Projet de recherche : Analyse des Abstracts

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Contents

Légende

- **Le thème et l'objectif principal du papier.** Quel problématique est-ce que le papier tente de résoudre ?
- **Introduction** : description du sujet principal.
- **Méthodologie** : quel est le type de recherche qui est effectué dans ce papier ?
- **Détails** : les informations qui ne sont pas aussi importantes, mais que nous pouvons prendre en compte, si nous avons une manque d'informations dans le résumé final. Par exemple : les participants sélectionnés pour conduire la recherche, ou le déroulement des recherches.
- **Résultats** de la recherche : ces informations pourraient ne pas être importantes pour le résumé final.
- **Conclusions** : À quoi sont arrivés les auteurs de la recherche ? Quels peuvent être les travaux futurs ?

Ce qui suit est une liste exhaustive d'abstracts avec des parties de phrases surlignés en 6 couleurs différentes. Cette liste n'est pas représentative de tous les abstracts, mais cela permet d'avoir une idée de comment extraire les informations dont on a besoin. L'extraction des informations a été fait à la main.
Les abstracts sont séparés par des clusters. J'ai sélectionné les cinq premiers abstracts dans chacune des cinq clusters fourni dans le DF-Hover.
Nous supposons que les informations de dates et de lieux ne sont pas important pour la génération du résumé.
Si vous avez d'autres questions, vous pouvez m'écrire à l'adresse *Nikita.Missiri@etu.unige.ch*.

1 Cluster n°1

Abstract n°1: « Integrating Enhanced HIV Pre-exposure Prophylaxis Into a Sexually Transmitted Infection Clinic in Lilongwe: Protocol for a Prospective Cohort Study. »

Pre-exposure prophylaxis (PrEP) reduces HIV acquisition risk by >90% and is a critical lever to reduce HIV incidence. Identifying individuals most likely to benefit from PrEP and retaining them on PrEP throughout HIV risk is critical to realize PrEP's prevention potential. Individuals with sexually transmitted infections (STIs) are an obvious priority PrEP population, but there are no data from sub-Saharan Africa (SSA) confirming the effectiveness of integrating PrEP into STI clinics. Assisted partner notification may further enhance STI clinic-based PrEP programming by recruiting PrEP users from the pool of named sexual partners of individuals presenting with an incident STI. However, the acceptability, feasibility, and effectiveness of these integrated and enhanced strategies are unknown.

This study aims to describe the implementation outcomes of acceptability, feasibility, and effectiveness (regarding PrEP uptake and persistence) of integrating an enhanced PrEP implementation strategy into an STI clinic in Malawi.

The enhanced PrEP STI study is a prospective cohort study enrolling patients who are eligible for PrEP (aged $\geq$ 15 years) who are seeking STI services at a Lilongwe-based STI clinic. Data collection relies on a combination of in-depth interviews, patient and clinic staff surveys, and clinic record review. All enrolled PrEP users will be screened for acute HIV infection and receive quarterly testing for Neisseria gonorrhea, Chlamydia trachomatis, and syphilis. Participants will be asked to name recent sexual partners for assisted notification; returning partners will be screened for PrEP eligibility and, if interested, enrolled into the cohort of PrEP initiators. We will also enroll patients who are eligible for PrEP but choose not to initiate it, from the STI clinic. Patient participants will be followed for 6 months; we will assess self-reported PrEP use, PrEP refills, sexual behaviors, perceived HIV risk, and incident STIs. Clinic staff participants will be interviewed at baseline and at approximately 6 months and will complete surveys examining the perceived acceptability and feasibility of the integrated and enhanced PrEP strategy.

Enrollment began in March 2022 and is projected to continue until February 2023, with patient participant follow-up through August 2023. The results of this study are expected to be reported in 2024.

This study will generate important evidence regarding the potential integration of PrEP services into STI clinics in SSA and preliminary data regarding the effectiveness of an enhanced intervention that includes assisted partner notification as a strategy to identify potential PrEP users. Furthermore, this trial will provide some of the first insights into STI incidence among PrEP users recruited from an STI clinic in SSA-critical data to inform the use of etiologic STI testing where syndromic management is the current standard. These findings will help to design future PrEP implementation strategies in SSA.

ClinicalTrials.gov NCT05307991; https://clinicaltrials.gov/ct2/show/NCT05307991. DERR1-10.2196/37395.

Abstract n°2: « Determinants of therapy failure among adults on first-line antiretroviral therapy in Asmara, Eritrea: a multicenter retrospective matched case-control study. »

Information on treatment failure (TF) in People living with HIV in a data-poor setting is necessary to counter the epidemic of TF with first-line combined antiretroviral therapies (cART) in sub-Saharan Africa (SSA). In this study, we examined the risk factors associated with TF in Asmara, Eritrea from 2001 to 2020.
A multicenter, retrospective 1:2 matched (by age and gender) case-control study was conducted in four major hospitals in Asmara, Eritrea on adults aged $\geq$ 18 years who were on treatment for at least 6 months . Cases were patients who fulfills at least one of the WHO therapy failure criterion during the study period. Controls were randomly selected patients on first-line treatment and plasma viral load $<$ 1000 copies/ml in their latest follow-up measurement . Multivariable logistic regression analysis was conducted to identify risk factors for TF. All P-values were 2-sided and the level of significance was set at $P < 0.05$ for all analyses.
Of the 1068 participants (356 cases; 712 controls), 585 (54.7%) were females. The median age at treatment initiation was 46 years [interquartile range (IQR): 39-51]. Median time to combined antiretroviral therapy (cART) failure was 37 months (IQR = 24-47). In the multivariate analysis, factors associated with increased likelihood of TF included initial nucleoside reverse transcriptase inhibitors (NRTI) backbone (Zidovudine + Lamivudine (AZT + 3TC): adjusted odds ratio (aOR) = 2.70, 95% Confidence interval (CI): 1.65-4.41, P-value $<$ 0.001), (Abacavir + lamivudine (ABC + 3TC): aOR = 4.73, 95%CI: 1.18-18.92, P-value = 0.028], and (Stavudine + Lamivudine (D4T + 3TC): aOR = 5.00; 95% CI: 3.03-8.20, P-value $<$ 0.001) in comparison to Emtricitabine and Tenofovir diproxil fumarate (FTC + TDF). Additional associations included prior exposure to cART (aOR = 2.28, 95%CI: 1.35-3.86; P-value = 0.002), record of sub-optimal drug adherence (aOR = 3.08, 95%CI: 2.22-4.28; $P < 0.001$), ambulatory/bedridden at presentation (aOR = 1.61, 95%CI: 1.12-4.28; P-value = 0.010), presence of comorbidities (aOR = 2.37; 95%CI: 1.36-4.10, P-value = 0.002), duration of cART ($<$ 5 years: aOR: 5.90; 95% CI: 3.95-8.73, P-value $<$ 0.001), and use of SMX-TMP prophylaxis (aOR = 2.00, 95%CI, 1.44-2.78, P-value $<$ 0.001).
Our findings underscore the importance of optimizing cART adherence, diversification of cART regimens, and interventions directed at enhancing early HIV diagnosis, prompt initiations of treatment, and improved patient-focused monitoring of treatment response .

Abstract n°3: « Predicting HIV Status among Men Who Have Sex with Men in Bulawayo & Harare, Zimbabwe Using Bio-Behavioural Data, Recurrent Neural Networks, and Machine Learning Techniques. »

HIV and AIDS continue to be major public health concerns globally. Despite significant progress in addressing their impact on the general population and achieving epidemic control, there is a need to improve HIV testing, particularly among men who have sex with men (MSM) . This study applied deep and machine learning algorithms such as recurrent neural networks (RNNs), the bagging classifier, gradient boosting classifier, support vector machines, and Naïve Bayes classifier to predict HIV status among MSM using the dataset from the Zimbabwe Ministry of Health and Child Care. RNNs performed better than the bagging classifier, gradient boosting classifier, support vector machines, and Gaussian Naïve Bayes classifier in predicting HIV status. RNNs recorded a high prediction accuracy of 0.98 as compared to the

Gaussian Naïve Bayes classifier (0.84), bagging classifier (0.91), support vector machine (0.91), and gradient boosting classifier (0.91). In addition, RNNs achieved a high precision of 0.98 for predicting both HIV-positive and -negative cases, a recall of 1.00 for HIV-negative cases and 0.94 for HIV-positive cases, and an F1-score of 0.99 for HIV-negative cases and 0.96 for positive cases. HIV status prediction models can significantly improve early HIV screening and assist healthcare professionals in effectively providing healthcare services to the MSM community. The results show that integrating HIV status prediction models into clinical software systems can complement indicator condition-guided HIV testing strategies and identify individuals that may require healthcare services , particularly for hard-to-reach vulnerable populations like MSM. Future studies are necessary to optimize machine learning models further to integrate them into primary care. The significance of this manuscript is that it presents results from a study population where very little information is available in Zimbabwe due to the criminalization of MSM activities in the country. For this reason, MSM tends to be a hidden sector of the population, frequently harassed and arrested. In almost all communities in Zimbabwe, MSM issues have remained taboo, and stigma exists in all sectors of society.

Abstract n°4: « Trends and predictors of modern contraceptive use among married women: Analysis of 2000-2016 Ethiopian Demographic and Health Surveys. »

Accessing family planning is a key investment in reducing the broader costs of health care and can reduce a significant proportion of maternal, infant, and childhood deaths. In Ethiopia, use of modern contraceptive methods is still low but it is steadily increasing. Identifying the contributing factors to the changes in contraceptive use among women helps to improve women's contraceptive use and helps to plan strategies for family planning programs. Thus, the current study aimed to analyze the trends and predictors of changes in modern contraceptive use over time among married women in Ethiopia.
Secondary data analysis of the national representative data of 2000-2016 Ethiopian Demography and Health Survey was employed.
This secondary data analysis was considered using 2000 through 2016 Ethiopian Demographic and Health Surveys. The study used data from the four DHSs conducted in Ethiopia (2000-2016). The data from all EDHS was collated so as to follow the trends throughout the period considered for the survey. Married women aged 15-49 years with sample sizes of 36,721 (9,203 in 2000, 8,438 in 2005, 9,478 in 2011, and 9,602 in 2016) were included. The analysis involved three levels , including trend analysis (to see changes from 2000 to 2005, 2005-2011, 2011-2016 and 2000-2016) . Bivariate and multivariate analysis were also considered to identify predictors of modern contraceptive use. Data was extracted from the EDHS datasets for which authorization was obtained from the DHS Program/ICF International using a data extraction tool. SPSS 24 was employed for data management and analysis.
Among married women of reproductive age, modern contraceptive prevalence increased from 6.2% in 2000 to 35.2% in 2016. This 5-fold increment in modern contraceptive use was due to being in the age group of 25-29 years (AOR = 1.4; 95% CI (1.1, 1.7)), having two children (AOR = 1.3; 95% CI (1.1, 1.6)), the richest wealth category (AOR = 3.0; 95% CI (2.5, 3.5)), currently working (AOR = 1.3; 95% CI (1.2, 1.5)) and attending secondary and above education (AOR = 1.2; 95% CI (1.1, 1.6)) were found to be predictors .
Over the past 15 years, an annual average of a 1.9% point increment has been observed in modern contraceptive use, but the country lags behind the SDGs's 2030 target of achieving zero unmet needs for contraception. Program interventions, and continued education of women, are mandatory, as education is one of the major factors contributing to increasing contraceptive use.

Abstract n°5: « Burden of sexually transmitted infections from acute HIV infection among women in South Africa: Evidence from a prospective cohort study. »

HIV and other sexually transmitted infections (STIs) often co-occur. However, less evidence exists on the long-term STI dynamics among persons living with HIV in sub-Saharan Africa to inform interventions. We investigated the incidence, prevalence and factors associated with STIs , starting from acute HIV infection in a cohort of South African women .
The CAPRISA002 study enrolled women with acute HIV infection and performed STI testing and treatment 1-2 times annually from 2004-2020. We estimated STI incidence, re-infection, and prevalence trends before and after antiretroviral treatment (ART). We fitted Cox regression models to identify factors associated with STIs .
We followed up 235 women (median age = 25 years, IQR 22-29) for 7.5 years (IQR 5.7-10.8). New STI and re-infection cases per 100 person-years (PYs) were 5.1 and 9.5 for Neisseria gonorrhoeae (NG), 7.4 and 14.7 for Chlamydia trachomatis (CT), 8.0 and 26.6 for Trichomonas vaginalis (TV), 7.7 and 16.7 for Mycoplasma genitalium (MG) and 25.2 and 37.3 for any STI. STI incidence, was associated with HIV log_{10} viral load (AHR = 1.24, 95% CI 1.06-1.44), active syphilis (AHR = 16.55, 95% CI 7.49-36.55), a positive HSV-2 PCR (AHR = 1.54, 95% CI 1.01-2.35), bacterial vaginosis (AHR = 1.48, 95% CI 1.01-2.18), recent regular sexual partners at enrolment (one vs none: AHR = 2.62, 95% CI 1.41-4.87; two plus vs none: AHR = 3.68, 95% CI 1.79-7.59) and age (5-year fold: AHR = 0.80, 95% CI 0.70-0.92). The persistent STI/HIV co-infection burden among South African women highlights that early HIV diagnosis and ART initiation needs to be combined with better STI care for women and their partners to prevent HIV and STI transmission.

2 Cluster n°2

Abstract n°1: « Subtle Longitudinal Alterations in Env Sequence Potentiate Differences in Sensitivity to Broadly Neutralizing Antibodies following Acute HIV-1 Subtype C Infection . »

To study the structure of human immunodeficiency virus (HIV)-1 drug resistance (DR) in patients with newly diagnosed infection . Residents of the Republic of Guinea (N = 2168) were tested for HIV using enzyme-linked immunosorbent assay (ELISA). Individuals with a positive result were further examined for the presence of viral load in blood plasma. HIV was analyzed using Sanger sequencing. The obtained sequences were genotyped using REGA (version 3.0) and analyzed in MEGA 7. Analysis for the presence of DR mutations was performed using the Stanford University HIV DR Database. Serological markers of HIV were detected in 239 people, which represents 11.02% of the entire sample. HIV RNA was detected in 58 people. The following subtypes were seen: HIV CRF02_AG (41.9%); A1 (29.1%); A3 (12.9%); URF A1_G (12.9%); and G (3.2%). In 25% of patients, at least one significant mutation was encountered leading directly to HIV DR. The mutations encountered cause resistance to NRTI and NNRTI; one case of multiple resistance was identified. Major resistance to protease inhibitor was not seen. The detection of HIV-1 mutations associated with DR, in individuals who have never received antiretroviral therapy, is a cause for concern. It suggests that: new infections are occurring with strains that already have resistance; and the expansion of resistance is not

always directly associated with selective drug pressure. Among the likely reasons for the high prevalence of primary HIV DR in the Republic of Guinea, drug availability is probably the key. The consequence of this is the lack of adherence of patients to treatment, the formation and transmission of resistant variants of the virus in the population. These findings suggest the need to test patients for resistant virus variants before initiating treatment.

Abstract n°2: « CCR5-Δ32 gene variant frequency in the Nigerian and Zimbabwean populations living in North Cyprus. »

The cystine-cystine chemokine receptor 5 (CCR5) is the primary HIV co-receptor involved in the viral entry process into human cells. The 32 bp deletion variant within the CCR5 gene (CCR5-Δ32) plays a very important role in viral recognition and progression of AIDS.
The current study was aimed at evaluating the CCR5-Δ32 gene variation frequency in Nigerian and Zimbabwean populations residing in Northern Cyprus.
A total number of 211 subjects (103 Nigerians and 108 Zimbabweans) were analyzed . Nigerian population was further analyzed with respect to the three major ethnicities: Igbo, Hausa, and Yoruba. Polymerase Chain Reaction was used to determine the CCR5-Δ32 gene variant status.
All studied subjects from both sampling groups were homozygous for the CCR5 wild type gene (CCR5-wt), meaning neither heterozygous nor homozygous genotypes of CCR5-Δ32 gene variant were observed.
This study observed the absence of CCR5-Δ32 deletion gene in the Nigeria and Zimbabwean populations living in Northern Cyprus. These populations lack the genetic advantage over HIV infection and may also show a rapid progression towards AIDS. Additionally, these populations could impact the local gene frequency as these two populations interact more and more.

Abstract n°3: « Infection with HIV-1 subtype D among acutely infected Ugandans is associated with higher median concentration of cytokines compared to subtype A. »

The observation that HIV-1 subtype D progresses faster to disease than subtype A prompted us to examine cytokine levels early after infection within the predominant viral subtypes that circulate in Uganda and address the following research questions: (1) Do cytokine levels vary between subtypes A1 and D? (2) Do cytokine profiles correlate with disease outcomes? To address these questions, HIV-1 subtypes were determined by population sequencing of the HIV-1: HIV-1 subtype D . Our results suggest that increased production of cytokines in early HIV infection may trigger a disruption of the immune environment and contribute to pathogenic mechanisms underlying the accelerated disease progression seen in individuals infected with HIV-1 subtype D in Uganda.

Abstract n°4: « CD4 T cells are rapidly depleted from tuberculosis granulomas following acute SIV co-infection. »

HIV/Mycobacterium tuberculosis (Mtb) co-infected individuals have an increased risk of tuberculosis prior to loss of peripheral CD4 T cells, raising the possibility that HIV co-infection leads to CD4 T cell depletion in lung tissue before it is evident in blood. Here, we use rhesus

macaques to study the early effects of simian immunodeficiency virus (SIV) co-infection on pulmonary granulomas . Two weeks after SIV inoculation of Mtb-infected macaques, Mtb-specific CD4 T cells are dramatically depleted from granulomas, before CD4 T cell loss in blood, airways, and lymph nodes, or increases in bacterial loads or radiographic evidence of disease. Spatially, CD4 T cells are preferentially depleted from the granuloma core and cuff relative to B cell-rich regions. Moreover, live imaging of granuloma explants show that intralesional CD4 T cell motility is reduced after SIV co-infection. Thus, granuloma CD4 T cells may be decimated before many co-infected individuals experience the first symptoms of acute HIV infection.

Abstract n°5: « **A neutralizing antibody target in early HIV-1 infection** was recapitulated in rhesus macaques immunized with the **transmitted/founder envelope sequence** . »

Transmitted/founder (T/F) HIV-1 envelope proteins (Envs) from infected individuals that developed neutralization breadth are likely to possess inherent features desirable for vaccine immunogen design. To explore this premise, we conducted an immunization study in rhesus macaques (RM) using T/F Env sequences from two human subjects, one of whom developed potent and broad neutralizing antibodies (Z1800M) while the other developed little to no neutralizing antibody responses (R66M) during HIV-1 infection . Using a DNA/MVA/protein immunization protocol, 10 RM were immunized with each T/F Env. Within each T/F Env group, the protein boosts were administered as either monomeric gp120 or stabilized trimeric gp140 protein. All vaccination regimens elicited high titers of antigen-specific IgG, and two animals that received monomeric Z1800M Env gp120 developed autologous neutralizing activity. Using early Env escape variants isolated from subject Z1800M as guides, the serum neutralizing activity of the two immunized RM was found to be dependent on the gp120 V5 region. Interestingly, the exact same residues of V5 were also targeted by a neutralizing monoclonal antibody (nmAb) isolated from the subject Z1800M early in infection. Glycan profiling and computational modeling of the Z1800M Env gp120 immunogen provided further evidence that the V5 loop is exposed in this T/F Env and was a dominant feature that drove neutralizing antibody targeting during infection and immunization. An expanded B cell clonotype was isolated from one of the neutralization-positive RM and nmAbs corresponding to this group demonstrated V5-dependent neutralization similar to both the RM serum and the human Z1800M nmAb. The results demonstrate that neutralizing antibody responses elicited by the Z1800M T/F Env in RM converged with those in the HIV-1 infected human subject, illustrating the potential of using immunogens based on this or other T/F Envs with well-defined immunogenicity as a starting point to drive breadth .

3 Cluster n°3

Abstract n°1: « Evaluation of **multi-assay algorithms for cross-sectional HIV incidence estimation** in settings with universal antiretroviral treatment. »

Multi-assay algorithms (MAAs) are used to estimate population-level HIV incidence and identify individuals with recent infection. Many MAAs use low viral load (VL) as a biomarker for long-term infection. This could impact incidence estimates in settings with high rates of

early HIV treatment initiation. We evaluated the performance of two MAAs that do not include VL.
Samples were collected from 219 seroconverters (infected < 1 year) and 4376 non-seroconverters (infected > 1 year) in the HPTN 071 (PopART) trial; 28.8% of seroconverter samples and 73.2% of non-seroconverter samples had VLs ≥ 400 copies/mL. Samples were tested with the Limiting Antigen Avidity assay (LAg) and JHU BioRad-Avidity assays. Antibody reactivity to two HIV peptides was measured using the MSD U-PLEX assay. Two MAAs were evaluated that do not include VL: a MAA that includes the LAg-Avidity assay and BioRad-Avidity assay (LAg + BR) and a MAA that includes the LAg-Avidity assay and two peptide biomarkers (LAg + PepPair). Performance of these MAAs was compared to a widely used MAA that includes LAg and VL (LAg + VL).
The incidence estimate for LAg + VL (1.29%, 95% CI: 0.97-1.62) was close to the observed longitudinal incidence (1.34% 95% CI: 1.17-1.53). The incidence estimates for the other two MAAs were higher (LAg + BR: 2.56%, 95% CI 2.01-3.11; LAg + PepPair: 2.84%, 95% CI: 1.36-4.32). LAg + BR and LAg + PepPair also misclassified more individuals infected > 2 years as recently infected than LAg + VL (1.2% [42/3483 and 1.5% [51/3483], respectively, vs. 0.2% [6/3483]). LAg + BR classified more seroconverters as recently infected than LAg + VL or LAg + PepPair (80 vs. 58 and 50, respectively) and identified 25% of virally suppressed seroconverters as recently infected.
The LAg + VL MAA produced a cross-sectional incidence estimate that was closer to the longitudinal estimate than two MAAs that did not include VL. The LAg + BR MAA classified the greatest number of individual seroconverters as recently infected but had a higher false recent rate.

Abstract n°2: « Blood Center Testing Allows the Detection and Rapid Treatment of Acute and Recent HIV Infection . »

Blood donations in South Africa are tested for HIV RNA using individual donation NAT (ID-NAT), allowing detection and rapid antiretroviral therapy (ART) of acute HIV infections. We enrolled a cohort of acute and recent HIV-infected blood donation candidates in South Africa in 2015-2018, measured HIV antibody, ID-NAT, and recency of infection < 195 days (Sedia LAg) at enrollment and initiated early ART. A small cohort of HIV elite controllers was followed without treatment. HIV reservoir measurements included ultrasensitive plasma RNA, cell-associated HIV RNA, and total DNA. Enrollment of 18 Fiebig I-III and 45 Fiebig IV-VI HIV clade C subjects occurred a median of 18 days after index blood donation. ART was administered successfully and compliance with follow-up visits was excellent. There were only minimal differences in HIV reservoir between ART initiation in Fiebig stages I-III vs. IV-VI, but ART noncompliance increased HIV reservoir. In 11 untreated HIV elite controllers, HIV reservoir levels were similar to or higher than those seen in our early treated cohort. National blood services can identify acute HIV cohorts for subsequent HIV cure research studies. Among HIV clade C-infected donors, HIV reservoir differed little by Fiebig stage at treatment initiation, but was smaller than in chronically treated HIV and those with ART noncompliance.

Abstract n°3: « Testing strategies to detect acute and prevalent HIV infection in adult outpatients seeking healthcare for symptoms compatible with acute HIV infection in Kenya: a cost-effectiveness analysis. »

Detection of acute and prevalent HIV infection using point-of-care nucleic acid amplification testing (POC-NAAT) among outpatients with symptoms compatible with acute HIV is critical to HIV prevention, but it is not clear if it is cost-effective compared with existing HIV testing strategies.
We developed and parametrised a decision tree to compare the cost-effectiveness of (1) provider-initiated testing and counselling (PITC) using rapid tests, the standard of care; (2) scaled-up provider-initiated testing and counselling (SU-PITC) in which all patients were tested with rapid tests unless they opted out; and (3) opt-out testing and counselling using POC-NAAT, which detects both acute and prevalent infection . The model-based analysis used data from the Tambua Mapema Plus randomised controlled trial of a POC-NAAT intervention in Kenya, supplemented with results from a stochastic, agent-based network model of HIV-1 transmission and data from published literature. The analysis was conducted from the perspective of the Kenyan government using a primary outcome of cost per disability-adjusted life-year (DALY) averted over a 10-year time horizon.
After analysing the decision-analytical model, the average per patient cost of POC-NAAT was $214.9 compared with $173.6 for SU-PITC and $47.3 for PITC. The mean DALYs accumulated per patient for POC-NAAT were 0.160 compared with 0.176 for SU-PITC and 0.214 for PITC. In the incremental analysis, SU-PITC was eliminated due to extended dominance, and the incremental cost-effectiveness ratio (ICER) comparing POC-NAAT to PITC was $3098 per DALY averted. The ICER was sensitive to disability weights for HIV/AIDS and the costs of antiretroviral therapy.
POC-NAAT offered to adult outpatients in Kenya who present for care with symptoms compatible with AHI is cost-effective and should be considered for inclusion as the standard of HIV testing in this population.
Tambua Mapema ("Discover Early") Plus study (NCT03508908) conducted in Kenya (2017-2020) i.e., Post-results.

Abstract n°4: « Quantitative interpretation of Sedia LAg Assay test results after HIV diagnosis. »

Testing for 'recent HIV infection' is common in surveillance, where only population-level estimates (of incidence) are reported. Typically, 'recent infection' is a category, obtained by applying a threshold on an underlying continuous biomarker from some laboratory assay(s). Interpreting the biomarker values obtained for individual subjects, as estimates of the date of infection, has obvious potential applications in the context of studies of early infection, and has also for some years attracted significant interest as an extra component of post-test counselling and treatment initiation. The applicable analyses have typically run aground on the complexity of the full biomarker growth model, which is in principle a non-linear mixed-effects model of unknown structure, the fitting of which seems infeasible from realistically obtainable data.
It is known that to estimate Mean Duration of Recent Infection (MDRI) at a given value of the recent/non-recent -infection discrimination threshold, one may compress the full biomarker growth model into a relation capturing the probability of a recent test result as a function of time t since infection, given a value of assay threshold h which defines the recent/non-recent discrimination. We demonstrate that the derivative (gradient), with respect to h. of the prob-

ability of recent infection, seen as a function of both t and h, is identical to the formal likelihood relevant to Bayesian inference of the time since seroconversion, for a subject yielding an assay result h, at or close to the date of their first positive HIV test. This observation bypasses the need for fitting a complex detailed biomarker growth model. Using publicly available data from the CEPHIA collaboration, we calibrated this likelihood function for the Sedia Lag assay, and performed Bayesian inference on hypothetical infection data.
We demonstrate the generation of posteriors for infection date, for patients with various delays between their last negative and first positive HIV test, and a range of LAg assay results (ODn) hypothetically obtained on the date of the first positive result.
Depending on the last-negative / first-positive interval, there is a range of ODn values that yields posteriors significantly different from the uniform prior one would be left with based merely on interval censoring. Hence, a LAg ODn obtained on the date of, or soon after, diagnosis contains potentially significant information about infection dating. It seems worth analysing other assays with meaningful dynamic range, especially tests already routinely used in primary HIV diagnosis (for example chemiluminescent assays and reader/cartridge lateral flow tests which admit objective variable line intensity readings) which have a sufficient dynamic range that corresponds to a clinically meaningful range of times-since-infection that are worth distinguishing from each other.

Abstract n°5: « The Impact of Early Antiretroviral Treatment (ART) for HIV on the Sensitivity of the Latest Generation of Blood Screening and Point of Care Assays. »

Rapid initiation of antiretroviral therapy (ART) in early HIV infection is important to limit seeding of the viral reservoir. A number of studies have shown that if ART is commenced prior to seroconversion, the seroconversion may, or may not, occur. We aimed to assess whether seroreversion or no seroconversion occurs using samples collected during an early treatment study in South Africa.
We tested 10 longitudinal samples collected over three years from 70 blood donors who initiated ART after detection of acute or early HIV infection during donation screening on fourth- and fifth-generation HIV antibody and RNA assays, and three point of care (POC) rapid tests. Donors were allocated to three treatment groups: (1) very early, (2) early, and (3) later. Longitudinal samples were grouped into time bins post-treatment initiation.
On all three high-throughput HIV antibody assays, no clear pattern of declining signal intensity was observed over time after ART initiation in any of the treatment initiation groups and 100% detection was obtained. The Abbott Determine POC assay showed 100% detection at all time points with no seroreversion. However, the Abbott ABON HIV1 and OraSure OraQuick POC assays showed lower proportions of detection in all time bins in the very early treated group, ranging from 50.0% (95% CI: 26.8-73.2%) to 83.1% (95% CI: 64.2-93.0%), and moderate detection rates in the early and later-treated groups.
While our findings are generally reassuring for HIV detection when high-throughput serological screening assays are used, POC assays may have lower sensitivity for detection of HIV infection after early treatment. Findings are relevant for blood safety and other settings where POC assays are used.

4 Cluster n°4

Abstract n°1: « Maternal retention and early infant HIV diagnosis in a prospective cohort study of HIV-positive women and their children in Malawi. »

Post-partum loss to follow-up and lack of early HIV infant diagnosis (EID) can significantly affect the efficiency of programs for the prevention of mother-to-child transmission.
In a prospective observational study 167 women were enrolled at week 36 of gestation and followed with their infants up to one year after delivery . Retention was defined as the proportion of women who attended the 12 months visit and EID as an HIV PCR test performed within 2 months. Determinants for retention and EID were assessed in univariate analyses and in multivariable logistic regression models.
Women lost to follow-up (24/167 or 14.4%) had a shorter duration of antiretroviral therapy (ART) at enrolment in comparison to women retained in care ($p = 0.025$). Lack of EID (occurring in 18.9% of the cases) was directly correlated, although not significantly, with a history of child death (p = 0.071), a higher educational level ($p = 0.083$), and female infant gender ($p = 0.064$).
Longer duration of ART at enrolment significantly predicted a better post-partum retention, suggesting that specific counselling interventions should be targeted to recent ART initiators. A low proportion of infants did not receive an EID, but predictive factors were difficult to identify.

Abstract n°2: « Efficacy of Mobile phone use on adherence to Nevirapine prophylaxis and retention in care among the HIV-exposed infants in prevention of mother to child transmission of HIV: a randomized controlled trial. »

HIV is a major contributor to infant mortality. A significant gap remains between the uptake of infant and maternal antiretroviral regimens and only a minority of HIV-exposed infants receives prophylaxis and safe infant feeding. Losses to follow-up of HIV-exposed infants are associated with shortcomings of facility-based PMTCT models with weak community support of linkages. Use of mobile phones offers an opportunity for improving care and promoting retention assessed by timely attendance of scheduled appointments for the mother-baby pairs and achievement of an HIV-free generation. The objective of this study was to compare self-reported adherence to infant Nevirapine (NVP) prophylaxis and retention in care assessed by timely attendance of scheduled appointments over 10 weeks in HIV exposed infants randomized to 2-weekly mobile phone calls (intervention) versus no phone calls (control) .
In this open label randomized controlled study , one hundred and fifty HIV infected women drawn from 3 health facilities in Western Kenya and their infants were randomly assigned to receive either phone-based reminders on PMTCT messages or standard health care messages (no calls) within 24h of delivery . Women in the intervention arm continued to receive fortnightly phone calls. At 6- and 10-weeks following randomization we collected data on infant adherence to Nevirapine, mode of infant feeding, early HIV testing and retention in care in both study arms. All analyses were intention to treat.
At 6 weeks follow-up, 90.7% (n = 68) of participants receiving phone calls reported adherence to infant NVP prophylaxis, compared with 72% (n = 54) of participants in the control group (p = 0.005). Participants in the intervention arm were also significantly more likely to remain in care than participants in the control group [78.7% (n = 59) vs. 58.7% (n = 44), p = 0.009

at 6 weeks and 69.3% (n = 52) vs. 37.3% (n = 28), p < 0.001 at 10 weeks].
These results suggest that phone calls are potentially an important tool to improve adherence to infant NVP prophylaxis and retention in care for HIV-exposed infants. PACTR202007654729602. Registered 6 June 2018 - Retrospectively registered, https://pactr.samrc.ac.za/TrialDisplay.aspx?TrialID=3

Abstract n°3: « National-level effectiveness of ART to prevent early mother to child transmission of HIV in Namibia. »

Namibia introduced the prevention of mother to child HIV transmission (MTCT) program in 2002 and lifelong antiretroviral therapy (ART) for pregnant women (option B-plus) in 2013. We sought to quantify MTCT measured at 4-12 weeks post-delivery .
During Aug 2014-Feb 2015, we recruited a nationally representative sample of 1040 pairs of mother and infant aged 4-12 weeks at routine immunizations in 60 public health clinics using two stage sampling approach. Of these, 864 HIV exposed infants had DNA-PCR HIV test results available . We defined an HIV exposed infant if born to an HIV-positive mother with documented status or diagnosed at enrollment using rapid HIV tests. Dried Blood Spots samples from HIV exposed infants were tested for HIV. Interview data and laboratory results were collected on smartphones and uploaded to a central database. We measured MTCT prevalence at 4-12 weeks post-delivery and evaluated associations between infant HIV infection and maternal and infant characteristics including maternal treatment and infant prophylaxis. All statistical analyses accounted for the survey design.
Based on the 864 HIV exposed infants with test results available, nationally weighted early MTCT measured at 4-12 weeks post-delivery was 1.74% (95% confidence interval (CI): 1.00%-3.01%). Overall, 62% of mothers started ART pre-conception, 33.6% during pregnancy, 1.2% post-delivery and 3.2% never received ART. Mothers who started ART before pregnancy and during pregnancy had low MTCT prevalence, 0.78% (95% CI: 0.31%-1.96%) and 0.98% (95% CI: 0.33%-2.91%), respectively. MTCT rose to 4.13% (95% CI: 0.54%-25.68%) when the mother started ART after delivery and to 11.62% (95% CI: 4.07%-28.96%) when she never received ART. The lowest MTCT of 0.76% (95% CI: 0.36% - 1.61%) was achieved when mother received ART and ARV prophylaxis within 72hrs for infant and highest 22.32% (95%CI: 2.78% -74.25%) when neither mother nor infant received ARVs. After adjusting for mother's age, maternal ART (Prevalence Ratio (PR) = 0.10, 95% CI: 0.03-0.29) and infant ARV prophylaxis (PR = 0.32, 95% CI: 0.10-0.998) remained strong predictors of HIV transmission.
As of 2015, Namibia achieved MTCT of 1.74%, measured at 4-12 weeks post-delivery. Women already on ART pre-conception had the lowest prevalence of MTCT emphasizing the importance of early HIV diagnosis and treatment initiation before pregnancy. Studies are needed to measure MTCT and maternal HIV seroconversion during breastfeeding.

Abstract n°4: « Factors associated with non-attendance at scheduled infant follow-up visits in an observational cohort of HIV-exposed infants in South Africa, 2012-2014. »

Since 2001 the South African guidelines to improve child health and prevent vertical HIV transmission recommended frequent infant follow-up with HIV testing at 18 months postpartum . We sought to understand non-attendance at scheduled follow-up study visits up to 18 months, and for the 18-month infant HIV test amongst a nationally representative sample of HIV exposed uninfected (HEU) infants from a high HIV-prevalence African setting .
Secondary analysis of data drawn from a nationally representative observational cohort study

(conducted during October 2012 to September 2014) of HEU infants and their primary caregivers was undertaken. Participants were eligible (N = 2650) if they were 4-8 weeks old and HEU at enrolment. All enrolled infants were followed up every 3 months up to 18 months. Each follow-up visit was scheduled to coincide with each child's routine health visit, where possible. The denominator at each time point comprised HEU infants who were alive and HIV-free at the previous visit. We assessed baseline maternal and early HIV care characteristics associated with the frequency of 'Missed visits' (MV-frequency), using a negative binomial regression model adjusting for the follow-up time in the study, and associated with missed visits at 18 months (18-month MV) using a logistic regression model.
The proportion of eligible infants with MV was lowest at 3 months (32.7%) and 18 months (31.0%) and highest at 12 months (37.6%). HIV-positive mothers not on triple antiretroviral therapy (ART) by 6-weeks postpartum had a significantly increased occurrence rate of 'MV-frequency' (adjusted incidence rate ratio, 1.2 (95% confidence interval (CI), 1.1-1.4), $p < 0.0001$). Compared to those mothers with ART, these mothers also increased the risk of '18-month-MV' (adjusted odds ratio, 1.3 (CI, 1.1-1.6), $p = 0.006$). Unknown infant nevirapine-intake status increased the rate of 'MV-frequency' ($p = 0.02$). Mothers > 24 years had a significantly reduced rate of 'MV-frequency' ($p \leq 0.01$) and risk of '18-month-MV' ($p < 0.01$) compared to younger women. Shorter travel time to health facility lowered the occurrence of 'MV-frequency' ($p \leq 0.004$).
Late initiation of maternal ART and infant prophylaxis under the Option- A policy and extended travel time to clinics (measured at 6 weeks postpartum), contributed to higher postnatal MV rates. Mothers older than 24 years had lower MV rates. Targeted interventions may be needed during the current PMTCT Option B+ (lifelong ART to pregnant and lactating women at HIV diagnosis) to circumvent these risk factors and reduce missed visits during HIV-care.

Abstract n°5: « HIV prevalence and risk factors in infants born to HIV positive mothers , measured by dried blood spot real-time PCR assay in Tigray, Northern Ethiopia. »

Infants infected during pregnancy or while breastfeeding requires early HIV diagnosis at 6 weeks after birth to identify HIV infection and timely treatment. The objective of this work was to determine the prevalence and associated risk factors of HIV among HIV exposed infants in the Tigray regional state, Northern Ethiopia.
A cross-sectional study was conducted on 350 exposed infants born to HIV seropositive mothers from September 01 to December 30, 2016. Convenient consecutive sampling technique was employed to enroll HIV exposed infants from age 6 weeks to 18 months attending prevention of mother to child transmission (PMCT) clinic at Anti Retroviral Therapy (ART) site facility in Tigray, Ethiopia. Sociodemographic data and associated risk factors were collected using a structured questionnaire. Dried Blood Spot (DBS) samples were collected from each infant and transported by post to Tigray Health Research Institute to detect HIV infection using real-time Polymerase Chain Reaction (PCR) . Data were entered into EPI Info version 7, exported and analyzed using Statistical Package for Social Sciences (SPSS) version 22. p-value less than 0.05 was deemed to be statistically significant by Fisher's exact test.
Three hundred forty infants (175 males, 165 females) met the criteria for selection during the completion of the study and the overall HIV prevalence was found to be 2.1% (n = 7). The majority of infants were from urban areas (n = 246, 72.4%). 45.5% (5/11, $p = 0.001$) infants were without ARV prophylaxis, 60% (3/5, $p = 0.001$) infants born to mothers who did not take maternal PMTCT intervention, 43% (3/7, $p = 0.001$) infants born to mothers who were

not enrolled to ART care, and 6.1% (4/66, p = 0.029) infants of unmarried mothers showed statistically significant difference.
The overall prevalence of HIV among exposed infants was high but lower than the Millennium Development Goal targets. In order to eliminate the mother to child HIV transmission (MTCT) ARV prophylaxis in infants must be strengthened, and enrollment of HIV positive pregnant women to PMTCT and ART care and treatment is needed.

5 Cluster n°5

Abstract n°1: « Tuberculosis prevalence, incidence and prevention in a south african cohort of children living with HIV . »

We describe tuberculosis (TB) in children living with HIV (CLHIV) eligible for HIV treatment in South Africa to highlight opportunities to prevent TB.
We analyzed additional data from our original study of CLHIV who were 0˜12 years old and due to start HIV treatment in five health facilities in Eastern Cape Province from 2012 to 2015 and assessed characteristics associated with existing and new TB.
Of 397 enrolled children, 114 (28.7%) had existing TB. Children with a higher measure of household income had higher odds of existing TB. CD4+ cell count < 350 cells/μl and malnutrition were also associated with existing TB. There were 5.2 new cases of TB for every 100 child-years. New TB was 4.7 times more likely for children with delayed HIV treatment start, 1.8 times more likely for children with malnutrition and 2.3 times more likely for children who did not get cotrimoxazole. Among 362 children with data, 8.6% received treatment to prevent TB.
A mong these CLHIV, existing and new TB were common. Early HIV treatment, cotrimoxazole and addressing malnutrition may prevent TB in these children.

Abstract n°2: « The magnitude of opportunistic infections and associated factors in HIV-infected adults on antiretroviral therapy in southern zone Tigray, Ethiopia: a cross-sectional study. »

Greater than twenty known opportunistic infections have been associated with HIV infection and usually patients experience co-infections during the stage of illness, HIV-related opportunistic infections are associated with significant morbidity and mortality.
A hospital-based retrospective study was conducted in HIV-infected adult patients on antiretroviral (ART) from April to June 2017; secondary data were collected from review of clinical records. A total of 400 study participants selected through a systematic sampling technique and a pre-tested checklist was used to collect data from records of study subjects. The data was entered and analyzed using SPSS version 22.
A total of 400 patients included in the study, in which more than half (51.0%) were females. The mean age of patients was 34 (standard deviation [SD] ±1.96) years. The overall of opportunistic infections (OIs) among HIV/AIDS patients on ART was 55.3%. The highest rates of OIs observed were oral candidacies 11.0%, followed by herpes zoster (10.8%) and tuberculosis (TB) (9.5%). The odds of having college and above educational levels were less likely to developed OIs compared to illiterate (AOR = 0.007; 95% CI = 0.053, 0.634). The odds of having OIs in WHO clinical stage I were less likely to have OIs compared to WHO clinical stage III and V (AOR = 0.001; 95% CI = 0.000, 0.015 and AOR = 0.00; 95%CI = 0.00 respectively).

There was a high prevalence of OIs observed in this study. Illiterate educational level and advanced WHO clinical stages were found to be predictors of OIs. Interventions were aimed at promoting early HIV testing and ART enrollment of HIV-infected.

Abstract n°3: « Intact HIV Proviruses Persist in Children Seven to Nine Years after Initiation of Antiretroviral Therapy in the First Year of Life. »

In adults starting antiretroviral therapy (ART) during acute infection, 2% of proviruses that persist on ART are genetically intact by sequence analysis. In contrast, a recent report in children treated early failed to detect sequence-intact proviruses. In another cohort of children treated early, we sought to detect and characterize proviral sequences after 6 to 9 years on suppressive ART . Peripheral blood mononuclear cells (PBMC) from perinatally infected children from the Children with HIV Early antiRetroviral (CHER) study were analyzed. Nearly full-length proviral amplification and sequencing (NFL-PAS) were performed at one time point after 6 to 9 years on ART. Amplicons with large internal deletions were excluded (< 9 kb). All amplicons of ≥ 9 kb were sequenced and analyzed through a bioinformatic pipeline to detect indels, frameshifts, or hypermutations that would render them defective. In eight children who started ART at a median age of 5.4 months (range, 2.0 to 11.1 months), 733 single NFL-PAS amplicons were generated. Of these, 534 (72.9%) had large internal deletions, 174 (23.7%) had hypermutations, 15 (1.4%) had small internal deletions, 3 (1.0%) had deletions in the packaging signal/major splice donor site, and 7 (1.0%) were sequence intact. These 7 intact sequences were from three children who initiated ART after 2.3 months of age, one of whom had two identical intact sequences, suggestive of a cell clone harboring a replication-competent provirus. No intact proviruses were detected in four children who initiated ART before 2.3 months of age. Rare, intact proviruses can be detected in children who initiate ART after 2.3 months of age and are probably, as in adults, maintained by clonal expansion of cells infected before ART initiation.

Abstract n°4: « Neurological disorders in HIV in Africa: a review. »

Neurological disorders in HIV infection are a common cause of morbidity and mortality. The aim of this paper is to provide a narrative overview of up to date information concerning neurological disorders affecting HIV infected persons in Africa.
Seminal research concerning neurological disorders among HIV-infected adults in sub-Saharan Africa from prior to 2000 was combined with an in-depth search of PubMed to identify literature published from 2000 to 2017. The following Mesh terms were used. "Nervous System Diseases" "HIV Infections" and "Africa South of the Sahara" and "Seizures" or "Spinal Cord Diseases" or "Peripheral Nervous System Diseases" or "AIDS Dementia Complex" or "Opportunistic Infections" or "Immune Reconstitution Inflammatory Syndrome" or "Stroke". Only those articles written in English were used. A total of 352 articles were identified, selected and reviewed and 180 were included in the study. These included case series, observational studies, interventional studies, guidelines and reviews with metanalyses. The author also included 15 publications on the subject covering the earlier phase of the HIV epidemic in Africa from 1987 to 1999 making a total of 195 references in the study. This was combined with extensive personal experience diagnosing and treating these neurological disorders.
Neurological disorders were common, typically occurring in WHO stages III/IV. These were

in three main categories: those arising from opportunistic processes mostly infections, direct HIV infection and autoimmunity. The most common were those arising from direct HIV infection occurring in > 50%. These included HIV-associated neurocognitive dysfunction (HAND), neuropathy and myelopathy. Opportunistic infections occurred in >20% and frequently had a 6-9-month mortality rate of 60-70%. The main causes were cryptococcus, tuberculosis, toxoplasmosis and acute bacterial meningitis. Concurrent systemic tuberculosis occurred in almost 50%.
Neurological disorders are common in HIV in Africa and the main CNS opportunistic infections result in high mortality rates. Strategies aimed at reducing their high burden, morbidity and mortality include early HIV diagnosis and anti-retroviral therapy (ART), screening and chemoprophylaxis of main opportunistic infections, improved clinical diagnosis and management and programme strengthening.

Abstract n°5: « Causes of hospitalization and predictors of HIV-associated mortality at the main referral hospital in Sierra Leone: a prospective study. »

HIV infection is a growing public health problem in Sierra Leone and the wider West Africa region. The countrywide HIV prevalence was estimated at 1.7% (67,000 people), with less than 30% receiving life-saving ART in 2016. Thus, HIV-infected patients tend to present to health facilities late, with high mortality risk.
We conducted a prospective study of HIV inpatients aged ≥ 15 years at Connaught Hospital in Freetown-the main referral hospital in Sierra Leone-from July through September 2017, to assess associated factors and predictors of HIV-related mortality .
One hundred seventy-three HIV inpatients were included, accounting for 14.2% (173/1221) of all hospital admissions during the study period. The majority were female (59.5%, 70/173), median age was 34 years, with 51.4% (89/173) of them diagnosed with HIV infection for the first time during the current hospitalization. The most common admitting diagnoses were anemia (48%, 84/173), tuberculosis (24.3%, 42/173), pneumonia (17.3%, 30/173) and diarrheal illness (15.0%, 26/173). CD4 count was obtained in 64.7% (112/173) of patients, with median value of 87 cells/μL (IQR 25-266), and was further staged as severe immunosuppression: CD4 < 100 cells/μL (50%, 56/112); AIDS: CD4 < 200 cells/μL (69.6%, 78/112); and late-stage HIV disease: CD4 < 350 cells/μL (83%, 93/112). Fifty-two patients (30.1%, 52/173) died during hospitalization, 23% (12/52) of them within the first week. The leading causes of death were anemia (23.1%, 12/52), pneumonia (19.2%, 10/52), diarrheal illness (15.4%, 8/52) and tuberculosis (13.6%, 7/52). Neurological symptoms, i.e., loss of consciousness (p = 0.04) and focal limb weakness (p = 0.04); alcohol use (p = 0.01); jaundice (p = 0.02); cerebral toxoplasmosis (p = 0.01); and tuberculosis (p = 0.04) were significantly associated with mortality; however, only jaundice (AOR 0.11, 95% CI [0.02-0.65]; p = 0.01) emerged as an independent predictor of mortality.
HIV-infected patients account for a substantial proportion of admissions at Connaught Hospital, with a high morbidity and in-hospital mortality burden. These findings necessitate the implementation of specific measures to enhance early HIV diagnosis and expand treatment access to all HIV-infected patients in Sierra Leone.