In Brazil, the transmission of HIV drug resistance strains has increased from 6.6 per cent in 2001 to 9.5 per cent in 2015. Besides being associated with virological failure in first-line antiretroviral therapy, drug resistance can also compromise pre-exposure prophylaxis, mother-to-child transmission prevention, and post-exposure prophylaxis. In order to monitor HIV primary resistance in Brazil, we aimed to identify pre-treatment drug resistance transmission chains in both national and regional levels. Sampling strategy was based on the HIV Threshold Survey methodology (HIV-THS, WHO). Subjects were selected from fifty-one highly populated cities present in all five Brazilian macro-regions. HIV pol subtype was determined by Rega HIV Subtyping Tool and maximum likelihood phylogenetics. The presence of pre-treatment drug resistance transmission clades was verified by maximum likelihood tree (PhyML 3.0) for subtypes B, C, and F, separately, in both national and regional levels. Phylogenetic trees were edited using FigTree v1.4.3. We analyzed 1,566 HIV pol sequences from antiretroviral naive individuals with recent HIV infection. The presence of surveillance drug resistance mutations (SDRM) was previously characterized by Stanford HIVdb Program, with a nationwide prevalence of 9.5 per cent. Overall, subtype B (66 per cent) was the most prevalent, followed by subtypes C (13 per cent), F (11 per cent) and recombinant forms (10 per cent). Subtypes A, D, and CRF 02_AG were identified in < 1 per cent. The distribution of HIV subtypes was slightly different among the different geographic regions, especially in the South, where subtype C represented 51 per cent of analyzed sequences. Sequences presenting SDRM appeared dispersed on all phylogenetic trees, showing no specific pre-treatment drug resistance transmission clade, when considering both the national level or the five Brazilian geographic regions, separately. The HIV subtype distribution is in accordance with previous reports, emphasizing the high prevalence of subtype C in the Southeast Brazil and the introduction of CRF 02_AG in the Northeast. Phylogenetic analyses showed no specific SDRM transmission clade. Hence, HIV SDRM transmission in Brazil does not seem to occur in a particular population group or geographic region. These results further illustrate the important contribution of phylogenetic studies in predicting future trends in SDRM transmission.

**Development of HIV drug resistance in HIV-infected patients failing second line regimen in Zimbabwe: A public health concern**

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The countries in southern Africa are not only the most heavily impacted in the world by HIV/AIDS but are now home to the world’s largest HIV/AIDS treatment programs, providing care and treatment to millions of people. As antiretroviral therapy (ART) programs in sub-Saharan Africa continue to expand, individuals on ART should be closely monitor to ensure favorable treatment outcomes and to minimize the development and transmission of HIV drug resistance, given the limited antiretroviral drug regimen choices available in these settings. We sought to investigate the frequency and determinants of virologic failure of acquired drug resistance-associated mutations (DRMs) in patients failing protease inhibitor-based antiretroviral treatment in Zimbabwe, using a prospective cohort study with cross-sectional analysis. All participants attended the HIV Clinic at Newlands Hospital-Harare and were on ART for at least twelve months. Participants with virologic failure (VL > 1,000 copies/ml) were tested for HIV-DRM. Demographic and clinical data were abstracted from medical records. DRMs were defined according to the Stanford HIV database guidelines. A total number of 187 plasma samples were genotyped, out of the 187 participants. Only 114 participants were on second line regimen. From the 114 participants, ART-associated PI major DRM were identified in forty-five patients (39.47 per cent) with multiclass resistance being the combination of M46I+I50L+V82A (2.63 per cent). The most common mutations were M46I (24.77 per cent), V82A (21.43 per cent), I50L (17.70 per cent), I84A (7.08 per cent), and L90M (4.42 per cent). No PI mutations were observed in adolescents with the mean age of < 20 years old and yet were prevalent in adults with mean age of > 35 years old. Virologic failure rates in adults were high with the majority of ART-failing adults harboring HIV-DRM, yet in adolescents and young adults this remains an adherence problem. Viral load monitoring and drug resistance testing are urgently needed to maintain future treatment options for the millions of African living with HIV.

**Phylogenetic characterization of HIV transmission in Belgium between 2013 and 2015**

Kenny Dauwe on behalf of all Belgian AIDS Reference Laboratories

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A good insight in regional HIV transmission dynamics is important for policy decisions and improved prevention and testing strategies. We present the phylogenetic analysis of a well characterized and dense sampled population of most newly diagnosed HIV patients in Belgium. The patient population consisted of 1,665 individuals newly diagnosed with HIV-1 in 2013, 2014, and 2015 for whom baseline resistance testing has been performed, which is a standard procedure in Belgium. Protease-RT sequences as well as clinical and epidemiological data were collected. Maximum likelihood phylogenetic analysis was performed on concatenated protease-RT sequences trimmed to a total length of 876 nucleotides. Clusters of at least two sequences with a bootstrap value > 0.97 and a mean pairwise distance < 0.015 were considered as transmission pairs or clusters (n = 177). Since the major aim of the work was a better insight on ongoing HIV transmission, occasional sequences with a genetic distance to the closest relative in the cluster of > 0.030 were removed and considered as individual sequences. Based on tree topology, bootstrap and distance analysis, 873 individual sequences, 93 pairs, 67 small clusters (three to seven individuals), and 17 large clusters (more than seven individuals) were identified. The median cluster size for small and large cluster was respectively 4 (IQR: 3–6) and 10 (IQR: 9–19). Comparison of the characteristics of patients on individual branches and patients in clusters (less than two individuals) revealed that clustered patients are more frequently male (92.6 vs. 65.8 per cent), MSM (77.2 vs. 41.3 per cent), of Belgian origin (68.2 vs. 32.8 per cent), self-reporting infection in Belgium (95.1 vs. 47.4 per cent), infected with subtype B or F (respectively 69.0 vs. 40.5 per cent and 18.8 vs. 2.8 per cent), diagnosed with an infection of < 6 months (55.4 vs. 28.8 per cent). They have higher CD4 counts (mean 487 vs. mean 376) and higher viral load (mean log
4.93 vs. 4.73). There was no difference in presence of transmitted drug resistance. This study confirms the current epidemiological knowledge of local spread of HIV-1 in Belgium and provides a solid base for more in-depth characterization of transmission and for future real-time follow-up of cluster dynamics.

A5 Using phylodynamic modelling to estimate the population attributable fraction of HIV spread due to key populations in Dakar, Senegal

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Although it has long been believed that certain key populations contribute disproportionately to HIV infection, the proportion of transmission events attributable to them is poorly understood. Most existing methods for estimating the population attributable fraction (PAF) are derived from the proportion of prevalent infections found in each group, or from static modes of transmission studies. Although these methods are useful in obtaining a cross-sectional estimate of the fraction of incident infections acquired in each group, they do not take into account the chain of transmission, and thus may underestimate the contribution of key populations. Using a transmission dynamics model, we aim to estimate the PAF of female sex workers, clients, and men who have sex with men to the HIV epidemic of Dakar, Senegal. On top of behavioural and epidemiological data, we will have access to genetic data from these key populations from an ongoing study, as well as historical samples from the Los Alamos database. As genetic diversity is shaped by epidemiological history, population genetic modelling of our sequence data can be informative about epidemic size and the migration of lineages through space and between risk groups. Our model will be first parameterised and fitted to behavioural and epidemiological data. We will then perform a phylogenetic analysis on our sequence data, using known dates of sampling and a molecular clock model of sequence evolution. Using structured coalescent models, we can look at the balance of phylogenies and infer patterns of transmission (although we will not have a large enough sample to determine clusters). We can then refit the transmission model to the sequence data as well, and provide new estimates of the PAFs. The comparison of PAFs estimated with or without using sequence data will provide an insight into the added value of phylodynamic modelling, and may help reassess the role of key populations in this setting.

A6 The effect of the mechanism and amount of missingness on phylodynamic inference of heterosexual HIV transmission networks

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Successful HIV prevention requires a better understanding of the structure and the dynamics of the sexual network. The latter evolves over time and the transmission network emerges from that dynamic sexual network. At the same time, the genetic material of the virus evolves across the transmission network. Due to the fact that population-level HIV transmission dynamics and HIV evolutionary dynamics are on the same time scale, the molecular evolution of the virus becomes a footprint of the transmission network. Therefore, the analysis of HIV phylogenetic trees holds the promise to provide more objective methods to estimate transmission network characteristics. We aimed to investigate the effect of sub-optimal sequence coverage on the characteristics of the transmission network (e.g., degree distribution and link density) inferred from the phylogenetic tree. We simulated a small epidemic (seventy-two transmission events) using agent-based models. Across the transmission chain, the molecular evolution of the virus was simulated using appropriate substitution models and evolutionary rates for HIV-1. We considered one consensus sequence per individual, and we simulated five levels of sequence coverage. In addition, we simulated two sampling strategies: a cross-sectional sampling design at the end of the simulation time window, and longitudinal sampling design. For each level, we constructed a phylogenetic tree and the subsequent transmission network, which were compared to the true transmission network. We found that a reconstructed transmission network from a phylogenetic tree has characteristics close to those of the true transmission network when sequence coverage was at least 60 per cent of the infected individuals (forty-five sequences). The increase of taxa (sequence coverage) improves the inferred transmission network characteristics. In addition, transmission networks reconstructed with the cross-sectional sampling design had less overestimation of links (which are seen as potential transmission events).

A7 Improving the accuracy and precision of estimated temporal trends in HIV incidence among MSM populations by calibrating agent-based simulation models to phylogenetic tree data

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Effective prevention of sexually transmitted HIV infections requires knowledge of the sexual networks across which these infections are transmitted. Sexual behaviour surveys are routinely being conducted to ask people about their recent sexual partners, leading to emergence of star-shaped ego-centric network data. At the same time, phylogenetic tree analysis has long been conducted to analyse HIV transmission clusters. In an ongoing project, we aim to show that (1) agent-based simulation models, embedded in a Bayesian framework, can provide a platform for combining these complementary data sources, and that (2) such an integrated approach can lead to more accurate and robust inferences in HIV epidemiology. Within this project, a first case study aims to provide evidence that phylogenetic tree data can increase the validity of agent-based model projections. Specifically, in a small-scale proof-of-concept study, we use synthetic data from a ‘master model’ to demonstrate that the accuracy and precision of estimated temporal trends in HIV incidence improves when agent-based simulation models of HIV transmission in MSM populations in Western Europe are not only calibrated to reported behavioural and epidemiological data, but also to phylogenetic tree data. Our model calibration

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