NATIONAL CENTER FOR HIV, VIRAL HEPATITIS, STD, AND TB PREVENTION

Contribution of HIV Transmission Bursts to Future HIV Infections, United States

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BACKGROUND

- The Respond pillar of the Ending the HIV Epidemic in the U.S. initiative includes strategies to detect and respond to clusters and outbreaks representing rapid transmission
- Assessing the contribution of rapid transmission to future infections can help improve understanding of the potential impact of responding to clusters and outbreaks

Objectives:

1. **Systematically identify periods of rapid HIV transmission as "transmission bursts" and estimate the relative contribution of transmission bursts to future transmissions**
2. **Describe characteristics of populations disproportionately impacted by transmission bursts**

METHODS

- Used subtype B HIV *pol* sequences from the U.S. National HIV Surveillance System for persons with HIV (PWH) diagnosed during 2014–2019 to infer time-scaled phylogenetic trees
- Constructed separate phylogenies for six geographic regions comprising 19 jurisdictions with >50% sequence completeness
- Inferred internal nodes in phylogenies (representing the most recent known common ancestors of divergent lineages) as estimated transmissions

Contribution to future transmission

- Detected transmission bursts, defined as ≥3 adjacent internal nodes in a 2-year period, and descendant transmissions from burst- and non-burst-associated lineages (see central figure)
- Calculated the relative contribution of transmission bursts in a fixed 2-year detection period (2015–2016) to transmission in a follow-up period (2017–2019) compared to non-bursts

Characteristics of PWH impacted by bursts

- Detected bursts in sliding 2-year detection periods during 2014–2019 to evaluate impact of bursts throughout full study period
- Assessed characteristics of PWH diagnosed 2017–2019 for association with any sliding window transmission burst membership or descendance using unadjusted risk ratios (RRs)

RESULTS

- 5,017/88,882 (5.6%) lineages associated with transmission bursts during 2015–2016 contributed to 623/4,171 (14.9%) transmissions during 2017–2019
- Relative contribution of lineages associated with transmission bursts to future transmissions was 2.94x that of lineages not associated with transmission bursts
- Among PWH diagnosed during 2017–2019, 6,463/43,721 (14.8%) were associated with transmission bursts
- Characteristics most strongly associated with burst membership or descendance:
  - Younger age at diagnosis
  - Self-identification as transgender or an additional gender identity, or as a cisgender man
  - Reporting male-to-male sexual contact, injection drug use, or male-to-male sexual contact and injection drug use
  - Diagnosis during acute or early infection

CONCLUSIONS

- Transmission bursts contribute disproportionately to future transmissions, underscoring the value of detecting and responding to clusters to prevent transmission
- Bursts of rapid HIV transmission may contribute to enduring disparities in overall HIV incidence among some key populations

Bursts of rapid HIV transmission contribute to nearly 3 times as many future transmissions as non-bursts

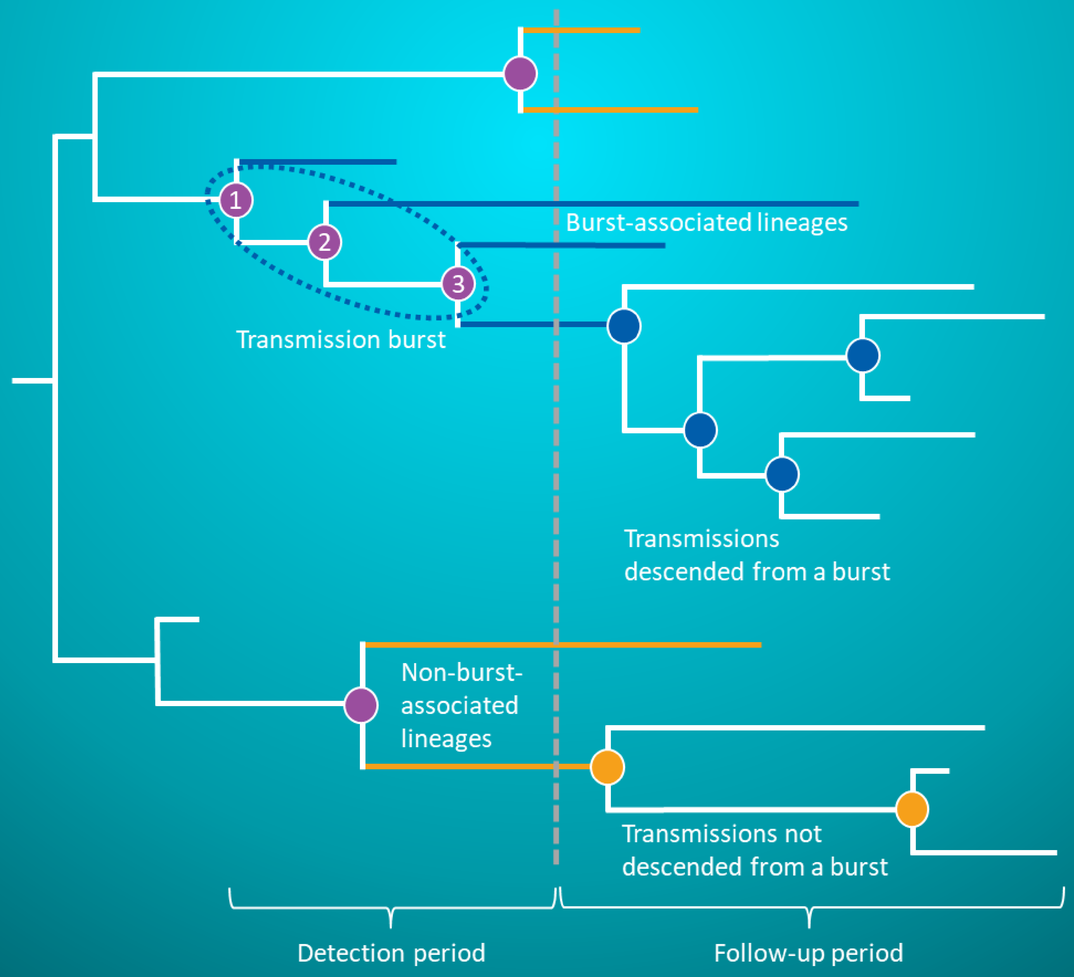


Table. Relative contribution of HIV transmission bursts to future transmissions during 2017–2019

Burst detection period	Lineages during the burst detection period		Transmissions 2017-2019		Relative contribution of bursts to future transmission[1]
	Not burst-associated, N (%)	Burst-associated, N (%)	Not descended from bursts, N (%)	Descended from bursts, N (%)	
2 Years	83,865 (94.4)	5,017 (5.6)	3,548 (85.1)	623 (14.9)	2.94
Sensitivity analyses					
1 Year	76,503 (97.8)	1,693 (2.2)	3,920 (94.0)	251 (6.0)	2.89
1.5 Years	80,209 (96.2)	3,153 (3.8)	3,770 (90.4)	401 (9.6)	2.71
2.5 Years	86,454 (92.5)	7,042 (7.5)	3,377 (81.0)	794 (19.0)	2.89
3 Years	87,596 (90.1)	9,628 (9.9)	3,198 (76.7)	973 (23.3)	2.77

[1]Burst-descended transmissions during 2017–2019 divided by the number of lineages associated with bursts during the burst detection period, compared to the number of non-burst-descended transmissions divided by non-burst-associated lineages.

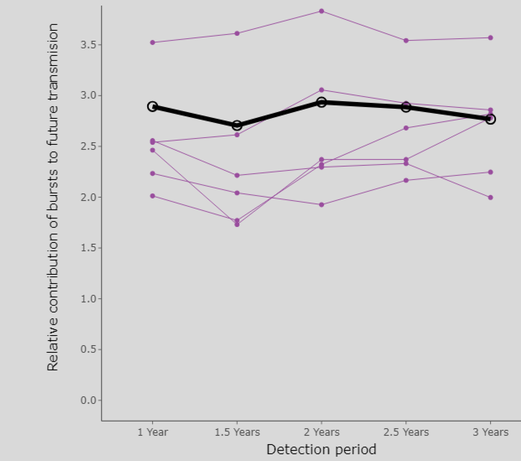


Figure 1. Relative contribution of HIV transmission bursts identified during a fixed burst detection period ending December 31, 2016 to future transmissions during 2017–2019, overall and within six regions. The length of the burst detection period is shown on the x-axis. Combined estimates across all regions are shown as hollow black points and estimates within individual regions are shown as solid purple points.

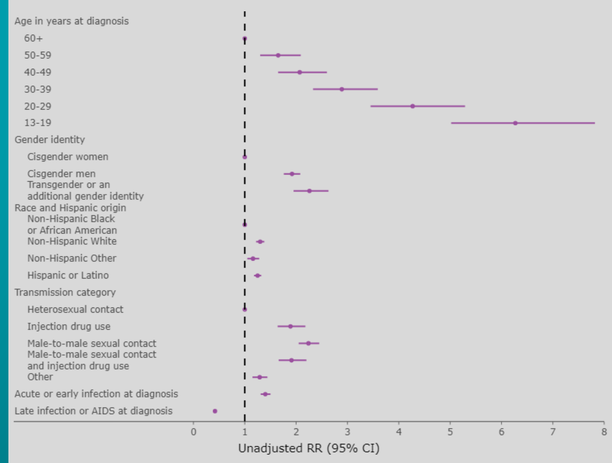


Figure 2. Demographic and clinical characteristics among people with HIV diagnosed during 2017–2019 associated with transmission burst membership or descendance. Unadjusted risk ratios with 95% confidence intervals (95% CIs) are calculated in comparison to a referent category for each characteristic, shown as solid points at RR = 1 for multi-level characteristics or not presented for two-level characteristics.

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