3rd Asia Pacific AIDS & Co-infections Conference

Translating Science into Clinical Practice in Asia Pacific

Abstracts
Oral Presentations

1

Derivation of population mixing patterns from virus sequence data and their impacts on the modelling of HIV epidemics in MSM

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Background: Population mixing forms one key concept for modelling epidemics. While random mixing is commonly assumed for model simplicity, overestimation could occur for sexually transmitted infections. Conventionally the HIV population is subcategorised by behavioural characteristics. Their delineation by available HIV sequence data could be an alternative approach.

Methods: We developed deterministic compartmental model with a number of submodels to simulate the epidemic growth of HIV among MSM in Hong Kong. The model is structured by the natural history of HIV infection and cascade of HIV care including the following status: undiagnosed, diagnosed, on treatment and loss to follow-up. Phylogenetic analyses (neighbour-joining methods) on HIV genotype resistance testing sequence of MSM were performed to generate phylogenetic trees for population delineation. We calculated the diagnosis rate, treatment initiation rate and loss to follow-up rate of each subgroup based on the corresponding clinical data for model parameterization. We then randomly distributed non-locally acquired infections to each subgroup. To compare between random mixing and sub-population delineation, a separate model with random mixing assumption was developed.

Results: A total of 143 clusters were identified from 1135 sequences with bootstrap value of ≥90. We summarized them as 19 MSM subgroups, ranging from non-clusters (1 node), small, intermediate and large clusters with 2-3 nodes, 4-10 nodes to >10 nodes respectively. Susceptible and infected population were further categorised by high/low risk groups. Annual number of new HIV diagnoses is estimated to increase from 9 in 1986 to 240 in 2010, and to 309 in 2014. Model estimation of annual new diagnoses was close to surveillance data in 1981-2014, but with moderate overestimations (2 to 3-folds higher) in 1996-2004. In the random mixing model, overestimation was 25 to 57-folds higher than the surveillance data

Conclusions: Despite the reporting of the continuous growth of HIV epidemics among MSM in Hong Kong and in many other places, the moderate non-exponential rise of the epidemic curve might be explained by the segregation of MSM population.

2

Transmitted drug resistance and impact on long-term clinical outcomes in the VMVN clinical trial in Hanoi, Vietnam

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Background: Transmitted drug resistance (TDR) has been shown to impair treatment outcomes. Baseline drug resistance testing is recommended to guide therapy in resource-rich countries. However, drug resistance screening is expensive, is not widely available, and its impact on treatment outcomes in resource-limited countries remains unclear.

Methods: We investigated TDR mutations and their clinical impact in antiretroviral-naïve patients initiating first-line ART in the VMVN study, a randomized controlled trial of routine virological monitoring versus targeted virological monitoring at Bach Mai Hospital in Vietnam between April 2011 and May 2017. TDR mutations were identified by Sanger sequencing of the partial pol gene and were defined based on the 2009 WHO surveillance drug resistance mutation list. The association of TDR and treatment failure, defined as virological failure (confirmed HIV RNA >200 copies/mL) and/or death over 36 months, was investigated using Logistic regression analyses.

Results: Among 650 patients enrolled in the trial, 603 patients were ART-naïve; successful sequencing was obtained for 564 patients. The median age was 33; 65% were male; the median CD4 count was 119 cells/mm3, interquartile range (IQR): 29-273. CRF01_AE was the predominant subtype, accounting for 530 (94.0%) patients. The other subtypes included: subtype A (4.1%), CRF08_BC (0.9%), CRF07_BC (0.7%), CRF03_AB (0.2%) and CRF01_AE/B (0.2%). TDR mutations were identified in 32 (5.6%) patients: 15 (2.7%) patients harbor mutations conferring resistance to NRTIs, 10 (1.8%) to NNRTIs, 11 (2.0%) to PIs, 4 (0.7%) to both NRTIs and NNRTIs. Complete outcome data were available for 500 patients. 50 (10%) patients died after a median of 4.9 (IQR: 2.2-14.8) months. In both univariate and multivariate analyses (with routine versus targeted virological monitoring as a covariable), the risks of virological failure or death at 36 months were higher in patients who had TDR; however, the differences in risk were not statistically significant, univariate odds ratio (OR)=1.30, 95% confidence interval (CI): 0.37-3.52, P=0.664 and adjusted OR=1.30, 95% CI: 0.37-3.54, P=0.641, respectively. We performed a sensitivity analysis examining the risk of treatment failure only in patients who harbored NRTI and NNRTI mutations conferring resistance to the standard first-line efavirenz-based combination therapy in Vietnam, and we found that the differences in risk were not statistically significant, OR=1.07, 95% CI: 0.17-3.94, P=0.929 and adjusted OR=0.108, 95% CI: 0.17-3.99, P=0.917.

Conclusions: We demonstrated in this clinical trial conducted at a large HIV referral center in Hanoi that TDR remains stable at <10% despite over 10 years of ART scale up in Vietnam. TDR does not increase the risk of virological failure or death over 36 months of follow up. Our data do not support baseline drug resistance testing. The increase in number and diversity of non-CRF01_AE subtypes raise a need for surveillance of circulating HIV strains to understand recent transmission networks in Vietnam and in the wider region.

3

Treatment outcome and drug Resistance mutations among patients on LPVr-containing second-line antiretroviral therapy in Vietnam

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Background: Achieving viral suppression is one of the key elements of the global strategy toward the end of HIV epidemic. However, the levels of viral suppression have yet to be described in many resource-limited settings, especially for the second-line antiretroviral therapy (ART).

Methods: Analyses were conducted with a longitudinal dataset from the Hanoi HIV Cohort Study, established in October 2007 in National Hospital of Tropical Diseases and Bach Mai Hospital in Hanoi, Vietnam. Clinical data was obtained retrospectively and prospectively at enrollment and every 6 months. Data of those on a lopinavir/ritonavir (LPVr)-containing second-line ART for more than 6 years were used for the analysis. We assessed the time to virologic failure (VF; defined as a viral load of ≥1000 copies/mL) and factors related to time to VF by using the Cox proportional hazards model. Drug resistance mutations were retrospectively identified by direct-sequencing with samples obtained when viral load was ≥1000 copies/mL.

Results: In 2156 cohort participants until Dec 2014, 172 experienced VF for the first-line ART and were switched to the second-line ART. Of those, 155 met the criteria and were assigned to the analysis. During a median observation of 39 months, 26 were identified as having VF. Viral suppression rate at 12 months was 91.5% and the survival without VF had maintained above 90% until 16 months. At the time of first-line ART failure, 95 were performed drug resistance testing and 87 (92%) were found to carry any of the drug resistance mutations on the 2015 IAS-USA mutation list, including M184V in 87 (92%) and thymidine analog-associated mutations in 67 (73%) for resistance to nucleoside reverse transcriptase inhibitors and K103N in 31 (33%) and Y181C/I/V in 51 (54%) for resistance to non-nucleoside reverse transcriptase inhibitors. No protease inhibitor (PI)-associated mutation was detected at switch. In univariate analysis, viral load before switch ≥100,000 copies/mL was associated with earlier VF (hazard ratio [HR] 4.83, 95% Confidence Interval [CI] 1.63-14.4, p=0.005, vs.<100,000 copies/ml) and those whose previous ART contained nevirapine (NVP) were less likely to have VF (HR 0.34, 95%CI 0.13-0.91, p=0.03). After controlling age, gender, and first-line regimens with NVP and any protease inhibitors in the multivariate model, only viral load ≥100,000 copies/mL was predictive for VF (HR 4.25, 95%CI 1.49-11.4, p=0.006). Among 26 with second-line VF, 11 were performed drug resistance testing after failing second-line ART and 2 (18%) carried multiple PI-associated mutations at the time of second-line failure, including primary mutations for lopinavir resistance I47V and L76V.

Conclusion: High rate of viral suppression was noted in the cohort of patients on a LPVr-based second-line ART despite high levels of drug resistance after failing first-line ART in Hanoi.

4

Chemsex: prevalence, characteristics and associated risk profiles of men who have sex with men in South Australia: a cross-sectional cohort study

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Background: Chemsex (Intercourse under the influence of psychoactive substances that heighten sexual arousal and disinhibition) is common among men who have sex with men (MSM). We report the prevalence, associated risk profiles and characteristics of MSM who engage in chemsex in South Australia.

Materials and Methods: Over 6 months (February to August 2017), MSM attending SA's only public sexual health clinic, a high HIV caseload General Practice and a drop in/appointment based non-government organization were invited to complete an anonymous survey about chemsex. Participants provided socio-demographic information and reported on sexual practices, drug use, HIV/STI testing and status. We assessed the proportion of respondents reporting chemsex and the associated factors. For statistical associations of interest, we present adjusted prevalence ratios (APR) and 95% Confidence Intervals (95%CI).

Results: Among 410 GBM participants, 31% were under 26 and 32% were 26-35 years old; 76% were Australian-born; 2.0% were of Aboriginal or Torres Strait Islanders (ATSI); 66% were employed fulltime or part time. In the preceding six months, 82% reported having multiple (>/=2) partners, 67% had condomless anal intercourse with other males; 42% engaged in group sex. By self-report: 12% were HIV-positive and 78% HIV-negative. Receiving PrEP: 6.4%. Chemsex was reported by 120 (29%) of participants. Substances used included crystal methamphetamine (14%) and gamma hydroxybutrate or butyrolactone (GHB/GBL, 5%), among other drugs, mainly for fun (18.5%), 'party and play' (10.2%), to have sex for longer (9.3%) and become less inhibited (9,5%). In the multivariate regression analysis, chemsex was associated with being Australian-born (APR=1.45; 95%CI: 1.02-2.06), engaging in group sex once/a few times (APR=1.86; 95%CI: 1.35-2.57) or at least monthly (APR=2.30; 95%CI: 1.23-4.29) in the last six months, hooking-up for sex online or via mobile applications (APR=1.70; 95%CI: 1.19-2.43), being HIV positive vs. negative (APR=2.46; 95%CI: 1.62-3.73) or taking PrEP (APR=1.85; 95%CI: 1.06-3.23).

Conclusions: In this clinical sample of MSM in South Australia, chemsex, being born in Australia and being HIV positive were found to be a key predictors of condomless anal sex. Understanding prevalence and risk profiles may help inform the development of intervention strategies to address decreasing STI and HIV transmission in South Australia

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Human Papillomavirus Prevalence and Behavioral Risk Factors among HIV-Infected Men in central Taiwan

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Objective: Human papillomavirus (HPV) infection is associated with cancer and is preventable by vaccination. We examined the prevalence of HPV infection in HIV-infected and HIV-uninfected men and then what behaviors are risk factors in order to provide information regarding vaccination strategy.

Methods: We conducted a prospective cohort study to collect clinical data from men who have sex with men (MSM), aged 20 years or older, at medical center in Taichung City, Taiwan during the period 2013–2016. We initially used a questionnaire in a face-to-face interview, then collected oral, anal, and genital specimens from HIV- infected and uninfected individuals. The data included demographic data, sexual behavior, sexual partners, drug use, circumcised status, and history of sexually transmitted infections (STI), diagnosis of syphilis and anogenital warts, and previous HIV test results. We applied the multivariate logistic regression models to predict which variables are associated with high risk HPV (HR-HPV) types of HPV infection.

Results: A total of 279 individuals were enrolled, consisting of 166 (59.5%) HIV-uninfected and 113 (40.5%) HIV-infected men. The median age of participants was 26.0 years, with 198 participants (71%) younger than 30 years. Most participants were never married (96.8%) and were employed (73.5%). The significant risk factors for HPV infection included receptive anal sex (91.3% vs. 75.6%; p=0.001), substance use (22.6% vs. 11%; p=0.009), and histories of STI (75.7% vs. 38.4 %; p<=0.001) in the 6 months prior to joining the study. Our findings also showed that HPV-positive participants had significantly higher rates than HPV-negative ones of anogenital or oral warts (39.1% vs. 6.72%; p<=0.001), syphilis (32.2% vs. 11.6%; p<=0.001) and HIV infection (69.6% vs. 20.1%; p<0.001). We detected 489 HPV DNA types through 379 usable specimens from 279 participants. 43.6% (n=213) of the HPV DNA were HR-HPV types and 5.7% (n=28) were HPV type 16. 56.4% (n=276) were low risk HPV types and 10.4% (n=51) were HPV type 6. The multivariate logistic regression analysis showed an association of HR-HPV infection with subjects who were employed (OR, 3.85; 95% CI, 1.54-9.66; P<0.05) and were HIV-infected (OR, 2.57; 95% CI, 1.07-6.14; P<0.05).

Conclusion: As a preventative measure, we recommend routine HPV vaccination with 4vHPV or 9vHPV vaccines (preferably the latter) for the MSM community, including HIV-infected individuals. It is probable that it would be urgent need to extend vaccination to the male population.

6

Malignancies in adults living with HIV in Asia

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Background: Hematological malignancies, predominantly lymphomas, have remained the most common cancer-related causes of death in people living with HIV (PLHIV). In Asia, little is known about the prevalence of hematological and non-hematological malignancies in PLHIV. This study assessed the occurrence, risk factors for, and outcomes of malignancies in the TREAT Asia HIV Observational Database (TAHOD) of IeDEA Asia-Pacific.

Methods: Cohort patients who had initiated antiretroviral therapy (ART) were eligible for the analysis. The proportion diagnosed with a malignancy was evaluated pre- and post-cohort entry. Factors associated with development of hematological and non-hematological malignancy after cohort entry were analyzed using competing risk regression and survival time using Kaplan-Meier.

Results: A total of 7720 patients (70% male) from 20 sites across 12 Asian countries were included. There were 69 patients (80% male) with a hematological malignancy (0.9%) and 126 (74% male) with a non-hematological malignancy diagnosis (1.6%). Of the hematological malignancies, non-Hodgkin lymphoma (NHL) was the most common (n=57, 83%): immunoblastic lymphoma (n=30, 43%), Burkitt lymphoma (n=12, 17%), diffuse large B-cell lymphoma (n=5, 7%), and unspecified (n=10, 14%). Other hematological malignancies were central nervous system lymphoma (n=11, 16%), and myelodysplastic syndrome (n=1, 1%). The most common non-hematological malignancies were Kaposi's sarcoma (n=51, 40%) and cervical cancer (n=19, 15%). After cohort entry, the incidence of hematological and non-hematological malignancy were 0.08 per 100 person-years (/100PYS) and 0.17/100PYS, respectively. Risk factors for hematological malignancy after cohort entry, adjusted for ART status, included age >50 years vs. age <30 years at cohort entry (sub-hazard ratio [SHR]=6.00, 95%CI 1.74-20.77, p=0.005), and being from a high-income country vs. a lower-middle-income country (SHR=4.00, 95%CI 1.47-10.90, p=0.007). Risk was reduced with higher CD4 count vs. CD4 ≤200 cells/μL (SHR for CD4 351-500 cells/μL 0.16, 95%CI 0.05-0.59, p=0.006; SHR for CD4 >500 cells/μL 0.14, 95%CI 0.04-0.52, p=0.003). Similar risk factors were seen for non-hematological malignancy, with country income and prior AIDS diagnosis showing a significant association. Patients diagnosed with a hematological malignancy had poorer survival time (median=1.4 years) compared to those with a non-hematological malignancy (p log-rank=0.008).

Conclusions: Hematological malignancies, predominantly NHL, were associated with poorer survival in our cohort. While associations with age and CD4 count are anticipated, the association with country-income level could indicate that these cancers are under-diagnosed in lower-income settings.

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Drivers for mental health issues among young and old HIV-infected individuals and opportunities for intervention

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Background: Mental health disorders among HIV-infected individuals is a growing concern, especially in the Asia-Pacific region where effective integrated healthcare models are lacking. In this study, we explored the prevalence of depression, anxiety and stress in treated HIV-infected individuals compared to matched controls and explored risk factors and health outcomes associated with this condition. Participants' media preference for access to health information was also assessed to explore the most appropriate platform for future interventions.

Methods: This was a cross-sectional study which recruited 329 HIV-infected individuals attending the University Malaya Medical Centre, of which 198 were matched for age, gender and ethnicity with uninfected community controls. All participants were ≥25 years, had no acute illness and virologically suppressed (HIV RNA <50copies/ml) for at least 12 months prior to recruitment. Depression, anxiety and stress were measured using DASS-21 and responses normalised using Z-statistics to a single score with higher values denoting a more severe negative emotional state. Multivariate regression analysis was performed to explore risk factors associated with normalised DASS scores in young (<45 years) and old (≥45 years) HIV-infected individuals as well as their impact on health outcomes. Internet use for daily activities and preference for health-related information delivery was also surveyed using standardised questionnaires.

Results: The median (interquartile range, IQR) age in the cohort was 44 (38-50) years and 83% were male while median CD4 T-cell count was 561 (393-739) cells/µl. Depression and anxiety were significantly higher in the HIV-infected vs matched controls; 42 vs 20%, 68% vs 50%, respectively (p<0.01 for both) and marginally so for stress 85% vs 77% (p=0.05). Among the HIV-infected, younger participants (n=186) had significantly higher normalised DASS 21 scores compared to older individuals (n=143); 13.6(7.3-20.9) vs 8.4 (3.7-17.3), p<0.01. Being female (ß=6.65, 95%CI=2.95-10.71, p=0.001), having a prior drinking history (vs never) (ß=6.59, 95%CI=1.75-11.4, p=0.025) and current efavirenz use (ß=4.84, 95%CI=1.06-8.62, p=0.012) were all positively associated with higher normalised DASS scores among the younger participants. Risk factors in older individuals were different however, with higher scores associated with low physical activity (ß=5.49, 95%CI=2.44-8.53, p=0.001) and poorer cognitive function (ß=1.01, 95%CI=0.14-1.89, p=0.023). Social isolation, partnership status and number of financial dependents were all not associated with DASS scores. In adjusted analysis, higher DASS scores were associated with poorer quality of life, poorer self-rated perceived health and higher healthcare utilisation in both the young and old (p<0.01 for all). Most respondents recorded wifi access (67%) and internet use for their daily activities (73%). Younger individuals overwhelmingly preferred the internet as their main source for health information (66%) while older individuals were more varied in their preferences; internet (34%), newspapers (31%) and television (33%).

Conclusions: We found a high prevalence of depression, anxiety and stress especially among young HIV-infected individuals. Drivers for these negative emotional states varied in the young and old, with efavirenz use and low physical activity identified as potential points of intervention. Our data also suggests that mobile technology platforms are suitable means for promoting mental health awareness and intervention in our setting.

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Asymptomatic talaromyces marneffei infection is associated with HIV mortality

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Background: Talaromyces marneffei (Tm) infection is an important cause of HIV-associated morbidity and mortality in Southeast Asia and southern China. Culture diagnosis is protracted, and a delay in diagnosis is associated with high mortality. In large patient cohorts, we have demonstrated that the novel Tm-specific mannoprotein (Mp)1p antigen detection assay is 90% sensitive (compared to blood culture at 70%) and 98% specific in diagnosing culture-confirmed infection from any sterile site. We hypothesize that infection can be detected during the pre-clinical stage and is associated with poor clinical outcomes.

Methods: We performed Tm antigen (TmAg) testing in archived plasma samples from HIV-infected patients starting antiretroviral therapy with a CD4 count ≤100 cells/mm3 from 22 outpatient clinics across Vietnam. These patients enrolled in the Vietnam Cryptococcal Retention in Care (CRICS study) between August 2015 and April 2017. We excluded patients with a diagnosis of talaromycosis at enrollment. Multivariable logistic regression analysis accounting for age (+10 years), baseline CD4 counts (< or ≥50 cells/mm3), and cryptococcal antigen positivity (prevalence = 2.9%) was performed to investigate whether TmAg positivity was associated with six month mortality.

Results: Baseline plasma samples were available for 1081 of 1174 enrolled patients. 802 (74%) patients were male. The median age was 35 (interquartile range, IQR: 30-41) years. The median CD4 count was 25 (IQR: 11-50) cells/mm3. At the optical density (OD) cut-off value of 0.5, TmAg was positive in 45/1081 patients, 4.2% (95% confidence interval, CI: 3.1%-5.6%), with significantly higher TmAg prevalence in northern Vietnam compared to southern Vietnam, 33/496 (6.7%) and 12/585 (2.1%) respectively, P-value <0.001 (Chi Square test). Follow-up data six months after enrollment were available for 760 patients. TmAg positivity was independently associated with death, Odds Ratio (OR) = 3.3, 95% CI: 1.4-7.6, P=0.01. The sensitivity analyses treating loss-to-follow-up (N=48) as deaths gave consistent results.

Conclusions: Asymptomatic T. marneffei infection was detected in 4.2% of patients with a CD4 count <100 cells/mm3 in Vietnam and was independently associated with six month mortality. The TmAg-detection assay should be evaluated as a screening tool to identify patients for pre-emptive antifungal therapy which has the potential to reduce mortality in patients with advanced HIV infection in Asia.

9

Outcome of HCV treatment by direct acting antiretroviral (DAAs) among HCV/HIV co-infections in Vietnam

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Background: HCV prevalence in the general population in Vietnam ranges between 0.4% and 1.7% in the north and between 1.0% and 4.3% in the south. The HCV prevalence is particularly high among HIV+ populations and injecting drug users with range between 30% and 97.2%. It is estimated that there are around one million people living with HCV in Vietnam. Treatment by direct acting antiviral (DAAs) is limited at the national level and few provincial facilities. High cost of DAAs drug and treatment by DAAs is not yet covered by health insurance leads to low treatment accessibility, especially among high risk and vulnerable groups including HCV/HIV co-infection. Vietnam launched a pilot program to increase access to DAAs treatment in 5 facilities (1 at national level, 3 at provincial level and 1 at district level) in 3 provinces. Treatment prioritization is given to patients with HIV/HCV co-infection patients, mono-infected patients with mild fibrosis or with metabolic disorders. The aim of this data analysis provides a preliminary result of treatment outcome among HCV/HIV co-infections patients who initiated DAAs in 2017 in this project.

Methods: Demographic and clinical data from diagnosis, treatment initiation to treatment completion was calculated from initial cohort of HCV/HIV co-infection patients who initiated DAAs in 2017. SVR12 was calculated as treatment outcome regardless genotype, fibrosis level or administrative level. Data analysis was done using SPSS.

Results: By end of December 2017, there are 775 patients initiated HCV treatment by DAAs in 5 facilities, among which 112 HCV/HIV co-infection completed treatment and performed SVR12 test to evaluate treatment outcome. The median age was 40 years old, 93.7% were male, and 59.8% had ever injected drug. Only 4.5% of patients had exposed to HCV treatment and 9.8% presented to clinic with signs and symptoms of HCV infection. 6.5% of HCV/HIV patients has HBsAg positive. 67% of patients had genotype 1 infection and 29% of patients had genotype 6 infection. 17.8% had advanced fibrosis and 2.7 % had decompensated cirrhosis. 88.3% of patients were treated with SOF+DCV and 11.7% with SOF+DCV+RBV. 57% of patients initiated treatment at national level and 24% at district level. Almost 100% of patients received 12 weeks of treatment except 3 cases with fibrosis received 24 weeks of treatment. Only 4% of patients reported side affects during treatment. 99% of patients completed treatment with 1 death due to the end-stage liver disease. 99% of patients achieved SVR 12 with only one case of treatment failure. There is no significant different in cure rate among patients who were initiated treatment at district level or at national level facility (p<0.05).

Conclusion: The preliminary treatment outcome among HCV/HIV co-infection patients in the pilot project in Vietnam showed a positive result. The results demonstrate that very high cure rate can be achieved using SOF+DCV±RBV regimen among HCV/HIV co-infection, people who inject drugs and patients with genotype 6 infection. In addition, decentralization of treatment to lower level is very much needed in Vietnam to increase accessibility to HCV treatment.

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Feasibility and outcome of rapid initiation of antiretroviral treatment among newly-diagnosed HIV-positive patients at a tertiary center in Taiwan

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Background: Taiwan has adopted the "treat-all" antiretroviral therapy (ART) policy from 2015 to catch up the global trend. WHO guidelines of combination ART also recommends a rapid initiation of ART, defined as ART initiation within 7 days after diagnosis, to reduced morbidity and mortality among HIV-positive patients in 2017. However, the feasibility and clinical outcome of rapid initiation of ART remains unknown in Taiwan.

Materials & Methods: Medical records of 647 newly diagnosed HIV-positive patients who were diagnosed or referred to the National Taiwan University Hospital (NTUH) between March 2014 and December 2017 were reviewed and information on clinical characteristics were collected. Patients who were aged less than 18 years (n=9) or enrolled in clinical trials (n=48) were excluded.

Results: During the 4-year study period, 590 HIV-positive patients were included, with a mean age of 32.9 years and 98.6% being male. Acute HIV infection accounted for 12.0% (71/590) of all patients. The median CD4 count was 294 cells/µl (IQR, 128-441) and 34.5% (192/556) of patients had advanced HIV disease, defined as CD4 counts less than 200 cells/µl. The median duration from diagnosis to ART initiation decreased from 18 days (IQR, 7-216) in 2014 to 7 days (IQR, 6-11) in 2017. The achievement of rapid ART initiation increased from 31.6% in 2014 to 64.1% in 2017. The median duration from HIV diagnosis to viral suppression (plasma HIV RNA load <200 copies/ml) were 112 days (IQR, 42-138) among the patients who received rapid ART initiation and 173 days (IQR, 111-513) among the patients who initiated ART after at least 7 days after HIV diagnosis, respectively. Before HIV viral suppression, 30 incident symptomatic sexually transmitted infections and 42 incident syphilis infections were identified. The rate of retention in care was higher (91.2%) in the patients who received rapid ART initiation than that in patients who received standard of care (91.2% vs 82.4%, p=0.009). Moreover, people who initiated cART within 7 days of diagnosis had a higher increase of CD4/CD8 ratio (p=0.002).

Conclusions: An increasing trend of HIV-infected patients initiated ART within 7 days of HIV diagnosis in Taiwan between 2014 and 2017; and rapid ART initiation shortened the interval from diagnosis to viral suppression. The finding of an high rate of sexually transmitted infections before viral suppression suggested the urgency of rapid ART initiation among this sexually active population. Meanwhile, the high rate of retention in care after rapid ART initiation suggests the feasibility of rapid ART initiation.

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Impact of initiation of combination antiretroviral therapy according to the WHO recommendations on the survival of HIV-positive patients in Taiwan

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Background: The TEMPRANO and START trials have demonstrated that early initiation of combination antiretroviral therapy (cART) reduces the risks of developing serious infections and mortality among HIV-positive patients. We aimed to assess the outcomes of initiating cART among HIV-positive patients in Taiwan according to the CD4 cut-off values by the WHO recommendations.

Materials & Methods: Between 2007 and 2015, we included 3 groups of patients who received HIV diagnosis at the National Taiwan University Hospital according to the timing of cART initiation recommended by WHO. Group 1 were patients with HIV diagnosis made between 2004 and 2009, when WHO recommended cART initiation if CD4 count was <200 cells/mm3; Group 2 were those between 2010 and 2012, when WHO recommended cART initiation if CD4 count was <350 cells/mm3; and Group 3 were those between 2013 and 2015, when WHO recommended cART initiation if CD4 count was <500 cells/mm3. The primary outcome was all-cause mortality. All patients were followed until death, loss to follow-up, or the end of observation on 31 December, 2017, whichever occurred first.

Results: During the 9-year study period, 2,027 patients were included, with a median age of 31 years, 96.5% being male and a median baseline CD4 count of 262 cells/mm3. In Group 1, 2 and 3, 729, 612, and 686 patients were included, respectively. The mortality rate of the respective group was 20.93, 16.63, and 11.18 deaths per 1,000 PYFU. In a multivariable Cox regression analysis, independent factors associated with mortality were age (per 1-year increase, adjusted hazard ratio [AHR], 1.06; 95% CI, 1.05-1.08), opportunistic infection (OI) at HIV diagnosis (AHR, 1.90; 95% CI, 1.14-3.16), cART use (AHR, 0.07; 95% CI, 0.04-0.13), and baseline CD4 count (per 1-cell/mm3 increase, AHR, 0.997; 95% CI, 0.995-0.998). For those without OI at HIV diagnosis, the estimated HR in multivariate Cox proportional hazards regression analysis for mortality in Group 3 compared to Group 1 was 0.25 (95% CI, 0.07-0.88), after adjusting for age, gender, baseline CD4 count, HBV infection and cART initiation. By Fine-Gray competing risk regression model for AIDS-defining diseases-related death, the HR for Group 2 versus Group 1 was 0.82 (95% CI, 0.46-1.47), while that for Group 3 versus group 1 was 0.532 (95% CI, 0.28-1.01). For non-AIDS-related death, the respective HR was 0.46 (95% CI, 0.18-1.17) and 0.27 (95% CI, 0.09-0.80, p=0.018). The hazard of all-cause mortality was analyzed via Kernal smoothing density estimation. The smoothed hazard appeared to decrease within 2-year follow-up period after HIV diagnosis, which dropped dramatically within the first 6 months. Rate ratio of all-cause mortality between the first 6 months and 6th-12th months was 8.12.

Conclusions: Our study support that early initiation of cART improved survival among HIV-positive patients with no OI as initial presentation according to the progressively increasing CD4 cut-off values overtime recommended by the WHO.

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Renal and liver function changes among post-exposure prophylaxis clients at the Thai Red Cross Anonymous Clinic in Bangkok

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Background: Post-exposure prophylaxis (PEP) is one of the key interventions in the combination HIV prevention packages. Three-drug PEP regimens for 28 days to be started within 72 hours of exposure are recommended in Thailand National Guidelines on HIV/AIDS Treatment and Prevention. Tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) or lamivudine (3TC) are the recommended backbones. Preferred third drugs recommended include rilpivirine (RPV), boosted atazanavir (ATV/r), boosted lopinavir (LPV/r) or boosted darunavir (DRV/r). Alternative third drugs include raltegravir (RAL), dolutegravir (DTG) or efavirenz (EFV). In this study, we evaluated renal and liver function changes among PEP clients of the Thai Red Cross Anonymous Clinic (TRCAC) in Bangkok, Thailand.

Materials and Methods: We collected the data from TRCAC clients who started PEP during 28 April 2016 to 31 December 2017. Serum creatinine (Cr) and alanine aminotransferase (ALT) were performed by Beckman Coulter (AU480) at baseline (pre-PEP) and around 4 weeks after PEP initiation (post-PEP). PEP clients were scheduled to come back at month 1 and month 3 after PEP initiation to determine HIV status. Median (interquartile range, IQR) of Cr and ALT were reported. Comparisons of Cr and ALT at pre-PEP and post-PEP time points were made by paired t-test.

Results: There were 3,568 clients who walked into TRCAC for PEP services. Of these, 82 (2.3%) came in after 72 hours of exposure, 48 (1.4%) had HIV-negative test results from elsewhere but not at TRCAC, and 8 (0.2%) tested HIV-positive at baseline. These clients were excluded from the analyses. Among remaining clients who started PEP, 3,160 clients (2,815 male and 345 female) had Cr results and 3,153 clients (2,808 male and 345 female) had ALT results at baseline. Median (IQR) pre-PEP Cr was 0.93 (0.83-1.03) mg/L and median (IQR) pre-PEP ALT was 22 (16-33) U/L. PEP regimens prescribed were TDF/FTC/RPV (93.61%), TDF/FTC/LPV/r (0.16%), TDF/FTC/EFV (0.03%)and others (6.21%).
Among 2,073 PEP clients who returned to TRCAC for HIV testing after 4 weeks of PEP, 890 clients also had ALT measured and 925 clients also had Cr measured. Median (IQR) post-PEP Cr was 0.99 (0.89-1.09) mg/L and median (IQR) post-PEP ALT was 26 (19-33) U/L. Comparing pre-PEP and post-PEP data using t-test, this study found significant increase in Cr and ALT after taking PEP (all p-values < 0.001). These findings were true for men (0.96 vs. 1.02, p=<0.001 for Cr and 31.09 vs. 37.00, p=<0.001 for ALT) and women (0.71 vs. 0.76, p=<0.001 for Cr and 17.44 vs. 22.78, p=<0.001 for ALT).

Conclusions: Although Cr and ALT increased significantly after PEP, the increase does not seem to be at the level with clinical significance. As PEP use indicates high risk behavior, clients coming in for PEP service should be the main target for pre-exposure prophylaxis (PrEP).

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Changes in creatinine and estimated glomerular filtration rate during the first 12-month period of pre-exposure prophylaxis among PrEP-30 clients at the Thai Red Cross Anonymous Clinic

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Background: Pre-exposure prophylaxis (PrEP) is recommended as part of the combination HIV prevention packages for people at high risk for HIV infection in Thailand National Guidelines on HIV/AIDS since 2014. A daily oral fixed-dose combination of tenofovir disoproxil fumarate (TDF) 300 mg and emtricitabine (FTC) 200 mg is currently the only recommended PrEP regimen. Renal side effects from PrEP with an increase in serum creatinine (Cr) and a decrease in estimated glomerular filtration rate (eGFR) were reported to be less than 1% from clinical trials and demonstration programs. We studied changes in Cr and eGFR over a 12-month period among clients of the PrEP-30 service at the Thai Red Cross Anonymous Clinic (TRCAC) in Bangkok, Thailand.

Materials and Methods: PrEP-30 is the first fee-for-service PrEP program in Thailand, started in December 2014. PrEP pills along with baseline and monitoring laboratory services are available at 30 Baht (or approximately 1 USD) per day from TRCAC. PrEP-30 clients are scheduled every 3 months for HIV testing and Cr/eGFR. We analyzed Cr and eGFR data from PrEP-30 clients who started PrEP during January 2016-January 2017. Comparisons were made between values at baseline, month 3, month 6, month 9 and month 12, and were also analyzed by ethnicity (Thai vs.non-Thai).

Results: A total of 616 clients (578 male and 38 female) started PrEP at TRCAC. Of these, 310 (50.3%) were Thais, 206 (33.4%) were non-Thais, and 100 (16.2%) did not report nationalities. Mean (standard deviation, SD) age was 34.2 (9.4) years old. Baseline Cr data was not available from 16 clients.

Over a 12-month period, 274 (45.7%), 127 (21.2%), 141 (23.5%) and 172 (28.7%) visited month 3, month 6, month 9 and month 12 clinic visits, respectively. Median creatinine (interquartile range, IQR) values were 1.01 (0.90-1.13), 1.01 (0.89-1.14), 0.98 (0.88-1.12), 0.95 (0.86-1.05) and 0.96 (0.88-1.07) mg/dL and median eGFR were 95.60 (82.95-107.90), 96.70 (83.40-109.30), 103.10 (90.40-111.80), 103.10 (90.40-114.80) and 101.00 (88.35-114.00) ml/min/1.73m2at baseline, month 3, month 6, month 9 and month 12, respectively. Comparing Cr between visits, Cr at month 6 (p=0.03), month 9 (p<0.001) and month 12 (p<0.001) were lower than baseline value. eGFR was also higher at month 6 (p=0.015), month 9 (p<0.001) and month 12 (p<0.001) than at baseline. Fifteen clients (2.4%) were advised to stop PrEP due to eGFR < 60 ml/min/1.73m2 at one or more time points, including seven (2.3%) of Thais and eight (3.9%) of non-Thais.

Two men who have sex with men (MSM) had HIV seroconversion giving an incidence rate (95% confidence interval) of 0.75(0.19-2.99) per 100 person-years as compared to 6.2 (4.5-8.6) per 100 person-years among MSM in the Test & Treat cohort at the TRC in 2012-2015. In both cases PrEP was discontinued 8-9 months before seroconversion.

Conclusions: Experience from our real-life PrEP-30 service confirmed the low incidence of serious renal side effects among PrEP users in the first 12 months. Frequency of Cr/eGFR monitoring should be tailored to fit the convenience of individual PrEP client although fixed timing serves only as reminder.

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Abstracts
Poster Presentations

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Peripheral T cell responses against HBV similar between TDF-based and LMV-based antiretroviral therapy in HIV-HBV coinfection

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Background: Hepatitis B virus (HBV)-specific T cell responses play a crucial role in viral control. Tenofovir disoproxil fumarate (TDF) is more potent against HBV than lamivudine (LMV). However, whether TDF-based antiretroviral therapy (ART) leads to better HBV-specific T cell responses than LMV-based ART in HIV-HBV coinfection remains unclear.

Methods: Twenty HIV-HBV coinfected Chinese patients received TDF+LMV-based (TDF group, N=10) or LMV-based (LMV group, N=10) ART for 48 weeks. Peripheral blood mononuclear cells were collected pre-ART and every 24 weeks. The HBV-specific CD4+ and CD8+ T cell responses were measured by flow cytometry to detect IFN-γ, IL-2 and TNF-α production following stimulation by peptide pools containing epitopes from HBV polymerase (P), surface antigen (S), core (C) and X protein (X). The magnitude of response was defined as the sum of the percentage of cytokine-producing CD4+ and CD8+ T cells for each peptide pool after subtraction of background. Chi-square, Kruskal-Wallis and Mann-Whitney U tests were used for statistical analysis, as appropriate.

Results: Prior to ART initiation, median CD4+ T cell count was 116 cells/μL in the LMV group and 197 cells/μL in the TDF group (P=0.03), whereas HIV RNA, HBV DNA, and the proportion of hepatitis B e antigen+ patients were comparable in the two groups. After 48 weeks of ART, CD4+ T cell count was still lower in the LMV than in the TDF group (267 cells/μL vs. 445 cells/μL, P=0.02). Undetectable HIV RNA and HBV DNA levels were achieved in 90% and 80% patients, respectively. Both groups did not differ in the proportion of patients achieving undetectable HIV RNA and HBV DNA.

Pre-ART, both groups had 9 patients with detectable cytokine-producing CD4+ T cells against at least one peptide pool and only one patient gained responses in the TDF group following ART (versus none in the LMV group, P>0.05). The magnitudes of CD4+ T cells responses to peptide pools were comparable between the two groups pre-ART (0.32% vs. 0.37%, P>0.05). Following ART, the median magnitudes of CD4+ T cells responses decreased to 0.24% in TDF group (P=0.03) and 0.07% in LMV group (P=0.02).

Pre-ART, HBV-specific CD8+ T cell responses were detected in 9 and 8 patients in the TDF and LMV groups, respectively. One and two patients in the TDF and LMV groups gained CD8+ T cell responses following ART. Pre-ART, the magnitudes of CD8+ T cell responses to each peptide pool were similar between the two groups. Following treatment, the magnitude of HBV-specific CD8+ T cells in the LMV group did not change significantly (0.19% at pretreatment vs. 0.10% at week 48, P>0.05). In the TDF group, a trend towards an increased total proportion of IL-2-producing CD8+ T cells against the four peptide pools was seen at 48 weeks, but that did not reach statistical significance (median 0.04% vs. 0.18%, P=0.05).

Conclusion: Neither LMV- or TDF-based ART significantly increased the peripheral HBV-specific T cell responses after 48-week treatment. Compared to LMV, TDF-based ART is not associated with an improved T cell response to HBV.

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The association of D-amino acids with markers of immune activation and functional aging in HIV-infected individuals

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Background: Amino acids (aa) occur naturally as chiral molecules, either as L- or D-isoforms. In humans, all aa were initially thought to be L-enantiomers while D-isoforms were mainly of bacterial origin. Reports of D-amino acid (D-aa) residues identified in tissues particularly in the elderly, and its association with age-related diseases, suggests its potential role in aging. Novel multidimensional high-performance liquid chromatography (HPLC) platforms have recently uncovered an extensive presence of D-aa in circulation but its biological relevance is currently unknown. Here, we investigated D-aa levels in plasma samples of HIV-infected individuals and explored its association with markers of immune activation, organ function and age-related conditions.

Method: Fifty-nine random samples were analysed from 39 treated HIV-infected and 20 uninfected controls from the Malaysian HIV and Aging study in University Malaya Medical Centre, Malaysia. All participants were ≥ 25 years, reported no acute illness at recruitment and all HIV-infected were virologically suppressed. An integrated multi-loop three-dimensional HPLC system was used to measure the D- and L-isoforms of serine (Ser) and alanine (Ala) with readouts expressed as D-aa concentrations and the proportion of D to D+L-isomers (%D). Kidney and liver function were expressed as eGFR and Fib-4 scores, respectively. Plasma soluble(s) CD14 (sCD14), a marker of LPS-induced immune activation, IL-6 and IL-10 were measured by ELISA while kynurenine (K) and tryptophan (T) by LC-MS/MS and expressed as K/T ratio, a marker for indolamine-2,3-dioxygenase activity. HIV-related parameters were extracted from medical records while assessments for geriatric syndromes were performed by trained personnel. Mann-Whitney and Spearman rank correlation coefficients were used for statistical analysis.

Results: The median (IQR) age for both HIV-infected and uninfected groups were 40 (34-58) and 28 (26-69) years, respectively, while median CD4 T-cell count was 483 (336-604) cells/μL. Both D-Ser and D-Ala were detectable in all plasma samples and significantly correlated with age in both HIV-infected (D-Ser: r=0.441, p=0.005; D-Ala: r=0.518, p=0.001) and uninfected (D-Ser: r=0.605, p=0.006; D-Ala: r=0.516, p=0.024), respectively. The concentrations were however not significantly different between the two groups after adjusting for age and not correlated with CD4 T-cell counts. %D-Ser and %D-Ala were positively correlated with sCD14 (r=0.344, p=0.032; r=0.448, p=0.004, respectively) and K/T ratio (r=0.609, p<0.001; r=0.551, p<0.001, respectively) but not IL-6 and IL-10. %D-Ser was correlated with kidney and liver function (r=-0669, p<0.001; r=0.331, p=0.039, respectively), whereas %D-Ala with kidney function (r=-0.408, p=0.010). Both markers were correlated with Veterans Aging Cohort Study (VACS) scores, a marker for mortality risks in HIV (r=0.345, p=0.031; r=0.362, p=0.024, respectively). In combined analysis controlling for HIV status, D-Ser and D-Ala concentrations were associated with the presence of cognitive impairment, urinary incontinence, functional impairment, polypharmacy and polypathology. These associations were lost, when controlling for age.

Conclusion: Plasma D-aa levels correlated with LPS-mediated markers of immune activation in the HIV-infected and is associated with increasing age, decline in organ function and age-associated disease. These molecules may be a sensitive surrogate for microbial translocation in HIV and their role in modulating age-related processes warrants further investigations.

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Immunological correlates of sarcopenia in HIV-infected individuals on suppressive antiretroviral therapy

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Introduction:
Sarcopenia is a condition characterized by the loss of skeletal muscle mass and quality, leading to a detrimental decline in physical function. Sarcopenia may precede the occurrence of frailty and while it is most commonly associated with older individuals, it is not strictly age-dependent and has been observed in younger individuals made vulnerable by chronic conditions. We recently found middle–aged HIV-infected individuals undergoing effective antiretroviral therapy (ART) to have higher rates of sarcopenia compared to age-matched controls. While sarcopenia in the general older population has been associated with persistent inflammation; to date, the immunological correlates in younger HIV-infected individuals has not been described. Here, we explored if markers of immune activation and senescence are associated with sarcopenia and its components of muscle loss, muscle function and muscle quality among HIV-infected individuals receiving ART.

Methods: Sarcopenia was assessed in 160 HIV-infected participants from the Malaysian HIV and Aging cohort. All participants were ≥ 25 years old, on stable ART (HIV RNA levels ≤50 copies/mL for at least 12 months), not pregnant and had no acute illness at the point of recruitment. Sarcopenia was defined as low muscle mass plus low muscle strength (grip strength) and/or low physical function (walking speed) as recommended by the Asian Working Group for Sarcopenia (AWGS). In all participants, whole blood immunophenotyping was performed for markers of activation (CD38+, HLA-DR+) and senescence (CD57+, CD28-) on T-cells, NK cells and monocyte subsets. Plasma IL-6, IL-10 and sCD14 levels were measured by ELISA and kynurenine and tryptophan by liquid chromatography tandem mass spectrometry (LC-MS/MS). Associations between immunological markers with sarcopenia and its components of grip strength (GS), walking speed (WS), muscle quality (MQ) and skeletal muscle index (SMI) were assessed using multivariate logistic regression analysis.

Results: The majority of participants were males (73.8%) and of Chinese descent (67.5%). Median (interquartile range, IQR) age was 42 (34-52) years while median current CD4 T-cell counts were 536 (397-760) cells/μl. Of this, 9.4% presented with sarcopenia while 8.1% were pre-sarcopenic. After adjusting for gender, sarcopenia was positively associated with the proportion of activated monocytes (%CD38+ on CD14++ monocytes, P=0.04). GS was associated with the proportion of intermediate monocytes (%CD14++ CD16+ monocytes, P=0.041) and IL-6 levels (P=0.003) while WS with IL-6 (P<0.001) and the proportion of non-classical monocytes (% CD14dim CD16++, P=0.005). SMI was associated with activation markers on both NK cell (NK HLA-DR+ and NK CD38+ HLA-DR+; P=0.011 and P=0.004, respectively) and non-classical monocytes (%CD14dimCD16++CD38+ and %CD14dimCD16++CD38+HLA-DR+; P=0.037 and P=0.020, respectively). Muscle quality was associated with IL-6 levels (P=0.0028) and the proportion of activated intermediate monocytes (%CD38+CD14++ CD16+, P=0.0147). No correlates were found with activation and senescent makers on CD4+ and CD8+ T-cells.

Conclusion: Sarcopenia and its components were found to be predominantly correlated with changes in the innate rather than acquired immune system in our study participants. These changes mainly involved the intermediate and non-classical monocyte subsets which are known to be pro-inflammatory. Larger studies which are powered to account for clinical covariates are needed to confirm our findings.

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Examination of circulating blood plasma protein in HIV patients with and without kidney dysfunctions

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Background: Patients with human immunodeficiency virus (HIV) are likely to develop chronic kidney disease (CKD) despite being treated with antiretroviral therapy (ART). This is because HIV-infected patients are exposed to various risk factors of CKD, including (i) committing to long-term ART that are nephrotoxic, (ii) higher incidence of co-morbidities, particularly diabetes mellitus (DM) and hypertension (HTN) known to exert negative effects on the kidneys and, (iii) the presence of an accelerated ageing phenomenon. However, it remains unknown why some HIV-infected patients are more susceptible whereas some are more resilient towards CKD, despite sharing a similar risk factor profile. The primary aim of this study is to compare the blood plasma proteome between adult HIV-infected patients with and without CKD, as the first step towards understanding the molecular mechanisms of kidney dysfunction among HIV-infected patients.

Material & Methods: Blood samples were previously collected upon the recruitment of the Malaysian HIV and Aging (MHIVA) cohort. These samples were processed within two hours of collection and the plasma samples were stored in a -80°C freezer in 1.5 ml aliquots. Patients were selected based on their estimated glomerular filtration rate (eGFR) values, namely <60 mL/min/1.73m² for disease cases and >90 mL/min/1.73m² for controls. Eight case-control pairs were matched according to their age, gender, and co-morbidities (DM and HTN). All blood plasma samples were subjected to two-dimensional gel electrophoresis (2-DE) and silver staining. The gels were then imaged with ImageScanner III (GE Healthcare) and analysed using ImageMaster 2D Platinum v7.0 (GE Healthcare). Protein spots were quantified as a percentage of spot volume in a given gel. An analysis of variance (ANOVA) test was used to compare the difference in the means of both groups.

Results: The protein spots were individually analysed and adjustments were made where necessary, including spot editing, spot propagation, and spot matching. Following these adjustments, eight spots were found to be statistically significant, with a fold difference of >1.5 and a p-value of <0.05, between the cases and controls. By referring to the human proteome maps previously published, one of the significant spots identified could be an isoform of the haptoglobin beta chain. Haptoglobins function to prevent iron loss and damage to the kidneys during hemolysis. They are also acute phase proteins that are elevated during inflammation. Of special note, haptoglobins were previously reported to be elevated in HIV-infected children with CKD, therefore implying that iron-related proteins may in fact play a role in the pathogenesis of kidney disease in HIV patients.

Conclusions and future work: There is a difference in the blood plasma protein profile between HIV-infected subjects with and without CKD. Our preliminary data calls for further investigation to identify the protein that are differentially present in these two groups with Quadrupole Time-of-Flight-liquid chromatography/mass spectrometry (Q-TOF-LC/MS) and to further validate the difference with Western blotting. The identified proteins shall provide clues towards mechanism of kidney dysfunction, may be further developed into biomarkers, and may serve as potential therapeutic targets in the future.

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Gender differences in outcomes of antiretroviral treatment among HIV-infected patients in China: a retrospective cohort study, 2010—2015

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Background: Women now account for about half of all people living with HIV worldwide, but researchers lack clear information and large

population-based study about gender differences in treatment outcomes.

Methods: A nationwide retrospective observational cohort study with data from the China National Free Antiretroviral Treatment Program was carried out. Antiretroviral-naïve patients older than 18 years initiating standard antiretroviral therapy between January 1, 2010 and December 31, 2011 were included and followed up to Dec 31, 2015. We used modified Poisson regression models to estimate the impact of gender on virological suppression and retention in treatment, and Kaplan-Meier analysis and Cox proportional hazard models to evaluate gender difference in mortality.

Results: 68646 patients (46083 (67.1%) men and 22563 (32.9%) women) with HIV met eligibility criteria. Women were significantly more likely to achieve virological suppression than men both at 12 months (adjusted relative risk [aRR] 1.02, 95%CI 1.01-1.03, p<0.001) and 48 months (aRR 1.01, 95%CI 1.00-1.02,p=0.005) after initiating antiretroviral treatment. Women were also more likely to remain in treatment at 12 months (aRR 1.02, 95%CI 1.01-1.02,p<0.001) and 48 months (aRR 1.04, 95%CI 1.03-1.05,p<0.001), although the difference became insignificant in alive patients. All-cause mortality was lower in women than in men (2.34 vs. 4.03 deaths/100PY, adjusted hazard ratio 0.72, 95%CI 0.67-0.77, p<0.001).

Conclusions: In China, women are more likely to achieve virological suppression, remain in treatment and have a significantly lower risk of death than men. Future studies could take both biological and socio-behavioral factors into analysis to clarify the influence factors.

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Cost-effectiveness of Dolutegravir in HIV-1 treatment-naïve patients in China

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Objectives: To evaluate the cost-effectiveness of dolutegravir (DTG) comparing to ritonavir-boosted lopinavir (LPV/r) and raltegravir (RAL) among treatment-naïve HIV-1 infected patients in China.

Methods: A decision tree model was developed taking the perspective of the healthcare system. Response rates defined by the probability of virologic suppression (HIV RNA<50 copies/mL) at 48 weeks were obtained from a published network meta-analysis. Responders were distributed across CD4 health states based on their baseline CD4 counts, allowing the calculation of quality-adjusted life-years (QALYs). Baseline patient characteristics were informed using pooled data from DTG phase 3 clinical trials (SINGLE, SPRING-1, SPRING-2 and FLAMINGO). Cost included were drug costs, routine care, and treatment for complications, adverse events and loss of productivity. A 10 year analysis was conducted using the societal perspective. Outcomes included QALYs, life-years (LYs), incremental cost per QALY ratio (ICER) and incremental cost per responder (ICPR). The year of analysis was 2018. Sensitivity analyses were also conducted explore the impact of differences in drug prices.

Results: At the same price of 340 RMB/month for the three treatment alternatives, the total cost of treatment/patient was RMB352,914, RMB358,752 and RMB369,029 for DTG, RAL and LPV/r, respectively. After 10 years of treatment, DTG, RAL and LPV/r generated 7.24, 7.17 and 7.04 QALYs, respectively resulting in DTG dominating RAL and LPV/r. For a longer time horizon of patient lifetime, DTG was cost effective compared to RAL and LPV/r with ICERs of RMB22,217/QALY and RMB18,006/QALY, respectively.

Conclusions: DTG in the treatment of HIV-1-infected patients in China was likely to be a cost-effective strategy comparing to LPV/r and RAL. These results need to be further confirmed with further long-term real world studies.

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Elevations of serum creatine kinase among HIV-positive individuals taking dolutegravir-based therapy versus non-integrase inhibitor-based therapy

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Background: Integrase strand transfer inhibitor (InSTI) is an increasingly used antiretroviral agent in both initial and salvage therapy across different local and international guidelines. Reports from randomized clinical trials and real-life cohort study have suggested that first generation InSTI, raltegravir, might be associated with an elevated risk of creatine kinase (CK) elevation and skeletal muscle toxicity. However, real-life data systematically evaluating the risk of CK elevation among HIV-positive patients receiving dolutegravir (DTG)-containing antiretroviral therapy are scarce.

Methods: HIV-positive patients who sought medical attention at the National Taiwan University Hospital between February 2017 and January 2018 were included in this study. Patients were prospectively interviewed to inquire into their practices of weight training and alcohol consumption. Laboratory tests including liver function, renal function, creatine kinase, plasma HIV RNA load and CD4 cell counts were tested every 3-6 months in accordance with the national HIV treatment guidelines. The incidence of elevation of serum CK and rhabdomyolysis (defined as >10-fold of the upper limit of normal) was estimated among patients who received DTG-containing antiretroviral therapy versus patients who received non-InSTI based therapy.

Results: 1335 HIV-positive patients with a median 37.9 age of years and 96.6% being male were included in this study: 339 patients who received DTG-containing antiretroviral therapy provided 651 laboratory results of CK measurements while 996 who received non-InSTI-based antiretroviral therapy contributed 1544 laboratory results of CK measurements. Among patients receiving DTG-containing therapy, the rate of CK elevation was 15.8% (103/651), which was similar to the 13.7% (211/1544) among those who received non-InSTI based therapy (difference, 2.1%; 95% CI, -1.1-5.6%). The rate of rhabdomyolysis was also similar between both groups (1.1% versus 0.7%; difference, 0.4%; 95% CI, -0.5-1.6%). The risk of CK elevation increased with patient's self-reported intensity of weight training (≤0.5 or >0.5 hours per day), but was not associated with the use of DTG-containing antiretroviral therapy. All episodes of elevated CK or rhabdomyolysis in either group of patients were self-limited during the study period and no specific treatment were required.

Conclusion: In this single-center prospective cohort study, DTG-containing antiretroviral therapy was not associated with an increased risk of asymptomatic CK elevation or rhabdomyolysis.

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No correlation was observed between adverse events and plasma dolutegravir concentrations in dolutegravir containing regimen

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Background: Dolutegravir (DTG) is a second generation HIV-1 integrase inhibitor that is high potent against both wild-type and drug-resistant HIV-1 strains. DTG has a good toleration, few drug interactions, minimal drug resistance and once-daily dosing for treatment-naïve patients. Therefore, DTG is approved for use in a broad population of HIV-1 infected patients. However, there are few data for reasons of DTG discontinuation during antiretroviral therapy. In this study, we intended to investigate major causes of DTG discontinuation and relationship with plasma DTG concentrations.

Methods: We examined 933 HIV-1 infected patients (male:female=852:81) who were treated with DTG containing regimen from May 2014 to Jan 2018, retrospectively. All patients had been administered with 50mg DTG once daily in combination with other antiretrovirals. Plasma DTG concentrations were determined by our developed LC-MS method. Adverse events were assessed by laboratory data and interviews at outpatient clinic.

Results: Of 933 patients treated with DTG, 10 patients (male:female=9:1) discontinued DTG because of some adverse events, and switched from DTG to other antiretrovirals. The median age for 10 patients was 46 years old (range; 28-81). Three patients were treatment-naïve and 7 patients were therapy-experienced. The adverse events were rash (5 patients; median duration 110 days), insomnia and unusual dreams (2 patients; median duration 76 days), diarrhea (1 patient; duration 42 days), arthralgia (1 patient; duration 112 days) and drowsiness (1 patient; duration 3 days), respectively. Co-administered nucleoside reverse transcriptase inhibitors were tenofovir disproxil fumarate/emtricitabine (5 patients), abacavir/lamivudine (2 patients), tenofovir alafenamide (1 patient), respectively. No correlation was observed between these adverse reactions and plasma DTG concentrations in individual patient.

Conclusions: These findings suggest that we need to pay attention for rash and insomnia during DTG containing antiretroviral regimen, for long term therapy specially. As the patients with adverse events had no higher DTG plasma concentrations, DTG pharmacokinetics were not related to these adverse reactions. In further study, we have to make clear cause of adverse reactions for DTG containing regimen.

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Dual therapy with ritonavir-boosted protease inhibitor(PI) plus lamivudine versus triple therapy with ritonavir-boosted PI plus two nucleoside reverse transcriptase inhibitor (NRTI) in stable-switched patients: a retrospective observational study

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Background: Dual therapy with lamivudine plus boosted PI in viral suppressed HIV-infected patients is recommended by DHHS, EACS and BHIVA guidelines. However, few studies were observed and compared with triple therapy of ritonavir-boosted PI plus two NRTIs.; therefore, we conducted the retrospective observational study to analyze the efficacy and tolerability of dual therapy.

Methods: The retrospective observational study was conducted in one HIV center in Taoyuan, northern Taiwan, from April 2015 to June 2017. We aim to compare efficacy of viral suppression, serum CD4/CD8 count, and safety, including LDL, total cholesterol and HbA1c in enrollment and after 48 week of treatment. Patients were eligible for enrollment if they had HIV viral suppression (virus load <200 copies/uL) under HIV therapy with ritonavir-boosted lopinavir or ritonavir-boosted darunavir, in combination with lamivudine and one NRTI of zidovudine/abacavir/tenofovir disoproxyl fumerate. The primary endpoint was virological response rate, defined as the proportion of patients with HIV RNA less than 50 copies per mL at 48 weeks. Dual therapy was classed as non-inferior to triple therapy if the lower bound of the 95% CI for the difference between groups was no lower than -12%.

Results: Between April, 2015, and June, 2016, 78 patients were shifted to the dual-therapy and 57 patients maintained triple therapy, and these 135 patients completed 48 weeks of treatment. At week 48, 76 patients (97.4%) in the dual-therapy group and 51 (89.5%) in the triple-therapy group had viral response (difference 7.9%, 95% CI -0.2% to 16.2%; p=0.059). No statistically significant changes were seen in CD4 T-cell count from baseline to week 48 between dual therapy group and triple therapy group [517 (290) to 569 (259) cells/µL versus 550 (259) to 554 (267) cells/µL, p = 0.32]. Moreover, no statistically significant changes were seen in cholesterol and LDL level after 48 weeks of treatment between 2 groups [cholesterol:194.5 (55.5) mg/dL versus 176 (49) mg/dL; p=0.406, LDL: 108 (50) mg/dL versus 105 (56) mg/dL; p=0.578].

Conclusion: Dual therapy with ritonavir-boosted protease inhibitor(PI) plus lamivudine showed good efficacy for HIV suppressed patients, but longer duration of observation is recommended in aspects related to lipid profile.

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Safety and Efficacy of E/C/F/TAF in HIV-Infected Adults on Chronic Hemodialysis

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Background: Elvitegravir (EVG)/cobicistat (COBI)/emtricitabine (FTC)/tenofovir alafenamide (E/C/F/TAF) is approved for use in HIV-1 infected individuals with mild to moderate chronic kidney disease (estimated glomerular filtration [eGFR] 30-69 mL/min). Current HIV treatment for individuals with renal failure on hemodialysis (HD) requires complex regimens with multiple pills. This is the first study to evaluate safety, efficacy, and pharmacokinetics (PK) of a daily single-tablet regimen (STR) in HIV-infected adults with end stage renal disease (ESRD) on chronic HD.

Material & Methods: HIV-1 infected, virologically suppressed adults with ESRD (eGFR <15mL/min) on chronic HD for ≥6 months were switched to open-label E/C/F/TAF 150/150/200/10 mg once daily for 48 weeks (W). Efficacy was assessed as the proportion of participants with HIV-1 RNA <50 copies (c)/mL (Snapshot algorithm). Maintenance of virologic suppression (<50 c/mL), safety, and patient satisfaction (Treatment Satisfaction Questionnaire) were assessed throughout the study. A PK substudy was done at or between W2 and 4. W24 data are presented here and W48 data will be available for the conference.

Results: We enrolled 55 participants; median age 51yrs (range 23-64), 24% female, 82% Black, median time on HD 6yrs (range 1-17), median CD4 count 515 cells/μL (IQR 387, 672), and 22% Hepatitis C Ab positive, and 27% history of diabetes. At W24, 87% (48/55) had HIV-1 RNA <50 c/mL. The other 7 participants discontinued due to lack of efficacy (n=1), AE (n=2), or other reasons not related to efficacy (n=4). EVG, COBI, and TAF PK were consistent with exposures in normal renal function. As expected, exposures of FTC and TFV (metabolite of TAF), which are renally eliminated, were higher v. historical data in normal renal function Mean (%CV) AUC ng*h/mL for FTC, TAF and TFV in ESRD when compared to individuals with normal renal function were 62900 (48) vs 11400 (12), 232 (53) vs 230 (47) and 8720 (39) vs 320 (15), respectively. Sixteen (29%) participants had Grade (G) 3 or 4 AEs unrelated to study drug; 6 (11%) participants experienced study drug related AEs (all were G1-2, including nausea in 4). Two participants discontinued E/C/F/TAF due to AEs (allergic pruritis, related; staphylococcal endocarditis, unrelated). The participant with endocarditis died from heart failure after entering hospice. 24 (44%) participants had G3-4 laboratory abnormalities, all of which were present at baseline. 79% of participants felt "much more satisfied" with the STR convenience compared to baseline.

Conclusions: Switching to E/C/F/TAF STR maintained virologic suppression at W24, was well tolerated, and more convenient for adults with ESRD on HD.

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A Phase 3b Open-Label Pilot Study to Evaluate Switching to Elvitegravir/Cobicistat/ Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) Single Tablet Regimen (STR) in Virologically-Suppressed HIV-1 Infected Adults Harboring the NRTI Resistance Mutation M184V and/or M184I (GS-US-292-1824)

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Background: Switching to a once-daily STR of E/C/F/TAF in HIV-1 infected patients was shown to be effective and safe through 144 weeks. No data exist evaluating the efficacy of E/C/F/TAF in subjects whose HIV-1 harbors the M184V/I resistance mutation.

Material & Methods: 1824 is an ongoing, prospective, open-label, single arm, multicenter study evaluating the efficacy and safety of switching to E/C/F/TAF in subjects receiving a stable regimen (≥6 months) of emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) or abacavir/lamivudine (ABC/3TC) plus a third antiretroviral agent. Subjects had a historical genotype report showing M184V and/or M184I and no evidence of previous virologic failure or resistance to boosted PIs or INSTIs. At screening, HIV-1 RNA <50 copies/ mL was required as well as sequencing of integrated HIV DNA (GenoSure Archive Assay, Monogram Biosciences) with no presence of other NRTI or PI resistance mutations. The pre-specified primary objective is to evaluate the efficacy of switching to E/C/F/TAF in maintaining HIV-1 RNA <50 copies/mL at Week 12 using pure virologic response (PVR). Subjects with discontinuation or missing values were considered responders if last HIV-1 RNA <50 copies/mL.

Results: Thirty-seven subjects were enrolled and switched to E/C/F/TAF. Mean age was 50 years (range 22-76), 73% White, 19% Black, 22% women and median CD4 count was 724 cells/μL. All subjects had HIV RNA <50 copies/mL at baseline. Prior to switching to E/C/F/TAF, the regimens at screening were 2 NRTIs plus boosted PI (54%), INSTI (32%), NNRTI (11%), and INSTI+NNRTI (3%). All subjects had the M184V, M184I or both mutations and 51% (19/37) had NNRTI resistance mutations on historic resistance tests. Archive DNA resistance testing found 43% (16/37) of subjects had either M184V, M184I or both, 5% (2/37) had only NNRTI resistance and 51% (19/37) had wild type virus.
All 37 subjects (100%) maintained HIV-1 RNA <50 copies/mL by Week 12 based on PVR. Three subjects discontinued prior to Week 12 with the last recorded HIV-1 RNA <50 copies/mL. There were no virologic failures and no cases of emergent resistance. There was no significant change in CD4 count to Week 12. Four serious adverse events (AEs) occurred were not considered study drug-related: 1 each of squamous cell carcinoma, acute kidney injury (due to poorly controlled hypertension and diabetes), transient proteinuria which resolved

while on study drug and pulmonary embolism. There were 19% (7/37) subjects experiencing any study drug-related AE; none were grade 3 or 4. Only one subject experienced an AE (muscle spasms) leading to premature E/C/F/TAF discontinuation.

Conclusions: In this primary analysis, 100% of HIV-1 suppressed subjects with baseline M184V and/or M184I mutations who switched to E/C/F/TAF maintained HIV suppression at Week 12 with no emergent resistance. E/C/F/TAF was well tolerated. Subjects will be followed for 48 weeks to establish the durability of HIV suppression on E/C/F/TAF.

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Efficacy and Safety of Tenofovir Alafenamide (TAF) Versus Tenofovir Disoproxil Fumarate (TDF) in Treatment-Naïve Asian Adults: Week 144 Results:

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Background: In treatment-naïve adults, the single-tablet coformulation of elvitegravir/ cobicistat/emtricitabine/TAF (E/C/F/TAF) demonstrated high efficacy and significantly reduced effects on renal biomarkers and bone mineral density (BMD) compared with E/C/F/TDF. We describe the efficacy and safety of TAF in treatment-naïve Asian adults through 144 weeks.

Material & Methods: This analysis consisted of pooled data from two Phase 3, randomized, double blind studies (Study 104 and 111) of HIV-infected, naïve adults who initiated E/C/F/TAF or E/C/F/TDF. We examined the efficacy and safety of two regimens through Week 144 in Asian and non-Asian adults.

Results: Of 1,733 adults, 10% were Asians (91 TAF vs 89 TDF). Baseline (BL) characteristics were

balanced between groups (15% and 17% with CD4 count <200 cells/μL; median eGFRCG 109 and 105 mL/min). Among Asian subjects, at Week 144, 93% on TAF vs 88% on TDF achieved virologic suppression. Mean increases in CD4 cell count were 297 cells/μL TAF and 278 cells/μL TDF. Both were well-tolerated with 1% discontinuation of TAF due to adverse events (AEs) vs 2% of TDF. No Asians discontinued due to renal AEs and there were no cases of proximal renal tubulopathy or Fanconi syndrome. Median changes in eGFR at Week 144 were -9 mL/min for TAF and -10 mL/min for TDF. Median change from BL in proteinuria for TAF and TDF [urine protein to creatinine ratio (CR): -1% vs 31%; urine retinol binding protein to CR: 47% vs 114%; urine beta-2-microglobulin to CR: -22% vs 74%] demonstrated that TAF had less impact on renal tubular function. There were significantly less spine and hip BMD loss for TAF compared to TDF (mean change at spine: -0.5% vs -3.4%; and hip: -1.3% vs -4.4%). Median changes in Total cholesterol to HDL ratio at Week 144 were 0.1 TAF and -0.2 TDF.

Conclusions: E/C/F/TAF and E/C/F/TDF have high and durable efficacy in treatment-naïve Asian adults, with changes in markers of renal and bone safety that favored TAF over TDF through Week 144.

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Efficacy and Safety of Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir alafenamide (E/C/F/TAF) in Virologically Suppressed Asian Adults with Renal Impairment: 144 Week

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Background: TAF is a novel prodrug of tenofovir (TFV) that results in 80-90% lower plasma TFV levels as compared to tenofovir disoproxil fumarate (TDF), and has been shown to be efficacious with an improved renal and bone safety profile.

Material & Methods: Study 112 is a Phase 3 single arm study in which HIV suppressed adults on TDF or non-TDF regimens with stable renal impairment (eGFRCG 30 to 69 mL/min) were switched to open-label E/C/F/TAF. Efficacy and safety endpoints through Week 144 were examined.

Results: 240 adults (34 Asian and 201 non-Asian) switched to E/C/F/TAF: median CD4 cell count 498 and 649 cells/mm3, and eGFRCG 44 and 58 mL/min at baseline. NRTIs in pre-switch regimens included 65% TDF, 22% abacavir, and 13% other. At Week 144, 91% of Asian and 82% of non-Asian maintained virologic suppression. E/C/F/TAF was well-tolerated with no discontinuations due to adverse events (AEs) in Asians versus 12 (of which 5 were renal AEs) in the non-Asian group. There were no cases of proximal renal tubulopathy or Fanconi syndrome. From baseline to Week 144, median eGFRCG remained stable (Asian vs. non-Asian: -0.6 vs +1.5 mL/min) with large decreases in multiple measures of proteinuria [Median % change from baseline in Asian and non-Asian: urine albumin to creatinine ratio (CR) (-36% and -35%), urine retinol binding protein to CR (-62% and -64%), and urine beta-2-microglobulin to CR (-80% and -82%)], demonstrating improvement in renal tubular function. Both groups experienced recovery of spine and hip bone mineral density (BMD) at Week 144 [Median % change from baseline in Asian and non-Asian: spine BMD (+1.9% and +2.8%); hip BMD (+2.7% and +1.9%)].

Conclusions: Through week 144, Asian adults with renal impairment who switched to E/C/F/TAF maintained high and durable efficacy with a favorable renal and bone safety. These data support E/C/F/TAF as a switch regimen in HIV suppressed Asian adults with renal impairment.

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Switching from TDF to TAF improves bone and renal safety independent of age, sex, race, or 3rd agent: Results: from pooled analysis (N=3816) of virologically suppressed HIV-1-infected adults

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Background: Five randomized trials evaluating switching from a tenofovir disoproxil fumarate (TDF)-containing regimen to a tenofovir alafenamide (TAF) regimen demonstrated improved bone and renal safety.

Material & Methods: We pooled data at Week (W) 48 from five trials of HIV-infected, virologically suppressed individuals who switched from a TDF-containing to a TAF-containing regimen to assess outcomes in subgroups at risk of bone and renal complications: age, sex, race, baseline eGFR, and 3rd agent prior to switch (PI, integrase, or NNRTI).

Results: Of 3816 participants, 2205 (58%) switched to TAF and 1611 (42%) remained on TDF. 48 weeks after switching to TAF, there were statistically significant improvements in hip and spine BMD, eGFR, and total and tubular proteinuria overall and in all subgroups. Of note, greater magnitude benefits were seen in those at greater bone and renal risk. Significant improvements in mean BMD % change were seen after switching to TAF vs TDF in women (hip: +1.4% vs +0.1%, spine: +2.3% vs -0.4%) and adults ≥50 years (hip: +1.1% vs -0.3%, spine: +1.9% vs -0.1%). Those on TAF with baseline eGFR < 90 mL/min had greater improvements in median eGFR (+6.2 vs +1.0 mL/min), significant median % declines in total (UPCR: -30.2% vs +14.8%, UACR: -25.1% vs +22.4%) and tubular proteinuria (RBP:Cr: -45.4% vs +43.7%; B2M:Cr: -62.6% vs +45.3%) compared with increases with TDF. Black participants who switched to TAF had improvements in both bone (hip: +1.2% vs +0.1%, spine: +1.9% vs -0.3%) and renal (UPCR: -15.6% vs +8.5%) safety. Improvements in bone and renal safety were independent of 3rd agent.

Conclusions: For >2200 individuals who switched to TAF, those at greater bone and renal risk had more benefit. These data support switching from TDF to TAF, in particular in TDF-treated individuals at high risk for low BMD or renal disease.

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Switch to Bictegravir/F/TAF From DTG and ABC/3TC

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Background: Bictegravir, a novel, unboosted INSTI with a high barrier to resistance and low potential for drug interactions, has been coformulated with the recommended NRTI backbone of emtricitabine and tenofovir alafenamide (B/F/TAF) as a fixed-dose combination (FDC). We report the primary Week (W) 48 efficacy and safety Phase 3 results: of switching to B/F/TAF from dolutegravir plus abacavir/lamivudine (DTG+ABC/3TC) or FDC of DTG/ABC/3TC.

Material & Methods: HIV-infected adults virologically suppressed on DTG/ABC/3TC or DTG plus ABC/3TC (DTG/ABC/3TC group), with estimated glomerular filtration rate (eGFR) ≥50 mL/min were randomized 1:1 to switch to B/F/TAF (50/200/25 mg) once daily or continue current regimen as DTG/ABC/3TC through week 48 in a double-blinded fashion. Primary endpoint was proportion with HIV-1 RNA ≥50 copies/mL (c/mL) at W48 (FDA snapshot). Noninferiority was assessed through 95.002% confidence intervals (CI) using a margin of 4%. Secondary endpoints were proportion with HIV-1 RNA <50 copies/mL and safety (adverse events [AEs], laboratory results, bone mineral density [BMD], and renal biomarkers).

Results: 563 participants were randomized and treated (B/F/TAF n=282, DTG/ABC/3TC n=281): 11% women, 22% Black, median age 46 yrs (range 20-71). At W48, 1.1% switching to B/F/TAF and 0.4% continuing DTG/ABC/3TC had HIV-1 RNA ≥50 c/mL (difference 0.7%; 95%CI -1.0% to 2.8%, p=0.62), demonstrating noninferiority. At W48, proportion with HIV-1 RNA <50 c/mL was 93.6% on B/F/TAF and 95.0% on DTG/ABC/3TC. No participant developed resistance to any study drug. The most common AEs were upper respiratory tract infection (10% B/F/TAF, 10% DTG/ABC/3TC), diarrhea (9%, 5%), nasopharyngitis (7%, 8%) and headache (7%, 7%).

Few participants (6 [2%], 2 [1%]) had AEs leading to premature study drug discontinuation. Mean BMD increased similarly in both groups. Percentage changes from baseline in renal biomarkers were similar between treatment groups. Lipid parameters were similar between groups with the exception of a small decrease in triglycerides (-5 mg/dL) seen in the B/F/TAF group vs +3 mg/dL in the DTG/ABC/3TC group (p=0.028).

Conclusions: Switching to B/F/TAF was noninferior to continuing DTG/ABC/3TC with low rates of W48 virologic failure, high rates of maintained virologic suppression, and no resistance. B/F/TAF was well tolerated, with a similar bone and urine protein safety profile to DTG/ABC/3TC.

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Phase 3 Randomized, Controlled Trial of Switching to Fixed-Dose Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) from Boosted Protease Inhibitor-Based Regimens in Virologically Suppressed Adults: Week 48 Results:

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Background: Boosted protease inhibitor regimens (bPIs) are effective and often used in HIV-infected individuals with difficulties with adherence, but they can have drug-drug interactions and GI adverse effects. Bictegravir (B), a novel, potent integrase strand transfer inhibitor with a high barrier to resistance and low potential for drug-drug interactions, was coformulated with the recommended nucleoside reverse transcriptase inhibitor backbone emtricitabine (FTC)/tenofovir alafenamide (F/TAF) and demonstrated high efficacy and tolerability in randomized studies in treatment-naïve adults. This randomized Phase 3 study assesses efficacy and safety of switching to B/F/TAF from a multi-tablet regimen containing a bPI.

Material & Methods: HIV-infected adults suppressed on regimens of boosted atazanavir (ATV) or darunavir (DRV) + abacavir/lamivudine (ABC/3TC) or FTC/tenofovir disoproxil fumarate (TDF), were randomized 1:1 to continue their current bPI regimen or switch to open-label coformulated B/F/TAF (50/200/25 mg) once daily. Primary endpoint was proportion with HIV-1 RNA ≥50 copies/mL (c/mL) at W48 (FDA snapshot). Noninferiority was assessed through 95.002% confidence intervals (CI) using a margin of 4%. Secondary endpoints included proportion with HIV-1 RNA <50 c/mL and safety measures at W48.

Results: 577 participants were randomized and treated with B/F/TAF (n=290) or current bPI regimens (n=287): 17% women, 26% Black, median age 48 yrs. Most were receiving a bPI with FTC/TDF (85%) at screening. At W48, switching to B/F/TAF was noninferior to continuing bPI with 1.7% in each group having HIV-1 RNA ≥50 c/mL (difference -0.0%; 95.002%CI -2.5% to 2.5%, p=1.00); the proportion with HIV-1 RNA <50 c/mL was 92.1% in B/F/TAF vs 88.9% in bPI. No participant on B/F/TAF developed resistance to study drugs. One participant on DRV/ritonavir + ABC/3TC developed a treatment-emergent L74V mutation. Incidence of grade 3 or 4 AEs was similar (B/F/TAF 4%, bPI regimens 6%). No renal discontinuations or tubulopathy cases occurred with B/F/TAF.

Conclusions: Adults switching to B/F/TAF from a boosted PI maintained high rates of virologic suppression without resistance. B/F/TAF was safe and well tolerated.

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Persistence among Treatment Naïve HIV-1 Patients: Single Versus Multiple Tablet Regimen Comparison

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Background: Antiretroviral therapy (ART) is a cornerstone of HIV management, working by suppressing viral replication and delaying disease progression. ART is chronically administered, and discontinuation of therapy may result in poor patient outcomes and increased costs associated with switching to more expensive subsequent lines of therapy. Once-daily single-tablet regimens (STRs) have been associated with higher adherence, persistence, and viral suppression when compared to multi-tablet regimens (MTRs). In order to 1) assess persistence among STRs, between MTRs, and among MTRs, and 2) update findings regarding persistence among Department of Health and Human Services recommended HIV regimens for treatment naïve patients in light of new therapeutic options, the QuintilesIMS longitudinal prescription claims database (LRx) was examined.

Materials & Methods: Quintiles IMS's longitudinal prescription claims database (LRx) was used to identify patients with ≥1 claim for any ART from 1/1/2014–5/31/2017, with the first ART claim within the index window (1/1/2015-5/31/2016) serving as the index date. All patients were ≥18 years of age at index, and did not have ART claims during a 12 month washout period. Persistence was evaluated using a <90 day refill gap and reported as mean days on therapy and the proportion of patients remaining on therapy 12 months post-index. Persistence with STRs and MTRs was assessed overall and by regimen using the Kaplan-Meier method. Log-rank test was used to compare persistence.

Results: A total of 39,253 and 10,847 patients on STR and MTR were identified with mean (SD) age of 41.8 (12.8) years for STR patients (77.1% male) and 43.4 (12.3) years for MTR patients (70.8% male). Patients initiating with a STR had more days on therapy (mean [SD]: 419.0 [1.47] vs 327.0 [2.51]; p<0.0001); more STR patients remained on therapy at 12 months (49.7% vs 36.1%) than those on MTRs. Among regimens, 62.6% of patients initiating E/C/F/TAF were still persistent at 12 months compared to 57.5% and 43.6% initiating ABC/3TC/DTG and E/C/F/TDF (STRs); there were 39.7%, and 33.5% still persistent with F/TDF +DTG and F/TDF+ boosted DRV (MTRs), respectively.

Conclusion: This study reinforces previous studies which suggested better persistence with STR versus MTR HIV regimens. In light of new therapeutic options, persistence in this commercially insured population was highest with STRs and lowest among patients using MTRs with a boosted third agent. To maximize the benefits of increased treatment durability, it's important to consider STRs versus MTRs to improve persistence when managing HIV patients.

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Superior Efficacy of Dolutegravir (DTG) Plus 2 Nucleoside Reverse Transcriptase Inhibitors (NRTIs) Compared With Lopinavir/Ritonavir (LPV/r) Plus 2 NRTIs in Second-line Treatment – Interim Data From the DAWNING Study

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Background: DAWNING is a noninferiority study conducted to compare a protease inhibitor–sparing regimen of dolutegravir (DTG) + 2 nucleoside reverse transcriptase inhibitors (NRTIs) with a current WHO-recommended regimen of lopinavir/ritonavir (LPV/r) + 2 NRTIs in HIV-1 infected participants failing first-line therapy of a non-nucleoside reverse transcriptase inhibitor (NNRTI) + 2 NRTIs (ClinicalTrials.gov: NCT02227238). An independent data monitoring committee (IDMC) performed periodic reviews of data to protect the ethical and safety interests of participants.

Methods: Adult participants failing first-line therapy, with HIV-1 RNA ≥400 copies/mL, were

randomised (1:1, stratified by Baseline plasma HIV-1 RNA and number of fully active background NRTIs) to 52 weeks of open-label treatment with DTG or LPV/r combined with an investigator-selected dual-NRTI background, including at least 1 fully active NRTI. An IDMC review was performed, which included data from 98% (612/627 randomised) of participants through 24 weeks on therapy.

Results: At Week 24, 78% (n=240) of participants on DTG versus 69% (n=210) on LPV/r achieved HIV-1 RNA <50 copies/mL (adjusted difference 9.6%, 95% CI: 2.7% to 16.4%, P=0.006 for superiority). The difference was primarily driven by lower rates of snapshot virologic nonresponse in the DTG group. The safety profile of DTG + 2 NRTIs was favourable compared with LPV/r + 2 NRTIs, with more drug-related adverse events reported in the LPV/r group, mainly because of higher rates of gastrointestinal disorders.
Following a review of Week 24 data and large subsets of data from Weeks 36 and 48, the IDMC recommended discontinuation of the LPV/r arm because of persistent differences in rates of snapshot virologic nonresponse and protocol-defined virologic failure favouring the DTG arm.

Conclusions: The IDMC recommended discontinuation of the LPV/r arm because of superior efficacy of DTG + 2 NRTIs and the potential to harm participants on LPV/r based on available data. Final Week 24 results: of this study will be presented. DAWNING provides important information to help guide second-line treatment decisions in resource-limited settings.

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INSPIRING: Safety and Efficacy of Dolutegravir-Based Antiretroviral Therapy in Tuberculosis/HIV Coinfected Adults at Week 24

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Background: Concurrent treatment of tuberculosis (TB) and HIV is complicated by drug interactions, overlapping toxicities, and immune reconstitution inflammatory syndrome (IRIS). The efficacy and safety of dolutegravir (DTG) in antiretroviral therapy (ART)–naive adults with HIV/TB coinfection were assessed.

Methods: INSPIRING (NCT02178592) is a phase IIIb, noncomparative, active-control, randomised, open-label study in HIV-1 infected ART-naive adults (CD4+ cell count ≥50 cells/µL) with drug-sensitive TB. Participants on rifampin-based TB treatment for up to 8 weeks were randomised (3:2) to receive DTG (50 mg twice daily during and for 2 weeks after TB therapy, followed by 50 mg once daily) or efavirenz (EFV; 600 mg once daily), with 2 investigator-selected nucleoside reverse transcriptase inhibitors, for 52 weeks. For this Week 24 interim analysis, the proportion of participants with plasma HIV-1 RNA <50 copies/mL was derived using the FDA snapshot algorithm in the intent-to-treat exposed population. Safety was assessed in all participants who received study drug. An independent committee adjudicated IRIS episodes. The study was not powered to show a difference between study arms; no formal statistical hypothesis was tested.

Results: Of 113 participants enrolled, 69 were randomised to DTG and 44 to EFV. Median baseline HIV-1 RNA and CD4+ cell counts were 5.10 $\log_{10}$ copies/mL and 208 cells/µL, respectively, in the DTG arm and 5.24 $\log_{10}$ copies/mL and 202 cells/µL, respectively, in the EFV arm. Forty percent of participants were women. The proportions of participants with HIV-1 RNA <50 copies/mL at Week 24 were 56/69 (81%; 95% CI: 72%, 90%) in the DTG arm and 39/44 (89%; 95% CI: 79%, 98%) in the EFV arm. The lower DTG response rate was driven by non–treatment-related snapshot failures; 5 participants (7%) in the DTG arm and 0 in the EFV arm discontinued for non–treatment-related reasons (lost to follow-up, protocol deviations). Median CD4+ cell count increases at Week 24 were 146 cells/µL (IQR: 71, 214) for DTG and 93 cells/µL (IQR: 47, 178) for EFV. Two participants discontinued study treatment because of adverse

events (both on EFV). Tuberculosis-associated IRIS rates (adjudicated and investigator reported) were low (DTG, n=4 [6%]; EFV, n=4 [9%]). No participants discontinued because of IRIS or liver events.

Conclusions: Interim Week 24 results from this ongoing study show that DTG 50 mg twice daily appears to be effective and well tolerated in HIV/TB coinfected adults receiving rifampin-based TB therapy. Rates of IRIS were low. There were no new toxicity signals for DTG and no discontinuations due to liver events. These data support the use of DTG-based regimens in HIV/TB co-infection.

most failures were due to AE in DTG group (26/27, 96.3%), DDI (18.2%) and resistance related virologic failure (9.1%) were observed as failure reasons in EVG/c group following AE (72.7%) . Most common AEs leading to regimen failure were central nervous system and gastrointestinal in both groups (37.5% and 20.8% in DTG group; 37.5% and 25.0% in EVG/c group). In Kaplan-Meier survival analysis, the durability was not different between DTG and EVG/c (p=0.346).

Conclusions: The frequency of STR regimen failure and durability were not different between DTG and EVG/c. Most STR regimen failure was due to AE in DTG group while DDI and resistance were also observed in EVG/c failure cases.

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Similar durability of DTG and EVG/c based STR

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Background:: Two integrase inhibitors (INSTIs), dolutegravir (DTG) and elvitegravir/cobicistat (EVG/c) are available in fixed-dose combinations with a nucleoside reverse transcriptase inhibitors backbone. In this study, we evaluated the durability of INSTI based STRs, DTG and EVG/c.

Materials and Methods: In November 2015, DTG based STR was introduced to National Medical Center following EVG/c based STR in 2014. Eligible cases were individuals who were on or started INSTI based STRs from November 2015 to June 2017. Demographic data and antiretroviral therapy (ART) history were retrospectively reviewed as well as ART related adverse event (AE) until December 2017. Durability was compared between DTG and EVG/c and it was considered as regimen failure in case the STR regimen was changed due to AE, resistance related virologic failure, or drug-drug interaction (DDI).

Results: During the study period, 255 INSTI based STR regimens were prescribed to 245 individuals. 157 were DTG and 98 were EVG/c. STR regimen failure was observed in 17.2% among DTG group and it was 11.2% in EVG/c group (p=0.193). While

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DTG Versus LPV/r in Second Line (DAWNING): Outcomes by WHO-Recommended NRTI Backbone

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Background: DAWNING is a noninferiority study conducted to compare dolutegravir (DTG) plus 2 nucleoside reverse transcriptase inhibitors (NRTIs) with a current World Health Organization (WHO)–recommended regimen of lopinavir/ritonavir (LPV/r) + 2 NRTIs in HIV-1 infected adult participants failing first-line therapy (HIV-1 RNA ≥400 copies/mL) of a non-nucleoside reverse transcriptase inhibitor (NNRTI) + 2 NRTIs (ClinicalTrials.gov: NCT02227238).

Methods: Participants were randomised (1:1, stratified by plasma HIV-1 RNA and number of fully active background NRTIs) to 52 weeks of open-label treatment with DTG or LPV/r combined with an

investigator-selected dual-NRTI background, including at least 1 fully active NRTI. The primary endpoint was the proportion of participants achieving HIV-1 RNA <50 copies/mL at Week 48 (FDA snapshot algorithm), with an interim analysis at Week 24. Post hoc analyses were performed to evaluate efficacy based on whether a WHO-recommended second-line NRTI backbone was chosen according to participants' first-line NRTIs; 59 participants not taking WHO-recommended first-line NRTIs were excluded.

Results: Of 968 participants screened, only 78 (8%) were screen failures because they did not have 1 fully active NRTI available; 624 participants were randomised and treated. At Week 24, DTG + 2 NRTIs was superior to LPV/r + 2 NRTIs, with 82% (257/312) and 69% (215/312) of participants, respectively, achieving HIV-1 RNA <50 copies/mL (adjusted difference 13.8%, 95% CI: 7.3% to 20.3%, P<0.001). The difference was primarily driven by lower rates of snapshot virologic nonresponse in the DTG group. Response rates were higher for the 56% (347/624) of participants who received a WHO-recommended second-line NRTI backbone than for participants who did not in both the DTG (87% vs 75%, respectively; treatment difference [95% CI], 12.0% [2.2 to 21.7]) and LPV (72% vs 66%, respectively; treatment difference [95% CI], 5.6% [−5.4 to 16.6]) treatment groups. Response rates were higher with DTG- versus LPV/r-based regimens among participants who received WHO-recommended second-line NRTIs (87% vs 72%, respectively; treatment difference [95% CI], 15.1% [6.6 to 23.5]) and those who did not (75% vs 66%, respectively; treatment difference [95% CI], 8.7% [−3.4 to 20.7]). The overall safety profile of DTG + 2 NRTIs was favourable compared with LPV/r + 2 NRTIs, with more drug-related adverse events reported in the LPV/r group. There were no treatment-emergent primary integrase strand transfer inhibitor or NRTI resistance mutations in the DTG + 2 NRTIs group by the data cutoff date for this analysis.

Conclusions: In the DAWNING study, response rates were higher with DTG versus LPV/r-based regimens, regardless of the NRTI backbone. Within each arm, participants had a higher rate of success when receiving WHO-recommended versus NRTIs not recommended by WHO. The DAWNING study provides important information to help guide second-line treatment decisions in resource-limited settings.

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Assessing the efficacy of Lopinavir /ritonavir based preferred and alternative second-line regimens on HIV-infected patients: a meta-analysis as a key evidence support for WHO recommendations

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Background: Standardize first-line and second-line regimens include nucleoside reverse-transcriptase inhibitors(NRTIs) and non-NRTI (NNRTI) with boosted protease inhibitor. Recent WHO guidelines recommend a boosted protease inhibitor (PI) combined with 2 nucleoside reverse-transcriptase inhibitors(NRTIs) or raltegravir as second-line regimen. Object: Ritonavir-boosted lopinavir (LPV/r), is known as a key medicine of second-line antiretroviral therapy(ART) in resource-limited settings. We carried out a meta-analysis in order to analyze virologic suppression and effectiveness of LPV/r based second-line therapy on HIV-infected patients.

Methods: In this meta-analysis, we searched randomized controlled trials and observational cohort studies to evaluate outcomes of second-line ART for patients with HIV who failed first-line therapy. A systematic search was conducted in Pubmed, Cochrane Library, Embase from inception to January, 2018. Outcomes included viral suppression, CD4 cell counts, drug resistance, adverse events and self-reported adherence. We assessed comparative efficacy and safety in meta-analysis. Data analysis was performed using RevMan 5.3.

Results: Nine literatures comprising 3923 patients were included in the meta-analysis. The overall success virologic suppression rate of second-line regimen was 76.75% (ITT) and 85.70%(PP) in 48 weeks, 77.06% (ITT) in 96weeks and 73.23%(ITT) in

144 weeks with the plasma HIV RNA load < 400 copies/mL. No statistical significance was found in CD4 cell counts recovery between LPV/r plus 2-3NRTIs and simplified regimens (LPV/r plus raltegravir) at 48 (P=0.09) , 96 weeks (p=0.05) and 144 weeks (P=0.73). Four studies indicated that the virus has low-level resistance to LPV/r , and the most common clinically significant PI-resistance mutations are 46I, 54V, 82A/82F and 76V, however, no virologic failure due to LPV/r resistance was detected. In addition, no statistical significance was found between two groups in self-reported adherence (RR=1.03, 95% CI 1.00, 1.07, P=0.06), grade 3 or 4 adverse events (RR=0.84, 95% CI 0.64, 1.10, P=0.20) and serious events (RR=0.85, 95% CI 0.77, 1.17, P=0.62).

Conclusions: These results suggest that the LPV/r-based regimen demonstrated efficacious and low resistance as second-line antiretroviral therapy. LPV/r plus 2-3NRTIs and LPV/r plus RAL regimens are both improve CD4 cell counts, there was no evidence of superiority of simplified regimens over LPV/r plus 2-3NRTIs.

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Comparative efficacy and safety of raltegravir-based simplified regimens for people living with HIV: a meta-analysis of randomized controlled trials

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Background: and **Objective:** Simplifying antiretroviral therapy (ART) enhances tolerability, decreases toxicities and reduces costs. However, more evidence is still needed to demonstrate the benefit and risk of simplified ART regimens. This study is to evaluate the efficacy and safety of simplified ART regimens based on raltegravir (RAL) for people living with HIV.

Methods: We systematically searched electronic databases to identify RAL-based randomized controlled trials (RCTs) containing only two drugs and then compared the efficacy and safety between RAL-based simplified regimens and traditional protease inhibitor-based three-drug or four-drug regimens. Outcomes were included viral suppression, CD4 cell counts and so on. We pooled data across studies and estimated summary effect sizes. The included data were analyzed using Review Manager 5.3 software.

Results: Eight RCTs involving 4327 patients with HIV-1 infection were included in this study, 2570 patients receiving RAL plus ritonavir-boosted protease inhibitors (PIs/r) were compared with combined with 2511 patients receiving PIs/r plus two or three nucleoside reverse-transcriptase inhibitors (NRTIs). The viral suppression rates of RAL-based simplified regimens were 66.7% (intention-to-treat, ITT) and 70.4% (per protocol, PP) at 24 weeks, 78.8% (ITT) and 75.2% (PP) at 48 weeks, 73.6% (ITT) and 81.4% (PP) at 96 weeks respectively, while the viral suppression rates of PIs/r plus two or three NRTIs (NRTIs-based regimens) were 66.7% (ITT) and 70.4% (PP) at 24 weeks, 78.4% (ITT) and 73.5% (PP) at 48weeks, 71.1% (ITT) and 79.8% (PP) at 96 weeks respectively. At 24 weeks, the efficacy of RAL-based two-drug regimens was greater than that of PIs/r plus two or three NRTIs(ITT) (risk ratio 1.11, 95% CrI [1.02, 1.21], P=0.01). Patients had significantly higher CD4 cell counts compared with those receiving NRTIs-based three-drug or four-drug regimens at 48 weeks and 96 weeks. RAL-based simplified regimens had less grade 3 or 4 adverse events than traditional NRTIs-based regimens at 48 week(P=0.007).

Conclusion: The results of this meta-analysis supported that regimens containing RAL plus ritonavir-boosted PIs were non-inferior to regimens containing boosted PIs/r plus two or three NRTIs in viral suppression. However, simplified regimens resulted in better CD4 cell counts levels and lower adverse events.

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First Line Antiretroviral Treatment Failure: Prevalence and Associated Risk Factors in Non-governmental Hospital in Cambodia

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Background: The aim of antiretroviral therapy (ART) was to sustain viral suppression and brought HIV/AIDS related disease under control. While ART were universal assessed the key challenge of HIV program in low and middle income countries is the first line treatment failure. There are few studies had assessed to the long-term use of first line HAART in resource-limited countries. We aim to describe the prevalence of first line ART treatment failure and its associated factors in HIV program in Cambodia.

Methods: We conducted a retrospective descriptive analysis of HIV program data in a non-governmental hospital in Phnom Penh, Cambodia. We included all ART naïve adult (age >18 years old) who enrolled in HIV program from 1st January 2003 to 31st December 2017 into the analysis. Treatment failure was define according to WHO as patient had HIV viral load >1,000 copies/ml. Criteria to start standard first line and switching to second line ART regimen based on WHO guideline. Data was analyzed by using STATA version 13.

Results: Over the 13 years period, 3,789 patients were initiated first line ART. The median age was 44 years (IQR 38-50), 54% (2,064/3,789) were female and 60% (2,292/3,789) were presented with WHO clinical stage 3 and 4. The median CD4 cell count at ART initiation were 137 (IQR 39-327). Among all patients, 6% (227/3,789) were switched to second line treatment due to first line ART failure. Of all first line treatment failure patients, 55% (124/227) were male (P: 0.005) 73% (166/227) age between 35 to 55 years old and 72% (163/227) had WHO clinical stage 3 and 4 (P: 0.004) at the time of switching to second line treatment. Median time to first line ART treatment failure was 2.4 years (IQR 1.4- 4.3). Among all ART failure patients the median CD4 cell count at the enrolment were 43 (IQR 18-155) and increase to 136 (IQR 63-247) at the time of treatment failure. For those with ART and those without ART experience the percentage of failure were 18% (62/351), 5% (165/3,435) respectively (P: 0.001). Regarding to first line ART regimen, failure was found in 10% (132/1,287) in Nevirapine base, 4% (92/2,334) in Efavirenz and 4% (1/23) in triple nuke base regimen (P: 0.001).

Conclusion: In this study, the prevalence of first line treatment failure was 6%. Being male, history of ART exposure, and NVP based first line ART regimen, low CD4 cell count were associated risk factor of treatment failure. Develop WHO clinical stage 3 and 4 after initiation fist line ART was predictor of treatment failure. Further study should be conducted in all OIs/ART sites in Cambodia for its generalizability.

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High Prevalence Rate of Antiretroviral Drug Resistance in HIV Infected Patients with Virological Failure in Taiwan

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Objectives: Few data are available for resistance prevalence among HIV-1 infected patients with virological failure in Taiwan, especially after the implementation of integrase strand transfer inhibitors (INSTIs) in the treatment of HIV-1 infected individuals in recent years. The aim of the present study was to monitor the prevalence of HIV drug resistance in treatment-experienced patients to guide the antiretroviral therapy in Taiwan.

Methods: A retrospective cohort study on prevalence of HIV-1 drug resistance in HIV-1 infected patients with virological failure was conducted in Taiwan from January 2013 to Dec 2017. Resistance testing for PR/RT (pol gene) was performed on plasma samples using the ViroSeq HIV-1 Genotyping System. INSTI resistance was determined by the in house population sequencing. Anti-retroviral resistance mutations were defined using the 2017 IAS-USA HIV drug resistance algorithm, while drug resistances were compared by using the HIVdb program of the Stanford University HIV Drug Resistance Database.

Results: A total of 52 HIV-1 infected treatment failure patients had tested for resistance, of whom 90% were infected by MSM. Subtype B HIV-1strains were found in 92% of the individuals. The resistance rates to any 4 classes of antiretroviral therapy (NRTI, NNRTI, PI and INSTI) were 77%. The prevalence rate for NRTI, NNRTI, PI and INSTI resistance was 65%, 48%, 12% and 37%, respectively. The most common

NRTI resistance associated mutation was M184V (59.6%), K219E (11.5%) and D67N (11.5%). For NNRTI resistance associated mutation, they were K103N (17.3%) and Y181C (17.3%). The most PI resistance associated mutation was M46I (5.8%), I84V (3.8%) and L90M (3.8%). For INSTI resistance associated mutations, they were G140S (17.3%) and Q148H (17.3%). Twenty-five percent of the patients with treatment failure had cross resistance to dolutegravir.

Conclusion: Our findings showed the high rate of HIV drug resistance (77%) to any four classes of antiretroviral regimens in treatment failure patients. With the widely use of INSTI in recent years, routine viral load monitoring and early genotypic drug resistance testing were mandatory to combat resistance.

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Accumulation of HIV Drug Resistance Mutations after Multiple Treatment Failures in A Resource-limited Setting

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Background: Antiretroviral therapy (ART) has led to better survival and quality of life in HIV-infected patients in resource-limited settings. After over a decade of scaling up of ART, treatment failure has emerged and some patients have experienced multiple treatment failures. This study aimed to compare the number and patterns of HIV drug resistance-associated mutations (RAMs) between patients single and multiple treatment failures.

Methods: An observational cohort study was conducted in HIV-infected patients who had treatment failure in a medical-school hospital. HIV genotypic resistance test was performed at treatment failure. Patients were categorized into two groups: patients with single failure (Group A) and those with multiple failures (Group B). All RAMs

according to the IAS–USA drug resistance mutations list in 2017 were analyzed and compared between the two groups.

Results: A total of 141 patients were studied. Mean age was 39.8±11.9 years and 62.4% were males. Of all, 106 (75.2%) patients were in Group A. Of 35 in group B, 21 (60%), 7 (20%) and 7 (20%) patients had treatment failures of 2, 3 and 4 regimens, respectively. Of all, 66.7% had NNRTI-based ART as first-line regimens. Among patients in Group B, PI-based ART was mostly used (75.9%) in second-line regimens, and darunavir/ritonavir and raltegravir were used in third-line and forth-line regimens. Demographics, risk of HIV acquisition, HBV or HCV co-infection, first ART regimen, CD4 cell count and HIV RNA were similar between the two groups (p >0.05). Median (IQR) duration of ART in Group B was significantly longer than that in Group A (6.6 vs 2.4 years, p <0.001). NRTI-RAMs more commonly observed in Group B included TAMs (71.4% vs 36.8%, p <0.001), M184V/I (100% vs 67.0%, p <0.001) and K65R (20.0% vs 6.8%, p=0.022). This resulted in higher rate of resistance to abacavir (60.0% vs 46.2%, p=0.006), lamivudine (100% vs 79.2%, p=0.013), tenofovir (51.4% vs 30.2%, p=0.023) and zidovudine (57.1% vs 34.0%, p=0.015) in Group B. NNRTI-RAMs were found at high rate in both groups (97.1% vs 92.5%, p=0.325) and resulted in high rate of resistance to efavirenz, nevirapine and rilpivirine in both groups (all >90%, p >0.05). Etravirine resistance in Group B was slightly higher in Group B but not statistically significant (54.3% vs 49.1%, p=0.592). Major PI-RAMs including M46I/L, I47V/A, G48V, I50L/V, I54M/L, L76V, V82A, I84V and L90M were more frequently observed in Group B (all p <0.05) and led to a higher rate of PI resistance in Group B (71.4% vs 16.0%, p <0.001).

Conclusion: Accumulation of HIV RAMs after multiple treatment failures is common in resource-limited setting. Options of the further regimens of ART are markedly limited. Intervention to prevent the development of HIV drug resistance in patients receiving ART is mandatory. Access to newer antiretroviral agents for HIV-infected patients with multiple treatment failure is crucial for scaling up of ART in resource-limited settings.

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Kidney dysfunction related to combination antiretroviral therapy containing tenofovir disoproxil fumarate/emtricitabine among HIV-positive patients in Taiwan

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Background: While combination antiretroviral therapy (CART) containing tenofovir disoproxil fumarate (TDF) may be associated with kidney dysfunction among HIV-positive patients, such data on kidney dysfunction among HIV-positive patients receiving TDF/emtricitabine (FTC)-containing regimens are relatively limited in Asia-Pacific region.

Materials and Methods: Between 12 May, 2015 and 31 March, 2017, HIV-positive patients with available baseline estimated glomerular filtration rate (eGFR) who were switched to or initiated TDF/FTC-containing regimens were included for assessing the trends of eGFR overtime. Five categories of cART were defined: TDF/FTC plus boosted protease inhibitor (PI); TDF/FTC plus unboosted atazanavir; TDF/FTC plus efavirenz or nevirapine; TDF/FTC plus rilpivirine; and TDF/FTC plus raltegravir. The endpoint for kidney dysfunction was defined as a decline of eGFR to less than 60 ml/min/1.73m2 for those with eGFR of 60 ml/min/1.73m2 or greater before switch; or a decline of eGFR by 25% or greater for those with eGFR<60 ml/min/1.73m2. The patients were observed until the end of the study on 30 March, 2018, loss to follow-up or death, or discontinuation of TDF, whichever occurred first. Time to the endpoint of kidney dysfunction was shown by Kaplan-Meier plot and Cox proportional hazards models were used to identify factors associated with kidney dysfunction after switch to or initiation of TDF/FTC-containing regimens.

Results: During the study period, 1224 HIV-positive patients switching to (n=1032) or initiating (n=192) TDF/FTC-containing regimens were included; of them, the mean age was 41.3 years (standard deviation [SD], 10.9), 95.5% were male, 89.6% were men who have sex with men, 18.9% had chronic hepatitis B infection and 8.6% tested positive for anti-HCV antibody. The plasma HIV RNA load was 1.99 (SD, 1.37) log10 copies/ml and CD4 count 579 (SD, 294) cells/mm3. Baseline eGFR was 103.2 (SD, 23.04) ml/min/1.73m2, with 19 patients (1.6%) having eGFR less than 60 ml/min/1.73m2. CART included TDF/FTC plus boosted PI (n=222), unboosted atazanavir (301), nevirapine or efavirenz (479), rilpivirine (136), and raltegravir (86). Diabetes mellitus was present before switch in 2.7%, 7.3%, 2.7%, 3.7%, and 9.3%, of the patients receiving TDF/FTC plus boosted PI, unboosted atazanavir, nevirapine or efavirenz, rilpivirine, and raltegravir, respectively. The mean follow-up duration was 115.5 weeks (SD, 38.4). Overall, 49 patients (4.0%) reached endpoints: 43 (3.5%) because of a decline of eGFR from baseline to less than 60 ml/min/1.73m2 and 6 (0.5%) because of a decline of eGFR by 25% from baseline. The rate of kidney dysfunction was 4.5%, 7.0%, 1.9%, 2.2% and 7.0% for patients receiving TDF/FTC plus boosted PI, unboosted atazanavir, nevirapine or efavirenz, rilpivirine, and raltegravir, respectively. In multivariate analysis, we found that age (per 1-year increase, adjusted hazard ratio [aHR], 1.083 [95% CI, 1.058, 1.109]) and receiving TDF/FTC plus nevirapine or efavirenz (vs TDF/FTC plus raltegravir, aHR, 0.289 [95% CI, 0.102-0.821]) were associated with kidney dysfunction.

Conclusions: We conclude that kidney dysfunction related to short-term exposure to TDF/FTC-containing regimens remains infrequent among HIV-positive Taiwanese patients. Compared with patients receiving TDF/FTC plus raltegravir, patients receiving regimens containing TDF/FTC plus nevirapine or efavirenz were less likely to develop kidney dysfunction.

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Platelet Function Upon Switching to TAF Vs Continuing ABC: A Randomized Substudy

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Background: Abacavir (ABC) use has been associated with increased risk of myocardial infarction (MI), with altered endothelial and platelet function as proposed underlying mechanisms. We hypothesized that a switch from ABC to tenofovir alafenamide (TAF) would result in decreased platelet reactivity.

Material & Methods: In a platelet function substudy of a randomized double-blind trial of virally suppressed, HIV1-positive individuals on ABC/lamivudine (3TC), randomized to switch to TAF/emtricitabine (FTC) or remain on ABC/3TC while continuing their 3rd agent, we measured platelet aggregation (PAg) at baseline (BL), week (wk) 4, and 12 in response to increasing concentrations of five agonists: collagen (Col), thrombin receptor-activating peptide (TRAP), adenosine diphosphate (ADP), epinephrine (Epi) and arachidonic acid (AA). We compared population-derived agonist concentrations inducing 50% platelet aggregation (EC50) between-groups at BL, wk4 and 12 by four parameter logistic regression. We measured platelet surface expression of the GPVI receptor, CD42b and P-selectin (P-sel) by flow cytometry and compared between-group differences at BL and wk12 pre- and post-stimulation with collagen-related peptide (CRP) by Wilcoxon rank sum test.

Results: The 61 participants (29 in TAF/FTC and 32 in ABC/3TC group) were well matched at BL. Although baseline PAg in response to Col, TRAP and ADP was similar between groups, wk4 PAg with Col, TRAP and ADP was significantly lower in the TAF/FTC arm (reflected by greater EC50) compared to the ABC/3TC arm. Reduced PAg in response to Col persisted through wk12, while differences in PAg with TRAP and ADP were no longer significant at wk12. PAg with Epi and AA did not differ between groups at any time point. Expression of the collagen receptor GPVI, which mediates endothelial-platelet interactions, was higher at wk12 in the TAF/FTC group (P=0.031) while wk12 GP42b and P-sel were similar between groups (P=0.10, P=0.8). There were no between-group differences in GPVI shedding or induction of P-sel with CRP activation (all P>0.1).

Conclusions: Within a randomised trial, switching from ABC/3TC to TAF/FTC was associated with significantly lower platelet reactivity to TRAP and ADP at W4 and Col through W12. Together with higher surface GPVI expression, these observations suggest improvements in measures of platelet function involving endothelial-platelet pathways with a switch from ABC/3TC and point to a potential underlying mechanism for increased risk of MI with ABC.

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Comparing Strategies for Reducing Myocardial Infarction Rates in HIV Patients

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Background: Studies show higher rates of myocardial infarctions (MI) with HIV and aging. Abacavir (ABC) has also been associated in some studies with an increased risk of cardiovascular (CV) events. To assess the relative impact of one intervention to reduce MI risk in HIV patients versus another, we modelled the impact of interventions that address traditional risk factors and replacing ABC on predicted MI rates. While other HIV antivirals have been associated with elevated MI risk, we used ABC as an example of the impact of changing HIV treatment in addition to a focus on traditional risk factors.

Materials & Methods: Strategies for reducing MI rates in HIV patients were compared over 10 years using a decision tree model. Assumptions about the effectiveness of smoking cessation counseling, substitution of ABC with an alternative regimen, anti-hypertensive and anti-hyperlipidemia medication use were based on publications from the HIV or general population. We adjusted for sex, age, and presence of the four MI risk factors. Interventions were compared based on published data on the probability of success of changing the risk factor and the impact of changing it when successful. For smoking cessation, the impact was

based on published quit rates following counseling, 36.5% after one year and 10% annual relapse rate.

Results: In the base case of 50-year old HIV positive male smokers who only replaced ABC, there was a 46% reduction in the MI rate compared to those who continued ABC (0.31/ 100 vs. 0.58/ 100 PY). Men who were counseled and treated for smoking cessation resulted in an 11% MI rate reduction versus those who did not attempt smoking cessation (0.52/ 100 vs. 0.58/ 100 PY). Over 10 years, compared to no MI intervention, ABC substitution prevented more MIs than counseling about smoking (2.64 vs 0.63 MIs per 100 persons). The impact of treating hypertension and hyperlipidemia was a 19% and 31% reduction in MI risk, respectively.

Conclusions: By incorporating the impact of CV risk factor modification based on real world data, this model suggests that replacing ABC, which can be accomplished in most patients, is potentially more impactful in reducing MI risk than interventions solely on traditional risk factors. While this model does not account for all tobacco risks, findings highlight the role that ABC substitution can have on MI risk over time compared to antismoking, hypertension and lipid lowering interventions. Interventions to address all CV risk factors are warranted.

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HIV-associated bacterial bloodstream infections in Cambodian adults: key pathogens and resistance patterns

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Background: In the combined antiretroviral therapy era, HIV-infected patients remain a vulnerable population for the onset of bacterial bloodstream infections (BSI) worldwide. However, data on HIV-infected patients presented with sepsis are scarce in developing countries. We describe key pathogens and their resistance patterns isolated from HIV-associated bacterial BSI in Cambodian adults.

Methods: We retrospectively reviewed the results of bacterial culture among all HIV-infected patients presenting with Systemic Inflammatory Response Syndrome (SIRS) as part of surveillance data of antibiotic resistance at Sihanouk Hospital Centre of HOPE (SHCH), Phnom Penh, Cambodia between January 2013 and December 2017. Cultures and isolate identification were performed by conventional methods antibiotic susceptibilities were assessed using disk diffusion and MicroScanH®, with additional E-test, D-test and double disk test where applicable, according to CLSI guidelines.

Results: A total of 125 blood samples with bacterial BSI from 105 HIV-infected patients (out of 4805 HIV-infected patients) were included. Among the included patients, median age was 39 years (range 19-64y), 58.7% were women, median CD4 cell count was 301cells/mm3, 55.2% patients on highly active antiretroviral therapy (HAART), and 24% viral loads were undetected at the time of sepsis. The main co-morbidity diseases include tuberculosis (n=10; 9.5 %), diabetes (n=8; 7.6 %), renal disease (n=3, 2.8%). Key bacterial pathogens included Escherichia coli (n = 49; 39.2 %), Salmonella spp. (n=29; 23.2 %), Staphylococcus aureus (n = 16; 12.8 %), and Klebsiella pneumoniae (n = 10; 8 %). Among the Salmonella spp, Salmonella Paratyphi A were predominant since 2013 (n=13). For resistance patterns, among the Escherichia coli isolates, we noted combined resistance to amoxicillin, sulphamethoxazole/trimethoprim (SMX-TMP) and ciprofloxacin in 27 isolates (55.1%); and 33 isolates (67.3%) were confirmed as producers of extended spectrum beta-lactamase (ESBL). All Salmonella isolates displayed high rates of decreased ciprofloxacin susceptibility (72.4%); 6 isolates (20.6%) were resistant to SMX-TMP; 5 Salmonella isolates (17.2%) had combined resistance to amoxicillin, SMX-TMP and ciprofloxacin; but all Salmonella isolates still have good susceptibility to ceftriaxone. Half of Klebsiella pneumoniae isolates had resistance to ceftriaxone. Methicillin resistance was seen in 9/16 (56.2%) S. aureus; 4 of them were co-resistant to erythromycin, lincomycin and SMX-TMP. The overall mortality was 16.8%.

Conclusion: Bacterial BSI for HIV-infected patients in Cambodian adults is mainly caused by difficult-to-treat pathogens. These data should be taken into account in the redaction of local treatment guidelines, nationwide surveillance and solid interventions to contain antibiotic resistance among HIV-infected patients.

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TB incidence among HIV-patients tested positive at baseline LTBI screening

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Background: Baseline latent TB infection (LTBI) screening among HIV patients could identify patients for timely treatment to reduce co-morbidities. HIV Patients without active TB but screened LTBI positive at baseline might continue to be at risk of TB reactivation over time. We aim at examining the risk factors of TB disease development among these patients.

Material & Methods: This is a retrospective observational cohort study with clinical and LTBI screening (mainly tuberculin skin testing) data of HIV patients accessed from the Integrated Treatment Centre, the largest HIV clinical service with a caseload of >3000 in Hong Kong. We included patients who were diagnosed with HIV between 2002 and mid-2017, aged 18 or above, and screened LTBI positive at baseline. Active TB cases (diagnosed with TB within 3 months of HIV diagnosis) were further excluded. Cox proportional hazard regression analyses were used to identify risk factors of TB disease development during follow-up.

Results: Among 2407 HIV-patients screened for baseline LTBI in the study period, 284 (12%) were positive. With 1748 person-years (PY) follow-up, the TB incidence from HIV diagnosis among patients screened LTBI positive at baseline was 1.43/100 PY (25 cases, 95%C.I. = 0.95 to 2.08). With 13518 PY follow-up, the TB incidence of patients screened LTBI negative at baseline was 0.21/100 PY (28 cases, 95%C.I. = 0.14 to 0.30). Among 284 patients tested LTBI positive at baseline, 253 (89%) were male, 208 (73%) were Chinese, 239 (84%) were local residents, 14 (5%) were diagnosed with diabetes mellitus (DM), and 214 (75%) received LTBI treatment (Isoniazid preventive therapy). TB incidence from HIV diagnosis was 0.48/100PY among patients received LTBI treatment and 6.12/100PY among those without treatment. At HIV diagnosis, 89% of these patients (n=284) were aged 18-49. Patients who were local residents (hazard ratio (HR)=0.25, 95% C.I.=0.11 to 0.55), Chinese (HR=0.27, 95% C.I.=0.12 to 0.59), who had higher baseline CD4 count (cells/µL) (HR=0.997, 95% C.I.=0.99 to 0.999) but lower baseline log10 viral load (copies/mL) (HR=0.33, 95%C.I.=0.19 to 0.57) were at lower risk of subsequent TB disease development. Patients who had received LTBI treatment (HR=0.15, 95%C.I.=0.06 to 0.37) were at lower risk of TB disease development. Seven patients (3%) were diagnosed with TB disease despite LTBI treatment, after a median follow-up period of 25 months (ranged 13-77 months). Overall, gender, history of DM diagnosis, age at HIV diagnosis, and body mass index were not significant risk factors of TB disease development among these patients.

Conclusion: TB incidence was 5-fold higher among HIV patients screened positive compared to those negative at baseline LTBI test. The risk was significantly lower after LTBI treatment, but the TB incidence remained higher than those screened LTBI negative. HIV patients screened LTBI positive at baseline deserve frequent attention and regular monitoring to reduce co-morbidity.

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Psychosocial domains contribute to frailty among HIV-infected individuals in Malaysia independent of assessment tool

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Background: Frailty is a state reflecting age-related, multidimensional decline leading to physical dysfunction, increased healthcare utilization and risk of death. Applicability of different frailty tools developed for the general population on HIV-

infected individuals is ambiguous. Our aims were to compare various health domains that characterize frailty determined by three frailty instruments; and investigate associations between frailty and negative health outcomes in HIV-infected individuals on stable antiretroviral therapy (ART).

Material and Methods: Frailty was assessed among participants of the Malaysian HIV and Aging cohort recruited in clinic with the following criteria; aged >25 years, on suppressive ART for at least 12 months, not pregnant and no acute illness at recruitment. Three instruments were used; (i) Frailty Phenotype, FP (ii) FRAIL Scale, FS (iii) Frailty Index, FI. Frailty status was ranked according to frail, pre-frail and robust to ease comparison. FI, known as the accumulation of deficits index was used as a common point of comparison among individuals categorized by frailty status using all instruments. It was calculated by number of frailty 'deficits' divided by total sum of variables. These deficits were distributed into domains of (i)physical/physiological, (ii)functional and (iii)psychosocial; whereby the proportional dominance of every domain was calculated by dividing the frequency of deficits in each domain over the total sum in all domains according to frailty status. Regression analyses were used to explore health-related frailty outcomes.

Results: We recruited 336 HIV-infected individuals. The majority were male (83%), Chinese (71%), with a median (IQR) age of 44(37-51) years and median CD4 T-cell count was 561(397-738) cells/μl. Using FP, 7% were considered frail, 56% pre-frail and 36% robust. Comparatively, FS found 16% frail, 53% pre-frail and 31% robust while FI identified 22% frail, 38% pre-frail and 40% robust. Frail individuals showed poorer social participation (FP:46%, FS:41%, FI:50%) and were more depressed (FP:60%, FS:44%, FI:65%) compared to pre-frail and robust regardless of instrument used. Poor consistency between instruments was depicted by the small number identified as frail (n=10) by all three instruments. Proportions of accumulated deficits in, psychosocial, functional and physical/physiological domains of each instrument were almost equally distributed among frail individuals (FP: 32.4%, 32.4% & 35.2%; FS: 31.6%, 34.8% & 33.5%; FI: 34.6%, 30.3% & 35.1%, respectively). In all three instruments, proportions of physical/physiological domains decreased from robust to frail. Conversely, in both FS and FI, proportions of psychosocial deficits increased from pre-frail to frail (FS: 29.6% vs 31.6%; FI: 32.3% vs 34.6%, respectively), while FP reported a small decline (33.2% vs 32.4%,

respectively). Healthcare utilization and functional disability were associated with frailty using FS and FI (p<0.005 for all) while QOL was associated with frailty when using FP (p=0.001) and FI (p<0.001).

Conclusion: Regardless of the frailty instrument used, psychosocial characteristics were equally dominant to physical/physiological and functional characteristics in frail HIV-infected individuals in Malaysia. In contributing to this condition, higher prevalence of social isolation and depression among frail individuals further highlight the importance of psychosocial influence on this population. Frailty was associated with negative health outcomes in all instruments used.

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Impact of HIV infection on epidemiology and outcome of blood stream infection in Cambodia

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BACKGROUND: Bloodstream infection (BSI) is an important cause of morbidity and mortality worldwide. HIV-infected patients are at increased risk of BSI, but data from developing countries are scarce. We observe the bacterial pathogens, the antibiotic resistance and treatment outcome for HIV-positive patients as compared to HIV-negative patients.

METHODS: Blood cultures were systematically performed in all patients suspected of BSI as part of surveillance of antibiotic resistance in Sihanouk Hospital Center HOPE, Phnom Penh, Cambodia. All patients with positive blood culture were prospectively recorded in a clinical logbook, and entered into a surveillance database, including demographic, microbiological and clinical data (including HIV status) with treatment outcome. We retrieved the data between January 2009 and December 2017 for analysis. The repeat culture performed more than 14 days after the initial one and grown an identical pathogen was considered as a new BSI episode and called as recurrent infection.

RESULTS: Of the 1614 patients having confirmed 1757 BSI episodes with true positive blood culture, 199 patients (12.3%) were HIV-positive with 239 BSI episodes (13.7%). The median CD4 value for HIV-positive patients was 199 cells/μL (IQR=33 - 416). Overall exposure to any antibiotics at the time of blood culture was 44.7% with similar proportion in HIV-positive and HIV-negative patients. There were more underlying diseases among HIV-negative patients: diabetes (27.9% vs 3.8%; p <0.001), chronic liver diseases (18.0% vs 2.1%; p < 0.001) and chronic renal disease (4.4% vs 1.2%; p=0.02). Gram-negative pathogens were more common in both HIV-positive and HIV-negative patients (78.2% and 82.2% respectively). Escherichia coli was overall the most common pathogen (n=565, 32.1%) and more frequent among HIV-positive patients (38.4% vs 31.2%; p=0.03). Staphylococcus aureus (14.2% vs 6.3%; p<0.001) and Salmonella Choleraesuis (3.8% vs 0.5%; p<0.001) were also more common in HIV-positive patients while Burkholderia pseudomallei and Salmonella Paratyphi A were more frequent in HIV-negative patients (10.3% vs 1.7% and 15.4% vs 6.7% respectively; p<0.001). Resistance rates to the commonly used antibiotics were high in both HIV-positive and HIV-negative patients, especially in Gram-negative bacteria. Overall, Echerichia coli presented Expanded Spectrum Beta-lactamase (ESBL) in 58.6% with similar rate in both patient groups while methycellin resistance Staphylococcus aureus (MRSA) were higher in HIV-positive patients (48.5% vs 28.1%; p<0.001). The overall mortality rate was 16.6% which was similar in both patients groups. In a sub-analysis of patients without the three underlying diseases (diabetes, chronic liver disease and chronic renal disease) which were more common in HIV-negative patients, there was a trend of worse outcome among HIV-positive patients compared to HIV-negative patients (14.4% vs 10.5%; p=0.051). Recurrent infection was also observed more frequently in the former patient group (8.4% vs 3.0%; p<0.001).

CONCLUSION: HIV-positive patients were more likely to have BSI with Escherichia coli, Salmonella Choleraesuis and Staphyloccus aureus and were more at risk for recurrent infections. While overall resistance patterns to antibiotics were high, HIV-positive patients had higher risk of MRSA. HIV-infection had negative impact on outcome of BSI, often with difficult to treat pathogens.

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HIV-associated neurocognitive disorder among HIV/AIDS patients in the highly active antiretroviral therapy (HAART) era in Vietnam: Implications for integrating with mental health care and treatment services

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Background:s: HIV-associated neurocognitive disorder (HAND) has been well-documented as an emerging comorbidity, which may associated with early mortality and cognitive impairment in HIV-infected people. This study assessed the prevalence of HAND and influenced factors among HIV/AIDS patients under ART in Vietnam.

Material & Methods: We enrolled 958 HIV-infected patients under care and treatment at Bach Mai hospital to participate in the study. Patients was self-reported about their level of HIV-associated dementia (HAD) and depression using The International HIV Dementia Scale (IHDS) and PHQ-9 Depression Test Questionnaire. Grooved Pegboard Test was also employed to screen for asymptomatic neurocognitive impairment among respondents (ANI). Multivariate logistic regression was performed to explore the factors related to outcomes of interest.

Results: In our sample, there were about 39.04%, 19.21%, and 8.04% of patients reported the symptoms of memory loss, slow-thinking, and difficulty in concentrating, respectively. Meanwhile, the mean IHDS total score among respondents was 10.01 (SD=1.23), with about 54% of them has considered as having HAD (cut-off of IHDS total score < or = 10). However, we found a significantly lower prevalence of depression according to PHQ-9 instrument (only 0.31%). About Grooved Pegboard Test, our results showed that the mean score for left-handed patients was 93.48 (SD=14.47), and for right-handed patients was 89.56 (SD=14.5). Compared to reference points, the estimation of patients having ANI was relatively low at 0.42%. In multivariate logistic regression, factors associated with HAD included female, older, lower education

level, had history of drug use, and currently used abacavir-contained regimen.

Conclusions: Our finding indicated a high proportion of HIV/AIDS patients under ART in Vietnam with HIV-associated dementia. This study suggested co-providing mental health counseling and treatment services with ART is necessary for people living with HIV.

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Early detection of anal cancer in men who have sex with men (MSM) living with HIV by incorporating digital ano-rectal examinations (DARE) into routine HIV care: a prospective cohort study

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Background: MSM living with HIV have the highest risk for anal cancer. The majority of anal cancers are detected in late stages where morbidity and mortality are high. We provide 'real-world' data on the feasibility of incorporating regular DARE into routine HIV care for MSM living with HIV.We monitored the referral rate to colorectal specialists, which may be a driver of cost.

Methods: In 2014, we recruited 327 MSM living with HIV, aged 35 and above, from Melbourne, Australia. Men were recruited from one major sexual health centre(n=187), two high HIV caseload general practices(n=118) and one tertiary hospital(n=22). Men were followed for two years and DARE was recommended at baseline, year 1 and year 2. Data were collected regarding patient and physician experience, and health service use. An ordered logit model was used to assess the relationship between sociodemographic factors and the number of DAREs received (1, 2 or 3). Potential confounding factors such as the site of recruitment, income level and HIV duration were adjusted for.

Results: Men had a mean age of 51 (SD+9) years, were Australian born (69%), current smokers (32%), and had a mean CD4 of 630 (SD+265) cells per mm3, with no significant differences between clinical sites. Overall, 232(71%) men received all three DAREs, 71(22%) received two DAREs, and 24(7%) only had one DARE. The referral rate to a colorectal surgeon was 3.8 referrals per 100 DAREs: lowest in the sexual health clinic (1.7/100 DARE), followed by GP clinics (5.6/100 DARE) and the tertiary hospital (13.2/100 DARE, P=0.01). One stage 1 anal cancer and eight anal intraepithelial lesions were detected. Receiving a greater number of DAREs was associated with: age >50 years (adjusted odds ratio(AOR)=1.98, 95%CI:1.10-3.55), ex-smoker(AOR=`2.32, 95%CI:1.17-4.56), and current smoker(AOR=2.00, 95%CI:1.00-3.98).

Conclusion: Integrating an early cancer detection program into routine HIV clinical care is feasible, particularly in settings where anal cytology and high-resolution anoscopy services are unavailable. Though referral rates to colorectal surgeons remained low over the two years, there was heterogeneity depending on site of recruitment. An education program to up-skill HIV physicians in early anal cancer detection could reduce the number of referrals.

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Reduced ovarian reserve in Chinese reproductive women with HIV infection

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Background: HIV-positive women are more prone to be infertile and earlier to go into menopause than HIV-negative women. Anti-Müllerian Hormone (AMH) has been proposed as a biomarker of ovarian reserve and gonadal aging. We aimed here to analyze the ovarian reserve function of HIV-positive fertile women by quantifying serum AMH levels and explore its correlation with CD4+ cell counts.

Methods: Totally 70 HIV-positive women aged 18~39 years (study group) regarded as the

reproductive age in the clinic of a tertiary hospital in Guangzhou were recruited between 2016 January to December, and 30 HIV -negative healthy women were enlisted as control group. Plasma AMH level and CD4+ cell counts were assayed.

Results: The average age of 70 HIV-positive women was comparable with that of 30 controls (32.6±5.0 vs 33.4±4.5 years old, t=-0.805, P=0.423). The AMH level of the study group was significantly lower than that of the control group [0.940（0.000~14.382）vs 2.973（0.270~8.300）ng/ml, Z=-3.937 P=0.000]. Among 70 HIV-positive women, 31 had CD4+ cell counts less than 200 /ul with the median CD4+ cell count being 64 cells/ul (range: 3~199 cells/ul), and the others had CD4+ cell counts between 200 and 500 cells/ul with the median CD4+ cell counts being 265 cells/ul /ul (range: 213~499 cells/ul). The AMH level of 31 patients with CD4+ cell counts less than 200 cells/ul was significantly lower than that of 39 patients with CD4+ cell counts between 200 and 500 cells/ul [0.013（0.000~14.382）ng/ml vs 1.511 (0.000~9.410）ng/ml, χ^2=15.486，P=0.000], however, the AMH level of 39 patients with CD4+ cell counts between 200 and 500 cells/ul was not statistically lower than that of 30 HIV -negative healthy women（χ^2=4.748，P=0.06).

Conclusion: Chinese HIV-positive fertile women had despaired ovarian reserve function, and the AMH level was associated with their CD4+ cell count.

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PROGNOSTIC VALUES OF CD4 COUNT, ANEMIA, AND LIVER FIBROSIS STAGE FOR FIVE-YEARS SURVIVAL OF HIV/HCV COINFECTED PATIENTS ON HIGHLY ACTIVE ANTI RETROVIRAL THERAPY

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Introduction: Human Immunodeficiency Virus (HIV)/Hepatitis C virus (HCV) coinfection accelerates liver fibrosis progression to end-stage liver disease and mortality. Liver disease due to chronic hepatitis virus is the most frequent cause of non AIDS–related death among persons with HIV on anti retroviral therapy (ART). HIV/ HCV coinfection was common among injecting drug users (IDUs) due to share route of transmission. This study aimed to analyze the prognostic value of CD4-count, anemia, and liver fibrosis stage for five-years survival of HIV/HCV coinfected patients on ART.

Materials and Methods: This retrospective study included 318 HIV/HCV coinfected patients from The Integrated Management for Prevention and Treatment of HIV/AIDS (IMPACT) study started ART from 2007 to 2011 in Teratai Clinic, Hasan Sadikin Hospital, Bandung. We performed Kaplan-Meier survival analysis to assess 5-years survival and Cox regression to evaluate potential prognostic factors, including CD4-count, anemia, and liver fibrosis stage(FIB-4 index). Findings were presented as hazard ratios with corresponding 95% confidence interval.

Results: Most subjects were male, injecting drug users (IDUs), and severely immunocompromised (CD4-count <50 cells/mm3). Thirty five patients died (11%) during follow-up. Overall incidence rate is 2.5 deaths persons-years. Kaplan Meier analysis showed HIV/HCV coinfected patients with low CD4-count, anemia, or advanced liver fibrosis had lower survival probability. On univariable analysis the following variables were predictive for death: CD4-count <50 cells/mm3 [hazard ratio (HR) 3.6; 95% CI 1.1–11.6; p=0.036], anemia [HR 3.0; 95% CI 1.3-7.0; p=0.009], and FIB-4 index ≥ 3,25 [HR 6.7; 95% CI 2.7-17.0; p<0,001]. Multivariable analysis showed the following variables were predictive for death: FIB-4 index ≥ 3,25 [HR=7.6; 95% CI 3.0-19.3; p<0.001], anemia [HR=2.7; 95% CI 1.1-6.3; p=0.026]. Proportional Hazard model by combining CD4-count <50 cells/mm3, anemia, and FIB-4 index ≥ 3,25 revealed 5-years survival probability to be 1,23% (p<0.001).

Conclusions: Low CD4-count, anemia, and advanced liver fibrosis predict poor survival among HIV/HCV coinfected patients on HAART.

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Routine Versus Targeted Viral Load Strategy Among Patients Starting ART in Hanoi, Vietnam

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Background: HIV viral load (VL) testing is recommended by the WHO as the most accurate method for monitoring patients on antiretroviral therapy (ART). VL monitoring has higher sensitivity and positive predictive value for diagnosing treatment failure compared to immunologic or clinical monitoring and allows earlier detection of virological failure and switch to 2nd-line ART before the accumulation of drug resistance mutations. However, evidence that routine VL (RVL) monitoring improves clinical outcomes is lacking.

Material & Methods: We conducted a prospective, randomized controlled trial of RVL monitoring every 6 months versus standard targeted VL (TVL, VL testing to confirm suspected treatment failure) in patients starting ART at Bach Mai Hospital in Hanoi. A total of 647 subjects were randomized to either RVL monitoring (n=305) or TVL monitoring (n=342) and followed for 3 years. Primary endpoints were death or WHO clinical stage IV events after 6 months of ART and rate of virological suppression at 3 years. Proportions were calculated and compared using Chi-squared test or Fisher's exact test. Survival analysis was used to compare time to occurrence of death or stage IV event between two groups. Person-time at risk was calculated from date of ART initiation up to date of death, new or recurrent stage IV event, or last study visit.

Results: Overall, 37.1% of the study subjects were female, the median age was 33.4 years (IQR: 29.5-38.6), and 47% had a CD4 count ≤ 100 cells/mm3 at the time of ART initiation. Approximately 44% of study events (death, lost to follow up, withdrawal, or new or recurrent stage IV event) and 68% of deaths occurred within the first 6-months of ART. Tuberculosis was the leading cause of death (22%).

Among patients on ART at 6-months, death or stage IV event occurred in 3.6% of RVL and 3.9% of TVL (p=0.823). Survival analysis showed no significant difference between the two groups (p=0.825). Viral suppression at 36 months of ART was 97.2% in RVL and 98.9% in TVL (p=.206) at a threshold of 400 cps/mL and was 98.0% in RVL and 98.9% in TVL (p=.488) at 1000 cps/mL. There was no difference in switching to 2nd-line ART (3.6% in RVL; 2.1% in TVL, p=.228). Trends of CD4 recovery were similar in both arms.

Conclusions: RVL monitoring every 6 months did not improve clinical outcomes compared to a TVL strategy after 3 years of follow-up. We found no difference in death, stage IV events, virological failure, CD4 recovery, or 2nd line switching in patients with RVL monitoring compared to those monitored with a TVL strategy. Most deaths occurred within the first 6-months of ART suggesting that earlier HIV diagnosis and initiation of ART may be needed to improve treatment outcomes in this group. Overall, there were high rates of viral suppression and relatively few adverse outcomes among patients alive and on ART after 6 months. These data suggest that the VL monitoring strategy may have less impact on patient outcomes compared to efforts to reduce early mortality and improve ART retention.

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Sensitivity and specificity of two dried blood spot Methods: for HIV-1 viral load monitoring among patients in Hanoi, Vietnam

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Background: The use of dried blood spot (DBS) specimens for HIV viral load (VL) monitoring is recommended to support the roll-out of routine VL monitoring in low and middle-income countries. To better understand the use of DBS for VL monitoring, we evaluated two DBS

testing methods, Roche TaqMan® Free Virus Evolution protocol (DBS-FVE) and Roche TaqMan® SPEX protocol (DBS-SPEX)) in patients receiving ART at an HIV clinic in Hanoi, Vietnam.

Material and Methods: DBS specimens were obtained from participants enrolled in the VMVN study, a prospective, randomized controlled trial of routine VL monitoring versus standard monitoring in a patient population starting ART between April 2011 and April 2014. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) with 95% confidence intervals (95% CI) were calculated for each DBS testing method at the thresholds of 1000 and 5000 copies/ml compared to plasma VL. DBS specimens were prepared by applying one drop of blood (~70 µL) on a Whatman 903® card. Specimens were dried at room temperature for a minimum of 4 hours and then were kept at 4-8C and either tested within two weeks or stored for future testing at -70C. A correction factor was added to each result obtained via FVE method as recommended by the manufacturer.

Results: A total of 757 specimens of 436 patients were tested via DBS. Of the 436 patients, 79 were ART-naïve (18%), and the remaining were on ART for at least six months. A large proportion of samples (81.0%) had an undetectable plasma VL (below 20 copies/ml); all from those who were already on ART. Only 10.7% (n = 81) had a plasma VL at or above 1000 copies/ml, and most of them (n = 77, 95.0) were from those who were not yet started on ART. At a threshold of 1000 copies/ml, sensitivity, specificity, PPV and NPV of the DBS-SPEX method were 98.8% (95% CI: 93.3%-100%), 74.3% (95% CI: 70.8%-77.5%), 31.5% (95% CI: 25.8%-37.6%), and 99.8% (95% CI: 98.9%-100%), respectively. Increasing the VL threshold value to 5000 copies/ml improved specificity (97.9%, 95% CI: 96.6%-98.9%) and PPV (83.9%, 95% CI: 74.5%-90.9%). Using the DBS-FVE method, at the threshold of 1000 copies/ml and with a correction factor of +0.3 log copies/ml, sensitivity, specificity, PPV and NPV were 95.1% (87.8%-98.6%), 98.8% (97.7%-99.5%), 90.6% (82.3%-95.8%), and 99.4% (98.5%-99.8%), respectively. Sensitivity decreased at the threshold of 5000 copies/ml (65.8%, 95% CI: 54.3%-76.1%). With a correction factor of +0.7 log copies/ml, the sensitivity was 96.3% (89.6%-99.2%) and specificity was 98.2% (96.9%-99.1%) at the threshold of 1000 copies/ml.

Conclusions: We found that the Roche DBS-FVE method, with a +0.7 log copies/ml correction factor, performed   well

with sensitivity and specificity greater than 96% at a VL threshold of 1000 copies/m. These findings add to the growing body of evidence supporting the use of DBS VL testing for ART monitoring. Future research should reconfirm the findings at different settings, under real-world conditions, and among populations with different distributions of VL.

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Adolescents living with HIV in transition from pediatric to adult care: Descriptive findings from a cross-sectional study in Cambodia

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Background: Older adolescents living with HIV experience worse HIV care outcomes compared to younger children or adults, often exacerbated by transition from familiar pediatric to new adult HIV care settings. However, there are limited data regarding this transition period. This paper reports characteristics of adolescents living with HIV preparing for transition from pediatric to adult care in Cambodia.

Material & Methods: In August 2016, a cross-sectional study was conducted among 328 adolescents aged 15-17, randomly selected from 11 antiretroviral therapy (ART) clinics across the country. A structured questionnaire was used to collect data on socio-demographic characteristics, experiences in HIV care, preparation for transition into adult care, adherence to ART, social support from different sources, disclosure of HIV status, knowledge and practices related to HIV and sexual and reproductive health, and substance use. Clinical data were obtained from individual medical record. Descriptive analyses were conducted to summarize participants' characteristics, and gender differences were explored. This study was approved by National Ethics Committee for Health Research.

Results: Of total, 55.2% were male and 40.8% were living with parents and 49.3% with either grandparents or relatives. Overall, 82.4% were on

first line ART treatment and had received treatment and care services for an average of 9.5 years, and ART for 8.4 years. The mean CD4 count from the most recent test was 672 cells/mm3, and viral load was 7,686 copies/mL. 95.6% were adherent to ART on Visual Adherence Scale. Half (50.7%) had never disclosed their HIV status to anyone, while the remaining half had disclosed it to their siblings (24.2%), friends (13.0%), schoolteachers (2.4%), or other (5.8%). A fifth reported having had boy or girlfriends, but few (2.1%) had ever had sexual intercourse. Girls were more likely to have been engaged in sexual intercourse, and to report not using a condom in their last intercourse. Few participants reported having ever used tobacco (1.8%), or any kind of illicit drugs (0.9%), but almost a fifth (20.7%), mostly girls, had a history of alcohol use. The majority (82.1%) were aware that they were receiving ART. HIV-related knowledge was suboptimal among the sample.

Conclusions: Findings from this study showed good adherence to ART, low likelihood of disclosure outside of family circles, sub-optimal condom use, and poor knowledge of HIV among adolescents living with HIV who are in transition into adult care. To provide individualized support for transition, pediatric and adult clinics will need to ensure that these characteristics are taken into account.

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Pressured HIV self-testing among men who have sex with men in China: a mixed Methods: analysis

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Background: HIV self-testing empowers users to test when and where they wish. However, there is potential for unintended consequences. We assessed the prevalence of pressured testing and its social context among Chinese men who have sex with men (MSM) using mixed methods

Methods: In 2017, we recruited MSM in China from Blued, a gay social networking mobile phone application. Pressured HIV testing was defined as being forced against one's will to test for HIV,

whether by physical violence, threats of violence, verbal abuse, psychological pressure, excessive control of activities, withholding of money/goods, or threats to end a relationship. We conducted multivariate logistic regression to identify factors associated with pressured HIV testing. In-depth interviews were conducted with 17 men randomly selected from the survey sample among those who reported pressured HIV testing. Content analysis was guided by grounded theory.

Results: Among 1,044 men, 96 (9.2%, 95% confidence interval(CI):7.5-11.1) reported ever experiencing pressured testing. Regular male sex partners were the most common source of pressure (61%, 59/96), and the most common form of pressure was threatening to end the relationship (39%, 37/96). Odds of having experienced pressured testing were higher in men who ever HIV self-tested compared to never self-tested (adjusted odds ratio(aOR) 2.39, 95%CI:1.38-4.14). The association between ever having self-tested and any history of being pressured to test was modified by education; only men with high school or less education had more common pressured testing associated with self-testing (AOR=5.88 (95%CI:1.92-17.99). Findings from the in-depth interviews suggested that perceptions of pressured HIV testing existed on a continuum and depended on relationship contexts. Often, the one who pressured did so 'in the name of love' or concern for their partner. Many men reported that although the experience of pressured testing itself was negative, they adopted better testing behaviours and safer sexual behaviours as a result of their experience.

Conclusion: Pressured testing among Chinese MSM was more common for those with less education who HIV self-tested. While pressured testing may increase testing uptake in some MSM, strategies are needed to reduce involuntary testing. In particular, in settings of scale-up of HIV self-testing, further research on pressured testing is needed.

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Social-support needs of adolescents living with HIV in transition from pediatric to adult care: Findings from a cross-sectional study in Cambodia

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Background: Adolescence is a period marked by changes in sexual behaviors, mental capacity, self-efficacy and independence. Given the dynamic changes during this period, studies have explored the outcomes of HIV care among adolescents living with HIV as distinct from those in adult populations. Understanding the circumstances of adolescents living with HIV is critical in designing adolescent-friendly services. This study describes the different aspects of social support adolescents living with HIV have and may need during the critical period preparing them to transition from pediatric to adult care in Cambodia.

Material & Methods: A cross-sectional study was conducted among 328 adolescents aged 15—17, randomly selected from major 11 antiretroviral therapy (ART) clinics across the country. A structured questionnaire was developed for face-to-face interviews, and clinical data were obtained from individual medical record at the clinics. Descriptive analyses were conducted to summarize their characteristics, access to social support, stigma experience and barriers to ART access. Gender differences were explored using Chi–square or Fisher's exact tests for significance. This study was approved by the National Ethics Committee for Health Research, Ministry of Health, Cambodia.

Results: Mean age of study participants was 15.8 (SD= 0.8) years. More than half (55.2%) were male, and 40.8% were living with parents and 49.3% with either grandparents or relatives. Almost half of them (48.4%) reported that their family had received social support for their health care, including food support (78.7%), school allowance (64.8%), transport allowance for going to ART clinic (55.6%), emotional counseling (32.4%), vocational training (25.9%) and home visit (10.2%). A third came from families with an ID poor card, and over half (55.0%) reported that their family had no ability to cover health expenses. Of these, 87.6% were covered by health insurance, and 38.4% had access to the health equity fund. About a third of respondents (13.7%) had been asked to come back earlier than their scheduled appointment, and 2.7% had been asked to purchase their own drugs. A third (32.0%) had experienced stigma, and 8.2% had been denied housing or food as a consequence HIV infection. Additionally, 16.8% had not attended school within the past month, and 22.9% reported having issues with school attendance.

Conclusions: Social protection mechanisms are reaching some adolescents in need, but the majority of them remain without aid due to significant discontinuities in health and social support. Multi-component interventions, supporting school attendance, reductions in child employment, mitigation of stigma and discrimination associated with HIV infection, peer support groups and improve coverage of social protection interventions are required for successful transition.

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The Impact of Late Presentation and Non-retention in Care on Subsequent Hospitalization due to Opportunistic Infections among HIV-infected Individuals Newly Engaged in Care: a Nationwide Population-based Study

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The ultimate goal of HIV care for HIV-infected individuals is to prevent patients from developing opportunistic infections (OI). Both of late presentation and non-retention may have negative impact of viral control and result in subsequent hospitalization due to OIs.
Knowing the effect of different steps of HIV care including decreasing late presenters and improving retention in care could provide useful information for reasonable allocating resources of HIV care.

We used Taiwan National Health Insurance Research Database to compare the impact of late presentation and non-retention in care on subsequent hospitalizations due to OIs in the second year of care among patients with newly-engaged in care.

Patients (N=9,185) were categorized into four groups based on initial status of retention or whether they were late presenters (retention/non-late presenters, n=4609, 50.18%; non-retention/

non-late presenters, n=3772, 41.07%; retention/ late presenters, n=750, 8.17%; non-retention/ late presenters, n=54, 0.59%). The two groups of non-late presenters had lower hospitalization rates (n=36, 0.78%; n=37, 0.98%, respectively) than the other two groups (retention/ late presenters, n=33, 4.4%; non-retention / late presenters, n=11 patients, 20.37%). Later presentation and non-retention remained as independent predictors of subsequent OI-related hospitalizations by multivariate logistic regression (OR: 3.58 and OR: 4.75, respectively)

There was a significant interaction between them (non-retention in care x late presentation, OR: 3.50) and that emphasized the importance of keeping patients retained in care when managing patients newly-engaged in HIV care and revealed the significant benefit of initial retention in care even for late presenters.

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Identifying MSM-competent physicians in China: A national online cross-sectional survey among physicians who see male HIV/STD patients

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Background: Men who have sex with men (MSM) are at high risk of human immunodeficiency virus (HIV) infection in China. Inadequate clinical services and poor clinical competency among physicians are major barriers to improving the sexual health of MSM. This study aims to understand physician clinical competency in providing MSM health services in China.

Methods: We conducted an online cross-sectional survey among Chinese physicians who have seen male patients for sexually transmitted disease (STD) concerns in the past year. We obtained information on individual demographics, clinical practice, attitudes toward MSM, and interest in contributing to MSM clinical services. We defined an MSM-competent physician as one who asked male patients about sexual orientation, sexual practices and recommended HIV/ STD testing at the same time. We conducted multivariable logistic regression to identify factors associated with MSM competency.

Results: In total, 501 physicians completed the survey. The most common subspecialties were dermatovenereology (33.1 %), urology (30.1%), and general medicine (14.4%). Roughly half (n=267, 53.3%) reported seeing MSM in the past 12 months. Among physicians who saw MSM in the past 12 months, 60.3% (n=167) met criteria as MSM-competent physicians, and most (n=234, 87.6%) MSM-competent physicians reported positive or neutral attitudes towards MSM. Over 60% of all physicians were willing to participate in further activities for improving MSM services (such as training and being on a MSM-friendly list). MSM-competent physicians showed no sociodemographic differences compared with non MSM-competent physicians, but were more interested in having their medical institution named on a MSM-friendly clinic list (aOR: 1.70, 95%CI: 1.01-2.86) and being on a list of MSM-friendly doctors (aOR: 1.77, 95%CI: 1.03-3.03).

Conclusion: MSM-competent physicians represented a broad range of individuals that practiced in diverse clinical settings. Most physicians were interested in improving and expanding MSM clinical services, despite having neutral attitudes toward same-sex behavior. Future interventions should focus on developing MSM clinical competency and expanding services that meet the needs of MSM.

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Relationship between types of main caregiver and oral health status among children living with HIV in National Pediatric Hospital, Cambodia

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Background: Worldwide, dramatic improvements in survival among children living with HIV, consequent to early antiretroviral therapy (ART) initiation, have necessitated the consideration of health-related factors in this population. Oral health is essential to an improved overall health status, and improvements oral health require the identification of related social factors and oral health behaviours. The child–caregiver relationship may be particularly important. This study aimed to examine the oral health status and identify related social factors or oral health behaviours among children living with HIV in Phnom Penh, particularly the association between the child's relationship with the caregiver and oral health status.

Material & Methods: A cross-sectional study of children (aged 8–15 years) living with HIV and their primary caregivers was conducted at the National Pediatric Hospital in Phnom Penh, the capital city of Cambodia. Separate face-to-face interviews of the children and caregivers were conducted using a semi-structured questionnaire. Each child's decayed, missed, filled permanent teeth (DMFT) index score and debris index of dental plaque were examined. The association of the child–caregiver relationship with other factors were evaluated using the chi-square test and T-test. Factors associated with the child's DMFT or debris index in bivariate analyses and in previous studies (e.g., age, gender) were included in a multiple linear regression analysis. This study was approved by the National Ethics Committee for Health Research, Ministry of Health, Cambodia and Ethical Committee of Kyushu University in Japan.

Results: The analysis included data of 143 dyads. The mean ages of children and caregivers were 12.3 (SD 1.8) and 44.8 (SD 10.6) years, respectively. Almost half (48.6%) of children had a biological parent and 29.6% had an organization staff member as a primary caregiver. The mean DMFT was 4.3. Children with an organization staff caregiver had significantly better DMFT and debris indexes and significantly higher rates of having ever visited a dentist and tooth brushing before sleep, compared to those whose caregiver was a biological parent. In a multiple linear regression analysis, having an organization staff caregiver was negatively associated with the child's DMFT score (β: -1.642, 95% CI: -2.925, -0.360).

Conclusions: According to this study of oral health-related factors among children living with HIV, child–caregivers play essential roles in oral health of children living with HIV, and children's needs may vary according to their relationship with their caregivers. Oral health interventions for these vulnerable children should provide room for improvement of oral and overall health knowledge and practices among their main caregivers.

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Oral health status in association with CD4 count level of children living with HIV: A cross-sectional study in Cambodia

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Background: To suppress an onset of AIDS, keeping a healthy immunity level is required among children living with HIV. Association between oral health status and immunity status has been suggested among HIV uninfected population including children. However, this association remains unclear among children living with HIV. This study aims to examine the association between oral health status and CD4 count level among children living with HIV.

Material & Methods: This cross-sectional study was conducted in 2016 at the National Pediatric Hospital in Phnom Penh, Cambodia. Participants were children living with HIV aged from 8 to 15 years receiving care and treatment services in the antiretroviral therapy clinic of the hospital. Face-to-face interviews, CD4 count examinations, dental checks, and saliva tests were performed. Oral health status was assessed by examining the number of decayed, missing, and filled teeth (DMFT) index, dental plaque status using a debris index, saliva

buffer capacity assessed by saliva pH level and oral health related quality of life (OHRQoL). Bivariate and multiple linear regression analyses were performed to examine the association between oral health status and CD4 count. Age, sex and duration under antiretroviral therapy were adjusted.

Results: Data of 143 children were analyzed. Male children accounted for 51%. Mean age was 12.2 years (SD 1.8). Mean CD4, DMFT index, debris index, and saliva pH were 826 (SD 286), 4.3 (SD 3.3), 1.6 (SD 0.5) and 5.7 pH (SD 0.6), respectively. DMFT, saliva pH and OHRQoL were significantly associated with CD4 counts in bivariate analysis. In multiple linear regression analysis, higher saliva pH was positively associated with higher CD4 counts (β = 0.053; 95% CI 0.005 – 0.101). Lower OHRQoL scores were negatively associated with higher CD4 counts (β= -0.004; 95% CI -0.007– 0.001).

Conclusions: Higher saliva pH level and better OHRQoL were identified as factors associated with higher CD4 counts among children living with HIV in Cambodia. These results suggest that better oral health status could be related to better immunity level among this population. Promoting oral health could contribute to suppress onset of AIDS among children living with HIV.

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Effects of supervised exercise program on physical health and quality of life in the people living with HIV in Hong Kong

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Background: Since the survival rate of HIV/ADIS patients improved, their physical health and quality of life become more important when they get older. The disease and the medication caused many side effects leading to declined physical function. Accelerated aging and poor exercise compliance were also found in the HIV population after middle age. Guided physical training could be a possible method to preserve or improve their physical health

and quality of life in the middle and old age HIV population.

Material and Methods: A single-blinded randomized control trial was done. With matching the inclusion and exclusion criteria, 21 HIV patients with age > 50 were recruited. Subjects were randomized into exercise group (n=11) or control group (n=10). The exercise group performed a moderate intensity 8-week, 2 times/week supervised exercise program by registered physiotherapist. In the control group, subjects had not given any exercises. Outcome measures included SF-36 questionnaire, Grip strength, 30 seconds chair stand, 6-mins walk test and subjective physical improvement. Outcomes were measured for both groups at baseline and post-8 week exercise. Between groups difference of outcomes improvement were analyzed by independent t-test or Mann-Whitney U test with SPSS version 23. Level of significance was set to be 0.05

Results: 1 subject in exercise group dropped out, the other 10 subjects (7 males, 3 females) completed the 8 weeks supervised exercise. All 10 subjects from control group (8 males, 2 females) completed the data collection. The exercises group showed statistical significant better improvement in all outcomes including SF-36 physical component (p=0.019) and mental component (p=0.008), Grip strength (p=0.015), 30 seconds chair stand (p=0.002), 6 mins walk test (p=0.021) and subjective improvement (p=0.004) compared to control group

Conclusions: The 8 weeks moderate intensity supervised exercise program showed significantly better improvement on the physical health and quality of life compared to control. Patients with HIV after middle age are strongly encouraged to participate in regular exercise in order to prevent early degeneration, improve physical health and enhance quality of life. Community NGOs could be a good place to carry out this type of supervised exercise program.

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Elsulfavirine/VM1500A Long-Acting Injectable, Once-Daily and Once-Weekly Oral Formulations for Treatment and Prevention of HIV-1 Infections

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Background: VM1500A is a new, potent non-nucleoside HIV-1 reverse transcriptase inhibitor. Its orally-bioavailable prodrug, Elsulfavirine/Elpida®, is marketed in Eastern Europe as an oral QD regimen for HIV/AIDS treatment. Red blood cells serve as a natural slow release depot for VM1500A. Unique pharmacokinetic properties (T1/2~9 days) of VM1500A suggest a possibility for long-acting formulation development.

Materials and Methods: Aqueous nanosuspensions of VM1500A were prepared by wet milling. Formulation safety and pharmacokinetics were studied in beagle dogs, following single or three once-monthly intramuscular (IM) injections. Blood samples were collected frequently up to 72 h after administration and every week up to 4 months. Elsulfavirine and VM1500A plasma concentrations were measured using LC-MS/MS. In phase I clinical study, uninfected healthy volunteers were randomized (7:1) to receive a single oral dose of VM-1500 20 mg, 40 mg or placebo. Plasma samples were collected frequently over 48 hours after dosing and then until day 36. In phase IIb randomized, double-blind, multi-center study, ART-naïve HIV-1-infected patients received Elpida 20 mg and various two NRTI regimens for 96 weeks. Plasma samples were collected at weeks 0-4 and 93-100. The VM-1500 and VM-1500A plasma concentrations were measured using LC-MS/MS method, and PK parameters were calculated.

Results: All studied formulations were well-tolerated at all doses, no adverse reactions were observed, including at the injection site. Following a single 10 mg/kg IM dose of VM1500A, its plasma levels were maintained above 50 ng/ml for at least 4 weeks and above or around 10 ng/ml for at least 14 weeks. In the repeat-dose studies in dogs, all studied formulations were well-tolerated, no adverse reactions were observed, including at the injection site. Following three once-monthly 10 mg/kg IM injections of selected VM1500A formulation, drug plasma levels were maintained above the clinically-efficacious VM1500A plasma concentrations for at least three month. In phase I

clinical study, the mean T1/2 of the prodrug after a single dose of Elsulfavirine was 1.7 and 2.6 hours for the 20- and 40-mg dose, respectively. In contrast, the T1/2 value for the parent compound VM1500A was 8.9 and 8.8 days for the 20 and 40 mg doses, respectively. After 7 days following a single oral 40 mg dose, VM1500A plasma levels exceeded clinically-efficacious drug concentration, suggesting a possibility of once weekly or less frequent dosing. In phase IIb study, the average Ctrough level of VM1500A at the end of treatment (weeks 93-96) was 60.8±17.7 ng/ml (n=10), similar (within 25%) to that at the beginning of treatment (weeks 1-4), and declined after the end of treatment with a kinetics similar to that after single dose or 7-day dosing, suggesting that Elpida neither significantly induced nor inhibited its own metabolism.

Conclusions: These studies support further development of VM1500A long-acting injectable formulations and Elsulfairine once weekly oral formulations to enable infrequent dosing for treatment and prevention of HIV-1 infections.

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Utilization of qualitative and participatory methodologies to inform development of a mobile health intervention among female entertainment workers in Cambodia

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Background: The HIV epidemic in Cambodia is strongly and disproportionately concentrated among key populations (KPs) including men who have sex with men (MSM), transgender women and female entertainment workers (FEWs). Additionally, other sexual and reproductive health (SRH) outcomes including STIs, contraception utilization and gynecologic health are poor among FEWs. mhealth interventions have been shown to be successful in collecting health data, increase access to health knowledge, and increase medication/appointment adherence in developing

countries. As part of the Mobile Link pilot program, focus group discussions (FGDs), in-depth interviews (IDIs) and revision workshops were conducted to better understand priority health messages, specifically for this population that would later rollout to FEWs mobile phones in a subsequent study.

Objective: To describe how and why in-depth FGDs, IDIs and revision workshops were conducted prior to development of SMS/Voice Call (VC) messages and illustrate how the findings informed roll-out and message design.

Methods: Qualitative and participatory methodologies were conducted through implementation of FGDs across 4 provinces to cover SRH topics. Additionally, IDIs were conducted with HIV-positive women in Siem Reap and Phnom Penh. The revision workshops were single day events which presented data from initial FGDs to FEWs and outreach workers (OW) for their feedback. The workshop included participatory activities to elucidate priority health topics and message sample feedback through a scoring rubric.

Results: There were 27 FGDs and 6 in-depth interviews (IDI) conducted along with 2 revision workshops after initial FGDs. The findings from the FGDs, IDIs and revision workshops highlighted that for many FEWs, health priorities such as adverse effects of high alcohol use (gastrointestinal issues) and gynecologic issues (STIs and vaginal infection/irritation) outweigh concerns around HIV and family planning. Participants also reinforced through discussions, a number of misconceptions related to contraception- particularly oral contraceptives and iUDS- as well as STI/HIV transmission. Lastly, many participants spoke to the important of outreach workers and the linkages that Smart Girl provides, further confirming the emphasis on Link within the Mobile Link program. The IDIs showed HIV-positive women would like to receive supportive/encouraging messages to address feelings of depression that may stem from the stigma they feel.

Conclusions: Following the revision workshop and FGDs, there was 312 final messages – reduced from 550 messages. The revision workshops allowed further refinement and clarification of both the message content and delivery. The input from the FGDs, IDIs and revision workshops were critical in providing more relatable and engaging messages to FEWs, which is expected to improve the overall effectiveness of the program.

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Factors associated inconsistent condom use with non-commercial partners among transgender women in Cambodia: Findings from the National Integrated Biological and Behavioral Survey (TG-IBBS 2016)

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Background: Globally, new HIV infections among transgender women continues to increase, and their engagement in sexual risk behaviors remains of great concerns. In Cambodia, the 100% condom use program has been successful in increasing condom use among the general population. However, the rates of consistent condom use, particularly in non-commercial relationships, remain consistently low in HIV key populations including transgender women. This study was conducted to explore factors associated with inconsistent condom use with non-commercial partners among transgender women in Cambodia.

Material & Methods: Data used in this cross-sectional study were collected as part of the National Integrated Biological and Behavioral Survey conducted between December 2015 and February 2016 in the capital city and 12 provinces with a high burden of HIV and transgender women population. Respondent Driven Sampling method was employed to recruit participants. A structured questionnaire was used for face-to-face interviews. A multivariate logistic regression analysis was performed to explore factors associated inconsistent condom controlled for potential confounding factors identified in this study and in previous studies. This study was approved by the National Ethics Committee for Health Research, Ministry of Health, Cambodia.

Results: This study included 1047 transgender women with a mean age of 26.0 (SD= 7.0). Of total, 40.6% of the respondents reported not always using condoms in anal sex with male non-commercial

partners in the past three months. After controlling for potential confounders, inconsistent condom use remained significantly associated with higher level of formal education (AOR= 0.95, 95% CI= 0.91-0.99), self-perception as 'female' (AOR= 1.49, 95% CI= 1.11-1.99), perception that they were unlikely to be HIV infected (AOR= 0.37, 95% CI= 0.22-0.64), lower frequency of alcohol intake (AOR= 1.81, 95% CI= 1.21-2.70), and lower likelihood of amphetamine-type stimulant use (AOR= 2.55, 95% CI= 1.38-4.39). It also remained significantly associated with other sexual behaviors such as lower number of non-commercial male partners (AOR= 1.03, 95% CI= 1.01-1.05) and consistent condom use with male commercial partners in the past three months (AOR= 0.37, 95% CI 0.13-0.83). The likelihood of inconsistent condom use was significantly lower among respondents who reported having had an HIV testing in the past 6 months (AOR= 0.67, 95% CI= 0.48-0.93) but higher among those who reported having an STI symptom in the past three months (AOR= 1.69, 95% CI= 1.10-2.59) compared to their respective comparison group.

Conclusions: The rate of inconsistent condom use with non-commercial male partners among transgender women in this study was considerably low and negatively associated with several other HIV and health risk behaviors as well as socio-demographic characteristics of the women. A tailored outreach and education program is needed to reach the right sub-groups of this high-risk population in Cambodia. Respondent Driven Sampling method remains an effective strategy to reach this hard-to-reach and stigmatized population.

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Replicating the Success: Using an HIV Model of Peer Driven Intervention (PDI+) to Increase TB New Case Detection in Cambodia

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Background: Cambodia has made great strides in tuberculosis (TB) control and achieved the Millennium Development Goals (MDG) target to halve TB deaths and prevalence by 2015. However, new case detection and treatment coverage remain a challenge. To increase new case detection rates, KHANA, under support of the national TB program, has implemented an innovative approach that was adapted from HIV model of peer driven intervention (PDI+) that was successfully employed in HIV new case detection.

Description: In 2017, KHANA was awarded a grant from TB Reach Wave 5 to implement the Community-based Innovations for Revitalized TB Active Case Finding (ACF) for Improved Detection and Linkage to Treatment. The existing KHANA's community HIV infrastructure and networks, allowed us to integrate, mainstream and build synergy among key stakeholders at grassroots levels. The project has been implemented in four Operational Districts from August 2017. Three approaches were used for the intervention: snowball active case finding (ACF); 2) integrated active case management (IACM); and 3) community mobilization for sustainability.

Lesson Learned: Working with community lay counselors, seeds and recruits have been identified. These included former people with TB and family contacts. They were given a coupon if agreed to be a seed and another five coupons to refer their peers. The eligibility screening tools and TB risk evaluation using a multi-TB symptom questionnaire were used to screen the participants. A TB pre-counseling and consent form were completed for TB screening. As the result, by March 2018, 3,382 of people coming with a coupon were verbally screened and met TB risk criteria, and all of them were tested for TB. In total, 899 people were diagnosed of TB (all form of TB), yielding a positivity rate of 26 %. The majority of the positive cases (97%) received TB treatment.

Conclusions: Findings from this intervention indicate that the PDI+ could be effectively adapted to increase TB new case detection in Cambodia. This innovative strategy should be scaled up as part of the National TB Program. Further studies are needed to more comprehensively evaluate the impacts and cos-effectiveness of the model in Cambodia as well as in other resource-limited settings.

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Leading by example: online sexual health influencers among men who have sex with men have higher HIV and syphilis testing rates in China

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Background: The spread of healthy behaviors through social networks may be accelerated by influential individuals. Previous studies have used lay health influencers to prevent sexually transmitted infections (STIs) among internet-using men who have sex with men (MSM). However, we know little about this subset of MSM. The purpose of this study was to examine socio-demographic characteristics, HIV/syphilis testing, and sexual behaviors of online MSM sexual health influencers (SHIs) in China, defined as individuals with relatively stronger influence on spreading HIV/STI information online.

Materials and Methods: An online survey of MSM was conducted in August 2017. Men were recruited through a gay social networking mobile phone application and were included if they were born biologically male, aged 16 years and above, ever had sex with another man, and HIV negative or with unknown HIV status. Information regarding socio-demographic characteristics, sexual behaviors and HIV/syphilis testing was obtained. We also assessed men's online sexual health influence using a standardized 6-item opinion leadership scale focused on HIV/STI information. Influencers were defined as those whose mean score ranked within the top 13% (men with higher scores have greater influence). We used multivariable logistic regression models to measure association between being an influencer and HIV/syphilis testing, controlling for intervention trial effects, age, education, income and marital status.

Results: Overall, 1031 men completed the survey. Most men were younger than 30 years old (819, 79.5%), and had at least college education (667, 64.7%). Influencers were more likely to get tested for HIV (55.3% vs 37.5%, p<0.001) and syphilis (26.5% vs 15.2%, p=0.001) in the last three months compared to non-influencers. There were no significant differences in condomless sex with male partners (19.7% vs 22.6%, p=0.46), mean number of male sex partners (1.32 vs 1.11, p=0.16) in the last three months, and mainly meeting male sex partners online in the last 12 months (73.5% vs 74.4%, p=0.82) between influencers and non-influencers. Regression analyses showed that influencers had higher odds of HIV testing (adjusted odds ratio [AOR]=2.16, 95% CI 1.48, 3.17) and syphilis testing (AOR=1.99, 95% CI 1.28, 3.10) in the last three months.

Conclusions: We identified online sexual health influencers who might be more likely to help promote healthy HIV/syphilis testing behaviors through online networks. This research may help to inform the development of network-based HIV/STI interventions for MSM.

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Pre-Exposure Prophylaxis (PrEP) Service in a South East Asian University Hospital – One Year Experience

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Introduction: Although PrEP, together with Treatment as Prevention, is considered instrumental in achieving UN 90-90-90 millennium goals, its implementation in Asia Pacific has been slow. In Singapore, until 2016 PrEP was offered only by a handful of private general practitioners at a high cost. Here we describe one-year experience (November 2016 – October 2017) of PrEP delivery in a sexual health clinic in a southeast Asian academic hospital.

Experience: National University Hospital is a 1,200 bed tertiary academic hospital in Singapore. In 2016, we started offering PrEP as part of a comprehensive sexual health clinic. It was designed to provide confidential, nonjudgmental sexual health services including PrEP and Post-Exposure Prophylaxis (PEP). Although only few similar services are available in Singapore and despite wide publicity, twelve months after opening, only twenty clients accessed our service. All were men. Eighteen (90%) were men who have sex with men (MSM), two were heterosexual. No transgender persons or commercial sex workers accessed our clinic during this period.

Clients cited several reasons for accessing our service: inconsistent condom use (50%); HIV discordant relationship (30%), recent PEP (15%); stealthing experience when partner removed condom during anal sex (10%).

While four (20%) clients had no indication for PrEP, they remained in follow up. Sixteen (80%) clients started PrEP; of those eleven (69%) daily PrEP and five (31%) event-driven PrEP. None of those taking event-driven PrEP reported issues with dosing schedules. Seven (44%) of those on PrEP purchased it from our pharmacy while nine (56%) purchased it from unofficial sources.

None of our clients were diagnosed HIV positive during initial assessment or follow up. Rates of sexually transmitted infections were low (one secondary and one latent syphilis case). Two (10%) clients were lost to follow up.

Main concerns when accessing our service were: stigmatization of gay sex by healthcare workers, confidentiality, perceived government's access to HIV test results and cost.

Discussion: Our experience indicates slow uptake of PrEP through a sexual health clinic at a university hospital in Singapore. Main barriers to entry seem to be costs and perceived stigma of PrEP and homosexuality by healthcare workers. However, lost-to-follow-up rates after first visit were low suggesting that perceived barriers such as stigmatizing attitudes of health care workers and costs, in reality may have less influence or simply be misconceptions. Almost a third of our clients accessed the clinic because they were in an HIV discordant relationship which shows that discussion regarding transmission prevention methods including PrEP is an essential part of taking care of people living with HIV.

Our experience shows that setting up PrEP services is also important for those who eventually will not be prescribed PrEP, offering them continuous education, counselling, HIV and STI testing and easy access to PEP.

The low uptake of PrEP services in our clinic and the fact that ninety per cent of our clients are MSM indicates alarmingly poor penetration of PrEP services into other key-populations in Singapore such as transgender persons, commercial sex workers and high-risk heterosexual men.

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Impact of Targeted Pre-Exposure Prophylaxis Strategies for Men who Have Sex with Men (MSM) in the United States

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Background: Pre-Exposure Prophylaxis (PrEP) with emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) has been demonstrated in various studies as effective HIV prevention, including among MSM. We aimed to estimate the impact of different prevention strategies using FTC/TDF for PrEP (FTC/TDF_PrEP).

Materials & Methods: CDC data were used as primary sources for epidemiological and behavioural assumptions, with an estimate of 3.9% of US adult males being MSM. The model was calibrated to 2010-2013 estimates of HIV prevalence, by age and race. PrEP efficacy-adherence relationship was derived from the iPrEx-OLE study and real world PrEP uptake, adherence and discontinuations from the PrEP DEMO project. Outcomes evaluated at 5 years included: (1) Number needed to treat (NNT) to prevent one transmission; (2) Percent reduction in HIV Prevalence (PRP) from 2015; (3) Public health benefits (PHB) measured as percentage of all avoided HIV infections that are among non-PrEP users.

Each of the following FTC/TDF_PrEP prevention strategies was considered: PrEP for MSM with CDC HIV Risk Index (HIRI-MSM) ≥10 (MSM-10+), PrEP for

black MSM with HIRI-MSM ≥10 (BMSM-10+), PrEP for young (age <25) black MSM with HIRI-MSM ≥10 (YBMSM-10+), and PrEP for MSM with HIRI-MSM ≥20 (MSM-20+).

Results: The proportion of FTC/TDF_PrEP eligible HIV-negative MSM in the US under each preventive strategy would be: 50.5%/21.6%/5.1%/2.3% with all MSM-10+/all MSM-20+/BMSM-10+/YBMSM-10+, respectively. PrEP uptake and adherence among eligible MSM are predicted to be lowest in YBMSM-10+ (uptake: 66.2%; adherence: 63.1%). The NNT to prevent one new HIV infection is 70 if FTC/TDF_PrEP is targeted to all MSM-10+. This is reduced to 33, 10, and 48 if targeted to BMSM-10+, YBMSM-10+, and MSM20+, respectively. PrEP availability to MSM-10+ would reduce HIV incidence by 50.0% and prevalence by 17.8% over 5 years, while the PRP with the other preventive strategies would be 4.0% for BMSM-10+, 2.9% for YBMSM-10+, and 9.4% with MSM-20+. PHB are estimated to be highest among YBMSM-10+ (37.8%).

Conclusions: Offering FTC/TDF_PrEP to MSM based on sexual risk, age and/or race, optimizes the NNT and increases PHB. Strategies that assist with uptake and utilization in populations most at risk will be most impactful.

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Awareness and acceptance of blood donors as regards the relaxation of blood donation deferral policy for men who have sex with men in Hong Kong

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Background: As men who have sex with men (MSM) have been disproportionately affected by HIV/AIDS, they used to be permanently deferred from blood donation in many jurisdictions, including Hong Kong. The permanent deferral mechanism is often considered discriminatory, as such lifetime deferral appears to be more stringent than other established donor deferral criteria for minimising the risk of transfusion-transmitted HIV infection. Since late September 2017, the permanent deferral policy for MSM has been replaced by time-limited deferral of one-year period in Hong Kong. This study aims to assess donors' awareness and acceptance of such change in deferral policy for MSM.

Material & Methods: A cross-sectional survey was conducted after the implementation of revised donor deferral policy for MSM. Chinese donors who had just given blood at donor centres in Hong Kong were invited to complete an anonymous self-administered questionnaire, embedded in a tablet computer. The questionnaire covered self-reported practice of deferrable behaviours related to HIV infection and one's attitudes towards the changed deferral policy relating male-to-male sex. Odds ratios (OR) were calculated to identify factors associated with the donors' awareness of the prevailing deferral policy for MSM. Statistical significance was defined as p value smaller than 0.05.

Results: Over an 8-week period between mid-December 2017 and mid-February 2018, a total of 1036 donors were recruited for the survey. Out of 551 male donors, 2 (0.36%) reported history of having sex with male, and their last sex with male took place within the one-year deferral period. Less than half of the respondents (443/1036;42.8%) were aware of the revision of deferral policy for MSM. A significantly higher level of awareness was observed among donors, who (i) were male (OR=1.52, 95% confidence interval (CI)=1.18-1.95), had attained post-secondary education (OR=1.59, 95%CI=1.22-2.08), had their last blood donation in the previous 6 months (OR=1.37, 95%CI=1.05-1.79) and donated blood for a higher number of times (Chi square=16.19, p=0.006). One third of the respondents (348; 33.6%) agreed with the policy change, while disagreement was reported by some 178 respondents (17.2%). On the length of deferral period for MSM, 180 (28.3%) out of 636 responding donors agreed with the one-year deferral period and 258 (40.6%) preferred a shorter deferral period or lifting any ban on blood donation from MSM.

Conclusions: Blood donation deferral policy for MSM remains a controversial issue in the society. This study reports a low level of awareness among donors on the change of deferral policy for MSM in Hong Kong. The public's acceptance of such policy is important as this would impact donors' compliance. Our results suggest that there is room for improving the understanding among less well-educated and

occasional donors. As the proportion of MSM among donors in this study was small, its relationship with their compliance to the deferral criteria shall be further evaluated. The deferral period shall also be reviewed and fine-tuned from time to time to maximise compliance for effective protection of blood safety.

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Treatment for anorectal Chlamydia trachomatis infection with azithromycin 1g single dose in men who have sex with men w/o HIV infection

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Background: Anorectal Chlamydia trachomatis infection (ACT) is important especially among non-HIV infected people since ACT raises the risk of HIV acquisition. The first line treatment for ACT in US is single dose (1 g) of azithromycin (AZM), whereas that in Europe and Australia is doxycycline (DOXY) 200 mg for 1 week based on the retrospective data. The retrospective data showed that failure rate of the AZM therapy is as high as 22 % and there is little prospective evidence on treatment with AZM. In this study, we prospectively evaluated the efficacy of treatment for ACT with AZM among men who have sex with men (MSM) with or without HIV infection.

Method: MSM with HIV infection (568 cases) were examined for ACT with Transcription Mediated Amplification (TMA) test between January and March in 2017, and MSM without HIV infection (173 cases) between January and December in 2017 for their first visit. For those who were diagnosed ACT, AZM 1g single dose were administered and test-of-cure were done at least 3 weeks after the treatment. Those who were detected ACT again, DOXY 200mg for 1 week was administered and test-of-cure was done at least 3 weeks after the treatment.

Results: Of 125 MSM with ACT infection, 118 MSM (97 with HIV infection and 21 without) were treated

with AZM 1g single dose and followed test-of-cure. Of the 118 MSM, 103 (87.3%) were cured (There was no significant differences in the efficacy between HIV positive or negative MSM). Of the15 MSM who failed the treatment with AZM, 12 were treated with DOXY 200mg for 1 week and followed test-of-cure. All the 12 (100%) MSM were cured.

Conclusion: This prospective study showed that the efficacy of AZM for ACT among MSM w/o HIV infection was high. AZM 1g single dose could be a reasonable option for ACT in a real clinical setting.

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AIDS incidence trends in the HIV-care continuum among HIV-at-risk populations: a 15-year nationwide cohort study in Taiwan

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Background: Although Taiwan has implemented several important interventions for various HIV-at-risk populations to combat the HIV epidemic, little is known regarding AIDS incidence in the HIV-care

continuum among the various HIV-at-risk populations in Taiwan. A better understanding of AIDS incidence trends would help improve patient care and optimize public health strategies aimed at further decreasing HIV-related morbidity and mortality.

Methods: Data from Taiwan Centers for Disease Control-operated Notifiable Diseases Surveillance System and Taiwan National Health Insurance Research Database (1998–2012) was divided into five cohort periods (consecutive 3-year groups). Logistic regression was employed to identify factors associated with AIDS incidence at presentation. Time-dependent Cox regression was used to identify factors associated with AIDS incidence during the follow-up period.

Results: Of 22,665 patients [mean age: 32 years; male (93.03%)], 6210 (27.4%) had AIDS incidence over 1.5 ± 0.82 (mean ± standard deviation) years of follow-up. AIDS developed in ≤3 months of HIV diagnosis in 73.61% AIDS patients. AIDS incidence trends in the HIV-care continuum differed according to HIV transmission routes over the five periods: AIDS at presentation increased in the sexual contact groups (P < 0.001 for homosexuals/heterosexuals; 0.648 for bisexuals) but decreased to a nadir in period 3 and then increased slightly in period 5 (P < 0.001) in intravenous drug users (IVDUs). AIDS incidence during the follow-up period increased from period 1 to a peak in period 3 or 4, before declining slightly in period 5, in the sexual contact groups (P < 0.001 for homosexuals/heterosexuals; 0.549 for bisexuals). However, it increased throughout the five periods in IVDUs (P < 0.001). Older age, sexual contact group versus IVDUs, high versus low income level, cohort periods, and HIV diagnosis regions helped predict AIDS in the HIV-care continuum.

Conclusions: Disparities in AIDS incidence trends in various HIV-at-risk populations reflect different sociodemographic variables of HIV exposure and the adopted HIV prevention strategies. This study suggests the urgent need for tailored strategies aimed at specific populations in the HIV-care continuum.

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A retrospective study on the cause of death and the risk factors of death in 442 deceased AIDS patients

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Objective: To conduct a retrospective analysis on AIDS patients who died in our hospital during the last 5 years and investigate the cause of death and risk factors of death.

Methods: We first collected all relevant information of those deceased AIDS patients, including disease diagnoses, demographic information, mode of transmission, antiretroviral therapy (ART) durations and laboratory

Results: And then, we analyzed the patients' demographic and clinical characteristics, disease diagnoses, and risk factors of death. Altogether, 442 deaths were included in this study. About 50 percent of them were diagnosed HIV infection less than 3 months before they died, had CD4 cell counts less than 200 cells/μl, and had HIV RNA over 5log copies/ml. 70 percent of all patients died of AIDS related diseases, and opportunistic infections accounted for 63.60%. The risk of death decreased for patients receiving ART compared with those not receiving ART, for patents whose ART duration over 6 months compared with those with ART duration less than 6 months, for patients with CD4+T cell counts more than 200 cells/μl at HIV confirmation compared with those with CD4+T cell counts less than 200 cells/μl. Whereas the risk of death increased for patients aged 60 years or older compared with those aged less than 30 years, and for patients with HIV RNA levels over 5 log copies/ml compared with those having HIV RNA levels less than 3log copies/ml.

Conclusions: Most patients in our study were late presenters and the coverage of ART was low among them. AIDS related diseases or opportunistic infections were major causes of death. Severe immunodepression, older age, and low ART coverage were risk factors for death.

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Epidemiological and clinico-biological characteristics of adults living with HIV and attending ART centers in Lao People's Democratic Republic (PDR)

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Background: Despite a low HIV prevalence rate (0.3% in 2015), about 1,000 new cases are reported each year in Lao PDR. Recent economic growth has been associated with an opening up of the country and increased population movements between Lao PDR and neighboring countries with higher HIV prevalence rates. Because of the limited data available in Lao PDR, it is topical to update our knowledge on the epidemiological and clinico-biological characteristics of people living with HIV (PLWH) in the country.

Methods: A cross-sectional observational study was performed in 10 antiretroviral therapy (ART) centers across Lao PDR from February to June 2017. Participants who were PLWH aged 17 and older were asked to complete a questionnaire and biological results were collected from the Center Infectiology Lao-Christophe Merieux. Co-morbidities associated with HIV infection were self-reported by participants and then assessed by healthcare staff. The study was approved by the Lao National Ethics Committee. Data were analyzed using STATA version 12.

Results: In total, 664 participants were included (51% female and 49% male). Our sample was statistically representative of the study population in terms of age and sex. Mean age was 36.3 (±9.4) years. Most of the participants were Buddhist (93%) and belonged to the lowland Lao ethnic group (93%). The majority (94%) had primary school education level or higher. From a socioeconomic standpoint, they were mostly from a vulnerable segment of the population because they were primarily involved in professional activities without regular remuneration and had low family incomes (<120 USD/month). HIV diagnosis was primarily made at ART centers and transmission of disease was thought to be heterosexual in 80% of cases. Within Lao PDR, HIV infection occurred not only in large cities but also in rural areas, while a high proportion of the participants (44%) reported that they were infected in Thailand. The majority of patients (78%) had low adherence to ARV treatment. When the last result of biological testing was considered, 37% had CD4 counts <250/mm3 and 10% had a viral load level above the detection threshold (>250 copies/mL). Besides the common HIV opportunistic infections and side effects of ARV medicines, a significant increase of psychological co-morbidities was observed after HIV diagnosis.

Conclusion: The high proportion of participants from a disadvantaged socioeconomic segment of the Lao population means that many PLWH are at risk of catastrophic expenses related to indirect costs of HIV care, which can lead to poverty. Regarding the low adherence to ARV treatment, it may clinically lead to treatment failure, and in terms of public health, increase the risk of ART drug resistance developing. Psychological disorders associated with HIV are often underestimated and neglected in low income countries, and we advocate for better screening and management of these pathologies in the HIV patient management program in order to improve their quality of life.

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Sexual risk behaviours and predictors for HIV among young men who have sex with men in Hong Kong

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Introduction: Men who have sex with men (MSM) are at high risk for HIV and sexually transmitted infection (STI). In recent years, increasing HIV infections have been reported among young MSM in Hong Kong. This study aimed to examine the

sexual risk behaviours and risk factors for HIV among young MSM in Hong Kong.

Material & Methods: MSM attending the community-based HIV/STI testing and counselling site were recruited using convenience sampling method. Questionnaire was self-administered to collect data on sociodemographic characteristics, sexual risk behaviours and recreational drug use practices. HIV and syphilis infections were diagnosed by rapid testing. Screening for C. trachomatis (CT) and N. gonorrhoeae (NG) infections at urogenital and extragenital sites was performed by nucleic acid amplification test. Predictors associated with HIV were analyzed by univariate logistic regression analysis.

Results: Of 368 MSM surveyed, 141 (38.3%) were young MSM aged 25 years or younger.
Among young MSM, the prevalence of HIV and syphilis was 10.6% (15/141) and 3.6% (3/84), respectively. HIV prevalence did not differ between young MSM and MSM above 26 years of age (10.6% vs 7.0%, P = 0.228). With regard to sexual behaviour, 54.5% (72/132) of young MSM reported having had condomless anal intercourse in the past 6 months, and 18.7% (26/139) engaged in group sex. Young MSM diagnosed with HIV had significantly higher rates of rectal STI infections (odds ratio (OR) = 4.14, 95% CI: 1.31-13.02, P = 0.015), and recreational drugs use before or during sex (OR = 4.27, 95% CI: 1.26-14.43, P = 0.019). The proportion of HIV-positive young MSM who had at least one STI in the past 6 months was nearly 7 times that of HIV-negative young MSM (26.7% vs 4.0%; P = 0.003).

Conclusions: Sexually transmitted infections are prevalent among young MSM, with the diagnosis of rectal STIs are associated with increased odds of HIV. Our study underscores the need for regular rectal STIs screening and interventions towards STI control for young MSM to reduce HIV acquisition and transmission in Hong Kong.

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Optimal timing of Antiretroviral Therapy for HIV-Infected patients with cryptococcal meningitis: A Systematic Review and Meta-analysis

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Background:/aims: Cryptococcal meningitis is one of the most opportunistic infections in HIV infection and progression to active cryptococcal meningitis after primary exposure or reinfection. Several studies reveals that cryptococcal meningitis is a major cause of mortality for patients with HIV-infected when without the antiretroviral therapy in the developed world, ranges from 10% to 25%. However, the optimal timing of ART initiation in HIV-infected persons with cryptococcal meningitis is still controversial. Thus, we conducted a systematic review and meta-analysis to synthesize the optimal timing on the efficacy of antiviral therapy in HIV-Infected patients with cryptococcal meningitis.

Search Methods and Selection Criteria: A systematic literature search was performed of PubMed, EMBASE, Clinical Trials gov and Cochrane Library databases for articles published from January 1980 to February 2018. All randomized controlled trials compared the early initiation of ART or delayed initiation of ART in HIV-infected patients with cryptococcal meningitis.

Data Extraction and Analysis: Two authors independently extracted data onto a standardised data extraction form. All-cause mortality and CM-associated immune reconstructive inflammatory syndrome (CM-IRIS) were main outcome in this analysis. All randomized effects estimated the relative risk (RR) and the 95% confidence intervals (95% CI).

Results: Six eligible randomized controlled trials were included (n=293) in our analysis. Overall, the HIV-infected CM patients who receiving to delayed ART had a lower all cause mortality than the patients assigned early ART at the end of follow up (relative risk [RR]=0.707, 95% CI: 0.529 to 0.944; I2=34.5%, P=0.019). Then, We analyzed the CM-IRIS data, the early ART was associated with a higher incidence of CM-IRIS compared with delayed ART in the HIV-infected CM patients (relative risk [RR]=0.516 ; 95% CI: 0.275 to 0.968; P=0.039; I^2 = 54.8%). The Secondary Outcomes of the 3-5 grade of adverse events (relative risk [RR]=0.976 ; 95% CI: 0.871 to 1.095; P=0.682; I^2 = 0.0%) and level of HIV RNA<400 uL (relative risk [RR]=1.089; 95% CI: 0.941 to 1.261; P=0.252; I^2 = 0.0%)had no statistically

difference between patients receiving early or delayed ART.

Conclusions: The systematic review shows that the delayed initiation of ART improves survival rate in HIV-infected patients with cryptococcal meningitis. For this moment, the early initiation of ART with the high risk of IRIS in patients. Thus, we recommend that ART initiation should be delayed until the clinical response to the antifungal therapy.

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Anonymous testing for HIV and syphilis at one HIV care designed hospital in Taiwan: surveillance data for 2013 to 2017

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Objectives: Using data from anonymous unlinked testing of routinely collected sera, trends in HIV are compared among sexually transmitted disease patients at one HIV care center in northern Taiwan.

Methods: Between 2013 and 2017, anonymous tests were obtained for routine syphilis testing and HIV combo tests from 14,325 patients in an unlinked survey. HIV combo and syphilis testing results were linked to anonymous demographic and risk information abstracted from the questionnaire.

Results: Of the 597 cases (4.2%) were ever diagnosed syphilis we followed, 324 cases (2.3%) were subsequently diagnosed as having HIV infection between 2013 and 2017. (figure 1) Five hundred and sixty-one cases (94.0%) were male, and 439 cases (73.5%) were men who have sex with men (MSM), 53 cases (8.9%) were bisexual and 105 cases (17.6%) were heterosexual persons. MSM and bisexual cases had significant risk to be infected by HIV (adjusted odds ratio: 5.20; 95% CI, 2.82-9.59), followed by age of between 25 and 34 years (aOR: 1.5; 95% CI, 1.02-2.22) and educational background of senior high school (aOR: 1.42; 95% CI, 1.01-2.07).

Conclusions: The cases were diagnosed syphilis at very high risk of HIV infection. More preventive methods and safe sex education are recommended in young MSM and people with educational background of senior high school.

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Molecular Characterization of Extended-spectrum β-lactamase Producing Enterobacteriaceae colonizing the gastrointestinal tract of HIV infected Individuals in Western Nepal

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Background: The gastrointestinal colonization by multi drug resistant bacteria has been increasing worldwide. Fecal carriage of ESBL producing Enterobacteriaceae has not been extensively investigated in HIV infected individuals. The aim of this study was to characterize the extended-spectrum beta-lactamase producing Enterobacteriaceae (ESBL-E) colonizing the gut of HIV infected individuals in Western Nepal.

Material & Methods: A cross sectional study was conducted. Participants in the HIV positive group were enrolled from day care centers and from those visiting Manipal Teaching Hospital and Western Regional Hospital, Pokhara for routine checkup. Detailed questionnaires including demographic and clinical characteristics were included. Rectal swabs from HIV infected patients (n=119) were screened for ESBL and CPE by using ESBL CHROM agar and MacConkey agar with 1 µg/ml imipenem (Hi-media, India) respectively. The phenotypic confirmation of ESBL production was performed by the double-disc synergy test as per CLSI guidelines. Antibiotic susceptibility testing was performed using Kirby-Bauer disk diffusion and E-Test methods. Two multiplex PCRs for blaTEM/blaSHV/blaOXA-1 genes and blaCTX-M including phylogenetic groups 1, 2 and 9 were used. CTX-M 15 genes were further characterized by singleplex PCR assay. AmpC

production was determined my phenotypic methods.

Results: Fecal samples or rectal swabs were collected from 119 HIV infected individuals (91 females and 28 males). Median age was 33.8 (inter-quartile range (IQR 26.5-43) years. Median time on antiretroviral (ART) was 3 years (IQR 0.9-8). ESBL Enterobacteriaceaes were isolated in 45 (38% [CI 22.9, 51.4]) participants. Majority of isolates were E coli followed by Klebsiella species. The ESBL-producing Enterobacteriaceae showed co-resistance to amoxicillin-clavulanate (66%), ciprofloxacin (62%), amikacin (8%), tetracycline (70%), cefoxitin (91%). Phenotypic AmpC production was observed in 49% (22/45) of study the subjects. Genotype blaTEM, blaSHV, blaOXA-1 were present in 22.2%, 13.3%, 11% respectively. blaCTX-M phylogenetic group 1 were found in 62.2%, and phylogenetic group 9 were 22.2%. 96 % of phylogenetic group 1 was of blaCTX-M-15 type. In this study no carbapenemase producing bacteria was isolated. The odd of ESBL carriage were 1.39 times (CI 0.29- 6.84) higher in those on ART (versus no ART history) and 0.27 times (CI 0.05- 1.4) higher in those who had close contact with livestock animals.

Conclusion: In this study we found high rate of gastrointestinal colonization of ESBL-E predominantly of blaCTX-M-15 genotype in HIV positive individuals that had not been identified previously in this geographical area. Further large scale study is warranted to identify the major predisposing factors for such colonization and to recognize and monitor associated risks for gut colonization.

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HIV community advisory boards for clinical trials in low- and middle-income countries: a scoping review of challenges

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Background: Community advisory boards (CABs) for HIV trials have expanded substantially beyond high-income countries (HICs), now playing a role in low- and middle-income countries (LMICs). Much research has examined HIV CABs in HICs, but fewer studies have examined CABs in LMICs. The purpose of this scoping review is to provide an overview of the evidence related to the challenges of CABs for clinical HIV research studies in LMICs.

Methods: We searched five databases (PubMed, Embase, Global Health, Scopus and Google Scholar), examining CABs in HIV research studies in LMICs. Two researchers independently reviewed articles for inclusion. Data were extracted regarding country, membership, activities, funding sources, research foci and challenges. Thematic analysis was used to identify the challenges of implementing CABs for HIV research in LMICs.

Results: Our search yielded 853 citations, of which 38 were included for analysis. Most studies (29) were published from 2008 to 2017. The five countries with the greatest number of studies included South Africa (12), China (9), Zimbabwe (4), Thailand (4) and India (4). The U.S. National Institutes of Health was the main source of support for CABs. CAB activities included reviewing clinical trial protocols, providing community literacy activities, and facilitating qualitative research related to clinical trials. Key challenges of implementing CABs for HIV research in LMICs included: (a) limited knowledge of science among community members, which contributed to poor communication between researchers and communities; (b) poor CAB management, e.g. lack of formal structure for participation and absence of CAB leadership; (c) incomplete ethical regulations that led to exploitation; (d) unbalanced power relationships between HIV researchers making decisions and local communities participating in studies; (e) competing demands for time that limited participation in CAB activities; and (f) language barriers between research staff and community members.

Conclusions: HIV research studies frequently use CABs to review clinical trials. Our results suggest several challenges with implementing CABs as part of HIV clinical trials in LMICs. These findings can help inform training and related activities to enhance HIV CABs in LMICs.

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Exposure to gender-based violence and depressive symptoms among transgender women in Cambodia: Findings from the National Integrated Biological and Behavioral Survey 2016

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Background: Transgender women are at significant risk of HIV and face intersecting barriers to health, social and legal services due to the hidden and stigmatized nature of the population. However, data regarding the unique needs and experiences of transgender people is scant globally. In Cambodia, HIV prevalence among transgender women remained high at 5.9% in 2016, despite the great success in reduction of the prevalence in the general population from higher than 2.0% in 1998 to 0.3% in 2014. Several cases of gender-based violence against transgender women have been routinely reported. This study examined the relationship between gender-based violence and depressive symptoms among transgender women in Cambodia.

Material & Methods: This cross-sectional study was conducted in December 2015 and February 2016 as part of the larger National Integrated Biological and Behavioral Survey. The study population included 1,375 sexually active transgender women recruited in the capital city of Phnom Penh and 12 provinces with high burden of HIV and transgender women population using the respondent-driven sampling method. Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression scale (CES-D). Multivariate regression analysis was conducted to explore factors associated with depressive symptoms controlling for potential confounding variables identified in bivariate analyses and previous studies. This study was approved by the National Ethics Committee for Health Research, Ministry of Health, Cambodia.

Results: Of total, 45.0% of the participants had depressive symptoms, and 21.8% had severe depressive symptoms. After controlling for other co-variates in the model, transgender women with depressive symptoms remained significantly more likely to report several negative experiences of gender-based violence such as a feeling that co-workers or classmates were not supportive regarding their transgender identity (AOR= 2.00, 95% CI= 1.22-3.28), having difficulties in getting a job (AOR= 1.67, 95% CI= 1.29-2.16), having been denied or thrown out of a housing (AOR= 1.53, 95% CI= 1.02-2.26), having difficulties in getting health services (AOR= 2.40, 95% CI= 1.50-3.82), having been physically abused (AOR= 1.54, 95% CI= 1.15-2.08), and having been fearful of being arrested by police or authorities (AOR= 2.18, 95% CI= 1.64-2.91) because of their transgender identity. Regarding their childhood experiences, transgender women with depressive symptoms remained significantly more likely to report that someone had tried to touch them or make them touch in a sexual way when they were growing up (AOR= 2.08, 95% CI= 1.61-2.68).

Conclusions: Transgender women in Cambodia experience high levels of depressive symptoms that are related to different forms of gender-based stigma and discrimination. To address this concern, a combination of service and policy interventions are required. These may include training and sensitization of trained and lay health providers in screening for depressive symptoms and integration of mental health services into facility- and community-based HIV services with enforcement of policies and laws that protect the rights of transgender women against gender-based violence.

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Potential barriers in access to community-based HIV services among transgender women in Cambodia: Using respondent driven sampling method to reach a hard-to-reach population

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Background: Cambodia is among a few countries in the world that has reversed HIV prevalence in the general population. However, the prevalence remains particularly high among key populations with high risks of HIV including transgender women. Moreover, transgender women face intersecting barriers to health, social and legal services due to their hidden and stigmatized nature. Despite the particular needs, data regarding the access to HIV services among transgender populations is scant globally. This study was conducted to explore barriers in access to community-based HIV services among transgender women in Cambodia.

Methods: Data used for this cross-sectional study were collected in late 2015 and early 2016 as part of the National Integrated Biological and Behavioral Survey. Sexually active transgender women were recruited from the capital city of Phnom Penh and 12 provinces with high burden of HIV and transgender women population using respondent-driven sampling method. A structured questionnaire was used for face-to-face interviews. Multivariate regression analysis was conducted to explore factors associated with access to HIV services controlling for potential confounding variables identified in bivariate analyses and in previous studies. This study was approved by the National Ethics Committee for Health Research of Ministry of Health, Cambodia.

Results: The study sample included 1375 transgender women with a mean age of 25.8 (SD= 7.1); of whom, 45.0% reported having received at least one community-based HIV service in the past three months. Transgender women with access to community-based HIV services remained significantly more likely to reside in a rural setting (AOR= 1.46, 95% CI= 1.04-2.04), report having used gender-affirming hormones (AOR= 1.37, 95% CI= 1.06-1.78), have been tested for HIV in the past six months (AOR= 6.08, 95% CI= 1.60-8.04), and have been arrested by police or authorities because of their transgender identity or expression (AOR= 1.51, 95% CI= 1.01-2.27) compared to transgender women without access to community-based HIV programs. However, transgender women with access to community-based HIV services were significantly less likely to report being in receptive role (AOR= 0.34, 95% CI= 0.15-0.82), using condom consistently with men not in exchange for money or gifts (AOR= 0.72, 95% CI= 0.55-0.94), and not using condoms because it was not available (AOR= 0.42, 95% CI= 0.23-0.76). Regarding gender-based discrimination and violence, transgender women with access to community-based HIV programs were significantly less likely to perceive that their co-workers or classmates were very supportive regarding their transgender identity (AOR= 0.58, 95% CI= 0.41-0.82) compared to that of transgender women without access.

Conclusions: We found that the respondent-driven sampling method was an effective strategy to reach a large proportion of transgender women who had not been reached by community-based HIV programs. This method may be adapted to increase the coverage of the programs reaching out subgroups of this hidden and stigmatized population who could not be reached by the existing interventions. Intervention programs should be tailored to respond to the needs of sub-populations of transgender women who are at greater risks of HIV and less likely to access the traditional outreach services.

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Factors associated recent HIV testing among transgender women in Cambodia: Findings from the National Integrated Biological and Behavioral Survey (TG-IBBS 2016)

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Background: Globally, the HIV prevalence among transgender women remains high, and a large proportion of transgender women are unaware of their HIV status. Cambodia is not exceptional. Despite the great success in reduction of HIV prevalence in the general population from more than 2.0% in 1998, the prevalence remains high at 5.9% among transgender women and less than half of them have been tested for HIV. This study aimed to identify factors associated with recent HIV testing among transgender women in Cambodia.

Material & Methods: This cross-sectional study was conducted in late 2015 and early 2016 as part of the National Integrated Biological and Behavioral Survey in 2016. A nationally representative sample of transgender women were recruited from the capital city and 12 provinces with a high burden of HIV and transgender population using the Respondent Driven Sampling method. Face-to-face interviews were conducted using a structured questionnaire. A multivariate logistic regression analysis was performed to explore factors associated with recent HIV testing controlling for potential confounders identified through bivariate analyses and reported in previous studies. This study was approved by the National Ethics Committee for Health Research, Ministry of Health, Cambodia.

Results: In this analysis, we included 1375 transgender women with a mean age of 25.8 years (SD= 7.1). Of total, 49.2% had been tested in the past six months. After controlling for several potential confounding factors, participants who had been testing for HIV in the past six months remained significantly less likely to be a student (AOR= 0.36, 95% CI= 0.20-0.65), to perceive that they were unlikely to be HIV infected (AOR= 0.50, 95% CI= 0.32-0.78), and to report always using condoms with male non-commercial partners in the past three months (AOR= 0.65, 95% CI= 0.49-0.85) compared to those who had not been tested. Regarding access to community-based HIV services, participants who had been testing for HIV in the past six months remained significantly more likely to report having been reached by community-based HIV services in the past 6 months (AOR= 5.01, 95% CI= 3.29-7.65) and receiving some forms of HIV education and materials in the past six months (AOR= 1.65, 95% CI= 1.06-2.58) compared to those who had not been tested.

Conclusions: More than half of transgender women in this study had not been tested for HIV in the past six months despite the extensive availability of free facility- and community-based HIV testing services across the country. HIV testing promotion programs with both HIV education and HIV testing services should be tailored to reach sub-groups of this hidden and stigmatized population who have not been reached by the existing strategies.

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Reducing Condomless Sex among Chinese Men Who Have Sex with Men through Repeated Exposure to Online Videos: Results: from an Online Cohort Study

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Background: Promoting condom use online is a cost-effective way to reduce condomless sex. However, condomless sex remains consistently high among Chinese men who have sex with men (MSM). This study aims to explore other factors that moderate the effects of online condom use promotion videos interventions in reducing condomless sex among Chinese MSM.

Methods: Data were collected from an online study comparing the effectiveness of two condom use promotion video interventions among Chinese MSM. We recruited MSM older than 16 years old who reported having condomless anal and/or vaginal sex within the past three months. After completing a baseline survey, participants viewed one of two condom use promotion video interventions. Participants from the two groups were combined since the two video interventions were shown to be non-inferior to each other. At the three-month follow-up survey, participants were asked if they had any condomless anal and/or vaginal sex, and whether they had viewed additional condom use promotion videos within the past three months. We used multilevel logistic regression models to identify factors associated with condomless sex. We tested the interaction between community engagement in sexual health and exposure to additional condom use promotional videos.

Results: Overall, 1172 participants completed the baseline survey and 791 (67%) completed the three-month follow-up. Most participants were under 30 years old (83%) and unmarried (83%). Self-reported condomless sex at the three-month follow-up was significantly associated with sex while intoxicated with alcohol (adjusted odds ratio(aOR)=1.80, 95%CI: 1.14-2.86), and receptive anal sex with stable male partners (aOR=1.86, 95%CI: 1.37-2.52). Moderate (aOR=0.65, 95%CI: 0.46, 0.93) and substantial levels of community engagement (aOR=0.49, 95%CI: 0.32, 0.75) and exposure to additional condom use promotion videos (aOR=0.67, 95%CI: 0.50-0.90) were significantly associated with more condom use. Moreover, additional condom use promotion videos had a larger effect in MSM with moderate (aOR=0.45, 95%CI: 0.28-0.72) or substantial (aOR=0.51, 95%CI: 0.29-0.90) community engagement.

Conclusions: Repeated exposure to condom use promotional videos and higher levels of community engagement in sexual health may help reduce condomless sex among MSM. Online interventions and offline community engagement activities should be integrated in future condom use promotion projects.

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The pattern of risk compensation in MSM enrolled in a pilot PrEP project

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Background: The use of pre-exposure prophylaxis (PrEP) may impact one's practice of unprotected sex, a phenomenon referred as risk compensation. With the launching of the first pilot PrEP project targeting men who have sex with men (MSM) in Hong Kong, we aim to profile the pattern of risk compensation through the characterisation of their condom using habit and incidence of sexually transmitted infections (STI) following initiation of PrEP.

Material & Methods: MSM with high risk sexual behaviours and an inclination to engage in unprotected sex were recruited to participate in PrEP. Daily oral TDF/FTC was prescribed to eligible participants for a maximum of 30 weeks. At each follow-up visit, participating MSM were required to complete a self-administered behavioural questionnaire, whereas STI screening (viz. syphilis, and urethral gonorrhoea and chlamydia) was performed at week 0, 12 and 28. Variables were assessed using univariate analyses.

Results: Over a five-month period, 40 MSM had enrolled in the project, with 32 having attended at least 2 clinic visits. During a follow-up period of 107 person-weeks, 2 incident STI occurred (incidence rate: 1.87 cases per 100 person-weeks). Both reported reduced condom use with "known" partners. Of 29 users with behavioural data collected from multiple visits, 24 reported sex with known partners. Half (50%) of them reported a reduction in condom use, 8% increased condom use and 29% had not changed their condom using habit. Reduction in condom use with known partners was associated with the history of recreational use of drug for sex (chem-sex) at baseline (odds ratio [OR]: 10.00, p=0.013) and reduced condom use with newly met partners (OR: 15.00, p=0.004). Some 27 of 29 users reported sex with newly met partners. Half (48%) of them reduced condom use, 37% reported no change and 11% increased condom use since PrEP initiation. Reduced condom use with newly met partners was associated with chem-sex at baseline (OR: 6.75, p=0.017), planned sex (OR: 12.10, p=0.004), and a higher degree of inclination to have unprotected insertive anal sex (Mann-Whitney U=57.00, p=0.04). Participants with HIV+ sex partners (n=4) reported decreased condom use. Reduced condom use was not associated with one's specific reason for starting PrEP (p=1.00).

Conclusions: About half of the MSM at high risk of HIV infection reported a reduction of their condom use following PrEP initiation, leading to a diagnosis of STI in some cases. Keen monitoring of HIV and STI will be important as risk behaviours tend to continue. Risk compensation is associated with one's behavioural profile at baseline, including a history of chem-sex.

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Differential preference of PrEP modalities among men who have sex with men

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Background: Daily dosing of oral antiretroviral is currently the standard modality for pre-exposure prophylaxis (PrEP) while alternatives are being studied. How these different modalities suit the needs of men who have sex with men (MSM) community has yet to be explored.

Material & Methods: A cross-sectional survey was conducted online in Hong Kong, where and when PrEP was not available. Respondents were inquired about their preference for four different PrEP modalities (1) daily, (2) time-driven, (3) event-driven (IPERGAY or ADAPT), and (4) injection (monthly to trimonthly). Other questionnaire items included demographics, body image type, preferred partner characteristics, and sexual behaviours. Multinomial logistic regression was performed to adjust and identify factors associated with preference of PrEP modality.

Results: Of 444 eligible MSM recruited over a two-month period in 2016, 349 (79%) expressed willingness in taking any form of PrEP. Assuming that the approval status, efficacy, price, and safety profile were identical, event-driven PrEP was preferred by almost half (45%) of respondents, followed by taking daily (25%). Some 18% and 13% respondents otherwise preferred injectable and time-driven PrEP, respectively.
The odds of non-preference for daily PrEP increased with age. Preference for event-driven PrEP was associated with not engaging in chem-sex, self-identification as being sporty, and a monthly income of less than HK$25,000 (about US$3,224). For them, dose schedule instead of efficacy was specifically considered when deciding on the use of PrEP. Separately, those preferring injection over daily modality were more active in seeking partners through physical venues. They were also more likely to be working full-time and having a monthly income of less than HK$25,000. MSM having seasonal sex pattern favoured injection.

Conclusions: MSM's preference for specific PrEP modality was associated with one's demographics, networking behaviours and lifestyles. Affordability may be an underlying factor as those earning less favoured with modalities with fewer doses. MSM who habitually planned their sexual activities were inclined to take on time-based modalities. High risk MSM who used drugs preferred daily PrEP as the perceived efficacy was higher. Long-acting injectables apparently suit MSM who could not take drugs as scheduled, which may be associated with one's job nature or networking pattern.

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A qualitative exploration of factors associated with delay in HIV diagnosis and linkage to care among HIV-infected women in Bandung, Indonesia

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Background: The majority of HIV cases in women in Indonesia were not attributable to drug use or sex work, and antenatal HIV screening has only recently been started in a few testing facilities. With no identified risk, delay in testing and treatment among women were observed. To improve HIV testing coverage and uptake of treatment in women in Indonesia, we investigated the reasons for delay in HIV diagnosis and linkage to care from the point of view of HIV-infected women in Indonesia.

Methods: We conducted 47 in-depth semi-structured interviews, 8 participant observations, and 1 focus group discussion with HIV-infected women, doctors, midwives, counselors, and brothel owners recruited through three main HIV clinics, a local non-government organization providing counseling and testing for sex workers, and peer support groups in Bandung, Indonesia. Women were identified based on point of entry to HIV

diagnosis and additional women were included through purposive selection based on emerging results.

Results: This abstract presented topics related to HIV testing and treatment delay identified in the study. Delay was found in various stages in the HIV diagnosis and linkage to care process. Partner notification delay of wives of HIV-infected men resulted in HIV diagnosis when the women or their child got symptoms. Women who were tested together with their male partner, regardless of result concordance between the couple, were diagnosed before having symptoms and stayed in treatment. HIV screening process for sex workers applying to a new sex work venue and for general population at Red Cross for blood donation both recommended people with positive result to access another HIV testing provider for confirmation testing, and these tests would be delayed due to lack of knowledge of a HIV testing provider, fear, and shame. Linkage to care was disrupted during the process of laboratory tests prior to getting ART, particularly among sex workers.

Conclusions: Delay in HIV diagnosis may be improved through more couple testing and faster screening with same-day result and facilitation of confirmation tests. Shorter ART initiation process may reduce loss of patients in the process and improve linkage to care.

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HIV infected heroin users' 1-year discontinuation rate from methadone maintenance treatment: Results: from survival analysis

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Background: Adherence to methadone maintenance could reduce the risk of HIV transmission by minimising the practice of sharing needles in heroin users. As a harm reduction strategy, ensuring a high level of adherence is relevant for HIV infected as well as uninfected heroin users. In Hong Kong, an extensive methadone maintenance programme has been in place since the 1970s. To examine the HIV transmission potential through needle-sharing, we aim to assess HIV+ methadone users' discontinuation rate and factors associated with such history.

Material & Methods: In Hong Kong heroin users could attend any one of the 20 methadone clinics for treatment. Administratively each user is required to register at the clinic again ('re-admission') if one had not used the daily methadone service for 28 consecutive days. In this study admission and re-admission records of HIV+ users were retrieved following data access approval from Department of Health. A non-attendance interval of 365 days was defined as a discontinuation event, the first occurrence of which was counted for further analyses. Cox regression analysis was conducted to identify factors associated with discontinuation using 31 December 2015 as the end of observation period. To allow at least two years of observation, those who first registered in or after 2014 were excluded from this analysis. Logistic regression was used to characterise those who had ever used methadone in 2016.

Results: Of 79 HIV+ methadone users recorded, 37 (47%) were male and 31 (39%) were ethnic Chinese. The median year of first admission was 2006 (inter-quartile range [IQR]: 2005-2008), while the median age was 43 years (IQR: 39-49 years) in 2015. Results from logistic regression model showed that, HIV+ users who attended methadone clinic in the year of 2016 were more likely male (odds ratio [OR]: 10.00, 95% confidence interval [CI]: 1.72-58.19), ethnic Chinese (OR: 7.80, 95% CI: 1.79-33.95) and younger (OR: 0.92, 95% CI: 0.84-1.00). A total of 68 had available data for Cox regression analysis, half (50%) of them had ever discontinued methadone for at least a year. Of these 5 (7%) did not return to the programme. Ethnicity, HIV subtype, age and years of admission and HIV diagnosis were not significantly associated with methadone discontinuation in the regression model. Only male HIV+ methadone users had a lower hazard of discontinuation (hazard ratio: 0.43, 95% confidence interval: 0.19-0.97).

Conclusions: Discontinuation of one or more year from methadone treatment was not uncommon in HIV+ heroin users. While a small proportion might have become rehabilitated from heroin addiction altogether, most required readmission to methadone maintenance treatment. No

demographic factors were associated with methadone discontinuation. Epidemiologic relevance of methadone discontinuation would require further assessment of addiction behaviours and HIV cascade of care.

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Low Pre-exposure Prophylaxis (PrEP) Uptake and Factors associated with PrEP initiation among people who received HIV voluntary counseling and testing (VCT) service in southern Taiwan

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Background: Little is known about predictors of pre-exposure prophylaxis (PrEP) initiation in Taiwan. We aimed to identify factors associated with PrEP interest and initiation among people who received HIV voluntary counseling and testing (VCT) service.

Methods: A cross-sectional survey was conducted during November 2016 and November 2017 to collect socio-demographics, sexual behavior and HIV perceived risk of clients for HIV VCT in an AIDS designated hospital in southern Taiwan. We applied "PrEP continuum of care model", which includes people who were: (1) PrEP candidates, (2) interested in PrEP, (3) successfully contacted, (4) received PrEP counseling, (5) scheduled appointments, (6) attended appointment, (7) initiated PrEP, and (8) retained in PrEP program. Characteristics of potential PrEP users were described. Mann-Whitney U test was used to compare HIV risk perception between PrEP initiators and PrEP non-initiators. Reasons for lacking of interest in PrEP were recorded. Multivariate logistic regression was used to predict factors associated with PrEP initiation.

Results: During study period, a total of 1,591 clients received VCT service, 1500 of them (94.3%) were PrEP candidates. The PrEP candidates had a mean age of 28.5 years (SD, 7.2 years), and 90.7% were male. Of 1500 PrEP candidates, 130 (8.6%) expressed interests in using PrEP. Reasons for lacking of interest in PrEP were low HIV risk perception (74.8%), in the relationship (11.7%) and financial barriers (4.4%). Of 1500 PrEP candidates, only 64 (4.3%) initiated PrEP. In multivariate analysis, seeking casual partners in gay bar, sauna or gym (aOR 5.40, 95% CI 1.51-19.04), had HIV positive partners (aOR 7.66, 95% CI 1.19-49.29), STI history (aOR 4.20, 95% CI 1.02-17.29) and recreation drug use (aOR 13.94, 95% CI 3.51-55.36) were more likely to initiate PrEP.

Conclusion: PrEP uptake rate among people who received VCT service in southern Taiwan was low. Low HIV risk perception was the main reason for lacking of interest in PrEP. More efforts should be focused on strengthening awareness of and willingness to use PrEP among people at risk and to reduce the cost of PrEP to scale up PrEP implementation in southern Taiwan.

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Association of First-Line and Second-Line Antiretroviral Therapy following enhanced adherence support in Phnom Penh, Cambodia

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Background: Adherence to first-line antiretroviral therapy (ART) plays an important role to sustain viral suppression. Evaluating this relationship was critical to identify patients at high risk for second-line failure, thereby exhausting their treatment options, and to intervene and improve patient outcomes. We describe program enhanced visual analog scale (VAS) suitable for illiterate patients to assess self-reported adherence in ART-treated HIV-infected individuals in a low income countries.

Method: We conducted a retrospective analysis of all HIV adult patients (≥ 18 years old) starting ART

from January 1999-22 March 2018 by using prospectively collected program data from a large ART program in a non-governmental hospital in Phnom Penh, Cambodia. Definitions of treatment failure and indications for second line treatment followed WHO guidelines for the different periods and with two consecutive viral loads (VLs) >1 000 copies/ml and VAS is a Valuable Tool to Assess Self-Reported Adherence in HIV-Infected Patients on Antiretroviral Treatment in a low income countries and VAS is measured to assess the level of adherence on week 2, week 4, month 3 then every six months from the second year onwards by a counselor. Cumulative adherence was defined as percentage adherence of VAS ≥95% good adherence and <95% bad adherence were analysis.

Results: A total of 225 of 3,724 (6%) participants reported to fail to first line ART regimen and were switch to second line treatment. The mean age at enrolment was IQR 44(21-70) and 2,030 (55%) were females. Of all failure the WHO clinical stage 3 and 4 were 109 (48%) and 53 (24%) respectively. The duration from first line ART initiation to second-line ART was 2. 4 years (IQR 1.4-4.3). Among all of HIV cohort, only 1% (51/3,724) of patient report to have VAS scores less than 95%. For those report VAS <95% were 6% (3/51) and VAS≥95% were 6% (222/3,673) fail to first line regimen respectively (P< 0.962).

Conclusion: The study found that the VAS intervention for assessing self-reported adherence in illiterate HIV-infected individuals had no effect to prevent ART failure. To prevent the failure, program should find another applicable tool to support patient adherence.

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Cost of medical care for HIV-infected inpatients in the context of free and universal access to antiretroviral treatment in China

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Background:. AIDS, hepatitis B and tuberculosis (TB) are the major infectious diseases in China, which cause a high economic burden to the patients. China has provided free antiretroviral therapy (ART) to HIV-infected patients since 2003. Little is know about the cost of medical care and the cause of hospital admission for HIV-infected inpatients in China in the context of free and universal access to ART.

Methods:. We retrospectively analyzed the costs of medical care for inpatients with AIDS, hepatitis B, and tuberculosis in a tertiary hospital in Shanghai, China, in 2017, respectively. The costs did not include ART drugs, anti-hepatitis B virus (HBV) drugs and anti-TB drugs. Costs were presented as mean medical cost per admission and mean medical cost per inpatient per admission in 2007 Chinese Yuan (RMB). The common causes for hospital admission for HIV inpatients were analyzed.

Results:. In 2017, 1064 HIV inpatients (1604 admissions), 1014 tuberculosis inpatients (1376 admissions) and 1581 hepatitis B inpatients (2681 admissions) were included in this study. The mean medical costs per admission for AIDS, TB and hepatitis inpatients were 15712.2 RMB, 12607.3 RMB, and 10524.4 RMB, respectively. The mean medical costs per inpatient for AIDS, TB and hepatitis inpatients were 23686.4 RMB, 16996.2 RMB, and 17845.1 RMB, respectively. The mean medical costs per admission and per inpatient for AIDS were higher than those for TB and hepatitis inpatients, respectively. The most common cause for hospital admission of HIV patient was pulmonary infection (account for 17.7% of admissions), followed by pulmonary TB (12.5%), lymphoma (5.5%), Disseminated Mycobacterium avium infection (4.5%), tubercular meningitis (3.0%).

Conclusions:. Medical care costs have remained relatively high for HIV-infected inpatients in the context of free and universal access to ART in China. The most common cause for hospital admission of HIV patient was pulmonary infection, mycobacterial disease and lymphoma. Enhanced testing to achieve earlier diagnosis and initiation of ART could potentially reduce costs of inpatient care.

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HIV Self-testing to Expand HIV Testing among Men Who Have Sex

with Men: Results: from a cohort study in China

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Background: The WHO recommends HIV self-testing (HIVST) as an additional approach for HIV testing. HIVST enables individuals to test themselves for HIV by themselves and at their own convenience. HIVST may be able to expand testing rates. The objective of this study is to evaluate factors that associated with using HIVST among a cohort of Chinese men who have sex with men (MSM).

Materials & Methods: This is a secondary analysis of longitudinal data collected as part of a stepped wedge randomized controlled trial. The trial collected data from MSM over a 12-month period starting in July 2016 in eight Chinese cities. Participants completed questions covering sociodemographic information, sexual behaviors, HIV testing (including HIV self-testing) history, social norms, and anticipated stigma. In addition, in a three-month period, men in the cohort could provide their address and receive a free HIVST by mail. Participants who remained in the trial during the last follow up prior to the intervention were include in the data analysis. We used univariate and multivariable analysis to examine factors associated with HIV self-testing during the study period.

Results: Overall, 1114 participants who met the inclusion criteria were included in this study. Among them, 62.8% were less than 30 years old, 87.3% were never married, and only 15.1% had an annual income of more than $8,500 USD. A total of 558 (50.1%) men received HIVST over the period, including 312 (28.0%) through the research study and 246 (22.1%) through other means. Multivariable analysis indicated that the people ever tested for HIV and people who ever self-tested were more like to take HIVST during the study period, with adjusted ORs (aOR) of 1.50 (95% CI 1.16-1.93) and 2.70 (95% CI 1.91-3.81), respectively. In addition, participants with higher social norm and self-efficacy score were also tended to conduct HIVST, with aORs of 1.15 (95% CI 1.00-1.06) and 1.04 (95% CI 1.00-1.08), respectively.

Conclusion: This study showed that a high proportion of MSM used self-test kits during the intervention period. Interventions and further implementation research that can create the demand and further expend HIVST among MSM are still needed.

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Health insurance to coverage antiretroviral treatment in Vietnam: Patients' preferences and barriers for expanding

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Background: With the rapidly losing funding from international donors, health insurance (HI) is an alternative strategy to sustain the HIV-related services for patients in Vietnam. At national-clinics, due to payment mechanism, patients were referred back to the lower-level clinics for care and treatment. This study explores the HIV patients' preferences and their perceived barriers to use HI among patients enrolled at Bach Mai hospital in Vietnam.

Materials & Methods: A cross-sectional study was conducted among 532 HIV-infected people under ART at out-patient clinic of Bach Mai hospital. Patients was asked about their HI status, type of HI, appointments' options, and their preference about continue treatment at the clinic. We also collected perceived barriers of respondents to use HI if transferred out.

Results: The prevalence of having HI among our sample was high with 88.87%, while about 6.42% of patients are waiting to be granted one. The majority of HI type was voluntary insurance (79.92%), followed by officer type (13.25%), and poor household type (5.02%). We found that 95% of respondents reported that they do not want to transfer to lower-level clinic despite the reduction in payment rate of health insurance. Among those, there was about 67% agreed to have appointment

on weekend, and 64.78% willing to pay the extra cost. The preferred frequency of appointment was one per three months. About the perceived barriers to continue treatment at lower-level clinic, the majority of patients concerned about stigma and discrimination at community level (accounted for 84.71%). On the other hand, quality of services which provided by commune- and district- level clinics might not satisfy them compare to national-level (22.35%).

Conclusions: Our study highlighted the high prevalence of HIV/AIDS patients having HI. However, the implementation and expansion of HI for ART in Vietnam may face many challenges, especially at national-level clinics. This study suggested HI payment mechanism should be more flexible, and future treatment strategy should be developed accordance with patients' preferences.

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Voices from the Hidden: Implementation of the People Living with HIV Stigma Index in Taiwan

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Background: Stigma toward HIV/AIDS has been recognized as a major obstacle in ending the global epidemic by deterring high risk populations to access equitable medical and psychosocial support. However, the formation of stigma in the society is a complex process and the measurement of stigma is difficult to approach. The aim of the study was to estimate the HIV stigma in Taiwan by measuring the discrimination encountered by people living with HIV in the society.

Method: During April 2017 to December 2017, a nationwide survey enrolling 842 (3% total HIV positive population) people living with HIV in Taiwan was conducted using The People Living with HIV Stigma Index questionnaire developed by GNP+, UNAIDS and ICW. Semi-structured questionnaire were filled during 1 to 1 interviews. Quantitative data were extracted and international comparisons were done by gathering the official reports on stigmaindex.org website.

Result: Despite the efforts in public health education done by the many HIV-associated NGOs and government in Taiwan over the past decade, stigma toward HIV/AIDS still exists, although in a silent way. There were 57.3% of the participants who did not let their adult family members know about their HIV status. Thirty-two percent of participants recalled their hesitance to take the HIV test due to the fears of other people's reaction if the result was positive. Seven percent of the participants reported refusals of medical services because of their HIV status in the past 12 months. Nevertheless, there was stronger supports from PLHIV communities as compare to the general society. Forty-seven percent of participants reported offering emotional, referral or physical help to other PLHIV in the past 12 months. Participants with higher education level/incomes were found to have less self-stigma and were more active in challenging social stigma and discriminations against HIV/AIDS.

Conclusion: HIV stigma and discrimination was evaluated in Taiwan by implementing the People Living with Stigma Index. Although there is still much to do before getting zero-discrimination, voices from the PLHIV were heard and further approaches are launched.

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Feasibility and effectiveness of Xpert® MTB/RIF assay in reducing the median time to diagnosis of tuberculosis in HIV infected patients

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Background: TB is the most common opportunistic infection among HIV-infected individuals affecting 10-30%. India ranks 2nd in the world and accounts for 10% of the global burden of HIV-associated TB. MDRTB is twice more prevalent in HIV/TB co-infected patients with high rates reported from Mumbai, India. HIV infected individuals are at greater risk of rapid progression of TB, reinfection after complete treatment and reactivation of TB from a latent infection.

Sputum smear microscopy is the mainstay in diagnosis of TB under Revised National Tuberculosis Control Programme (RNTCP), but has poor sensitivity owing to paucibacillary nature of TB in HIV-infected individuals. Culture has higher sensitivity and specificity but takes longer time and requires stringent biosafety measures. Delay in diagnosis increases risk of progression, infectivity and onward transmission of TB. Xpert® MTB/RIF assay, developed by Cepheid diagnostics, is a unique fully automated, molecular assay for detecting TB and rifampicin resistance within two hours. Xpert® MTB/RIF assay has become popular globally and has become routine diagnostic tool in India. The objective of our study was to assess feasibility and effectiveness of Xpert® MTB/RIF assay in reducing the median time to diagnosis of TB in HIV-infected individuals.

Materials and Methods: After approval from the institutional ethics committee, a prospective study was conducted over one and a half year, in a tertiary care hospital in Mumbai. Sputum smear microscopy, culture on LJ medium and Xpert® MTB/RIF were performed on specimens collected from 224 HIV positive adults suspected of TB. The results of all the three tests were observed, interpreted, recorded. Overall diagnostic yield and sensitivity were calculated with culture as reference standard. The results were statistically analysed using the Chi-square test. P value < 0.05 was considered as significant.

Results: Microscopy, culture and Xpert MTB/RIF were positive in 16 (7.1%), 36(16.07%) and 34(15.17%) suspected TB cases respectively. Xpert® MTB/RIF assay gave an additional yield of 8.04% (18/34) over microscopy. The higher yield by culture in comparison to Xpert® MTB/RIF assay was statistically significant (p = 0.0001). Overall sensitivity of Xpert MTB/RIF was 77.78% (28/36) and specificity was 96.81% (182/188). Xpert®

MTB/RIF sensitivity in smear positive culture positive and smear-negative, culture-positive cases was 100% and 61.90% respectively. Rifampicin resistance was detected in 11 out of 34 cases (32.35%) by Xpert MTB/RIF assay. Median time to detection of TB by Xpert MTB/RIF was 0 days, compared to 1 day for microscopy and 30 days for solid culture.

Conclusions: Xpert® MTB/RIF assay was able to establish a diagnosis of TB in a significantly high number of HIV infected individuals who are sputum smear negative. The assay significantly reduced the median time to diagnosis of TB facilitating early initiation of treatment. The minimal expertise and processing time required for preforming the assay with negligible bio-hazard component makes it feasible to implement Xpert® MTB/RIF assay as a routine diagnostic test in a high throughput microbiology laboratory.

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High HBV and HIV Suppression With Treatment of HIV/HBV Coinfection in B/F/TAF Studies

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Background: HBV is a common coinfection in HIV patients. We report HBV and HIV outcomes in ART-naïve and experienced HIV/HBV-coinfected subjects enrolled in 4 studies of bictegravir/ emtricitabine/ tenofovir alafenamide (B/F/TAF).

Material & Methods: HBV serologies were collected at baseline (BL) and week (W) 48 in 4 B/F/TAF studies: Studies 1489 (B/F/TAF vs abacavir/lamivudine/dolutegravir [DTG, ABC/ 3TC/

DTG] as initial therapy), 1490 (B/F/TAF vs F/TAF+DTG as initial therapy), 1878 (switch from PI + 2 NRTIs to B/F/TAF vs stay on BL regimen [SBR]), and 1844 (maintain ABC/3TC/DTG vs switch to B/F/TAF). Studies 1490 and 1878 permitted HBV-infected patients to enroll; HBV coinfection was excluded from Studies 1489 and 1844 due to ABC/3TC in control arms. HBV seropositive patients had HBV DNA at baseline and W48. Proportion with W48 HBV DNA <29 IU/mL using missing=excluded data imputation was pre-specified for studies 1490 and 1878. HBV serology and DNA results were analyzed to identify incident HBV infections in all 4 studies through W48.

Results: In Study 1490, 14 naïve coinfected subjects (n=12 HBV surface antigen [HBsAg] positive and n=2 HBsAg-/core antibody+ and HBV DNA detectable) were randomized to B/F/TAF (n=8) or DTG+F/TAF (n=6). 1 HBsAg positive subject (DTG+F/TAF group) discontinued study at Day 68. At W48, 11/13 (85%) had HBV DNA <29 IU/mL. 2/11 had HBsAg loss. In Study 1878, 14 treatment experienced coinfected subjects were randomized to stay on BL regimen (SBR, n=6) or switch to B/F/TAF (n=8). 2/14 had HBV DNA >29 IU/mL at BL: 1 (SBR) who discontinued at Day 1 and had no post BL HBV DNA, and 1 (B/F/TAF) who at W48 had HBV DNA ≥29 IU/mL. 12/12 with suppressed HBV DNA at BL maintained HBV DNA <29 IU/mL at W48; none had HBsAg conversion. W48 HIV-1 RNA was <50 copies/mL in 25/28 of those with HIV/HBV coinfection at BL in these two studies (89%). In these two trials plus Studies 1489 and 1844, no patient receiving B/F/TAF, F/TAF or F/TDF acquired HBV. One naïve subject randomized to ABC/3TC/DTG acquired HBV infection by W48.

Conclusions: High rates of HBV suppression were achieved at W48 in naïve HIV/HBV coinfected patients treated with F/TAF regimens. HBV suppression was maintained in experienced patients switching to B/F/TAF. At W48, HIV suppression among HBV coinfected patients was high and comparable to those with HIV mono-infection. Further studies of B/F/TAF and other regimens containing F/TAF for HBV treatment and prevention in HIV-infected patients are warranted.

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Syphilis influences the CD4/CD8 ratio and a scoring model predicts normalization of CD4/CD8 ratio in HIV-infected patients

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Background: HIV/syphilis co-infection may increase HIV viral replication and decrease CD4+ T cells levels in vivo after combination antiretroviral therapy (cART). Few studies demonstrate the effect of syphilis on the normalization of CD4/CD8 ratio, which is associated with recovery of immune competence. Effective models to predict immunological recovery among HIV-infected patients is urgently needed in clinical practice.

Setting: The study was conducted in a tertiary care hospital for HIV/AIDS in North China (Beijing Ditan Hospital).

Methods: Using a retrospective study, 965 cART-naïve HIV-infected patients were followed up to 72 weeks post-cART. Cox regression analyses were performed to determine a prediction scoring model to identify independent predictors. The hazard rates of the predictors were converted to integer risk scores.

Results: The prevalence of HIV/syphilis co-infection in participants was 24.18%. Normalization of CD4/CD8 ratio after a 72-weeks treatment was observed in 9.96% of HIV/syphilis co-infections and 20.03% of HIV mono-infections. Age ≥40 (Hazard Rate [HR]: 2.204, 95% confidence interval [CI]: 1.528-3.181, p<0.001), baseline HIV viral load <105 copies/mL (HR: 1.163, 95% CI: 1.058-2.459, p=0.026), baseline CD4+ T cells ≥ 350 cells/mm3 (HR=3.449, 95% CI: 2.475-4.808, p<0.001), HIV mono-infection (HR=2.039, 95% CI: 1.331-3.125, p=0.001) were more likely to achieve a normal CD4/CD8 ratio at week 72 after cART.

Conclusions: HIV/syphilis co-infection is a risk factor of CD4/CD8 ratio normalization among HIV-infected patients. The prediction scoring model at 72 weeks after treatment, based on baseline age, CD4+ T cells, HIV viral load, and HIV/syphilis co-infection, offered a reliable predictive value for the response to cART.

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Prevalence and predictors of tuberculosis among adults with newly diagnosed HIV/AIDS

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Background: Tuberculosis and HIV co-infections are associated with special diagnostic and therapeutic challenges and constitute a high burden on healthcare systems. The study was to estimate the prevalence of tuberculosis among antiretroviral-naive HIV-infected adults, and to identify immunological, demographic and clinical factors that were associated with the presence of tuberculosis.

Methods: A cross-sectional study was conducted among 2866 adult HIV-positive patients from 10 provinces and municipalities in China during 2009 to 2010. Clinical and laboratory investigations including chest x-ray, acid fast staining and culture were used to identify tuberculosis cases. Blood samples were collected to determine CD4+ lymphocyte count. A structured questionnaire was used to collect socio-demographic characteristics of study subjects. The data was entered and analyzed using SPSS version 19 software. Demographics and medical histories were recorded. Factors associated with the presence of tuberculosis were analysed by logistic regression.

Results: Among the 2866 patients, 75.3% were male. Median age was 40 years (range: 18-86 years). 29.8% had tuberculosis, 23.0% had pulmonary tuberculosis and 11.9% had extrapulmonary tuberculosis. The prevalences of smear-positive pulmonary tuberculosis and culture-positive pulmonary tuberculosis was 11.8% (211/1784) and 17.2% (123/714), respectively. Tuberculosis was more prevalent among men (31.3%), ethnic minority patients (44.7%), patients with CD4 count of $< 200/mm3$ (32.3%), and patients who were $<$ 50 years of age (31.2%). The prevalence of tuberculosis differed significantly according to province ($P < 0.001$) and HIV transmission route ($P < 0.001$). Tuberculosis was more common in patients with fever (67.4%), cough (76.0%), night sweats (85.6%), fatigue (68.3%), weight loss (70.7%), loss of appetite (72.3%), abnormal pulmonary imaging findings (44.7%), and history of tuberculosis (73.3%). In multivariate analysis, having been diagnosed in provinces Henan, Jiangxi, Shanghai and Xinjiang, male sex, ethnic minority, lower CD4 count, having abnormal pulmonary imaging findings, fever, cough, night sweats, weight loss, and history of tuberculosis were associated with increased adjusted odds of tuberculosis among HIV-infected patients.

Conclusions: Tuberculosis is highly prevalent among Chinese adults with newly diagnosed HIV/AIDS. Geographical areas, male sex, ethnic minority, lower CD4 count, having abnormal pulmonary imaging findings, history of tuberculosis, and presenting with non-specific symptoms including fever, cough, night sweats or weight loss were found to be the predicting factors for tuberculosis among HIV-infected patients. All newly diagnosed HIV/AIDS individuals should be routinely screened for tuberculosis. These findings provide focused targets for improving routine screening for tuberculosis in antiretroviral-naive HIV-infected individuals.

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Partner notification of patients with syphilis infection in Shenzhen: Results: from a Cross-Sectional Study

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Background: Partner notification is a cornerstone to syphilis control, but there are few Chinese evaluations of the outcomes of partner notification of syphilis cases published. The purpose of this study was to describe partner services of syphilis and potential correlates of partner services among syphilis patients in Guangdong.

Methods: Syphilis patients who visited hospitals in the Nanshan District of Shenzhen and were later transferred to Nanshan Center for Chronic Disease Control between April 2011 and June 2017 were enrolled. Information on all the syphilis patients

including age, gender, marital status, HIV infection status, syphilis stage and TRUST titre were collected. We used a logistic regression multiplication model to analyze the association of partner notification.

Results: Altogether 1298 participants were recruited in this survey. The mean age of participants was 36.25±12.19 years. About 160(12.33%) of the participants were primary syphilis, 290(22.34%) were secondary syphilis, 10(0.77%) were tertiary syphilis, 838(64.56%) were latent syphilis.

For spouse, fixed partner and temporary partner, the partner notification rate was 82.3%, 78.6% and 9.3%, the partner HIV testing rate was 72.9% ,62.6% and 6.2%, the syphilis positive rate of partners was 40.7%,45.7% and 50.0%, respectively.

For spouse partner notification, Multivariate analysis indicated that the participants who were married (aOR=80.632, 95% CI: 37.805~171.972) were more likely to have spouse notification. The participants who were HIV negative (aOR=4.548, 95% CI: 2.242~9.250) were more likely to have spouse notification. The participants whose syphilis titer were smaller were more likely to have spouse notification.

For fixed partner notification, multivariate analysis indicated that the participants who were unmarried (aOR=2.442, 95% CI: 1.070~5.574) were more likely to have fixed partner notification. The participants who were included in 2011~2012 year (aOR=0.115, 95% CI: 0.061~0.216) were less likely to have partner notification.

Conclusion: The rate of partner notification among syphilis patients in China is suboptimal, especially for casual sexual partner, which may result in continuing transmission of syphilis. Novel methods to enhance PN delivery and success is necessary, such as use of the internet and mobile phones as tools for PN interventions.

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Hepatitis D Virus Infections among Hepatitis B Virus (HBV) Infected Individuals with or without HIV Co-infection: A Cross-sectional Study in one Hospital in Sichuan, China

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Background: Hepatitis D virus (HDV), which is a defective RNA virus, requires the present of hepatitis B virus (HBV) for HDV virion assembly and transmission. Studies have shown that patients with HBV and HDV co-infection have more severe liver diseases than those with HBV infection alone. Longitudinal studies have shown a decrease in HDV prevalence in some endemic areas with successful HBV vaccination programs. However, the recrudescence of HDV infection may occur among people immigrating from endemic areas and/or with high-risk behaviors such as intravenous drug use. Because HBV and HIV share common routes of transmission, HDV transmission can also spread with HBV among HIV infected individuals.

In China, HDV infection could be prevalent due to the high HBV epidemic in the community, but the data is limited. Our study is aiming to exam the HDV infections among HBV surface antigen (HBsAg) positive patients with or without HIV infection in one tertiary hospital in China.

Methods: 353 individuals with HBsAg positive were recruited during June to December 2017 for HDV screening from The First People's Hospital of Liangshan Yi Autonomous Prefecture, Sichuan, China. There were 260 individuals as serologically positive for HBsAg without HIV co-infected and 93 HIV/HBV co-infected subjects in the hospital. Anti-HDV antibody (IgM and IgG) was measured using enzyme-linked immunosorbent assay kit (Wantai Biopharm Co., China). We used chi-square test and logistic regression models to estimate the risk factors associated HDV infection. Serum HDV RNA was tested by using Real Time quantitative PCR, and the HDV genotype of individuals with HDV RNA positive was identified.

Results: There were 48 individuals of anti-HDV (IgM or IgG) being detected among 353 participants with serologically positive for HBsAg, with 13.60% of HDV prevalence rate. In 260 HIV uninfected participants, only four individuals (1.54%) were positive for anti-HDV. However, there were 44 individuals (47.31%) of anti-HDV being detected among 93 HIV/HBV co-infected participants. The HDV prevalence was higher in participants with HIV co-infected (adjusted hazard ratio [OR] 14.132, 95% CI: 4.300-46.440)

than in those with HBV only. HDV infection occurred more frequently in male (7.110, 1.274-39.675). HDV infection was significantly associated with the increased aspartate-aminotransferase (AST). The HDV genome was amplified in 16 individuals with HDV RNA positive. The phylogenetic analysis indicated that all of 16 sequences clustered with HDV-2a.

Conclusion: The prevalence rate of HDV is as high as 47.31% among HBV infected patients with HIV Co-Infection but not in those without HIV infection in Yi Autonomous Prefecture, Sichuan, China. The predominant circulating HDV genotype was HDV-2a in Yi Autonomous Prefecture, Sichuan, China.

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Bridging the HIV-syphilis testing gap: Missed opportunities for syphilis testing for men who have sex with men who ever tested for HIV in China

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Background: The World Health Organization recommends dual (i.e. concurrent) testing for both HIV and syphilis among key populations, including men who have sex with men (MSM). Since 2010, China implemented policies recommending that syphilis testing should be added to all HIV testing. However, there has been limited implementation research to guide scale-up and widespread adoption. We assessed the proportion of MSM who dual tested during their last HIV test and explored associated factors.

Methods: In 2017, an online survey of 802 MSM who ever tested for HIV was conducted in eight cities from two provinces of China (Guangdong and Shandong). Descriptive analysis was used to summarize their experience of dual testing, including location and cost of dual testing, and reasons for not dual testing. Multivariable logistic regression identified characteristics associated with not dual testing.

Results: Among 802 men, 297 men dual tested with their last HIV test (37%), conducted a median of four months ago (IQR 2-10). The dual test was in a public hospital (35%), voluntary counselling HIV test site (28%), at home with a self-test (18%), community based organization (8%), community health centre (7%), other (4%) or in a private hospital (1%). Whilst HIV testing was free, about half of men reported paying out of pocket costs for their last syphilis test (43%) with a median payment of 18 USD (IQR 8-30). Greater odds for not dual testing was found in men who had not disclosed their sexuality to a health provider (AOR=1.61, 95%CI:1.10-2.34) and had minimal (AOR=1.85, 95%CI:1.11-3.08) or no community engagement in sexual health (AOR=2.26, 95%CI:1.34-3.81), compared to those with high community engagement. The most common reasons for not dual testing were not knowing that they could be dual tested (34%), did not ask the doctor to be dual tested (25%), and did not believe they were at risk for syphilis (19%).

Conclusions: There are missed opportunities for syphilis testing in men who are receiving HIV testing. Further strategies to integrate syphilis testing within HIV testing services are urgently needed.

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Uptake of HCV treatment and Barriers among drug users in methadone maintenance treatment clinics in Guangdong province, China

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Background: Despite the fact that methadone maintenance treatment (MMT) could reduce hepatitis C virus (HCV) incidence, prevalence of HCV infection among drug users in MMT clinics was still high in China. Treatment for HCV was the most effective strategy to curb HCV epidemic. Here, we demonstrated the current treatment status of HCV among drug users in MMT clinics and explored

barriers and related factors with HCV treatment in Guangdong province, China.

Methods: Cross-sectional survey was conducted in 17 MMT clinics in 9 cities from June 2017 to October 2017 in Guangdong Province, China. All eligible HCV antibody positive patients were included. Data was obtained including socio-demographic characteristics, drug-use and alcohol-use related behaviors, sexual behaviors, HIV and HBV infection status, status and reasons for HCV treatment. Descriptive statistics and logistic regression were used to analyze related factors with treatment naive.

Results: 678 HCV antibody positive patients with an average age of 43.3 ± 6.65 were enrolled with a history of abusing drugs for an average of 20.1 ± 6.06 years. Only 366 (54.0%) reported they were infected or ever infected with HCV, of these, 42.1% (154/366) were being or ever receiving treatment but with an average delay duration of 18.8 ± 33.5 months later after they knew their infection status, and 15.0% (55/366) did not complete treatment duration. The most common causes for treatment naive including unaffordable medical costs (42.0%, 89/212), quite mild symptoms and thought there was no need to treat (34.9%, 74/212), could not find HCV treatment sites (20.3%, 43/212), and did not believe in effect of HCV treatment (12.3%, 26/212). Multiple logistic regression revealed that having not stable residence (Adjusted odds ratio [AOR]: 0.510, 95%CI: 0.265-0.983), female (AOR: 0.405, 95%CI: 0.191-0.860), ever injecting drugs (AOR: 0.386, 95%CI: 0.212-0.705) were less likely intended to receive treatment.

Conclusions: Uptake of HCV treatment was relatively poor, education for HCV, HCV care including effective referral and on-site treatment in MMT clinics, and new treatment such as direct antiviral agents (DAA) should be implemented in MMT program in China.

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HIV-1/HCV Coinfection Treatment with Single-Tablet Antiviral Regimens (CoSTARs): 12 Weeks of Ledipasvir/Sofosbuvir (LDV/SOF) after Randomized Switch to Elvitegravir/Cobicistat/ Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) or Rilpivirine/F/TAF (R/F/TAF)

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Background: Clinical data on the use of TAF regimens in HIV/HCV coinfected patients are limited.

Material & Methods: CoSTARs is an open-label, prospective study. Participants with HIV-1 RNA <50 copies/mL and chronic HCV GT1 (HCV treatment-naïve ± compensated cirrhosis or HCV treatment-experienced non-cirrhotic) were randomized 1:1 to switch to E/C/F/TAF or R/F/TAF. If HIV suppression was maintained at Week 8 (W8), participants received 12 weeks of LDV/SOF. Participants without HIV RNA suppression at W8 were discontinued (evaluable only for HIV outcomes). The primary endpoint was sustained HCV virologic response (SVR) 12 weeks after HCV therapy. Secondary endpoints included HCV SVR4, W24 HIV-1 RNA ≥50 copies/mL (FDA Snapshot) and safety.

Results: Of 144 participants receiving LDV/SOF, 72 were randomized each to E/C/F/TAF or R/F/TAF and were 74% male, 41% Black, 83% GT1a; 94% HCV treatment-naïve; and 12% cirrhotic. At baseline: median age 53 years, CD4 count 651 cells/μL, and HCV VL 6.3 log10 IU/mL. SVR4 was 98.6% (142/144, 95% CI: 95.1-99.8%) including 100% (17/17) cirrhotic, 100% (9/9) HCV treatment-experienced and 98% (58/59) Black. Two did not achieve SVR4: 1 had end of therapy undetectable HCV RNA but died of metastatic carcinoma of unknown primary before SVR4; 1 non-responder had suboptimal adherence to LDV/SOF. Of 148 randomized to a TAF regimen, 4 discontinued prior to receiving HCV treatment at W8. Through W24, 95.3% maintained HIV suppression; no HIV resistance was seen. Grades 2, 3 or 4 adverse events and serious adverse events (treatment-related serious AEs) were 28% and 6% for E/C/F/TAF and 31% and 11% for R/F/TAF. No participant discontinued LDV/SOF or E/C/F/TAF due

to AEs and 1 discontinued R/F/TAF due to worsening of pre-existing hypercholesterolemia. No renal discontinuations occurred.

Conclusions: High rates (98.6%) of HCV SVR4 and maintenance of HIV suppression (95.3%) were seen in both TAF regimens. HIV suppression rates (viral load < 50 copies/mL) at Week 24 were 95.9% with E/C/F/TAF (n=74) and 94.6% with R/F/TAF (n=74). No difference in AEs was seen between TAF regimens during LDV/SOF therapy. CoSTARs supports the use of 12 weeks of LDV/SOF with a TAF regimen in HIV-1/HCV-GT1 coinfection.

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Use of multidisease testing devices as a way forward to tackle HIV/HCV in Asia-Pacific: Three-country experience

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Background: HCV infection is a great public health concern in many Asia Pacific countries. In particular, there are about 1.3 and closed to 1.0 million people living with chronic HCV infection in Myanmar and Viet Nam respectively. In Malaysia, 2.5% of adult population are estimated living with chronic HCV infection. HCV infection could lead to serious health conditions but is curable, however majority of the population living with HCV in these countries are not aware of their infection due to diagnosis bottlenecks. Through funding from UNITAID, the Foundation for Innovative New Diagnostics started piloting projects in Malaysia, Myanmar and Viet Nam with the aim to: 1. assess the feasibility of different testing approaches tailored to each country's healthcare system infrastructure and context – based on available polyvalent laboratory platforms being used for other mature programs such as HIV and TB; and 2.how well are the tested persons linked to HCV care and treatment. The ultimate goal is to identify HCV service delivery model(s) to be included in the national healthcare system sustainably in terms of health insurance reimbursement and acceptability to HCV infected population.

Materials and Methods: In each country, FIND engaged discussions with the Ministry of Health (MOH), National Hepatitis Control Programs (NHCP), National HIV/AIDS Program (NAP), the WHO and other stakeholders to define a set of activities and interventions relevant to the country context. The agreed upon interventions will be studied to understand the impact of various HCV service delivery models on the NAP regarding: uptake of HCV screening among HIV co-infected patients, polyvalent diagnostic laboratory platforms sharing, and linkage to care. Depending on particular context, decentralization of both screening and confirmatory testing, or decentralized screening and centralized confirmatory testing relying on dried blood sport (DBS) sampling will be deployed in order to optimize the already invested polyvalent molecular platforms for HIV viral load.

Results: First intervention includes mapping out the utilization rate of high-throughput and POC polyvalent platforms within NAP in order to identify the most effective approach for adding HCV confirmatory testing. Expanding access to centralized testing will be explored through the use of DBS sampling, both for serology and molecular testing. The introduction of HCV screening through RDTs at ART clinics will likely improve linkage to care and reduce the loss to follow up between screening and confirmatory testing.

Conclusions: The under-utilization of available polyvalent laboratory platforms and the urgency of optimizing the allocated resources offer the unique opportunity to facilitate the integration of HCV testing on polyvalent platforms belonging to NAP. The increased availability of pan-genotypic HCV medicines, in parallel with HCV treatment cost reduction due to competition among HCV medicine producers will provide great momentum for decentralization of treatment via accelerating further the integration of HCV services into public health services/programs i.e. HIV/AIDS.

3rd Asia Pacific AIDS & Co-infections Conference

Translating Science into Clinical Practice in Asia Pacific

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