Transmission Networks of HIV-1 Among Men Who Have Sex With Men in East and Southeast Asia

To the Editors:
The HIV epidemic among men who have sex with men (MSM) in Asia is expanding at an alarming rate, especially in several urban centers. Understanding the dynamics of HIV-1 transmission among MSM across large geographic areas may provide essential information on the origin of viral lineages and their epidemic expansion. Such estimates provide insights on the size and frequency of the disease spread, which can be used to facilitate the implementation of intervention strategies for prevention, such as the use of pre-exposure prophylaxis and combination antiretroviral therapy (cART). The availability of large data sets of genetic sequences from antiretroviral resistance surveillance activities and the use of phylodynamic tools allow for the identification and characterization of transmission clusters.

In this study, we characterized the transmission clusters of HIV-1 among MSM across Asia and Southeast Asia. A total of 1856 HIV-1 polymerase gene sequences from HIV-infected individuals were obtained from the TREAT Asia Studies to Evaluate Resistance—Monitoring (TASER-M) Database between 2006 and 2011. The details about this study have been described previously. Briefly, patients initiating first-line cART from participating urban hospitals in Hong Kong, Thailand, Malaysia, and the Philippines, were included. Ethics approvals were obtained from the local institutional review boards, and informed consent was obtained before baseline genotypic resistance testing. Polymerase gene sequences were sequenced (HXB2 position: 2252-3263 nt) in laboratories participating in the TREAT Asia Quality Assurance Scheme (TAQAS) using in-house and/or commercially available resistance assays on specimens collected within 6 months before initiating cART. A total of 364 antiretroviral-naive MSM sequences were identified from the TASER-M database (Hong Kong, n = 118; Thailand, n = 124; Malaysia, n = 56; Philippines, n = 66). Following manual inspection (to remove problematic sequences) and phylogenetic inference, 144 subtype B and 186 CRF01_AE sequences from antiretroviral-naive MSM were identified and subjected to phylogenetic analysis. Unique recombinant forms and other rare subtypes (n = 29) were excluded from further analysis. Global MSM reference sequences of HIV-1 subtype B (n = 362) and CRF01_AE (n = 40) were retrieved from the HIV sequence database, in which sequences from other Asian countries (China, Mongolia, and Myanmar) were also included. Transmission clusters from the time-stamped sequence data sets were first deduced by neighbor-joining tree reconstruction followed by the more robust maximum likelihood and Bayesian maximum clade credibility inference implemented in PAUP version 4.0 (Sunderland, MA) and BEAST 1.7, respectively. Transmission cluster was defined based on the recently reported criteria: a phylogenetic cluster consisting of at least 2 isolates that form a clade supported by high bootstrap values (>90%) and Bayesian posterior probability value of 1 at the tree node. The divergence times or time of the most recent common ancestor (tMRCA) for each subtype B and CRF01_AE transmission clusters were estimated using the Bayesian coalescent methods as described previously.

Phylogenetic reconstructions of the TASER-M data sets showed that a total of 68.1% of HIV-1 subtype B and 45.7% of CRF01_AE sequences were grouped in 50 transmission clusters of various sizes (mean size = 5.6, range = 2–32 sequences), with subtype B sequences having a higher tendency to form a cluster (P < 0.0001). Together with other Asian sequences from China, Mongolia, and Myanmar, a total of 34 clusters involving 154 subtype B-infected individuals and 16 clusters involving 125 subjects infected with CRF01_AE were estimated (Fig. 1A). In both subtypes, most clusters contained individuals from the same geographical origin (ie, country), although about 22.0% of the clusters comprised individuals from more than 1 country. This suggests that MSM networks in East and Southeast Asia were usually localized in their respective countries, with some clusters spanning beyond a single country. Genealogy-based analysis to estimate the tMRCA for each transmission network indicated the continued emergence of new subtype B and CRF01_AE clusters in the past 3 decades (Fig. 1B). The uninterrupted growth of each subepidemics of various cluster sizes suggests the role of transmission clusters as the continuous driving force of the epidemic among MSM in Asia.

Information on HIV-1 transmission clusters generated by identifying genetically close virus variants circulating at a population level provides real-time direct evidence of an ongoing forward transmission that otherwise cannot be readily detected by conventional epidemiological surveillance. Despite expanded access to cART in some developing and developed nations in Asia, our analysis showed continued emergence of recent HIV-1 subtype B and CRF01_AE

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networks compared with the period in the 1980s and early 1990s where cART was less accessible. Although incomplete sampling or cluster extinction (dead-end transmission) may influence our interpretation and the fact that most of the TASER-M data sets were sampled primarily in 2008–2009 (62.4%), the observed trend suggests that increased access to cART in general may not be sufficient in reducing transmission clusters. The seemingly reduced transmission rates among individuals on cART could have been outpaced by the rapidly growing networks among undiagnosed and untreated MSM. Therefore, strategies such as early diagnosis and initiation of cART to reduce the risk of transmission among serodiscordant partners need to be urgently implemented and expanded across the region.\(^3,4\) The overall success of prevention or even harm reduction methods can in turn be assessed by monitoring the development of transmission networks, where in the presence of effective transmission control strategy, a significant decrease in the size and number of clusters over time should be observed.

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APPENDIX 1. Members of the TASER Study

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REFERENCES


To the Editors:

We read with great interest the report on baseline data from the US pre-exposure prophylaxis (PrEP) Demonstration Project,1 the first study to assess the feasibility and acceptability of delivering PrEP to men who have sex with men (MSM) in the United States. The data describe the cohort participating in a prospective, open-label study assessing PrEP delivery through STD clinics in San Francisco and Miami, as well as a community health center in Washington DC. This is an important work given the potential for PrEP (emtricitabine/tenofovir) to have a significant impact in limiting HIV acquisition with >90% efficacy among those with high adherence, as evidenced by detectable drug levels.2 Moreover, identifying clients who are at increased risk for HIV, such as those who seek services at STD clinics, will have the greatest public health impact for every dollar spent.3 The authors make an important distinction between clients enrolled in the study who were self-referred and those who were referred by clinic staff and conclude that interest in PrEP is high among a diverse population of MSM in these settings. Although the overall results suggest that there is high interest among MSM, a few aspects of the study require further

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