Title: Subtype specific differences in transmission cluster dynamics of HIV-1 B and CRF01_AE in New South Wales, Australia

Author:
Di Giallonardo F1, Pinto AN1,2, Keen P1, Shaik A1, Carrera A3, Salem H4, Selvey C5, Nigro SJ5, Fraser N6, Price K7, Holden J8, Lee FJ4,9, Dwyer DE10, Bavinton BR1, Geoghegan JL11,12, Grulich AE1, Kelleher AD1, on behalf of the NSW HIV Prevention Partnership Project

1 The Kirby Institute, UNSW Sydney, Sydney NSW 2052, Australia.
2 Royal Prince Alfred Hospital, Sydney NSW 2050, Australia.
3 HIV reference laboratory, Sydney NSW 2010, Australia.
4 New South Wales Health Pathology-RPA, Royal Prince Alfred Hospital, Camperdown NSW 2050, Australia.
5 Health Protection NSW, Sydney NSW 2059, Australia.
6 Positive Life New South Wales, Sydney NSW 2010, Australia.
7 ACON, Sydney NSW 2010, Australia.
8 NSW Ministry of Health, Sydney NSW 2059, Australia.
9 Sydney Medical School, University of Sydney, Sydney NSW 2050, Australia.
10 New South Wales Health Pathology-ICPMR, Westmead Hospital, Westmead, NSW, Australia.
11 Department of Microbiology and Immunology, University of Otago, Dunedin 9016, New Zealand.
12 Institute of Environmental Science and Research, Wellington 5018, New Zealand.

Introduction:
The HIV-1 epidemic in New South Wales (NSW) is becoming more heterogeneous. NSW Health reported differences in drop in infections for Australian-born (41%) and non-Australian-born individuals (6%) since 2014. This suggests differences in transmission dynamics between risk groups that could be linked to an increase in non-B subtypes, which are more common in non-Australian-born individuals. We therefore sought to compare transmission dynamics between different subtypes and their associated demographic characteristics.

Methods:
We used reverse transcriptase sequences sampled from new HIV-1 notifications between 2004 – 2018 that classified as subtype B (n=2919) and CRF01_AE (n=473). We estimated maximum likelihood trees and identified NSW-specific clades as nodes with 100% NSW sequences. Sequence pairs contained only two sequences and clusters contained ≥3 sequences. All other NSW sequences were defined as singletons. Chi-Square statistics was used for comparison between demographic factors and sequences being associated with a cluster or not.

Results:
We identified 104 subtype B and 11 CRF01_AE growing clusters. For subtype B; sequences associated with clusters were more likely to be from individuals reporting men who have sex with men transmission, being Australian-born, and derived from the early stage of infection (p <0.01). For CRF01_AE sequences, only those derived from the early stage of infection were associated with clusters (p <0.05). We found 47 subtype B and seven CRF01_AE clusters that contained sequences sampled during the early stage of infection but with a large time gap in-between (>1 year) and did not have a close genetic
link. These are likely to be representing infections derived from intermediate transmission via undiagnosed individuals.

**Conclusion:**
We identified subtype specific transmission dynamics with subtype B being dominated by larger clusters and CRF01_AE by sequence pairs. We identified numerous active clusters potentially containing undiagnosed individuals that might play a major role in sustaining the ongoing epidemic.

**Disclosure of interest statement**
This work was supported by the Swiss National Science Foundation (P300PA_174462 to F.D.G.), and the NHMRC Postgraduate Scholarship (APP1074467 to A.N.P.). This analysis was further supported by funding from NHMRC Partnership (GNT1092852) and Practitioner Fellowship (GNT117907) Grants, the NSW Ministry of Health, and UNSW Sydney. The Kirby Institute receives funding from the Australian Government Department of Health and is affiliated with the Faculty of Medicine, UNSW Sydney. No pharmaceutical industry grants were received for this study.