efficiently (7 vs 12/100 infected person years over 2007-2018) than undiagnosed MSM (Table 1).

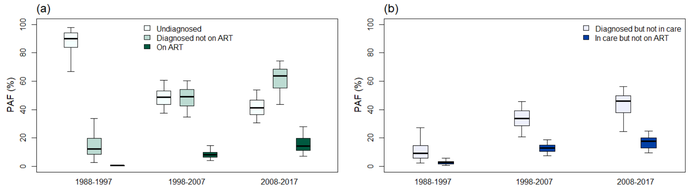
Figure 5. Estimated numbers fractions of HIV+ MSM in different care-continuum stages



We estimated that over the past 10 years:

- Two-thirds of the transmissions were attributable to HIV+ MSM not on ART despite being diagnosed (PAF=64% (44-74%)) (Figure 6a)
- MSM in care but not on ART contributed to 19% (12-28%) of transmissions (Figure 6b)
- MSM on ART modestly contributed to transmissions: 14% (7-28%), while representing 49% (30-56%) of all HIV+ MSM. Among them, those adhering to ART made very little contribution to transmission (PAF= 2% (1-5%)), despite comprising 42% (25-50%) of HIV+ MSM (not shown)

Figure 6. Estimated contribution of HIV+ MSM in different care-continuum stages to HIV incidence over 10-year periods



5. CONCLUSIONS

We estimated that undiagnosed MSM might have contributed to 40% of HIV transmissions among MSM in Baltimore over the past 10 years, with undiagnosed HIV+ MSM in the acute stage of the disease contributing to 20% of transmissions

Increases in the relative contribution to transmission of diagnosed MSM over time reflect improvements in HIV testing, but the majority of these transmissions arise from those who remain untreated, showing gaps in treatment provision and retention. Future interventions will need to address the remaining diagnosis and treatment gaps.

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