UNICEF Learning Collaborative
Summary of Selected Research Articles
April to June 2018

Topic I: Prevention of mother-to-child transmission (PMTCT)

Luogo, Ezekiel, et al., 'No HIV transmission from virally suppressed mothers during breastfeeding in rural Tanzania', *Journal of Acquired Immune Deficiency Syndromes*, Epub ahead of print. 16 May 2018.

- This prospective study enrolled 214 mothers from the Kilombero and Ulanga Antiretroviral Cohort (KIULARCO) and their 228 infants to assess the risks of a long breastfeeding period on mother-to-child transmission (MTCT). The primary outcome was the infant's HIV status after at least six weeks following cessation of breastfeeding.
- All mothers were on antiretroviral therapy (ART). During breastfeeding, 75 per cent of mothers had viral loads of <100 copies/mL and 16 per cent had viral loads of <1,000 copies/mL. The overall MTCT risk through breastfeeding was 4 per cent. Of 186 infants remaining after accounting for loss to follow-up, transfers and deaths, two tested positive for HIV infection.
- The authors noted that the mothers of the two infants who tested positive either had a high viral load one month post-delivery or self-reported ART interruption. They further confirmed prior research that the risk of MTCT while breastfeeding is very low when mothers adhere to ART.

Goodenough, Christopher, Kunjal Patel and Russell Van Dyke, 'Is there a higher risk of mother-to-child transmission of HIV among pregnant women with perinatal HIV infection?', *The Pediatric Infectious Diseases Journal*, Epub ahead of print, 4 May 2018.

- The Surveillance Monitoring of ART Toxicities Study (SMARTT) is a US-based prospective cohort study within the Pediatric HIV/AIDS Cohort Study (PHACS). SMARTT aims to evaluate the safety of in-utero exposure to maternal HIV infection and ART. In this sub-analysis, cases of MTCT and associated factors among women enrolled in the SMARTT study were identified from 2007 to 2015. The authors were particularly interested in the maternal and infant outcomes of pregnant women who themselves acquired HIV infections perinatally.
- Among 2,123 births in the period, the overall MTCT rate was 0.5 per cent. The MTCT rate for mothers with perinatal HIV infection was 1.1 per cent, almost three times that of mothers whowere not infected perinatally.
- The authors attributed the low overall rate of MTCT in the sample to participants being enrolled in SMARTT and receiving care at research sites at the time of analysis. The higher prevalence of transmission in mothers with HIV infections acquired perinatally in this setting demonstrates an emerging at-risk population that requires particular attention from PMTCT programmes.

Davey, Dvora J, et al., 'Risk perception and sex behaviour in pregnancy and breastfeeding in high HIV prevalence settings: Programmatic implications for PrEP delivery', *PLoS ONE*, vol. 13 (5), 14 May 2018.

- This qualitative study conducted in Cape Town, South Africa, sought to understand factors related to HIV-risk behaviours in pregnancy and post-partum periods and to assess the knowledge and acceptability of pre-exposure prophylaxis (PrEP) in pregnancy.
- From 26 in-depth interviews among HIV-uninfected at-risk pregnant and recently post-partum women, the study identified common themes associated with risky sexual behaviours during pregnancy. These include: lack of control over decisions concerning sex and condom use; low perceived risk with reported reasons such as unconfirmed partner HIV status or alcohol consumption; and socio-cultural beliefs that discourage condom use during pregnancy. PrEP knowledge was low at the time of interview. While hypothetical acceptability of PrEP during pregnancy was high in the sample, concerns remained around the potential impact on the infant.
- The authors point to gender-based power imbalance – experienced as a lack of control and potential barrier to adherence – and socio-cultural beliefs as important considerations in the design and delivery of prevention interventions targeting HIV-uninfected pregnant women in high-incidence settings.

Additional articles on PMTCT:

- Heffron, Renee, et al., 'Pregnancy outcomes and infant growth among babies with in utero exposure to tenofovir-based pre-exposure prophylaxis for HIV prevention', *AIDS*, Epub ahead of print, 11 May 2018.
- Chouraya, Caspian, et al., 'Mother-to-child transmission of HIV and HIV-free survival in Swaziland: A community-based household survey', *AIDS Behavior*, 25 April 2018.

Topic II: Paediatric HIV testing and treatment

Shiu, Stephanie, et al., 'Early antiretroviral therapy in HIV-infected infants: Can it lead to HIV remission?', *The Lancet HIV*, vol. 5 (5), May 2018, pp. e250–e258.

- There is some evidence and discussion on the possiblility of HIV remission with very early ART initiation among infants with HIV. Reviewing studies published from 1993 to 2017, the authors evaluated this potential link with a focus on the following factors: velocity of viral suppression and initial viral suppression rate with early ART, subsequent virological control and viral reservoir size after early treatment, outcomes of randomized trials with structured treatment interruption and the likelihood of viral rebound after ART cessation.
- Current data indicate that early ART initiation can achieve viral suppression. However, there is no strong evidence that initial viral suppression is higher in infants with early ART initiation compared to those who start later. There is evidence for better virological control after early ART, and some studies indicate that treatment at earlier ages is associated with smaller viral reservoirs; however, the authors note that more data are needed to support this finding. Randomized trials of supervised treatment interruption have been limited, and there has been little opportunity to investigate viral dynamics after ART cessation.

- In sum, there is not strong evidence supporting the link between early ART and HIV remission. The authors call for more prospective data with large cohorts and clearly defined measures of remission-related endpoints. They note that as the community explores the goal of long-term remission, it is crucial to weigh the benefits of very early ART with potential risks as well as the programmatic, logistic and structural challenges of implementing very early treatment.

Ibrahim, Maryanne, et al., 'Targeted HIV testing at birth supported by low and predictable mother-to-child transmission risk in Botswana,' *Journal of the International AIDS Society*, vol. 21 (5), 29 May 2018.

- This paper examines the first year of the Early Infant Treatment (EIT) study in Botswana, launched in 2015. The authors looked to identify the specific maternal risk factors that contribute to MTCT with the aim of allowing targeted birth testing of infants based on these risk factors.
- In the study, HIV-exposed infants were screened based on inclusion criteria that included a gestational age of ≥35 weeks and a birthweight of ≥2,000 g. The authors also assessed risk factors for MTCT, such as less than eight weeks of ART during pregnancy, CD4 count of <250 cells/mm3, HIV RNA measured at >400 copies/mL, self-reported poor maternal ART adherence, lack of maternal zidovudine (ZDV) in labour and lack of infant post-exposure prophylaxis.
- Of the 2,303 HIV-exposed infants tested in the study, 16 per cent were identified as high risk based on the criteria assessed above. Of these, 3.25 per cent (12 infants) were HIV-positive at birth. In-utero MTCT did not occur in any of the infants not identified as high risk at delivery. The authors noted that two risk factors were common to all positive infants: either less than eight weeks of maternal ART in pregnancy (75 per cent) or lack of maternal viral suppression (25 per cent).
- The authors conclude that the predictable association between the risk factors identified above and MTCT allows for birth testing that especially targets high-risk infants. The targeted testing will likely capture the majority of infants who will then benefit from early ART initiation.

Desmonde, Sophie, et al., 'Access to antiretroviral therapy in HIV-infected children aged 0–19 years in the International Epidemiology Databases to Evaluate AIDS (IeDEA) Global Cohort Consortium, 2004-2015: A prospective cohort study', *PLoS Medicine*, vol. 15 (5), 4 May 2018.

- This prospective study sought to describe attrition across the continuum of care for children living with HIV by analysing ART initiation probabilities and time. The researchers followed 135,479 children with HIV (ages 0–19) who had not previously received treatment from the International Epidemiology Databases to Evaluate AIDS (IeDEA) Global Cohort Consortium between 2004 and 2015. The sample included children from West and Central Africa, Eastern and Southern Africa, Asia-Pacific and Latin America.
- Overall, 68 per cent of the cohort initiated ART within 24 months of enrolment. The risk of mortality or loss to follow-up before initiation was 19.3 per cent. The authors further delineated ART initiation patterns by comparing the ART eligibility of the cohort; according to WHO criteria, nearly half (49.1 per cent) of the cohort were known to be eligible for ART initiation at baseline and an additional 3.95 per cent became eligible during follow-up. Among this subset of children eligible for ART, 19 per cent did not initiate ART within 24 months of enrolment.

- Infants under age 1, children under 10 years and adolescents aged 15 to 19 years at baseline were less likely to initiate treatment than children aged 10 to 14 years. Other characteristics of participants who were lost to follow-up before ART initation include: females compared to males; those becoming eligible for ART in the follow-up period compared to those eligible at baseline; and those living in sub-Saharan Africa compared to the other regions in the study.
- The authors note that the high attrition rate prior to ART initiation is particularly concerning and represents a missed opportunity to prevent mortality and loss to follow-up.

Pennazzato, Martina, et al., 'Catalysing the development and introduction of paediatric drug formulations for children living with HIV: A new global collaborative framework for action', *The Lancet HIV*, vol. 5 (5), May 2018, pp. e259–e264.

- This viewpoint describes key features, unique roles and opportunities of the Global Accelerator for Paediatric Formulations (GAP-f), a global collaborative framework to address the challenges of paediatric antiretroviral drug development.
- The GAP-f has four main areas of focus: accelerating critical research and approval of priority drug formulations; supporting rapid introduction and uptake of optimal formulations; ensuring strategic and sustainable financing for both upstream and downstream interventions; and linking other disease fields facing similar barriers to paediatric drug development and treatment scale-up.
- Together, the GAP-f's innovative efforts build on existing work to ensure a more streamlined continuum from paediatric drug development to market introduction and uptake.

Jani, Ilesh, et al., 'Effect of point-of-care early infant diagnosis on antiretroviral therapy initiation and retention of patients: A cluster-randomised trial', *AIDS*, Epub ahead of print, 8 May 2018.

- This cluster-randomized trial in Mozambique evaluated the effect of point-of-care early infant HIV testing on ART initiation rates and infant retention in care. The abstract of this study was previously presented at CROI 2017.
- There was a seven-fold improvement for ART initiation and a 43.7 per cent increase in retention in care with point-of-care infant diagnosis in primary health clinics. Among 2,034 infants enrolled in the point-of-care arm of the trial, 89.7 per cent initiated ART within 60 days of sample collection with a median time to initiation of less than a day; in the standard-of-care control arm, 12.8 per cent among the 1,876 infants initiated ART in the same period with a median time to initiation of 127 days. Of those who initiated treatment, retention in care at 90 days of follow-up was 61.6 per cent for the point-of-care testing group and 42.9 per cent for the control group.
- The authors concluded that the routine use of point-of-care infant HIV testing allowed clinics to provide test results rapidly, reduced opportunities for loss-to-follow-up and promoted same-day treatment initiation.

Topic III: Adolescent HIV testing and treatment

Hector, Jonas, et al., 'Acceptability and performance of a directly assisted oral HIV self-testing intervention in adolescents in rural Mozambique', *PLoS ONE*, vol. 13 (4), 5 April 2018.

- This prospective study evaluated the acceptability and performance of a directly assisted oral HIV self-testing intervention among adolescents (ages 16–20) in rural Mozambique.The intervention, tested at secondary schools in the catchment area of two hospitals with existing youth-friendly services (YFS), included a detailed explanation of the oral self-test and a demonstration on how to use it, followed by an invitation card to use the YFS for oral self-testing. Self-test results were confirmed with an additional finger prick HIV test performed by a trained nurse.
- Among 496 adolescents who consented to be included in the study, 299 followed-up and performedan oral HIV self-test. This included nearly half of adolescents recruited from area schools (372) and all of the adolescents (124) recruited from the hospital itself. About 70 per cent of those who administered the self-test did so for the first time. The rate of HIV positivity was 1.7 per cent.
- Overall, the majority of adolescents found the oral HIV self-test easy to use with only 7.1 per cent reporting difficulty. Over 80 per cent preferred it to the standard finger-prick testing. While some reported preference to self-test at home, 76 per cent preferred to self-test at the hospital, particularly because there was a trained counsellor available.
- The authors noted that sensitization in schools is an effective strategy to motivate adolescents to use YFS. The intervention was found feasible and acceptable in the studied rural area, and the results may be generalizable to similar settings.

Figueroa, Carmen, et al., 'Reliability of HIV rapid diagnostic tests for self-testing compared with testing by health-care workers: A systematic review and meta-analysis', *The Lancet HIV*, vol. 5 (6), June 2018, pp. e277–90.

- This systematic review and meta-analysis assessed the reliability of self-testing using HIV rapid diagnosic tests by examining research published between 1995 and mid-2016 that reported HIV self-testing performance.
- From 25 studies included in the review, the authors assessed measures of concordance (agreement between self-tester results and health worker results) and measures of accuracy (statistical estimates of the sensitivity and specificity of the self-test). Most studies (15) used oral fluid-based rapid diagnostic tests, six used blood-based rapid diagnostic tests and four used both.
- Overall, the studies demonstrated high concordance, with the raw proportion of agreement in test results between self-testers and tests performed by health care workers ranging from 85.4 per cent to 100 per cent. Both directly assisted and unassisted self-testing showed high accuracy with its sensitivity and specificity measurements as well as a high degree of agreement with test results found by health care workers.
- The authors conclude that self-testing is a promising and reliable method of HIV rapid diagnostic testing. The largest source of error was in the specimen collection phase; thus, the authors concluded that improvements in collection methods and additional instructions for use will contribute to more accurate self-testing results.

Cluver, Lucie, et al., 'Multitype violence exposures and adolescent antiretroviral nonadherence in South Africa', *AIDS*, vol. 32 (8), 15 May 2018, pp. 975–983.

- This study used a cross-sectional survey to explore the associations between adolescent ART adherence and exposure to violence at home, schools, health clinics and in the community.
- The authors interviewed 1,060 HIV-positive adolescents (ages 10–19) who had ever initiated ART at 53 clinics in South Africa and collected validation measures of self-reported non-adherence such as viral load data and concurrent pulomonary tuberculosis indicators. In the study, 36 per cent of adolescents self-reported ART non-adherence in the past week. Non-adherence was strongly associated with both virologic failure and symptomatic pulmonary tuberculosis.
- The four types of violence associated with past-week non-adherence were (in order of decreasing effect size): clinic victimization such as verbal abuse by health care staff; domestic violence witnessed; physical abuse by caregivers; and teacher violence. Some 25 per cent of participants with no exposure to violence did not adhere to ART in the past week compared to 74.9 per cent of participants who experienced all four of these types of violence.
- The study highlights the importance of considering violence prevention as part of HIV treatment programmes and particularly points to the effect of negative provider-patient interactions on adherence.

Bermudez, Laura G, et al., 'Does economic strengthening improve viral suppression among adolescents living with HIV? Results from a cluster randomized trial in Uganda', *AIDS and Behavior*, Epub ahead of print, 20 May 2018.

- This paper used data from a longitudinal, cluster randomized study in Uganda to assess the effect of an economic empowerment intervention on viral suppression in adolescents (ages 10–16) living with HIV.
- The intervention included a matched savings account that could be used to cover expenses related to medical, small business development or education as well as workshops on financial management and planning skills. For the 702 enrolled participants, mean savings in the intervention group increased from US$2.15 at baseline to US$19.34 at 24 months and from US$1.78 to US$4.44 in the control group.
- The results demonstrated significant improvement in viral suppression with the economic empowerment intervention. At 24 months after the start of the intervention, the proportion of virally suppressed participants in the intervention cohort increased tenfold relative to the control group. Odds of having a detectable viral load at 12 months and 24 months significantly decreased in the intervention group with no significant differences in the control group.
- The authors concluded that combination interventions addressing multiple components of economic insecurity may improve adherence to ART and improve health outcomes.

Wang, Julia Shu-Huah, et al., 'Effects of financial incentives on saving outcomes and material well-being: evidence from a randomized controlled trial in Uganda', *Journal of Policy Analysis and Management,* vol. 37 (2), 29 May 2018.

- This paper analysed data from the same cluster randomized study in Uganda to examine the effect of the economic empowerment intervention on the spending of low-income households on basic needs. The analysis explored how varied levels of matching savings plan contributions affected savings and consumption behaviour.
- The two intervention arms in this trial offered different savings-match incentives: 1:1 or 1:2. At 24 months after the start of the intervention, children in both intervention arms were more likely to have accumulated savings than children in the control group in which there was no economic empowerment intervention. The higher-match incentive demonstrated higher deposit frequency but not higher overall savings, suggesting that the degree of incentive is not as significant as receiving an incentive. Notably, households did not sacrifice the consumption of basic needs and necessary goods when given an opportunity to save in the intervention arms.
- Families with children in both intervention groups showed increased levels of asset holding and small business start-up than families with children in the control group. Children who were less likely to use the savings account tended to be older, did not live with either of their biological parents, or had lived in their current households for less time. The authors note that this points to the importance of early interventions for economic empowerment that target younger children with financial management skills and saving behaviours.

Additional articles on adolescent HIV testing and treatment:

- Slogrove, Amy, and Annette Sohn, 'The global epidemiology of adolescents living with HIV: Time for more granular data to improve adolescent health outcomes', *Current Opinion in HIV and AIDS*, vol. 13 (3), 1 May 2018.

Topic IV: Adolescent HIV Prevention

Lane, Catherine, Robert Bailey, Chewe Luo and Nida Parks, 'Adolescent male circumcision for HIV prevention in high priority countries: opportunities for improvement', *Clinical Infectious Diseases*, vol. 66 (S3), 3 April 2018, pp. S161–S165.

- The recent special supplement of *Clinical Infectious Diseases,* 'Adolescent Voluntary Medical Male Circumcision: Vital Intervention Yet Improvements Needed,' focuses on voluntary medical male circumcision (VMMC) as a critical part of HIV prevention.
- The commentary notes that the studies included in the supplement describe the successes and gaps in adolescent VMMC programmes at individual and family levels, facility and community levels, and country and international levels. Data from these studies capture up to 1,526 adolescent boys and young men along with other individuals and groups involved in VMMC decision-making and delivery.
- The studies noted gaps for younger adolescents (ages 10–14 years). Prioritizing this population with increased support for knowledge-sharing, familial and community engagement and effective counselling will improve VMMC uptake for HIV prevention.
- The nine articles included in the supplement and mentioned in this commentary focus on VMMC programmes in South Africa, the United Republic of Tanzania and Zimbabwe. Eight articles examine adolescent motivation, counselling, wound healing, parental involvement, female peer support, quality of communication and providers' perceptions in their analyses of how well adolescents are reached by the

WHO's minimum package for comprehensive HIV prevention. One article presents and compares models for scaling up VMMC coverage from 2017 to 2021.

Govender, Kaymarlin, et al., 'HIV prevention in adolescents and young people in the Eastern and Southern African region: a review of key challenges impeding actions for an effective response', *The Open AIDS Journal*, vol. 12, 9 May 2018.

- This review describes epidemiological patterns of the HIV epidemic among adolescents and young people, particularly aiming to identify where HIV prevention efforts need to be focused, and examines the limitations of current HIV prevention programmes.
- While noting the gaps in the epidemiological profiles of young populations, the authors identified three subpopulations for special attention: (1) girls and young women, who had double the HIV prevalence as young men across the Eastern and Southern African region in 2017; (2) young members of key populations, who are frequently excluded from services and face unique challenges in the legal, policy and social arenas; and (3) adolescent boys and young men, who are also generally missed by sexual and reproductive health services and face increasing rates of HIV incidence.
- The review also discusses broader developmental priorities, such as social protection programming to mitigate HIV vulnerability, innovative financing for HIV prevention and civil society involvement. The authors assert that cross-sector partnership and country-led processes are crucial to reach global goals for HIV prevention.

Thurman, Tonya, et al., 'Can family-centered programming mitigate HIV risk factors among orphaned and vulnerable adolescents? Results from a pilot study in South Africa', *AIDS Care*, 1 April 2018.

- This paper evaluates *Let's Talk*, a family-centred HIV prevention programme for adolescents in South Africa that targets orphaned and vulnerable adolescents and addresses factors such as elevated risk for poor psychological health and sexual risk behaviour. Notably, the programme includes a caregiver-specific component with support for mental health and parenting skills.
- The pilot study included 12 groups evaluated with participant interviews at baseline and three months post-intervention. Average changes in HIV prevention knowledge and self-efficacy, mental health and family dynamics were estimated.
- Among the 105 adolescents and 95 caregivers who completed two sets of interviews, significant improvements in adolescents' HIV knowledge, condom use knowledge and condom negotiation were found. Mental health improvements (for depression, anxiety and stress measures) were seen among both adolescents and caregivers. Connection and communication about healthy sexuality among the participants also improved. However, adolescents' agency and capacity to refuse sex did not improve in the period of study.
- The authors conclude that these preliminary results suggest significant potential for *Let's Talk* and similar family-centred interventions to mitigate adolescent HIV risk factors, and such programmes hold lessons in designing future models.

Gibbs, Andrew, et al., 'Childhood traumas as a risk factor for HIV-risk behaviours amongst young women and men living in urban informal settlements in South Africa: A cross-sectional study', *PLoS ONE*, vol. 13 (4), 6 April 2018.

- This cross-sectional analysis, drawing on data from a cluster randomized control trial, aimed to describe the relationship between physical, sexual and emotional childhood traumas and subsequent HIV-risk behaviours among young people (ages 18–30) in urban informal settlements in Durban, South Africa.
- Using questionnaires from 680 women and 677 men, the researchers found that all childhood traumas included in the study were associated with a range of HIV-risk behaviours. For example, among women, transactional sex was significantly associated with emotional abuse and its overall severity, as well as sexual abuse and its severity. Other risk behaviours demonstrating significant associations with childhood trauma for both men and women include: a higher number of main partners and casual sexual partners; intimate partner violence experience or perpetration; non-partner sexual violence experience or perpetration; and harmful alcohol use.
- The analysis suggests that childhood trauma plays a significant role in HIV-risk behaviours later in life and represents a key vulnerability for interventions to address. In addition, adolescent-friendly HIV prevention programmes may benefit from integrating trauma-focused therapies.

Topic V: Adolescent Girls and Young Women (AGYW)

Pilgrim, Nanlesta, et al., 'Provider perspectives on PrEP for adolescent girls and young women in Tanzania: The role of provider biases and quality of care', *PLoS ONE,* vol. 13 (4), 27 April 2018.

- This mixed methods study in the United Republic of Tanzania examined factors that influence health care providers' knowledge, attitudes, skills and perceptions of facility readiness to provide PrEP, which are associated with providers' willingness to provide PrEP to adolescent girls and young women (AGYW).
- Lower willingness to prescribe PrEP to AGYW was associated with negative attitudes towards adolescent sexuality and concerns that PrEP use would encourage young adults from protective behaviours. Other barriers raised were the need for technical competency and trainings for adolescent-friendly care; shortages of staff to provide PrEP and space in which to do so, which could affect the allocation of existing services; and stock-outs of HIV prevention and treatment options.
- The authors note when PrEP is introduced in the health system, it should be accompanied by preparatory interventions focusing on AGYW that aim to reduce health care provider bias and strengthen the health system infrastructure for additional services.

Kilburn, Kelly, et al., 'Transactional sex and incident HIV infection in a cohort of young women from rural South Africa enrolled in HPTN 068', *AIDS*, Epub ahead of print, 11 May 2018.

- This secondary analysis explores longitudinal data from young women (ages 13–20) in South Africa enrolled in the HIV Prevention Trials Network (HPTN) 068 study on

conditional cash transfers. The analysis aimed to assess the effect of transactional sex on HIV incidence over a period of six years. Transaction sex was defined by the authors as self-reported material exchanges with three most recent sexual partners at each clinic visit.

- The cohort included 2,362 young women who were HIV-negative at baseline, followed for up to four visits over six years. Of these participants, 3.6 per cent reported having had transactional sex; and among them, HIV incidence was significantly higher than among those who did not report having had transactional sex (adjusted hazard ratio: 1.50). The effect size was particularly higher when material gifts or money were received at least weekly (adjusted hazard ratio: 2.71).
- This cohort, followed from adolescence to young adulthood, also provided evidence that HIV risk differs by time period and age of exposure. There was a stronger association between transactional sex and HIV incidence among younger women, roughly before age 20.

Compiled and summarized by Carthi Mannikarottu and Jessica Rodrigues.