12TH INTERNATIONAL CONFERENCE ON HIV TREATMENT, PATHOGENESIS, AND PREVENTION RESEARCH (INTEREST)

Kigali, Rwanda
May 29 – June 1, 2018

MEETING REPORT

JULY 2018
# Table of Contents

1. Introduction .................................................................................................................. 3

2. Current status of the HIV epidemic and response in Rwanda ............................................. 4

3. Progress towards the 90-90-90 goals in sub-Saharan Africa ............................................. 6

4. HIV prevention .............................................................................................................. 8
   - HIV susceptibility among women ............................................................................... 8
   - Pre-exposure prophylaxis ......................................................................................... 9
   - Other novel HIV prevention methods .................................................................. 10

5. Meeting the needs of key populations .......................................................................... 12
   - HIV and Hepatitis C among key populations ....................................................... 12
   - Best practices in programming for key populations ......................................... 12

6. HIV testing and diagnostics .................................................................................... 14
   - Sustaining progress on “the first 90” .................................................................. 14
   - HIV self-testing .................................................................................................... 15
   - “The third 90”: Improving access to viral load testing .................................... 15
   - Point-of-care technology for early infant diagnosis and viral load testing in children .... 17

7. Towards a vaccine and cure .................................................................................... 17
   - Update on HIV vaccine research ........................................................................ 17
   - Towards a cure for HIV ..................................................................................... 18

8. HIV co-infections, comorbidities and aging ................................................................. 18
   - The challenges of tuberculosis control ............................................................... 18
   - Eliminating hepatitis in sub-Saharan Africa .................................................... 20
   - The next era of comorbidities: HIV and aging .................................................. 21

9. Nothing for us without us: Issues for adolescents and young adults .............................. 22
   - The challenge of demographic shifts in sub-Saharan Africa ............................ 22
   - Optimizing HIV treatment outcomes for young people .................................... 23

10. Current issues in HIV treatment ............................................................................. 25
    - Antiretroviral treatment initiation and retention: “the second 90” ..................... 25
    - Differentiated service delivery ........................................................................ 27
    - HIV in children ................................................................................................. 28
    - Mental health in people living with HIV ........................................................... 28

11. Harnessing new technologies for an accelerated response ........................................ 29

12. Building the next generation: Mentorship in the HIV response .................................. 31

13. Implementation science: what success looks like ....................................................... 32

14. Closing of the 12th INTEREST meeting .................................................................. 33
1. Introduction

The 12th International Conference on HIV Treatment, Pathogenesis and Prevention Research (the INTEREST meeting) was held in Kigali, Rwanda from May 29 – June 1, 2018, bringing together nearly 600 participants from 32 countries, half of whom came from the host country.

Taking advantage of the meeting’s intimate all-plenary format, INTEREST delegates engaged in lively debates over three and a half days on key challenges in the HIV response, including ethical approaches to HIV prevention trials and the potential and pitfalls of mobile technologies in the response to HIV. Delegates also explored key challenges facing the region as it seeks to end the AIDS epidemic by 2030, including how to better tailor services and interventions to meet the needs of key populations, adolescents, and young adults; scaling up innovations such as pre-exposure prophylaxis and HIV self-testing; continuing to expand access to viral load testing for patient management and early infant diagnosis; managing comorbidities in people living with HIV as they age and the continuing impact of co-infections such as tuberculosis (TB) and viral hepatitis; approaches to differentiated care for people taking antiretroviral therapy (ART); and promising advances in efforts to develop an HIV vaccine and cure.

The meeting featured eight oral and 30 mini-oral presentations and two debates, in addition to invited speakers and special symposia, as well as 343 poster presentations.

For the third successive year, in honour of the late conference co-founder, the Joep Lange Award was presented to the African researcher with the highest scoring conference abstract. The late Jacqueline van Tongeren's support for the arts was recognized by the availability of colourful handcrafts for sale from the local group, Inundo Association of People with Mental Disabilities.

As in previous years, many INTEREST delegates rose early in the morning to participate in discussions on selected poster presentations, attend the Joep Lange early-career mentorship sessions and seek grantspersonship advice in sessions led by the European and Developing Countries Clinical Trial Partnership (EDCTP), US National Institutes of Health-Fogarty International Center, and France’s Recherche Nord & Sud Sida-hiv Hépatites (l’ANRS).

Meeting co-sponsors included Abbvie, Becton Dickinson, GlaxoSmithKline, International AIDS Society, Joep Lange Institute, Johnson & Johnson, Mylan, NIH-Fogarty, Roche, and ViiV Healthcare.
Welcoming delegates and formally opening the 12th INTEREST meeting, the Minister of Health of Rwanda, the Honourable Diane Gashumba, highlighted the significant progress made in the response to HIV in both Rwanda and across the region, beginning with the availability of antiretroviral treatment in the early 2000s. She attributed the successes achieved in many countries in the region to factors such as task-shifting to nurses and community health workers, decentralization of HIV services, expansion and simplification of programs to prevent vertical HIV transmission, effective monitoring and evaluation using routinely collected patient data to guide decision-making, and political leadership within a culture of “always doing better”. Nevertheless, many countries are now facing significant challenges and constraints, notably with regard to declining donor funding that threatens the long-term sustainability of HIV programs and requires further commitments from African countries to increase domestic funding for HIV and other health priorities.

2. Current status of the HIV epidemic and response in Rwanda

Jeanine Condo, Director-General of the Rwanda Biomedical Centre, presented an overview of the current status of the HIV epidemic and response in the 12th INTEREST host country. Rwanda has achieved a major reduction in HIV prevalence from above 10% in the early years of the epidemic to around 3% today, with prevalence currently higher among women (3.6%) than men (2.2%). Prevalence remains extremely high among female sex workers (FSW), at more than 45%, and may be higher than the reported 4% among men who have sex with men, highlighting the need for close attention to HIV among key and vulnerable populations. Numbers of new infections and AIDS deaths have fallen substantially from their peaks in 1990 and 2003, respectively (Fig. 1).

Fig. 1

New HIV Infections and AIDS Deaths in Rwanda

Rwanda has also made impressive progress against the 90-90-90 targets, with 88% (198,000) of the 225,000 people living with HIV in the country diagnosed with HIV, 94% (187,000) of those diagnosed now on ART, and 91% of those on ART (170,000) achieving viral suppression. A slightly lower proportion of adolescents is diagnosed, on ART, and virally suppressed than adults (Fig. 2). Other notable achievements include reduction of the rate of mother-to-child HIV transmission
(MTCT) from nearly 11% in 2010 to 1.5% in 2018 through the provision of antiretroviral drugs in all antenatal care facilities, increasing coverage of voluntary male medical circumcision to 30% of prioritised men, and the steady scale-up of viral load testing using a “hub and spoke” model designed to extend access to laboratory diagnostics across the country, including rural and remote areas. Scale-up of ART in Rwanda has led to an average gain in life expectancy of 25 years among people living with HIV in Rwanda.

Rwanda is now setting its sights on achieving 95-95-95 by 2030. To accelerate progress on HIV testing and diagnosis, attention is being paid to ensure that testing reaches key populations, pregnant women, and male partners in serodiscordant couples, including through outreach to key populations in “hot-spot” areas, more effective referral of clients with sexually transmitted infections (STI) from pharmacies, and the scale-up of HIV self-testing. To improve ART initiation, attention is being paid to coverage gaps for key populations, adolescents, children, young women, and adult men, including through the further roll out of “treat all”, implementation of differentiated service delivery, increasing the number of adolescent friendly health services, and implementation of electronic medical records with unique patient identifiers. To improve viral suppression among people on ART, the country is focusing on effectively monitoring the risk of treatment failure through the further scale-up of viral load testing and addressing lower levels of viral suppression among adolescents, children, and adult men, including through the strengthening of community-based adherence support. Management of comorbidities in people living with HIV, including TB, viral hepatitis, and non-communicable diseases, is also an important priority.

The Rwandan Minister of Public Health and Primary Health Care, the Honourable Patrick Ndimubanzi, noted that his country is endeavouring to increase domestic spending for HIV, including by absorbing health personnel costs that were previously supported by PEPFAR and the Global Fund. He also highlighted the country’s move away from vertical programs and toward an increased focus on integrated health services.
Geraldine Umutesi from the Imbuto Foundation of Rwanda highlighted the important role played by community-based health organizations and services in her country. The Rwandan health system includes community-level care in nearly 15,000 villages provided by more than 45,000 community health workers, many of whom play a key role in supporting access to HIV services. Sage Semafara from the Rwandan National Network of People Living with HIV described how the network’s more than 120,000 members support HIV program implementation through activities such as peer adherence support and participation in national policy development.

3. Progress towards the 90-90-90 goals in sub-Saharan Africa

Karusa Kiragu, the UNAIDS Country Director for Uganda, presented an overview of the response to HIV in sub-Saharan Africa, including regional and sub-regional progress towards the 90-90-90 targets. The region as a whole has nearly 70% of the global burden of HIV, with adolescent girls and young women more likely to acquire HIV than boys and young men. Key populations account for around 25% of new infections in the region.

Eastern and southern Africa have more than 19 million people living with HIV, with the highest number of new infections occurring in South Africa, Mozambique, and Kenya. Between 2010 and 2016, the sub-region experienced a 24% decline in new infections among people 15 years and older, accompanied by a 56% decline in new infections in children due to the scale-up of programs to prevent mother-to-child transmission. The largest declines in new infections among adults have been reported in Zimbabwe, Mozambique, and Uganda.

Around 6 million people are living with HIV in west and central Africa, where declines in the number of new infections between 2010 and 2016 were lower, at 9% among people 15 years and older and 33% among children. The largest number of new infections in the sub-region – 60% - occurred in Nigeria, followed by Cameroon and Ghana. Guinea-Bissau has recorded the largest decline in new infections, followed by Burundi and Senegal.

East and southern Africa have achieved a 42% reduction in AIDS-related deaths since 2010, with ART coverage increasing from 23% in 2010 to 60% in 2016. In Botswana, eSwatini, Rwanda, and Zimbabwe, more than 75% of people living with HIV are accessing treatment. West and central Africa have achieved a 21% reduction in AIDS deaths since 2000, with ART coverage increasing from 13% in 2010 to 35% in 2016, but no country has achieved ART coverage higher than 75%.

Progress against the 90-90-90 targets also differs between the two sub-regions. All 21 countries in eastern and southern Africa have adopted the WHO “treat all” recommendation, while only half of the countries in west and central Africa have adopted the policy. West and central Africa lag significantly behind in the diagnosis of HIV among people living with HIV (42% of people know their status compared to 76% in eastern and southern Africa) and are also lagging in linking people who are diagnosed to treatment and care and in achieving viral suppression among those...
on treatment (Fig. 3). WHO and other partners are implementing a catch-up plan to accelerate progress against the 90-90-90 targets in west and central Africa. Stigma and discrimination continue to act as significant barriers to treatment access and outcomes across the region. Men and young people have lower uptake of HIV services compared to adult women.

Fig. 3

![Bar chart showing progress towards the 90-90-90 targets, 2016](image)

Although some countries - including eSwatini, South Africa, and Zimbabwe - provide virologic testing to diagnose HIV infection in more than 70% of HIV-exposed children in the first two months of life, more needs to be done to expand access to infant diagnosis across sub-Saharan Africa and to improve treatment coverage for children. ART coverage stands at 51% in eastern and southern Africa and 42% in west and central Africa.

Financial resources for HIV in eastern and southern Africa are currently near the levels needed to reach fast-track targets, with nearly half of all funding in the sub-region coming from domestic sources; however, both external and domestic funding levels in west and central Africa remain inadequate. Both sub-regions face the pressure of declining external funding.

Discussion following the session highlighted the importance of couples testing in antenatal care settings, the need to address persistently high levels of HIV-associated stigma, and strategies to enhance retention in care, including through adequate geographic coverage of services and community-based support systems.
4. HIV prevention

HIV susceptibility among women

In eastern and southern Africa, young women will acquire HIV five to seven years earlier than their male peers. In 2015, there were on average 4,500 new HIV infections among young women every week, double the number in young men. In west and central Africa, 64% of new HIV infections among young people in 2015 occurred among young women. The sex difference is particularly striking in Cameroon, Côte d’Ivoire, and Guinea, where adolescent girls aged 15–19 years are five times more likely to acquire HIV infection than boys of the same age.

HIV disproportionately affects women and adolescent girls because of vulnerabilities created by unequal cultural, social, and economic status, including attitudes towards sex outside marriage, the restricted social autonomy of women and young girls that reduces their ability to negotiate safer sex and access sexual health and HIV services, and gender-based violence. Addressing these social and structural vulnerabilities is an important element of national responses to HIV. Rwanda, for example, has used national cross-sectoral legal and policy frameworks, including the 2010-2014 National Accelerated Plan for Women, Girls, Gender Equality, and HIV, to promote gender equality and female empowerment within the national HIV response.

As Heather Jaspen of the Seattle Children’s Research Institute and the University of Cape Town emphasized in a presentation on women’s vulnerability to HIV, biological factors also play an important role in influencing women’s susceptibility to HIV. Masson et al (2015) have reported that women with pre-existing genital inflammation are much more likely to acquire HIV. Furthermore, the relatively higher diversity of the vaginal microbiome in African women compared to women in North America is associated with higher levels of vaginal inflammation (and possible damage to the mucosal barrier), likely predisposing African women to HIV acquisition. In addition, observational data from the Polis study and a randomized trial comparing different contraceptive methods (the U Choose study) indicate that there is lower diversity of vaginal microbiota among women who use oral contraceptives than among those who use long-acting injectable contraception, the latter being the most commonly used method in sub-Saharan Africa, especially among younger women. These findings suggest that combined oral contraceptives are protective against vaginal diversity. Studies also suggest that inflammation associated with high diversity of vaginal microbiota could undermine the efficacy of tenofovir-based pre-exposure prophylaxis (PrEP).
Pre-exposure prophylaxis

Interest in and momentum for the implementation of PrEP is growing in sub-Saharan Africa. Nelly Mugo from the Kenya Medical Research Institute presented a summary of the evolution of PrEP, from the reporting of pivotal clinical efficacy data and the first WHO recommendations in 2012 to the implementation and scale-up that are now taking place globally, including in a number of settings in Africa. She noted that the efficacy of PrEP in demonstration projects has exceeded 90%, indicating that rates of adherence are high when people recognize their own risk and the benefits of the intervention. When tailored for populations at high risk for HIV exposure, PrEP augments the impact of ART by increasing uptake of HIV testing, reducing the number of undetected infections, and increasing uptake of ART. Gender sub-analysis across three major studies showed that PrEP is well tolerated by women, has minimal toxicities, and is safe in terms of reproductive health. There is limited evidence of PrEP-related drug resistance to date. Recent evidence of population-level impact in high-income settings is very encouraging: PrEP was partly associated with a 51% decline in new HIV infections in San Francisco between 2012 and 2016, a 25% decline in the number of new HIV cases in Australia over a five-year period, and a 42% decline in new cases at a London clinic over two years.

Although a number of studies are currently underway to inform PrEP uptake and adherence among young African women, it is apparent that effective implementation and scale-up in Africa requires a clear implementation framework, effective demand creation strategies, supportive implementation tools, and delivery that is integrated with other desired health services. Above all, African women need to be able to choose from a range of HIV prevention methods. Dr Mugo concluded her presentation with a case study of scale-up in Kenya, where more than 20,000 people have accessed PrEP and the intervention is helping to re-energize prevention advocacy and the provision of combination prevention services.

Among the approaches being implemented in Kenya is an initiative to offer PrEP to young, pregnant, and post-partum women as part of routine care in 16 maternal and child health (MCH) clinics (the PrIYA Program) in Kisumu Country in Western Kenya. Results are promising in this setting with nearly 10,000 young women having been assessed over a six-month period for behavioural risk factors and willingness to consider PrEP and more than 1,800 of them initiating PrEP. Those who started PrEP were more likely to do so in the post-partum period, be young, have an STI, or had been forced to have sex in the last six months. The results suggest that routine MCH clinics could be a useful platform for PrEP delivery.

Rwanda is working to identify appropriate populations for implementation of PrEP. Recent recipients of post-exposure prophylaxis (PEP) may provide one entry point for reaching people at high risk of HIV transmission and expanding access to PrEP through existing services.

In eSwatini, the new national PrEP framework emphasizes PrEP for any person at high risk of HIV acquisition, in addition to six priority populations. A demonstration study conducted at primary health care clinics in 2017/18 found that a large proportion of clients expressing interest in PrEP and reporting risk factors for HIV did not belong to any of the priority populations, suggesting
that PrEP programs that are open to everyone at risk may be more effective in high HIV incidence settings than those focused only on specific populations.\textsuperscript{21}

In Zambia, PrEP was first incorporated into national guidelines in 2016, with eligibility expanded in 2017 to include risk-based criteria prioritising key populations and serodiscordant couples. Results from pilot initiation of PrEP at a referral site for key populations in Lusaka found near-universal positive perceptions of PrEP, however stigma, reticence on the part of health care workers, and negative media reports were barriers to access.\textsuperscript{22} Loss to follow-up one month after PrEP initiation was higher among at-risk men than among serodiscordant couples and female sex workers.

\textit{Other novel HIV prevention methods}

Nyaradzo Mgodi from the University of Zimbabwe emphasized that - in addition to PrEP – women have a strong interest in the range of other biomedical prevention methods that are currently in clinical development.\textsuperscript{23} The Voice D study, for example, found that women expressed strong preferences for injectables, implants, and vaginal rings over oral tablets.\textsuperscript{24}

The vaginal ring has the advantages of being long-acting (thereby promoting adherence and effectiveness), easy to use, safe, private, and discreet. However, the dapivirine vaginal ring has shown only moderate efficacy of around 30\% in the Aspire and Ring studies. Two ongoing open-label Phase IIIb extension trials (HOPE and DREAM) will further evaluate its safety and adherence to this product. Interim results from these trials indicate that HIV incidence is half the expected rate and that there is high uptake and adherence. The dapivirine vaginal ring is now being reviewed by the European Medicines Agency (EMA). If the EMA approves the product, World Health Organization (WHO) prequalification will then be sought.

Long-acting injectable antiretrovirals may represent the next generation of PrEP and offer advantages in terms of adherence by eliminating the need for daily pill taking. The first of these products, cabotegravir (CAB-LA), a long-acting injectable formulation of the integrase inhibitor dolutegravir, is being tested in two National Institutes of Health (NIH)-funded Phase III trials. HPTN 083 will test CAB-LA among at-risk cisgender men and transgender women who have sex with men in 43 sites in the US, Argentina, Brazil, Peru, South Africa, Thailand, and Vietnam. Concurrently, HPTN 084 will test the efficacy of CAB-LA among at-risk women in 20 sites in sub-Saharan Africa. Both trials currently include a four-week oral therapy induction phase to identify any adverse reactions before the long-acting injectable is given. Results from both trials are anticipated by 2022. The need for an oral lead-in phase and the long pharmacologic tail of the drug after the last injection may pose significant challenges to implementation.

Passive antibody-mediated approaches to HIV prevention are also being tested. Two harmonized cohorts of men who have sex with men and transgender women in North and South America and Europe and of heterosexual women in sub-Saharan Africa (the NIH-funded AMP studies, also known as HPTN 081/HVTN 703 and HPTN 085/HVTN 704) are examining the safety and tolerability of the monoclonal antibody VRC01 and optimal dosing based on intravenous infusions
every eight weeks, and whether there is a signal that this product reduces risk of HIV infection. Phase I trials of three other monoclonal antibodies are currently in developmental stages.

**Formal Debate 1:** “It is the responsibility of research funding organizations and researchers to ensure access, uptake, and adherence to free, onsite, oral HIV pre-exposure prophylaxis as the standard of care for all participants at risk of HIV infection in all HIV prevention clinical trials”.

Formal debates have become a popular component of INTEREST meetings over the last several years. This debate took place in a context in which it is becoming increasingly difficult to conduct Phase 3 HIV prevention trials ethically and effectively. With a highly efficacious standard of prevention (oral PrEP) available and highly-effective ART being rolled out, researchers will need to enrol very large cohorts to achieve statistically significant comparisons of HIV acquisition in different trial arms.

In favour of the proposition, Helen Rees of the Wits Reproductive Health and HIV Institute in South Africa and Imelda Mahaka of the Pangaea Global AIDS Foundation in Zimbabwe argued that it is the ethical and professional obligation of researchers conducting HIV prevention trials to provide study participants with the best standard of prevention available, and that this has always been the practice in HIV prevention trials. Providing a consistent standard of care is also important to ensure comparability of results across trials. They noted that studies and cohort size can be designed to take PrEP use into account and that anything new in prevention will inevitably roll out in a context in which PrEP is available – it is therefore important to understand synergies between PrEP and new interventions sooner rather than later. By being in the vanguard of providing accessible PrEP, investigators and trial participants can become advocates for PrEP use and develop strategies to optimize adherence and uptake outside the study context.

Arguing against the proposition, Linda-Gail Bekker of the Desmond Tutu HIV Centre in South Africa and Jacqueline Wambui Mwangi of AfroCAB Kenya warned against the unintended consequences of offering PrEP as the standard of care in HIV prevention trials, including costs of performing very large trials and potential abuses of trials by participants whose only motivation to participate in studies is to access services. They argued that it should be the responsibility of countries hosting trials to provide the standard of care to all people, not just to trial participants, and that new interventions such as PrEP require demand creation and other strategies to support uptake and adherence that fall well outside the responsibilities of prevention trial investigators.

In a lively audience discussion, several delegates supporting the proposition argued that many people access new interventions as part of trials and that doing so is a valid way to initiate access to new interventions. Other delegates supporting the proposition noted that while it the trial investigators’ responsibility to provide access to the standard of prevention, they should not be responsible for ensuring uptake and adherence. Delegates against the proposition argued that PrEP was unlikely to be a cost-effective or sustainable intervention in many low-income countries and offering it as the standard of prevention in trials posed risks to existing HIV programs. In a post-debate ballot, delegates voted 60/40 against the proposition.
5. Meeting the needs of key populations

The 12th INTEREST meeting highlighted the increased attention being paid to the needs of key populations in the region. Key populations are disproportionately affected by HIV in nearly all countries and experience major barriers to accessing services, including criminalization, stigma, and discrimination. A symposium supported by the International AIDS Society (IAS) explored opportunities for and models of providing comprehensive care to key populations, including men who have sex with men, sex workers, people who inject drugs, and transgender people.

HIV and Hepatitis C among key populations

Nathan Ford from WHO highlighted the vulnerability of key populations to HIV, high HIV prevalence among key populations in nearly all countries in sub-Saharan Africa, and the lack of data needed to respond effectively to their needs in many countries. Punitive laws - including criminalization of homosexuality, drug use, and aspects of sex work, along with stigma and discrimination, act as major barriers to accessing services. Dr Ford noted that law reform can have a significant impact in averting new HIV infections (Fig. 4) and that significantly more attention to harm reduction is needed to address worrying trends in growing prevalence of HIV and hepatitis C among people who inject drugs, especially in southern Africa.

Fig. 4

![Diagram showing the potential reduction in HIV infections through various interventions](image)

*Best practices in programming for key populations*

Case studies and oral abstracts presented at the meeting highlighted the growing attention being paid to the needs of key populations in the region. Drawing upon the experience of providing PEP
and PrEP to men who have sex with men in South Africa, IAS President Linda-Gail Bekker from the Desmond Tutu HIV Research Centre noted that health services in Africa tend to be heteronormative and rarely address risk factors such as anal sex and injecting drug use. In addition, health care providers frequently lack relevant training and stigma and prejudice are widely reported in many health care settings. Dr Bekker emphasized the need to scale up best practices such as championing a public health approach for men who have sex with men; differentiated service delivery; tailored approaches to prevention and care for key populations; increased access to PrEP – including on-demand PrEP - as part of comprehensive services; addressing the special needs of adolescent key populations; effective community engagement; peer outreach; increased emphasis on mental health; and sustained efforts to change the attitudes of health care providers.

In eSwatini, where HIV prevalence is estimated to be around 70% among female sex workers and 18% among men who have sex with men, structural drivers of HIV among key populations include criminalization of same-sex activities and sex work, police harassment, violence and arbitrary arrest, and stigma and discrimination in health services. With support from PEPFAR LINKAGES, the country is implementing a multisectoral strategy to address these challenges, including creating opportunities for dialogue between key populations and government; training and sensitization for police and health care workers; and engaging communities, lawyers, and the judiciary. A study from Senegal highlighted the importance of addressing structural factors such as safe working spaces and violence mitigation programs to increase the ability of female sex workers to consistently negotiate condom use.

Training of health care workers, political support from the Ministry of Health and focus group discussions with affected communities have been key factors in the success of a project to integrate LGBT²-specific services in 25 health facilities in five counties in Kenya. The program is beginning to focus more intensively on the needs of transgender people, who experience high levels of discrimination and gender-based violence. Similarly, a study reported from Malawi found that community empowerment and engagement by government, health care workers, and peer leaders are key elements in implementing prevention and care programs among key populations. A study from Rwanda reporting high HIV prevalence among clients of female sex workers emphasized the need to include these clients in HIV prevention programming. In Kenya, non-financial incentives (points redeemable for various purchases) have been shown to be effective in motivating peer educators to enrol female sex workers in an SMS³-based health information program. In Eastern Cape Province in South Africa, an LGBT-sensitization program has focused on changing attitudes among local government leaders with a view to better engagement of LGBT people in local affairs.

Temeke Municipal Council in Dar es Salaam, Tanzania runs one of the relatively small number of programs in the region providing harm reduction and services tailored to people who inject drugs, including HIV and TB screening, methadone, ART in health facilities, and referrals to

---

² LGBT: lesbian, gay, bisexual, and transgender people
³ SMS: short message service
community-based services, such as needle and syringe exchange. In Senegal, an integrated centre for the management of addictions offers medical and social support including opioid substitution therapy, but faces challenges as a result of the restrictive legal and policy environment for harm reduction.

Access to treatment and care for prisoners - among whom HIV, TB, and hepatitis prevalence is high - is frequently poor across the region. A study from Malawi reported that nearly half of prisoners had consensual sexual relations while in prison, while access to HIV-related services was inconsistent and nutrition was particularly poor.

6. HIV testing and diagnostics

*Sustaining progress on “the first 90”*

Presenting on behalf of the Rwanda Zambia HIV Research Group, Susan Allen of Emory University emphasized the importance of identifying serodiscordant couples to appropriately focus HIV prevention resources and avert new infections. Because a key barrier to couples testing in many African countries is the belief that it is not possible to be in a sexual partnership with someone of a different HIV status, demand creation strategies are essential. Successful models for providing and promoting joint testing exist in every African country, including Rwanda and Zambia, two countries that have made concerted efforts to make couples testing a social norm. In addition to prevention benefits, knowledge of being in a serodiscordant couple also enhances adherence to treatment by the HIV-positive partner.

Joint pre- and post-test counselling or facilitated joint disclosure are effective approaches to ensuring that test results are communicated accurately between partners. Couples testing can and should be provided in a range of settings depending on the context and priority population, including health facilities, community-based settings, through mobile outreach, and in the home. The latter approach helps to overcome logistical barriers such as distance and time travelling to health facilities but may be comparatively expensive.

More attention is being paid to male participation and the provision of couples testing in antenatal care (ANC) settings. A study in Malawi, for example, found that men are reluctant to attend ANC clinics due to peer pressure from other men and fear of losing income when taking time off work. In such cases, financial and other incentives may serve as additional motivation for male partner involvement. Research reported from Tanzania and Rwanda indicates that efforts to increase male involvement in prevention of MTCT (PMTCT) services can increase uptake of partner testing.

Research from several countries, including Kenya, Botswana, Nigeria, and Uganda, emphasized that sexual partner notification and testing of contacts of index patients continues to be an effective approach.
HIV self-testing

HIV self-testing offers the potential to increase testing uptake and linkage to prevention and treatment in sub-Saharan Africa, especially among men and adolescents who can be hard to reach. However, concerns exist about potentially low yield and ensuring appropriate linkages to care when this method is offered in community-based settings. A study presented by Frackson Shabacompared the offer of conventional provider-initiated HIV testing to the novel method of facility-based self-testing performed in the waiting area with results subsequently given to the patient in private. Much higher uptake was reported among those in the self-testing arm of the study and self-testing was associated with a higher absolute number of new positive cases identified. Participants who used self-testing were also more likely to want to test again using the same method and were more likely to recommend testing to others.

Partner-delivered HIV self-testing appears to be a promising approach. In a study reported from Malawi, 65% of HIV-positive partners surveyed preferred the idea of delivering HIV self-testing kits to partners rather than the conventional partner referral slips. When clients were asked whether they believed that their partners would actually be tested, self-testing was associated with an 18% increase in anticipated testing compared to referral slips. Overall, 69% of people surveyed believed their partner would prefer self-testing. A study from Kenya that enrolled women seeking antenatal and post-partum care also compared participants who received two self-testing kits with a comparison group that received referral slips. Male partner testing uptake was 92% in the self-testing group compared to 55% in the comparison group. Couples testing was also significantly more likely in the self-testing group. This approach has also met with success in South Africa and Malawi.

A costing study conducted as part of the STAR initiative in Malawi, Zambia, and Zimbabwe evaluated population-level impact of HIV testing and demand for ART from home distribution of oral fluid self-testing kits by trained community providers. Nearly 400,000 testing kits were distributed in the three countries. Costs per test were found to be significantly higher than facility-based testing, driven by the need for additional personnel and supply costs. However, the self-testing approach attracted higher absolute numbers of testers and more hard-to-reach men. Costs may be further reduced with price reductions, economies of scale, and more effective targeting of test distribution.

“The third 90”: Improving access to viral load testing

Access to viral load testing is critical to monitor viral suppression in patients on ART and progress against “the third 90”. Pascale Ondoa from the African Society for Laboratory Medicine provided an overview of opportunities and challenges related to the scale-up of viral load testing to improve patient management. Although many countries in the region are working to implement viral load testing, progress varies widely. For example, more than 90% of ART patients in South Africa have received at least one viral load test compared to only 9% of ART patients in

---

4 Winner of the 2018 Joep Lange Award.
Côte d’Ivoire. Patients are frequently lost along the complex cascade of steps required to collect and transport samples and return test results (Fig. 5).

**Fig. 5**

### Systems issues affecting the Viral Load testing cascades

<table>
<thead>
<tr>
<th>Step</th>
<th>Issue</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Policy &amp; Regulation</td>
</tr>
<tr>
<td>1</td>
<td>Sample referral system</td>
</tr>
<tr>
<td>2</td>
<td>Sample collection</td>
</tr>
<tr>
<td>3</td>
<td>Sample transport</td>
</tr>
<tr>
<td>4</td>
<td>Test performed</td>
</tr>
<tr>
<td>5</td>
<td>Result returned</td>
</tr>
<tr>
<td>6</td>
<td>Clinical consultation</td>
</tr>
<tr>
<td>7</td>
<td>Clinical action</td>
</tr>
</tbody>
</table>

- Poor demand from patients and clinicians
- HIV care services are overloaded
- Lack of SOP
- Issues with sample conservation
- Sample referral system with:
  - low coverage
  - no tracking system
  - Long turn around time of sample transport
- Poorly optimized workflow
- Shortage of human resources
- Insufficient testing capacity
- Insufficient quality
- Reagent stock out
- Equipment maintenance
- Long turn around time
- Ineffective laboratory clinic interface
- Lack of or poor compliance to guidelines to use results
- Lack of differentiated care models
- Stock out of ARVs

Strong sample referral systems, such as the “hub and spoke” model used in Uganda and other countries, can be effective in improving access to centralized viral load testing and increasing the coverage of the laboratory network. Point-of-care viral load testing further simplifies the cascade by reducing the need for sample transport and enabling rapid delivery of results. However, introducing new point-of-care technologies can be a lengthy process due to the need for regulatory approval in each country, limited normative guidance, relatively higher prices per test, and currently limited funding support.

Utilization of viral load test results to inform patient management is currently sub-optimal: studies in Kenya and Mozambique, for example, showed that only a small minority of patients with unsuppressed viral load undergo repeat testing.\(^{52,53}\) Reasons for poor test result utilization include lack of systems to connect results with patients or to flag unsuppressed viral load as an emergency, lack of responsible individuals in the clinic, and poor patient follow-up and recall. Effective approaches to overcoming these challenges include having viral load focal points in clinics; systematic, daily review of test results; the use of “unsuppressed viral load registers”; using stickers on charts; and case management approaches. Key challenges for the future scale up of viral load include helping countries with limited resources to access viral load testing by taking a systems-wide approach to ensure that improvements along the viral load cascade benefit other diseases, and broad stakeholder engagement in the scale-up process. The laboratory strengthening system community of practice (LabCoP) supported by the Bill and
Melinda Gates Foundation currently engages 11 countries in sub-Saharan Africa to share lessons and best practices for improving laboratory system functioning and accelerating the scale-up of HIV viral load testing.

**Point-of-care technology for early infant diagnosis and viral load testing in children**

Viral load testing for early infant diagnosis (EID) is beginning to become available in sub-Saharan Africa. Kenya has one of the most advanced conventional EID systems in the region, benefiting from investments in an electronic results database that expedites processing of test results. Despite this, only around half of HIV-exposed infants access testing by two months of age and many children are lost to follow-up, in part due to the need to transport blood samples and delays in the return of results to caregivers. A pilot study using point-of-care EID and a “hub and spoke” model led to 99% of caregivers receiving results within 30 days, compared to 19% using conventional EID. The median turnaround time for results decreased from 52 days to two days, with ART initiation rates increasing from 71% to 100%.54

A study in Zimbabwe highlighted current challenges in performing routine viral load testing to manage HIV in children in remote areas.55 Of nearly 4,000 children on ART in three rural districts, 57% had received a viral load test in 2017. Data from a sub-sample of these children found an average turnaround time for viral load test results of 41 days, with up to 70% reporting detectable viral load. Use of dried blood spot samples was found to be feasible and may promote uptake of viral load testing in remote settings, but the high viral load levels reported in the study indicate serious gaps in HIV management among children in the settings studied.

7. Towards a vaccine and cure

**Update on HIV vaccine research**

Linda-Gail Bekker from the Desmond Tutu HIV Research Centre presented an update on HIV vaccine research, focusing on trials underway through the HIV Vaccine Trials Network.56 Modelling suggests that adding a vaccine to the current repertoire of prevention interventions could have a major impact in averting new infections.57 The ideal characteristics of an HIV vaccine include effectiveness in a single dose; durable, cross-clade protection; ease of transport and preparation; and potential to be co-administered with other vaccines. To date, it has been difficult to develop a vaccine because of the genetic diversity of HIV, the unique envelope of the virus, challenges in translating animal modelling to efficacy in humans, and lack of engagement by the private sector. The two big questions currently facing the vaccine field are whether non-neutralizing antibodies can be potent enough to achieve durable efficacy (defined as >50% for at least two years), and how to elicit better T-helper responses to drive higher and more durable protection.

Dr Bekker presented an overview of vaccine efficacy trials, beginning with the unsuccessful VaxGen gp120 trial in the late 1990s, after which the field turned to T cell-based approaches;
however, the Step trial (HVTN 505) showed no efficacy and raised concerns that the candidate vaccine may cause harm. Results from the RV144 trial in in Thailand in 2009 energized the field when a ‘prime’ vaccine called ALVAC-HIV (vCP1521), combined with a boost of the AIDSVAX gp120 vaccine, showed efficacy of around 30%. Efforts to better understand and build on the RV144 findings and explore the use of monoclonal antibodies are underway in three trials (HVTN 702, HVTN 703/704 and HVTN 705) that are currently enrolling participants in several countries. These pivotal HIV vaccine efficacy studies will help to define whether neutralizing and/or non-neutralizing antibodies can be tweaked to provide reasonable vaccine efficacy and will set the stage for the design and development of vaccine research for the next decade.

Towards a cure for HIV

Carolyn Williamson from the University of Cape Town provided delegates with an overview of the current status of HIV cure research and implications for the future.58 The major challenge in HIV cure research is to address the persistent HIV viral reservoir in lymph nodes and other parts of the body. It is generally thought that eliminating a “small” reservoir will be easier. Although people who start ART during acute infection will have smaller reservoirs, a number of factors may increase the size of the viral reservoir, including non-adherence to treatment, immune activation, and concurrent chronic infections. To date, only one person has been completely “cured” of HIV and around 5-10% of adults are able to control HIV after early initiation and cessation of ART, but in most people, viral rebound will take place as early as two to three weeks after stopping treatment.

The main strategies currently being pursued in cure research to achieve viral remission are therapeutic vaccination and passive immunization, potentially in combination with latency reversing agents. More than 40 clinical trials of a range of therapeutic vaccine products have been undertaken to date, and although these products have been shown to be safe, they have so far been largely ineffective. Broadly neutralizing antibodies in development for HIV prevention also have potential for cure research and have shown significant promise in animal models; more research in humans is needed to test the efficacy of this approach. A key challenge for researchers in the future is to more clearly define the viral reservoir in African populations since most cure research to date has taken place in Europe and the United States.

8. HIV co-infections, comorbidities, and aging

The challenges of tuberculosis control

Jeremiah Chakaya Muhwa from the Kenya Medical Research Institute presented an overview of the global TB epidemic and prospects for controlling TB, including among people living with HIV.59 Of the estimated more than 10 million cases of TB in 2016, 1 million or 11% occurred in people living with HIV (Fig. 6). Many of the countries with the highest burden of TB, TB/HIV co-infection, and multi-drug resistant (MDR) TB are in sub-Saharan Africa. Poverty is one of the most important
drivers of TB globally and, in this region, HIV is an additional, extremely important driver of TB. Miners have 10 times the rates of TB, compared to the general population.

Fig. 6


Current challenges in TB control include the need for active case finding to close the huge gap between current numbers of estimated and reported cases; for new approaches to accelerate declines in TB incidence, including new drugs and diagnostics; for concerted efforts to reduce the current, high TB case fatality ratio; for measures to address catastrophic health expenditures experienced by many TB patients and their families; for action to address the rising global burden of drug resistance; for mobilising communities and advocates more effectively; for accelerating adoption and ensuring optimal use of new technologies; and for efforts to strengthen weak health systems to respond to TB more effectively, including to address inequities in service delivery in many poor, rural communities. Above all, tackling the root causes of poverty is essential: it is estimated that ending extreme poverty and expanding social protection would reduce TB incidence by 33% and 75% respectively; doing both would reduce global TB incidence by 84%. Discussion following Dr Muhwa’s presentation focused on the need to eliminate the DOTS approach and the critical need for a validated diagnostic tool to determine who is going to progress from latent TB infection to active disease.

Nesri Padayatchi of the Centre for the AIDS Programme of Research in South Africa discussed the major disparities in global investment and innovation in TB compared to HIV. Between 2000 and 2015, more than 2600 HIV clinical trials have taken place, compared to just 350 for TB, with the result that 28 new drugs have been discovered for HIV, compared to just two new drugs for TB. TB is critically underfunded: for every dollar spent on HIV research in the period 2005-2007, just 5 cents was spent on TB, while in 2015 the Global Fund disbursed 53% of its resources to HIV
programs and only 16% to TB programs. At the same time, approaches to HIV testing, prevention, treatment, and care focus on empowering people and their communities, while TB is notable for a top-down, disempowering model of detection, notification, and cure. Although there is stigma associated with both TB and HIV, HIV advocates have been more effective at challenging stigmatization through collective grass-roots action that leads to policy change, whereas the TB community has inadequately contested programmatic norms that reinforce stigma and disempowers patients and communities. To help change cultural and provider attitudes to TB and to enable the TB community to more effectively draw upon lessons from the HIV response, Dr Padayatchi called for HIV and TB programs to adopt a more collaborative and collective approach, as well as for increased efforts to meet the socio-medical needs of TB patients and for more patient-centred approaches to TB prevention, treatment, and care.

*Eliminating viral hepatitis in sub-Saharan Africa*

While global mortality from HIV, TB, and malaria has fallen over the last 15 years, mortality from viral hepatitis is growing (Fig. 7).

**Fig. 7**

A presentation by Ganiyat Kekelomo Oyeleke from Lagos University Teaching Hospital in Nigeria explored the actions needed to eliminate hepatitis in sub-Saharan Africa, which accounts for 25% of the global burden of hepatitis B (HBV) and 11% of hepatitis C (HCV).^62^ Co-infection with HIV worsens the condition of the liver. In Nigeria, the most populous country in Africa, 21 million people are infected with HBV and 4 million with HCV. Most people present with advanced disease and treatment for chronic HBV/HCV is limited to tertiary centres and the private sector. Although
coverage of the HBV vaccine birth dose is currently very low, many countries are in the course of planning to implement or are scaling up this important intervention.

Key challenges in the response to viral hepatitis in the region include limited government leadership and commitment; lack of funding; poor implementation of national strategies; lack of a public health approach to screening and treatment; the high cost of drugs; and gaps in data on disease burden and treatment need. Cultural beliefs and stigmatization also act as barriers to screening and linkage to care, with few health care workers being adequately trained in this area. Rather than vertical approaches, integration of hepatitis services into health systems and strategies is an essential element of effective future responses to hepatitis in the region. Multisectoral partnerships including civil society are also needed. Some encouraging initiatives to address viral hepatitis are underway, including an HCV treatment program supported by the Clinton Foundation and efforts to leverage the GeneXpert TB and the Roche PCR HIV platforms to improve access to HCV and HBV viral load testing. In addition, over 250 primary care physicians are being trained through the International Coalition of Hepatology Education Providers. However, greater political commitment, a public health approach, increased resources, and lower drug prices are all needed to further advance the regional response to viral hepatitis.

In 2017, Rwanda held a national, week-long campaign related to World Health Day to raise public awareness about viral hepatitis. More than 180,000 people were screened for HBV and HCV, with around 4% of people testing positive for HBsAg and 8% for HCV. The campaign helped to build capacity and leverage infrastructure for hepatitis screening in the country and provided a baseline of data for future interventions.63,64

**The next era of comorbidities: HIV and aging**

In a symposium sponsored by Gilead, Andrew Kambugu from Makere University and Mas Chaponda from the Royal Liverpool University Hospital presented overviews of the epidemiology of HIV and comorbidities related to aging, including a series of interactive case studies.65 In the era of effective ART, an aging population of people living with HIV, long-term toxicities related to treatment, and residual inflammation among people on treatment all have implications for the incidence of non-communicable diseases (NCDs) - including hypertension, cancers, renal and cardiovascular disease, fractures, and diabetes - in sub-Saharan Africa. This is particularly important among women, who comprise the majority of people on ART in the region.

Renal disfunction can be caused by a range of factors, including smoking and hypertension. ART – particularly the drug tenofovir disoproxil fumarate (TDF) – can contribute to this problem. TDF is also associated with changes in bone mineral density that are of particular concern for women over 50 years who are already more prone to fractures. Dr Chaponda recommended that where possible patients be assessed for risks of renal disfunction and changes in bone mass and that ART regimens be tailored accordingly. For example, tenofovir alafenamide (TAF) - a pro-drug of TDF - has been found to preserve bone mineral density and has significantly lower impact on
renal function. Cardiovascular disease and diabetes are also growing challenges among older people with HIV, especially men.66

Polypharmacy is an increasing challenge as more drugs are prescribed to older people living with HIV. Health care providers need to be aware of potential interactions between some antiretrovirals and other drugs, as well as with antacids, multivitamins, herbs, and traditional medicines. Boosted protease inhibitors are of particular concern, while integrase inhibitors have fewer interactions. The University of Liverpool HIV drug interaction website provides comprehensive guidance for health care providers in this area. In resource-limited settings, education and task-shifting to nurses and clinical officers is important for effective management of drug-drug interactions.

Data on HIV and aging in sub-Saharan Africa are limited. In Uganda, the number of people diagnosed with HIV aged 50-59 years more than doubled between 2011 and 2016.67 However, population data from that country suggest that co-morbidities associated with aging are in fact more prevalent in HIV-negative people than in people living with HIV. This may be because people with HIV access care more frequently and because traditional risk factors, such as smoking and alcohol use, are higher in the HIV-negative population. Nevertheless, qualitative studies suggest that older people with HIV face a range of challenges, including stigma; reluctance to disclose HIV status; mental health issues; delayed diagnosis and challenges with adherence; continuity of care; and end-of-life care. There is evidence that immune reconstitution in older patients commencing ART may also be suboptimal. More research into HIV and aging is needed in the region, including implementation research on approaches to integrating the management of HIV and NCDs.

9. Nothing for us without us: Issues for adolescents and young adults

The challenge of demographic shifts in sub-Saharan Africa

In a keynote address, Mark Dybul, former US AIDS Ambassador and former Executive Director of the Global Fund to Fight AIDS, TB, and Malaria, highlighted the challenges posed to the HIV response in sub-Saharan Africa by major demographic changes that are currently underway.68 Africa’s population is anticipated to increase from 1 billion people today to 2.5 billion by 2050 and 4 billion by the end of this century. In addition, the African population is young, with 61% of people under 25 years of age, compared to 33% in North America. In many countries in the region, only about half of young people 15-24 years of age are tested for HIV (Fig. 8), and fewer young people on ART achieve viral suppression than adults. At the same time, adolescent girls and young women in the region as a whole are 14 times more likely to be living with HIV than their male peers. The consequence is that the largest generation in history is reaching an age when they are most at risk of HIV, and with current trends, more young people will be living with HIV by 2030 than in 2000.
This “youth bulge” in Africa and its likely negative impact on the region’s ability to end AIDS by 2030 require a more intensive effort to keep adolescent girls and young women HIV-free, including by keeping them in school and preventing early pregnancies and sexual violence. For this population, HIV needs to be addressed in a broader context by providing more flexible, comprehensive, adolescent-friendly health and social services, including sexual and reproductive health and family planning services. Dr Dybul provided several examples of such programs already underway, including youth clubs in South Africa, community-based adolescent treatment support services in Zimbabwe and a “hub and spoke” model that links services provided in schools and community settings with adolescent-friendly health facilities. He urged INTEREST delegates to develop “communities of practice” linked to data and policy-making that will help enable such approaches to be brought to the scale needed to address the growing challenge of HIV among adolescents and young adults across the region.

Optimizing HIV treatment outcomes for young people

A special session sponsored by Johnson & Johnson focused on strategies to optimize treatment outcomes for young people and approaches to providing adolescent-friendly health and social services, including for HIV.

In Rwanda, where HIV prevalence in the general population is around 3%, young women aged 15-24 years have slightly higher prevalence at 3.5% than young men at 1.5%. Rwanda has developed a minimum package of adolescent HIV services that includes HIV counselling and testing, referral to health facility- and community-based services, ART, support for safe disclosure, psychosocial support, sexual and reproductive health services, voluntary male medical circumcision (VMMC), and nutrition support. To the extent possible, services need to be
integrated and available in the same setting and should have the flexibility to be meet special needs as they arise, such as housing and academic support. Designing services for young people requires specific attention to three elements: 1) time: flexibility in service hours is needed to accommodate youth needs, including after-school and drop-in services and avoiding holding consultations with adults and youth at the same time; 2) space: young people prefer private, dedicated spaces that enable them to freely express themselves; and 3) trained staff that have the knowledge and skills to address adolescent needs and tailor services to suit the age group and stage of social development of the clients.⁶⁹

Psychosocial support is a key component of youth-friendly services. In Lesotho, which has very high HIV prevalence among both adults and young people, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) has developed an integrated psychosocial support approach based on youth-led peer support groups that have now been offered to more than 18,000 young people. The groups have helped participants develop life skills and prepare for the transition to adult care and improved motivation for initiating and adhering to ART. They have also supported safe disclosure and strengthened referrals to social workers and psychologists. Data suggest that young people linked to the groups have improved clinical outcomes, including viral suppression.⁷⁰

A study of more than 1500 young people living with HIV in South Africa and neighbouring countries explored some of this population’s unique characteristics. It found that young people’s needs were complex given their developmental stage and included processes of releasing connections with caregivers and developing new romantic, sexual, and professional relationships. Balancing school attendance and health care is frequently a challenge. Health care providers found that loss to follow-up and issues related to stigma and disclosure were common. The researchers highlighted the need to go beyond “hashtags and beanbags” in providing youth-friendly services and proposed a “STACK” model based on adequate Stocks of medicines (to ensure adherence), adequate Time to address youth needs, Accompanying young people to clinics, Cash for food and transport, and Kind staff. This study also found associations between peer support and lower levels of unprotected sex, improved adherence, and viral suppression.⁷¹

A panel discussion highlighted additional important issues for youth living with HIV, including the use of social media platforms for peer support, the need to support young couples and those having children, gender-based violence and inability to negotiate condom use, the importance of supporting young women with HIV to stay in care after pregnancy, the need for youth-focused treatment literacy, and challenges associated with coming-of-age rituals and masculine norms when living with HIV.

Poster and oral abstract presentations covered a range of issues related to HIV and young people. A study from South Africa reported alarmingly low levels of viral suppression among adolescents 0-19 years of age. Older, vertically-infected adolescents were most at risk of poor virological monitoring and treatment failure.⁷² Data collected by EGPAF in adolescent-friendly services in eight African countries found that although adolescents 10-19 years of age represented just 4-10% of the population in HIV care, they had more intensive treatment, adherence counselling, and psychosocial support needs.⁷³ Clubs and peer support groups were found to be important
complements to clinical care but need to be further scaled up. More providers can be trained in providing youth-friendly services at facilities than off-site, capacity can be built with short courses, and multidisciplinary care teams can better address the needs of youth.

In South Africa, Wits Reproductive Health and HIV Institute’s USAID-funded Adolescent Innovations Project has provided an integrated model of care for adolescents living with HIV including out-of-facility testing, linkage to services with the support of a peer navigator, and support for adherence and retention through psychosocial support and “youth care clubs”. The intervention increased rates of treatment initiation over a 12-month period, as well as the number of viral load tests performed and rates of viral suppression. In Zimbabwe, a differentiated service delivery model for children and young adults living with HIV in rural settings found that double orphans and boys had higher virologic failure, suggesting that gender and family context influence adherence in these populations.

A secondary school-based nursing program introduced as part of the Zimele Project in South Africa involves weekly school attendance by a trained nurse. The initiative has been effective in bringing health care directly to adolescents at a time and place conducive to their needs. More than 44% of the female students accessing the services sought support related to sexual and reproductive health, highlighting a critical need and gap in care for this population. The project is supported by the local Department of Education and has been incorporated into its school health policy.

A study of young men and women living with HIV aged 14-21 years in Rwanda evaluated gender related roles and behaviours in relation to treatment adherence. It found that among young women, self-silencing (“doing what their partner wants them to do”) and gender-based violence were negatively associated with adherence, and that having more control in their relationships improved adherence. The study highlighted the importance of addressing structural and social factors to improve treatment outcomes for youth.

10. Current issues in HIV treatment

Antiretroviral treatment initiation and retention: “the second 90”

Nathan Ford from WHO provided an overview of issues related to ART initiation and retention, noting that there are still major gaps in the care cascade globally and at the regional level, including in sub-Saharan Africa (Fig 9).
The WHO “treat all” recommendation has been rapidly adopted in most countries, with widespread uptake in Africa over the last two years (Fig. 10). Recent data indicate that “treat all” increases the number of people starting ART within three months of diagnosis. Observational data and randomized trials show that starting ART within seven days of diagnosis is associated with lower levels of loss to follow-up, improved viral suppression, and reduced mortality.
Key outstanding research questions include the benefits and challenges of implementing “treat all” among key populations, adolescents, and pregnant women; optimal tools to assess patient readiness for same-day treatment initiation and to support adherence; long-term outcomes of rapid ART initiation; and the potential for ART initiation in community settings.

Barriers to adherence are well documented and include forgetting to take pills, travel, being busy, and changes to daily routine.83 A range of interventions has been proposed to address these challenges, including SMS messaging, decentralization of services, and mental health screening and support. Studies suggest that no single intervention will work in all settings and it is likely that a package of options will be most effective.84 More rather than fewer counselling sessions appears to be the best predictor of adherence. Differentiated service delivery can have a beneficial impact on patient retention and treatment outcomes. Viral load testing is the best indicator of adherence and of the need for adherence support or regimen change when treatment failure is confirmed. Key outstanding research questions in this area include the optimal frequency of clinic visits, options for ART dispensing, and optimal approaches to adherence counselling.

Advanced HIV disease is an enduring challenge, with 33% of people in South Africa in 2016 initiating ART at CD4 counts below 200 cells/mm$^3$ and 17% initiating treatment at CD4 counts below 100 cells/mm$^3$. Men are twice as likely as women to initiate treatment late. Advanced disease is also a consequence of ART discontinuation. The main causes of morbidity and mortality among people living with HIV with advanced disease are TB, bacterial infections, and pneumonia. A simplified package of care for advanced HIV disease using the public health approach recommended by WHO since 2017 has been shown to be effective.85,86 Key outstanding research questions in this area include the feasibility and impact of implementing a package of interventions to prevent advanced HIV disease and approaches to managing advanced disease in ART-experienced patients.

**Differentiated service delivery**

In the era of “treat all”, differentiated service delivery (DSD) models of care are being successfully implemented in many countries to reduce the frequency of clinic and pharmacy visits for people who are doing well on ART and to enable health services to focus on people experiencing complications, co-morbidities, or other serious health needs. In his presentation on ART initiation and retention, Nathan Ford of WHO described how differentiated service delivery involving six-monthly clinic visits for those stable on ART has been shown to improve patient retention in Zambia, how home delivery of ART has been shown to be feasible and improves patient outcomes in the UK and Spain, and how three-monthly clinic visits reduce costs to patients and health systems in Kenya and Uganda.87,88

Under the Rwanda DSD model implemented since mid-2016, patients taking ART are now categorized as either stable A (with six-monthly clinic visits and three-monthly pharmacy visits), stable B (with three-monthly clinic visits and three-monthly pharmacy visits), or unstable (with three-monthly clinic visits and monthly pharmacy visits). Nearly half the people taking ART in
Rwanda are currently categorized as stable. As in other countries, the Rwanda DSD model is helping to reduce the burden of clinic visits on both health facilities and patients, who also benefit from a community-based adherence support program.89

**HIV in children**

A study from Uganda included some of the first data on long-term treatment outcomes among African children living with HIV who are 12 years old or younger.90 Early virologic failure (<24 months after initiation of treatment) was found in 26% of the 316 children studied and was associated with reduced effectiveness of first-line regimens (based on drug resistance testing) and poor adherence. Late virologic failure occurred in 13% of the children and was associated with being older than three years when initiating treatment and having a WHO stage 3 or 4 disease classification. Acquired drug resistance was seen in 27% of children 0-24 months after treatment initiation and 14% of children at 24-48 months. The results highlight the importance of starting all children on ART regardless of age and WHO disease staging.

A study from Zimbabwe examined the high incidence of echocardiographic abnormalities in children living with HIV despite good control of HIV with ART.91 Echocardiograms conducted in 200 children found left heart abnormalities in 30% and right heart abnormalities in 8% of those examined. Follow-up found that some of the abnormalities are transient, most likely explained by acute illness in the period before echocardiography, while others are persistent. Further research is needed to examine long-term implications of these findings.

**Mental health in people living with HIV**

Mental health issues among people living with HIV are gaining increased attention. A study from Kenya noted that although HIV patients are two to three more times likely to be depressed compared to HIV-negative individuals, screening for depression is rarely done in public sector HIV clinics. Depressed people are more likely to have low adherence, poor clinical outcomes, and riskier behaviour. Co-morbid conditions such as hypertension increase the risk of depression among people with HIV on treatment.92,93,94 A study from Nigeria indicated that mental health screening and psychiatric services are usually limited to tertiary hospitals and are seldom available in secondary health facilities. Better integration of mental health services into routine HIV care can help support adherence and improve clinical outcomes for people living with HIV.95

**Emerging data on the safety of dolutegravir in pregnant women**

A special session was held to review and discuss emerging data on dolutegravir (DTG). DTG is an integrase inhibitor recommended by WHO in 2016 as part of an alternative first-line ART regimen. A preliminary analysis of an independent observational study in Botswana recently identified four cases of neural tube defects among new-borns of 426 women who became pregnant while taking DTG. This statistically significant rate of 0.9% compares to a rate of 0.05% seen among women treated with efavirenz (EFV)-based regimens and 0.09% among HIV-negative women. However,
as this is an interim analysis of an observational study from only a single country, the findings will need to be followed with a complete analysis and be confirmed by other studies. Based on these findings, WHO has advised that:

- Women who are already taking DTG should not stop ART and should speak with their health provider for additional guidance. (Note: The same observational study found no neural tube defects among new-borns of women who had started DTG after conception.)
- Women who plan to become pregnant (or who are not using consistent contraception) should avoid the use of DTG.
- ART regimens for women and adolescents of childbearing age, including those who are pregnant, should be based on drugs for which adequate efficacy and safety data are available; an EFV-based regimen is a safe and effective first-line regimen.
- If other first-line ARVs cannot be used in women and adolescents of childbearing age - for example, due to drug resistance to EFV - DTG may be considered in cases where consistent contraception can be assured.
- Women who take DTG should be fully informed about the potential risk of neural tube defects so that they can discuss options with their health care provider.
- Programmes should continue strengthening pharmacovigilance including monitoring of birth outcomes.

Further information may be found in the web statement and Q&A published by WHO in May 2018. New ART guidelines being developed by WHO in 2018 will contain updated guidance.

What is a neural tube defect?

The neural tube is the foundation of the spinal cord, brain and the bone and tissues that surround it. Neural tube defects occur when the neural tube fails to completely form in the embryo; this formation takes place between 0 and 28 days after conception, i.e. before most women have received confirmation that they are pregnant. Neural tube defects may be related to folate deficiency, other medications or family history. WHO recommends that women take daily supplements of folic acid before conception and during pregnancy to help prevent neural tube defects, but it is not clear whether taking folic acid while taking DTG will reduce the risk of neural tube defects.

Source: WHO, 2018

A symposium sponsored by GSK/ViiV on holistic HIV management addressed the efficacy, tolerability, resistance profile, safety, and convenience of dolutegravir. Its role in second-line regimens for HIV/TB co-infection was discussed, as was the prevalence in Kenyan populations of the human leukocyte antigen HLA-B*57:01 allele, which increases risk of hypersensitivity reactions to the drug abacavir.
11. Harnessing new technologies for an accelerated response

A symposium sponsored by the Joep Lange Institute explored opportunities offered by digital mobile technologies for personalized health care in response to HIV and other health challenges in Africa. Mobile phones are increasingly being used to support surveillance and diagnosis, as in the use of mobile phone photography as a surveillance tool for cervical cancer screening in Tanzania. Weekly, bi-directional text messaging is being used effectively in Ethiopia and other countries to support adherence and to remind patients to attend health clinics; however, one-way SMS messaging is less effective as a method of adherence support. In Kenya, a partnership with the country’s largest mobile phone company is using a “mobile health wallet” to connect malaria patients with providers and payers of health services. Current challenges in digital health include the proliferation of pilot projects, lack of integration of many mobile platforms, security issues, and long-term sustainability of some interventions. Some Ministries of Health are reluctant to support new vertical digital applications and approaches and are seeking to implement more open and integrated health information systems.

Debate 2: “Technological interventions will end the HIV epidemic in Africa”

In the second, lively debate of the 12th INTEREST meeting, sponsored in this instance by Roche, delegates discussed the potential and pitfalls of technological innovations as tools in the response to HIV. A poll taken prior to the debate found 75% in favour of the proposition ‘Technology Interventions will end the HIV Epidemic in Africa’ and 25% opposed.

Arguing for the proposition, Sergio Carmona of the National Health Laboratory Service (South Africa) and Allison Glass, Lancet Laboratories (South Africa) noted that new technology - including rapid HIV tests, viral load testing, and simplified fixed-dose drug combinations - has contributed enormously to the progress made against HIV in the region. Innovations such as electronic health information systems and digital drug stock management have also played a key role in enabling programs to scale up. New approaches - such as drone delivery of health commodities and the use of mobile phones for activities as wide-ranging as surveillance and adherence support - continue to emerge, and the pace of innovation is unlikely to slow. The proponents argued that it is impossible to imagine the end of AIDS without increased use of technologies in the HIV response.

Against the proposition, François Venter of the Wits Reproductive Health and HIV Institute and Richard W. Rodriguez of the Draper Richards Kaplan Foundation (USA) argued that health technology has largely overpromised and under-delivered, citing electronic medical records, “telemedicine”, “seamless and interconnected” health information platforms, point-of-care diagnostics, online training, and an wide range of mobile phone apps as examples of technologies that have been poorly implemented or failed to meet expectations. Health systems, they noted, cannot be fixed by technology alone, but require investments in physical infrastructure and people, and several countries in the region have come close to achieving 90-90-90 by focusing on these priorities. Poor adherence is influenced by factors such as distance to clinics, forgetting to
take pills, and drug stockouts that will not be solved by another new mobile phone app. While
the opponents agreed that new technology offered significant opportunities, they asserted that
it is frequently slowly implemented, lacks interoperability with other platforms, and is
unsustainable. Above all, technology needs to be designed for and in Africa, not “at” Africa.

In comments from the audience, several delegates emphasized that while some technologies had
been useful, and others held promise, they are never successful without responsible human
behaviour and appropriate investments in training and maintenance. Other participants pointed
to the growing tendency to treat people as “data opportunities” rather than as human beings.
However, many participants were of the view that significant gains had been achieved through
the use of technology in areas such as monitoring, tracking, and reminding patients to take
medication and attend health services. At the conclusion of the discussion, audience views
remained relatively unchanged, with the proposition supported 75% to 25%.

12. Building the next generation: Mentorship in the HIV response

Two sessions at the meeting highlighted the importance of clinical mentorship to improve
standards of HIV care in resource-limited settings and to build the next generation of African HIV
scientists.

In a session sponsored by Abbvie, clinical mentorship was described as an important bridge
between didactic training and clinical practice. Speakers from Zambia, Kenya, and Nigeria – three
countries that account for 6 million people living with HIV in Africa and that each have around 1
million people on ART – highlighted successful examples of national clinical mentoring and
training programs, including the use of clinical mentorship teams that support decentralized
delivery of comprehensive health care services and standardized clinical management of
patients. As HIV programs in these countries have scaled up, treatment guidelines have
continued to evolve and more people are accessing treatment. As a result, mentorship has
become an important, integrated component of training for all HIV care providers.

In a session focused on fostering research careers, speakers highlighted the challenges and
choices faced by young scientists seeking mentorship. Fredrick Kateera from Partners in Health
in Rwanda described the role of mentors and some of the key factors to consider in selecting a
mentor. Elizabeth Bukusi from the Kenya Medical Research Institute discussed her own
experiences of mentoring and paid tribute to the mentors who helped shape her career. Jean
Utumatwisha from Ruhengeri General Hospital in Rwanda highlighted research showing that
academic staff with a mentor were more likely to publish abstracts, to present a conference talk
or poster, and to publish a paper in a peer-reviewed journal. Annette Uwineza from the
University of Rwanda concluded the session with reflections on her own journey from mentee to
mentor and described the comprehensive mentorship program at her own institution.
13. Implementation science: what success looks like

Nicolette Naidoo from Wits Reproductive Health and HIV Institute in South Africa provided an overview of the role of implementation science in determining what novel tools and interventions to implement, how to implement them and who will do the work of implementation (Fig. 11).

Implementation science can be defined as the study of methods and strategies to promote the uptake of interventions that have proven effective into routine practice, examining what works, for whom and under what circumstances, and how interventions can be adapted and scaled up in ways that are accessible and equitable to achieve the greatest and most cost-effective public health benefit. Methods of effective implementation science include case studies, qualitative and quantitative research, process evaluation, quality improvement, participatory action research, and “pragmatic” trials that produce results to rapidly inform decision-making for policy and programming. Dr Naidoo presented three case studies exploring how implementation science has played an important role in recent years to guide implementation and scale-up of the human papillomavirus (HPV) vaccine to prevent cervical cancer, PrEP for HIV prevention, and HIV self-testing.

Dr Emmanuel Njeuhmeli from USAID eSwatini gave a presentation on how mathematical modelling can be used as a critical tool for HIV program planning and strategic decision-making, including to examine the impact of interventions over a range of timescales, settings, and populations. Such modelling enables estimates of outcomes that are otherwise difficult to measure, such as trends in HIV incidence or AIDS-related deaths, as well as the quantification of long-term gains in cost-savings and epidemiological impact. However, because there is often a
disconnect between modellers and policy-makers, it is important that these two groups collaborate to design and do modelling that can inform policy while also meeting the needs of end users of interventions. Dr Njeuhmeli presented a case study of the modelling and country engagement work commissioned by UNAIDS to guide policy on the scale-up of VMMC in 10 countries in eastern and southern Africa. The modelling - which produced scale-up scenarios including age prioritization for the intervention in different contexts and provided policy-makers with an online tool that could be used to test different approaches – has had a significant impact on global VMMC policies since the work began in 2007 and demonstrates the wide-ranging use of such tools for advocacy, data generation for planning and program monitoring.

14. Closing of the 12th INTEREST meeting

In concluding remarks, the conference co-chairs, Sabin Nsanzimana from Rwanda Biomedical Centre, Cate Hankins from the Amsterdam Institute for Global Health and Development, and Elly Kabira from Makere University in Uganda thanked presenters and delegates for the high standard of science presented and the engagement of participants in debate and discussion that helped to make the 12th INTEREST meeting one of the most successful ever. Diverse participants at the meeting ranged from three local Kigali high school students to senior researchers. The Joep Lange Award for the highest scoring abstract at the meeting was presented to Frackson Nuke Shaba from Malawi for his study “Facility-based HIV self-testing for outpatients dramatically increases HIV testing in Malawi: a cluster randomized trial”.

It is proposed to hold the 13th INTEREST meeting in Accra, Ghana in May 2019.

Acknowledgements: This report was researched and written by science writer Ian Grubb and edited by INTEREST’s Scientific Chair Catherine Hankins.

***
References

15. Lehman, D. et al. Risk of drug resistance among persons acquiring HIV within a randomized clinical trial of single- or dual-agent pre-exposure prophylaxis. JID 2015:211 (15 April)
34. Mwihumbo MM. Addressing the needs of people who inject drugs (Including harm reduction as well as HIV care) in Tanzania. 12th International Conference on HIV Treatment, Pathogenesis and Prevention Research (INTEREST), Kigali, Rwanda, May 2018. Invited speaker.
38. Sakala D. et al. Peer and economic influences on men’s decision to attend antenatal clinics including HIV testing: A qualitative study from Blantyre, Malawi. 12th International Conference on HIV Treatment, Pathogenesis and Prevention Research (INTEREST), Kigali, Rwanda, May 2018. Abstract 305.
51. Ondoa P. Improving access to and utilization of viral load testing for better patient management. 12th International Conference on HIV Treatment, Pathogenesis and Prevention Research (INTEREST), Kigali, Rwanda, May 2018. Invited speaker.
57. Medlock J. Effectiveness of UNAIDS targets and HIV vaccination across 127 countries. PNAS April 2017. 114 (15) 4017-4022. https://doi.org/10.1073/pnas.1620788114
68. Dybul M. At the precipice: Demographics and the risk of losing control of the HIV epidemic. 12th International Conference on HIV Treatment, Pathogenesis and Prevention Research (INTEREST), Kigali, Rwanda, May 2018. Invited speaker.
70. Mattee M. Fresh perspectives: The youth experience of living with HIV. 12th International Conference on HIV Treatment, Pathogenesis and Prevention Research (INTEREST), Kigali, Rwanda, May 2018. Invited speaker.
97. Tilahun B. Digital, bi-directional patient support systems to support ART adherence and MNCH. 12th International Conference on HIV Treatment, Pathogenesis and Prevention Research (INTEREST), Kigali, Rwanda, May 2018. Invited speaker.