(28%). There was no significant difference of adverse events between triple prophylaxis and AZT alone (Table 1). Median (IQR) hemoglobin level among infants who received triple prophylaxis were 9.9 (9.0 to 11.4) g/dL, 10.1 (9.3 to 11.0), and 11.7 (11.0 to 12.3) at aged one, two and four months, respectively, which did not significantly differ between groups. No infants required blood transfusion. NVP concentrations were available from 48 infants (135 samples); median predicted NVP C_{24} were 1336 ng/mL, 2241, 2782, 2197, and 812 on days 1, 2, 7, 14, and 28 of life, respectively (Figure 1). All infants maintained NVP concentrations above the proposed prophylactic target threshold of 100 ng/mL during the first four weeks. Maternal EFV treatment did not affect infant NVP levels.

Conclusions: Six-weeks of AZT/3TC/NVP in HIV-exposed infants did not increase the risk of toxicity compared with an AZT regimen. Administration of 4 mg/kg of NVP from birth provided adequate NVP concentrations for prophylaxis during the first four weeks of life.

THAC0101

The identification of a micro-epidemic in a hyper-endemic HIV setting using molecular epidemiology

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Background: Understanding transmission dynamics of infectious diseases is critical in developing effective interventions. Traditional epidemiological analyses are the bedrock of many public health decisions, but can be resource-intensive and may be limited by incomplete/inaccurate datasets. Since HIV gene sequences can provide information not contained in traditional case data, considerable efforts are now invested in generating genomic data. However, the value of such data for epidemiological surveillance remains unclear. We illustrate how incorporating genomic data with traditional epidemiological analyses provides additional insight for surveillance, with potential to inform prevention strategies.

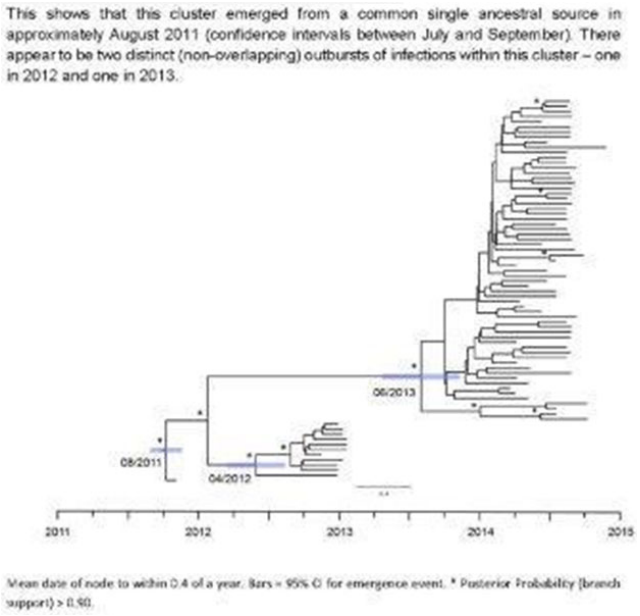
Methods: We used routinely-collected AHRI data to undertake a combined phylogenetic and epidemiological investigation.

A phylogeny of 2179 HIV-1 subtype-C partial pol sequences was reconstructed by maximum-likelihood inference. This included 1376 local sequences (2010 to 2014, 15% of the HIV-positive population) and 803 publicly-available South African control sequences (2000 to 2014). A dated phylogeny was inferred using Beast2 and reproduction numbers (R_e) estimated. We geo-located individuals to their residence and undertook space-time analyses to identify variations in HIV incidence.

Results: Phylogenetic reconstruction revealed a previously undetected distinct monophyletic cluster (75 local sequences; branch support>90%). The dated phylogeny suggests this outbreak emerged from a single common source, experienced two bursts of infection (2012&2013/4; R_e>1.8) and was still expanding at the time of sampling (2014) (Figure 1). Geo-locating individuals/sequences revealed over 40% resided within a rural area adjacent to a recent (2008) coal mine development. Baseline characteristics of the cluster suggest demographics compatible with those working in the mine (higher proportion of employed males). Space-time analysis confirmed the emergence of this rural cluster by identifying increased HIV incidence in the locality of the mine.

To our knowledge, this is the first time molecular methods have detected a micro-epidemic not identified via traditional epidemiological surveillance.

Conclusions: By uncovering a micro-epidemic our findings demonstrate that molecular epidemiology enhances traditional epidemiological analysis. Genomic data are a valuable addition to routine surveillance data, particularly in allowing detection of emerging micro-epidemics in a hyper-endemic region. Although, at present, implementation may be unrealistic in resource-poor settings, sequence data is becoming increasingly affordable, and molecular methods should be considered to enhance surveillance and guide the development of optimal intervention strategies.



Abstract THAC0101-Figure 1. Dated Phylogeny of identified cluster.

THAC0102

High prevalence fishing communities are not a major source of new HIV infections to the inland populations in Rakai District, Uganda: implications for geo-spatially targeted HIV prevention interventions

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Background: Targeting combination HIV prevention (CHP) to areas of high HIV prevalence is considered a cost-efficient and essential strategy for reducing HIV incidence in sub-Saharan Africa. Since 2014, the Ugandan National Antiretroviral Therapy Guidelines recommend targeted CHP to fishing communities on Lake Victoria, with an estimated HIV prevalence 25% to 40%, partly based on the assumption that fishing sites are a major source of HIV transmissions to the inland populations; however the validity of this assumption has not been empirically evaluated.

Methods: Between August 2011 and Oct 2014, individuals aged 15 to 49 years in 40 communities in Rakai District, Uganda, were tested

for HIV and interviewed (sociodemographic, behavioral and health information). Households were geocoded, and communities were classified as Lake Victoria fishing (n = 4), agrarian (n = 27), or main road trading (n = 9) communities. Viral RNA from newly diagnosed participants was deep sequenced via *Illumina* instruments. The *phyloscanner* software package (https://github.com/BDI-pathogens/phyloscanner) was used to reconstruct HIV transmission networks, and to infer the direction of HIV transmission from deep sequence data. Transmission flows between fishing sites and agragrian/trading communities were estimated with Bayesian multi-level models.

Results: Of 23,719 individuals surveyed, 6205 were HIV-positive, 4309 (69%) were antiretroviral naive, of whom 2803 (65%) were sequenced. 359 phylogenetically likely transmission events involving 676 individuals were reconstructed, with an estimated, expected 16% (11% to 23%) of false reconstructions. Direction of transmission could be inferred in 241 likely transmission events, with an estimated, expected 14% (7% to 26%) of false directions. Only 3/241 transmission events occurred from fishing sites to agrarian/trading communities. Adjusting for differences in participation and sequence sampling by age and community, an estimated 34.3% (28.6% to 40.5%) of transmissions occurred within fishing sites, 58.0% (51.2% to 64.6%) within agrarian/trading communities, 3.4% (1.7% to 6%) from fishing sites to agrarian/trading communities, and 4.0% (2% to 7.2%) from agrarian/trading communities to fishing sites.

Conclusions: HIV is infrequently transmitted from four high-prevalence fishing sites to the population in 36 agrarian/trading communities further inland, based on population-level NGS viral phylogenetic analysis. Our results suggest that targeted CHP to Lake Victoria fishing sites would not mitigate the broader HIV epidemic. Further studies in sub-Saharan Africa are needed to assess the strategy of targeting CHP to various high prevalence hotspots.

THAC0103

An RNA-seq gene expression signature identifies early HIV infection in rural Mozambique

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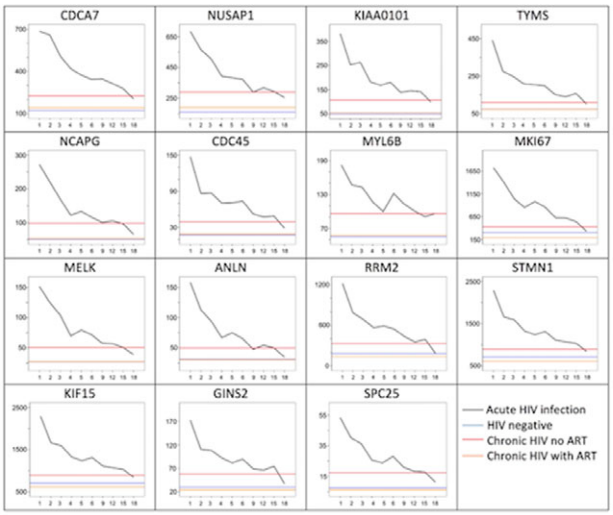
Background: Accurate measurement of HIV incidence is crucial in determining the effectiveness of preventative and therapeutic interventions, yet remains a global challenge. This study employed RNA-seq to investigate changes in human gene expression during early HIV-1 infection with the objective of identifying a transcriptomic signature able to differentiate early from long-standing infection.

Methods: Individuals presenting to Manhica District Hospital, Mozambique were screened for acute HIV infection (AHI), defined by positive viral load prior to seroconversion, with follow-up over 18 months. Uninfected subjects, plus those with longstanding HIV, with and without anti-retroviral therapy (ART), were recruited as controls. Peripheral blood mononuclear cells were collected and RNA extracted using RNeasy MinElute Clean-up kit (Qiagen). Illumina 50 bp, single-end RNA-seq was performed. Read quality was assessed using FastQC. Reads were aligned to human reference genome hg19 using HISAT. Alignment quality was assessed using Samstat. Quantification and normalisation of read counts was performed using summarizeOverlaps (*GenomicAlignments* package) and voom (*limma* package), both from Bioconductor. Random Forest assessed the predictive accuracy of sample classification. Statistical analyses were performed using R version 3.2.0.

Results: Fifty-three AHI individuals had a median estimated time since infection of nine weeks (IQR 7.8 to 19.3 weeks). RNA-seq was performed on 164 longitudinal samples from the AHI cohort, as well as 54 HIV negative, 24 chronic without ART, and 24 chronic with ART samples, resulting in an average of 23 million reads per sample, with 80% of reads mapped at high accuracy. All samples passed pre-and post-alignment QC. Fifteen genes were significantly differentially expressed during AHI compared with all controls (Figure 1). Random Forest analysis was able to predict biological group with a sample-level error rate of 0.26.



Horizontal axes are in units of months post-diagnosis. Vertical axes are in units of mean mapped reads per gene.

Abstract THAC0103-Figure 1. Expression patterns of the fifteen gene that are differentially expressed during early HIV infection compared to all controls.

Conclusions: This exploratory transcriptomic analysis was able to identify a gene expression signature unique to early HIV infection, most effective at distinguishing the initial three months from longer-term infections. For individual samples, acute infections and chronic infections with ART had high identification accuracy, however chronic untreated infection samples were harder to distinguish from early infection. The gene candidates in Figure 1 are clearly differentially expressed during early infection, compared with all controls, indicating useful pathways for future incidence assay optimisation.

THAC0104

Size estimation of key populations for HIV in Singapore using the network scale-up method

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Background: The size of populations at-risk for HIV in Singapore has yet to be systematically estimated. Using the network scale-up (NSU) approach, we developed a localised instrument and Bayesian statistical method to generate size estimates—adjusted for transmission error—of at-risk populations in Singapore.

Methods: We conducted nine in-depth interviews and four focus groups discussions with key stakeholders to guide the development of the survey questionnaire. In total 199 participants recruited from the