

8th International Workshop on HIV Treatment, Pathogenesis, and Prevention Research in Resource-limited Settings (INTEREST)

5-9 May 2014 - Lusaka, Zambia

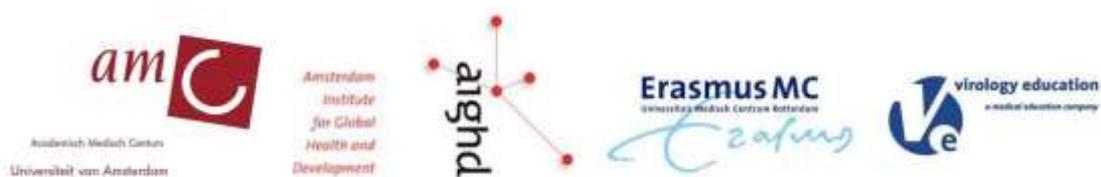


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Introduction

The **8th INTEREST Workshop** (International Workshop on HIV Treatment, Pathogenesis, and Prevention Research in Resource-limited Settings) took place in Lusaka, Zambia, 5-9 May 2014. Major highlights of the meeting included an update on basic HIV research; the impact of the new World Health Organisation (WHO) guidelines on HIV management; improving access to HIV prevention, testing, and care, especially for key affected populations; preventing and treating paediatric HIV infection; HIV co-infections and co-morbidities; and the impact of hormonal contraceptives on the risk of HIV transmission and acquisition. The majority of the 334 participants at the Workshop were from sub-Saharan Africa (SSA), especially Zambia and South Africa. Delegates also came from Europe and the USA to attend this meeting.

Before the Workshop officially opened, there were two pre-workshops: one chaired by Dr Luo (Zambia) and Dr Kankasa (Zambia) on paediatric HIV in the context of the elimination of new HIV infections in children and child survival and one chaired by Dr Hakim (Zimbabwe) and Dr Lange (The Netherlands) on implementation science. Major themes of the paediatric workshop included the need to focus on elimination of mother to child transmission of HIV (EMTCT); to follow the 2013 WHO guidelines in order to simplify and consolidate lifelong treatment of HIV-positive mothers and to protect their babies from HIV acquisition; and to decentralise EMTCT services and integrate them with strengthened mother and child healthcare systems, including immunisation clinics. Lessons learned in Zambia, Uganda, Swaziland, and South Africa were presented. The implementation science workshop focused on a number of practical issues such as the need for robust HIV-focused supply chains; how to transition adolescents to adult HIV care; the rationale and design of the POPART study; how to improve communication of HIV-related messages; scale up of voluntary medical male circumcision (VMMC); and issues facing patients co-infected with HIV and TB. A number of common themes emerged from the presentations: the need to involve the community in all HIV-focused initiatives; to maximise decentralisation of services while maintaining quality of care; to tailor healthcare appropriately for the intended priority population (e.g. adolescents, pregnant women, serodiscordant couples, etc.); to convey clear and accurate messages to the community; and to mobilise the political support that is essential to ensure the appropriate management of HIV and its co-infections. Many thanks to Abigail Mangimela (Zambia) and Natasha Namuziya (Zambia) for providing a summary of the two workshops.

The International AIDS Society-Industry Liaison Forum sponsored a symposium on expanding access to viral load monitoring in resource-limited settings. It was chaired by Dr Bekker (South Africa) and Dr Hankins (The Netherlands).

The Workshop was opened by the Minister of Health of Zambia, The Honourable Dr Joseph Kasonde. He said, "Research is the way forward to conquer today's diseases. We are making strides in clinical and biological sciences but the healthcare systems in resource-limited settings need to be strengthened." He noted that the Zambian government has reaffirmed its commitment to fighting HIV by increasing the budget for the purchase of antiretrovirals and healthcare commodities. "We have to achieve our goal of zero new HIV infections," he declared.

HIV prevention, treatment and care

Prevention methods using antiretrovirals

Catherine Hankins (The Netherlands) summarised the state of the art with respect to pre-exposure prophylaxis (PrEP) (Figure 1) [1]. The use of antiretroviral (ARV) therapy (ART) in HIV-positive people for their own health and to reduce the risk of onward transmission of HIV forms the basis for Treatment as Prevention (TasP) at population level, Treatment for Treatment (T4T), Treatment for Prevention (T4P) at an individual level, and Test and Treat strategies. Providing ARV PrEP to HIV-negative people reduces their risk of acquiring HIV. Variable results have been obtained from studies that evaluated diverse PrEP strategies: effect sizes ranged from 39% to 75%, depending on the intervention tested and the study population (Figure 1). Potential explanations for the different effectiveness results include higher drug levels achieved by oral PrEP in anal versus vaginal tissues; the effect administration route on local concentrations of ARVs (gels tend to generate a thousand-fold higher local drug level than tablets); and adherence to the regimen. In the FEM-PrEP study, 95% of the women reported that they 'usually/always took their study pill' but effective drug levels were only detected in the blood near to the time of infection in 26% of women. Dr Hankins commented that adherence is a major driver in PrEP study results: participants who adhered to their PrEP regimens experienced markedly higher levels of protection than those with low levels of adherence.

In the HPTN 052 study, ARV treatment of the HIV-positive partner reduced the risk of HIV transmission within a serodiscordant couple by 96%. However, 11 of the 39 individuals who were infected with HIV during the study acquired the virus from a sex partner outside the couple. Treatment of the HIV-positive person in a couple will only protect the HIV-negative partner if he/she only has the one sexual partner in the couple and the HIV-positive partner adheres well to his/her ART regimen.



Figure 1: Pre-Exposure Prophylaxis strategies

An alternative approach is for the HIV-negative partner to take ARVs; for example, until their HIV-positive partner's viral load is undetectable (which may take up to 6 months after initiating ART) or to prevent HIV acquisition from outside partners.

Serodiscordant couples who wish to conceive have a number of options, such as timed unprotected intercourse during the fertile period or ART for the HIV-positive partner to achieve an undetectable viral load before conception. Peri-conception PrEP could also be used to enable HIV-negative partners to conceive with their HIV-positive partners.

In 2012, the FDA approved the use of tenofovir (TDF)/emtricitabine (FTC) 'to reduce the risk of HIV infection in uninfected individuals who are at high risk of HIV infection and who may engage in sexual activity with HIV-infected partners'. A number of oral PrEP demonstration projects have been initiated or are planned in a range of low- and middle-income countries (www.avac.org). The aim is to identify the priority populations for PrEP and determine the levels of uptake and adherence, as well as the best methods of delivering PrEP. The safety of PrEP and its impact on sexual behaviour will be assessed. Strategies to maximise the cost effectiveness of PrEP will be evaluated.

Dr Hankins compared PrEP to oral contraceptives: both make sex safer, but concerns are expressed in some quarters about the resources required to provide these drugs. Just as a person's contraceptive needs change during his/her life, the requirement for PrEP will alter depending on his/her personal

circumstances. Dr Hankins expressed the opinion that new PrEP options will be available in the near future and people will be able to choose from a 'menu' of different ARVs (e.g. maraviroc +/- TDF/FTC, rilpivirine, S/GSK1265744) and delivery methods (e.g. rings, long acting injectables, gels, daily vs. intermittent administration).

Prevention: voluntary medical male circumcision (VMMC)

Voluntary medical male circumcision (VMMC) has been shown to protect HIV-negative men against HIV acquisition in three large clinical trials [2]. In 2007, the WHO and the Joint United Nations Programme on HIV/AIDS (UNAIDS) issued a recommendation to scale up VMMC in countries with high HIV prevalence and low male circumcision prevalence because it is a cost effective method of preventing HIV. It has been estimated that uptake of VMMC to achieve an 80% prevalence of male circumcision by 2015 in 13 priority countries in SSA would require 20 million VMMC. This would avert two million new infections and 0.3 million deaths over a ten-year period. By the end of 2012, 3.2 million MMCs had been carried out, Kasonde Bowa (Zambia) reported. It is likely that the 2015 target will not be achieved unless efforts are intensified.

HIV testing is carried out before a VMMC is carried out. Testing is not mandatory, and so acceptance of testing has ranged from 100% in Zambia to 75% in South Africa. HIV positivity rates range from 0.4% in Ethiopia to 5% in Lesotho. Early infant medical male circumcision is undertaken in three of the priority countries.

The majority of VMMC services (85%) are donor funded. There is a lack of doctors to perform MMCs and there are often seasonal fluctuations in demand for the procedure (e.g. increased demand during student holidays). Devices, such as the Prepex and the Shang Ring, are being evaluated because they can be used by nurses. Mobile campaigns can be used to access men in a range of environments, e.g. workplaces, and thus increase uptake of VMMC.

Treatment: the 2013 WHO consolidated guidelines

In 2013, the WHO issued a set of consolidated guidelines for the management of children, adolescents, and adults with HIV infection in resource-limited settings (RLS) [3, 4]. They reflected recent data that had demonstrated the benefits of early therapy for both individuals and society.

The recommended first line regimen is TDF/3TC (or FTC)/efavirenz, preferably as a fixed dose combination (FDC). Use of stavudine (d4T) should be discontinued because of its toxicities. Guidelines for RLS and resource-rich countries are now converging so that treatment approaches are similar worldwide. The trend is towards a 'Test and Treat' approach, Dr Lange (The Netherlands) noted.

Target Population (Age/Adult)	2010 ART Guidelines	2013 ART Guidelines	Strength of Recommendation & Quality of Evidence
NEW ASYMPTOMATIC	CD4 >500 cells/mm ³	CD4 >500 cells/mm ³ (OR >350 cells/mm ³ at a priority)	Strong, moderate-quality evidence
NEW SYMPTOMATIC	WHO clinical stage 3 or 4, regardless of CD4 cell count	No change	Strong, moderate-quality evidence
PREGNANT AND BREASTFEEDING WOMEN WITH HIV	CD4 >500 cells/mm ³ or WHO clinical stage 3 or 4	Regardless of CD4 cell count or WHO clinical stage	Strong, moderate-quality evidence
NEW TB CO-INFECTION	Presence of active TB disease, regardless of CD4 cell count	No change	Strong, low-quality evidence
RECURRENT CO-INFECTION	Presence of chronic active HIV disease, regardless of CD4 cell count	Presence of severe chronic HIV liver disease, regardless of CD4 cell count	Strong, low-quality evidence
NEW PARTNER ALSO COUPLE	No recommendation established	Regardless of CD4 cell count or WHO clinical stage	Strong, high-quality evidence

Figure 2: 2013 WHO consolidated guidelines – summary of changes between 2010 and 2013

An assessment by the International AIDS Vaccine Initiative (IAVI) of the time period between the known time of an incident HIV infection and reaching the <500 CD4 cells/mm³ threshold in individuals in East and Southern Africa demonstrated that the median time was six months for men and eight months for women. The opportunity costs of deferring ART for people who test HIV-positive but are not yet eligible for treatment substantially outweigh the costs of starting treatment at the time of diagnosis, i.e. for an additional 6-8 months. Dr Lange called for Treatment for Treatment (T4T), i.e. treating people for their own health, which has the added benefit for society that they are less likely to transmit HIV to their sexual partner(s) or, if they are pregnant women, to their babies.

Starting ART as early as possible is justified on the grounds of biological

evidence that suppressing viral replication as much as possible, as soon as possible, is associated with improved outcomes compared to starting ART after the immune system has deteriorated. There is overwhelming evidence that early therapy increases survival rates, minimizes damage to the immune system, diminishes the risk of TB in HIV-positive people, and reduces the risk of onward transmission of HIV. It has been suggested that early therapy may lead to a 'functional cure' in a subset of people who are treated during primary or acute infection. Starting ART when people are healthy facilitates task shifting because community health workers, rather than clinicians, can manage patients. Expanding access to ART may also be used as platform to diagnose and treat other chronic conditions, such as diabetes and hypertension. Dr Lange pointed out that although initiating ART for all HIV-positive individuals will initially be expensive, massive savings will be achieved eventually because of the number of new infections averted. He added that treating relatively healthy individuals is far less costly than managing patients with advanced HIV infection.

Zambia has been one of the leaders in implementing the consolidated 2013 WHO guidelines: the guidelines were adopted in 2013 and rolled out in 2014, Albert Mwango (Zambia) explained [5]. HIV prevalence amongst adult Zambians is 14.3%. The program goals for 2015 are to reduce new infections in adults by 50% compared to baseline rates in 2011-12; and reduce mother to child transmission (MTCT) of HIV from 9% in 2011 to <5%. In 2013, 94% of adults eligible for ART received therapy and paediatric ART coverage was 55%. At the same time, lifelong ART for pregnant and breastfeeding women, for both their own health and to prevent transmission to their babies, was introduced. First, second and third line ART is provided free of charge to all Zambians. The ARV budget has increased from US\$5 million to US\$45 million in three years. Dr Mwango concluded by saying that the new WHO guidelines are moving Zambia towards a 'Test and Treat' strategy. He commented that if someone is diagnosed with malaria or diabetes, he/she is treated immediately. Dr Mwango urged healthcare workers to

react in the same way to HIV infection – by starting ART early in order to prevent immune deterioration.

Test and Treat The PopART Study

The PopART study (HPTN 071) is investigating the hypothesis that the offer of universal testing and immediate ART will reduce HIV transmission and have a substantial impact on HIV incidence at the population level (Figure 3) [6]. Helen Ayles (Zambia) explained that a trial is needed to determine if Universal Test and Treat (UTT) can be delivered with a high rate of uptake and acceptability. It will provide information that will be of benefit to policymakers and healthcare workers concerning the potential adverse effects of this approach, such as sexual risk compensation and HIV-related stigma; the capacity of healthcare services to deliver HIV services at a high level initially and then, as new infection decrease, to scale back HIV care; the extent of drug toxicity and resistance; and the cost effectiveness of the intervention. The three-arm study is taking place in 21 communities in Zambia and South Africa (Figure 3). When the study was designed, the national treatment guidelines recommended initiating ART if the CD4 cell count was <350 cells/mm³ but Zambia has recently amended the treatment threshold to CD4 cell counts <500 cells/mm³. Community HIV Providers (CHiPs) will deliver testing, counselling, linkage to care, and treatment support in the community.

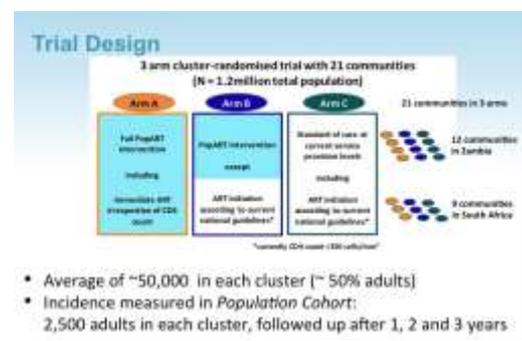


Figure 3: Design of PopART study

Annual door to door HIV counselling and testing will be offered in each community. Individuals assigned to Arm A will receive the full PopART intervention, including ART regardless of CD4 cell count; referral

for TB and STI (sexually transmitted infections) treatment, PMTCT (option B+) and/or voluntary MMC (VMMC) as appropriate. CHiPs will provide support to enhance adherence and retain patients in care, as well as supplying condoms. Individuals in Arm B will receive the PopART intervention but will only be treated with ART if they meet current national guidelines. Arm C will receive standard of care management at the current service provision level including ART initiation according to national guidelines. Data from the population cohort will provide information on the incidence of HIV and HSV-2; rates of retention and ART adherence; viral suppression rates; the community viral load; drug resistance levels; sexual risk behaviour; and HIV-related stigma.

Public randomisation ceremonies were held in Zambia and South Africa in February 2013 and the enrolment of the population cohort is in progress (n=5,484 to date). Uptake of universal treatment is higher in Zambia (~98%) than in South Africa but the reasons for the difference are not clear, Dr Ayles commented. Since the study is complex and involves many different stakeholders, regular meetings are held at different levels (international, national and regional) to ensure good governance and enable lessons to be learned as the study progresses. Challenges that have been identified to date include the need to perform 'catch up' couples testing, when one partner has already been tested e.g. as part of a PMTCT program; enabling men and hard to reach populations (e.g. sex workers, men who have sex with men [MSM], teenagers who are not at school, etc.) to access testing; and encouraging men to undergo VMMC. It is expected that the PopART study will be completed in 2017.

The ANRS 12249 TasP Study

The ANRS 12249 TasP Study is a cluster randomised trial (11 control clusters and 11 intervention clusters) that is taking place in rural KwaZulu-Natal, South Africa [7, 8]. The aim was to test all members of the community for HIV infection and to immediately initiate ART in all HIV-infected individuals, regardless of immunological or clinical staging, in order to prevent onward sexual transmission of HIV and to reduce the incidence of HIV in this population.

Initially, the feasibility and acceptability of the TasP intervention was evaluated at the community and health facility level to determine the uptake of HIV testing, linkage to care of HIV-infected individuals, HIV prevalence, rate of internal migration within the community, and ART uptake. The feasibility phase was completed in February 2014 and the main study will start in June 2014. Dr Tanser (South Africa) acknowledged that policy changes might overtake the gathering of research data; for example, if South Africa adopts TasP, the study will not be powered to detect a difference between the control and intervention clusters.

The study is being conducted in a poor, rural area in KwaZulu-Natal, where there are high levels of unemployment and the adult HIV prevalence rate is 24% [7]. The roll out of ART in recent years has been associated with a substantial increase in life expectancy: from 49 years in 2004 to 61 years in 2012. Despite this improvement, new HIV infections occur in this community at a very high rate and in distinct spatial clusters, particularly in the peri-urban populations that live near the highway. Since 2003, the community has participated in a longitudinal, dynamic cohort. HIV testing has been offered on an annual basis; 75% of those who are HIV-uninfected are subsequently re-tested. ART coverage in this community has increased from <10% in 2004 to >40% in 2011. The risk of HIV acquisition is lower in communities with high (>40%) ART coverage compared to those with low ART coverage.

MaxART

The MaxART project (initiated by STOP AIDS NOW! (The Netherlands) in collaboration with the Ministry of Health (MoH) of Swaziland and Clinton Health Access Initiative (CHAI)) is being conducted in two phases in Swaziland, which has the highest HIV and TB prevalence in the world [9]. The adult HIV prevalence rate is 26% and 80% of TB patients are also HIV-infected. ART coverage is >80% of eligible patients and the retention in care rate is 87%. The aim of MaxART is to contribute to the reduction of new HIV infections by 50% in a high prevalence setting. During Phase 1, preparations were made to achieve universal access to testing and treatment

for eligible patients (based on current guidelines) and to reduce loss to follow up. Social science research was conducted to understand the realities of PLHIV and to conduct epidemiological research. Phase 2 commenced in 2014 and will run until 2017. It will offer immediate access to ART for all HIV-infected people. A continuum of care has been developed to ensure access to HIV healthcare and retention in care. The study design is complex: it is a randomised, stepped wedge, open enrolment trial of all HIV-infected people aged ≥ 18 years in 15 sites in the Hhohho region of Swaziland. The primary study endpoints are retention in care and virological suppression. Secondary endpoints include ART uptake, adherence, drug resistance, TB, and cost per patient per year.

Ms Nyambe (Swaziland) offered a community perspective on MaxART [10]. She stressed the need to protect human rights when offering universal ART since there is a risk that individual health rights will be overridden for the community's good (HIV prevention). The aim of ART should be for the patient's own health. HIV prevention benefits for his/her sexual partner(s) and the rest of the community should be an additional benefit and not the main reason to initiate ART. HIV-infected people in Swaziland are often motivated to take ART so that they maintain their health and are not stigmatised because if they become ill, the community will assume that they are HIV-infected.

Achieving long term adherence

Improving adherence to ART in resource-limited settings (RLS) is essential for the success of T4T, T4P, UTT, or TasP [11]. A decade ago, adherence was shown to be better in African patients than North American patients. However, recent data suggests that adherence in RLS is decreasing and it is expected to fall even further. Causes of low adherence in SSA include lack of transport to clinics and dispensing facilities; intermittent drug supply; fear of stigmatisation; lack of access to accurate information; and ARV side effects.

A number of interventions that are appropriate for RLS have been developed to assist with ART adherence including: behavioural stimuli (text messages, directly observed therapy [DOT]);

education; peer support and counselling; food supplements; community structures; income generating schemes; and community mobilisation. Short, weekly text messages have been shown to be more effective in improving adherence (13-16% increase in the proportion of patients who achieved $>90\%$ adherence) than long and/or daily messages. Treating partners improved ART adherence by two fold in a Nigerian study and 10 fold in a study conducted in Mozambique. Time-limited DOT, using patient-nominated treatment supporters, is particularly useful for patients at high risk of non-adherence. Intensive adherence counselling at ART initiation resulted in a sustained and significant improvement in adherence compared to the use of an alarm device. Providing holistic care for HIV-infected patients enhances their health, adherence and wellbeing.

During the discussion of the WHO 2013 guidelines, several speakers stressed the need to achieve excellent levels of adherence long term so that patients derive benefit from their ART and HIV transmission rates decline at the community level. The success of Test and Treat depends on people being adherent to their ARV regimens.

New therapeutic options

Francois Venter (South Africa) reviewed the new ARV drugs and regimens that are becoming available in RLS and are in the pipeline [12]. He pointed out that regimens are becoming simpler, less toxic and more robust. Their effectiveness should now be monitored by viral load testing, as recommended by the WHO [3]. Initiation of ART takes place at a much higher CD4 cell count than a decade ago: CD4 cell counts of ≤ 500 cells/mm³ for many adults compared to ≤ 200 cells/mm³ in 2002. A public health approach has been taken to ART in RLS in order to minimise costs and maximise effectiveness: this has led to dramatic reductions in the prices of ARVs. Fixed dose combinations (FDC) have simplified treatment regimens and made ART much easier to take: a wide range of FDCs are now available or near to market. A number of interesting ARVs and FDCs are in the pipeline (www.pipelinereport.org).

Impact of hormonal contraceptives on HIV transmission and acquisition

Speakers at a roundtable on the impact of hormonal contraceptives on HIV transmission and acquisition during the INTEREST meeting included Helen Rees (South Africa), Mike Mbizvo (Zimbabwe), Chelsea Polis (USA), and Nelly Rwamba Mugo (Kenya).

Dr Rees explained that concerns had emerged about an apparent relationship between the use of hormonal contraceptives and HIV transmission and acquisition [13]. Contraception is an essential public health tool in the prevention of maternal mortality in women, whether or not they have HIV infection. In Africa, 57% of the population's contraceptive needs are met by hormonal contraceptives and, in recent years, the use of injectable contraceptives has increased substantially. There are several biological reasons why hormones may influence HIV acquisition but the data are sparse and conflicting; no clinical data are available. Concerns about potential interactions between hormonal contraceptives and virus acquisition emerged on the basis of data obtained in animal models that used non-physiological doses of hormones. However, when animal models using physiological doses of contraceptives were studied, no increases in plasma viral load or genital viral shedding were observed. Dr Rees cautioned that observations in animal models do not necessarily reflect human biology.

Conflicting evidence has been obtained in clinical trials. A South African study of family planning methods found no evidence of an association between HIV infection and injectable contraceptives. However, a sub-group analysis of the Partners study among serodiscordant couples found that women who used injectable contraceptives were at increased risk of acquiring and transmitting HIV. Alarmist media coverage of these data resulted in confusion and mixed messages. In 2012, the WHO convened a meeting of experts to examine the data. There is a considerable overlap with areas of high HIV prevalence having higher levels of injectable contraceptive usage and high maternal mortality rates.

However, Dr Rees cautioned that this did not mean that there is a causal relationship between HIV infection and hormonal contraceptive use. She added that, if hormonal contraceptives were withdrawn in high HIV prevalence settings, this would probably result in an increase in both unwanted pregnancies and maternal mortality rates.

Dr Mbizvo outlined the medical eligibility criteria (MEC) process that the WHO used to develop guidance on contraceptive use [14]. Extensive analysis of existing data and consultations with experts in the field were used to establish the recommendations and to grade the evidence available. After the document had been approved, an ongoing process of review and updating was set up to ensure that new information is incorporated into the guidelines as appropriate. The current WHO MEC recommendation for oral contraceptives is 1 (no restriction for the use of the contraceptive method). A caveat is attached to this recommendation: *Some studies suggest that women using progestogen-only injectable contraception may be at increased risk of HIV acquisition, other studies do not report this association. A WHO expert group reviewed all the available evidence and agreed that the data were not sufficiently conclusive to change current guidance. However, because of the inconclusive nature of the body of evidence on possible increased risk of HIV acquisition, women using progestogen-only injectable contraception should be strongly advised to also always use condoms, male or female, and other HIV preventive measures.*

USAID/PEPFAR/CDC issued a technical brief on hormonal contraceptives and HIV in 2012

(<http://www.usaid.gov/sites/default/files/documents/1864/hormonal-contraception-and-HIV.pdf>) [15]. It summarised the results of a systematic literature search that had identified 20 relevant studies. Only eight studies met the minimum quality criteria and the results were very heterogeneous (Figure 5).

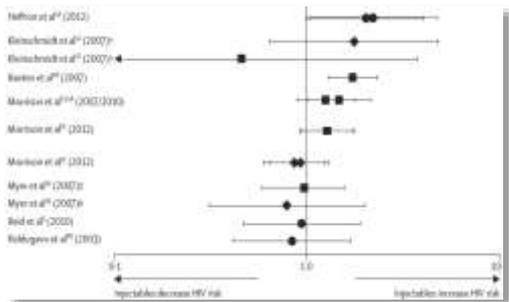


Figure 5: Injectable contraceptives and HIV acquisition: studies that met minimum quality criteria

Dr Polis pointed out that the term ‘hormonal contraceptives’ covers several products and each one may have a different effect on HIV transmission and acquisition. Women switch contraceptives frequently and so measuring the impact of a specific contraceptive is challenging. Ascertaining the exact time of HIV acquisition is only possible if frequent, repeated HIV testing has been performed. The levels of underlying exposure to HIV are not known in this analysis. Identifying a suitable comparison group of women is not simple. Women who are not using contraceptives or are using non-hormonal contraceptives are usually chosen as controls but it is likely that they differ from women who use hormonal contraceptives in a number of ways. Self reported data about sexual behaviour and contraceptive use are often subject to error and confounding factors, such as male or female condom use, may not be taken into account in the analysis.

An updated systematic review was presented to the March 2014 meeting of the WHO MEC committee. New guidance on the use of hormonal contraceptives by women infected with HIV is planned for release in July 2014.

Randomised studies are being planned to investigate whether different hormonal contraceptives have different effects on the risk of HIV transmission and/or acquisition. Dr Polis agreed with Dr Rees that the theoretical risks of HIV transmission through the use of injectable contraceptives must be balanced against the significant risks of unintended pregnancies in women living with HIV, both to the woman and her baby. The use of contraceptives prevents 44% of maternal deaths worldwide. The public health impact of injectable contraceptives on HIV transmission/acquisition depends on the effect size; as well as the incidence of HIV and the rate of maternal deaths in the region. Dr Polis stressed that additional data are urgently needed so that policy decisions can be made and women can be counselled about the risks and benefits of all contraceptive options.

Dr Mugo described the ECHO trial, which aims to compare the impact of progestin-only injectable contraceptives (DMPA and NET-EN or implants) and copper IUDs on fertility and HIV acquisition [16]. The proposal is in development and it has not yet been decided if NET-EN or implants will be included in the study. The trial will be randomised because high quality evidence is needed for public health decisions about the use of hormonal contraceptives in areas of high HIV incidence and to provide women with accurate information so that they can make informed decisions about their contraceptive choice(s). At present, only conflicting observational evidence is available. The aim is to enrol 8,600 women who do not want to conceive and are willing to be randomised to a contraceptive method. The primary endpoint will be HIV infection with secondary endpoints including pregnancy, continuation of contraceptive method, and side effects of each contraceptive method. The study will take place in Eastern and Southern Africa and is expected to run for ~36 months.

	Living with HIV		
	Acquisition	Progression	Transmission
OCPs	No current concern	No current concern	No current concern (based on very few studies)
DMPA	Some concern, more research warranted	No current concern (potentially protective effect based on very few studies)	Some concern (based on very few studies), more research warranted
NET-EN	Limited concern (based on very few studies)	No current concern (based on very few studies)	Limited concern (based on very few studies), more research warranted
LNG-IUD	No data available	No current concern (based on very few studies)	No current concern (based on very few studies)

* No data available for contraceptive implants, contraceptive patches, contraceptive rings, or emergency contraception.
 * Some ART medications (NNRTIs and monaiv-boosted PIs) may reduce efficacy of some HC methods (COCs, implants).
 * No drug interactions reported between ART medications and DMPA; this may be an important option for women living with HIV.

Figure 6: Conclusions of USAID/PEPFAR/ CDC review

Key: OCPs: Oral contraceptive pills; DMPA: Depot medroxyprogesterone acetate; NET-EN: norethisterone enanthate; LNG-IUD: long acting hormonal intrauterine device

Key affected populations

Helen Rees (South Africa) discussed the issue of key affected populations in HIV. She noted that social drivers are fundamental to high levels of disease burden in these populations, they have low levels of access to services, and experience social exclusion [17]. Key affected populations and their partners account for a high proportion of new HIV infections. Tailoring programmes for these populations is essential to control the HIV epidemic. In Africa, key affected populations include young women, orphans, refugees, sex workers, young men, prisoners, migrant workers, and men who have sex with men (MSM).

Although HIV prevalence amongst young African women has declined overall in recent years, it is still very high in certain regions. Young women do access HIV services via antenatal clinics but many of them are HIV-positive before they become pregnant. Interventions amongst this affected population have been shown to be effective but must be continued long term to protect young women from infection. Being a teenaged female orphan is associated with an increased risk of acquiring HIV infection (3-fold) or another sexually transmitted infection (2-fold), and of having a teenage pregnancy (4-fold).

HIV prevalence in refugee camps has been compared with that in the host communities in one study of seven SSA conflict-affected countries. It was lower in 9/12 camps, similar in 2/12 camps, and higher in only one camp than in the respective host communities. Although this evidence suggests that refugees are not an increased risk of HIV infection, there is still a need for HIV and TB services in refugee camps.

Data on female sex workers (FSW) are not available for many SSA countries. However, HIV prevalence in 16 SSA countries reported in 2012 demonstrates that it is considerably higher in FSWs than the general population: 36.9% (36.2-37.5%) vs. 7.42% (odds ratio 12.4 (8.9-17.2)).

Tailored interventions for sex workers are needed, Dr Rees commented.

Men and the HIV pandemic

Migrant male labour is very common in SSA: it is possible that the high rates of HIV prevalence in Swaziland and Lesotho are due to the large numbers of migrant miners employed in South Africa [17]. Many migrant workers have a wife at home (usually in a rural village) and an 'urban wife'. HIV rates are higher in miners, their wives and partners than in the general population. Miners and their wives or partners are less likely to adopt safer sex behaviours and to use condoms than non-miners and their wives or partners.

The prevalence of HIV in male prisoners in SSA is high: in one prison in Johannesburg, 25% of the offenders were HIV-positive and 3.4% had active TB. Multi drug resistant TB (MDR-TB) was detected in 4.3% of prisoners with undiagnosed TB. Partners of prisoners who return to the general population are at high risk of being infected with HIV and/or TB.

MSM are a key affected population: in all regions of the world, including SSA, MSM are infected at higher rates than the general population. In SSA, the overall adult HIV prevalence reported in 2012 was 5% but it was 17.9% in MSM. Population based estimates in African countries suggest that 0.03-2.3% of men are MSM but there is very little research carried out on this key population. Homophobia and punitive laws against MSM are major barriers to involving these men in HIV prevention and care programmes (Figure 7).



Figure 7: Global distribution of HIV-related punitive laws for MSM

Transgender individuals are another neglected population, both in terms of HIV interventions and research.

In Swaziland, considerable efforts are being made to involve men in HIV prevention, testing and care, Ms Nyambe reported [10]. Special men's HIV sessions are held during male-orientated community events, including the provision of information and testing.

In order to control the HIV epidemic, it is essential that key affected populations are tested for HIV infection and receive the appropriate care [10, 17]. Non-traditional approaches are being used in Ghana via the SHARPER project to reach MSM and involve them in HIV prevention, testing, counselling and care [18]. Social media was used to communicate HIV messages to MSM: in 2013, 15,291 MSM were reached in this way. Social network testing (SNT) and outreach to male sex worker (MSW) networks were undertaken. SNT was initiated with 25 'seed' members: 166 participants, excluding seeds, were tested and counselled. The majority of these men (63%) reported that they had not been exposed to HIV messages during the previous 12 months and the same proportion (62%) had not taken an HIV test during the previous year. One third (33%) tested HIV-positive. The MSW outreach programme reached 135 MSWs, of whom 97 (67%) underwent HIV testing; 25/90 (28%) were HIV-positive and all of them were linked to HIV services. A combination of complementary approaches was shown to be the most effective method of reaching MSM in Ghana.

HIV testing of infants

Between the 1990s and 2005, HIV rapid testing was undertaken in babies aged nine months in Zambia; repeat tests were carried out at 18 months for babies who had previously tested HIV-positive [19]. In 2014, the guidelines were updated to support virological testing at 6-8 weeks, at six months and six weeks after cessation of breastfeeding. Dr Chintu (Zambia) observed that it is challenging to convince

parents to have their babies re-tested and to train healthcare workers about the need to re-test babies. Between 2007 and 2012, over one million women were counselled and tested for HIV: 14% were found to be HIV-infected. The peak rate of maternal HIV positivity occurred in 2008 (~17%) and has fallen significantly since then (12% in 2012). Reductions in the HIV positivity rate in infants have also been observed: from 10% in 2007 to 3% in 2012. Dr Chintu reported that fewer infants born to HIV-infected mothers were tested in 2010-2012 than in 2009-2010 because of logistic difficulties with the supply of HIV testing commodities.

Four laboratories in Zambia carry out DNA PCR HIV testing for early infant diagnosis (EID) [19]. The median turnaround time between sample collection and the caregiver receiving the test result was 92 days in a study conducted in 2013. Results were not sent to the caregiver for 55/476 samples tested. Mortality peaks in HIV-infected babies at 2-3 months; delays in receiving test results mean that many babies do not receive ART and die prematurely. Electronic notification of test results by SMS (text messages) has recently been introduced and this has substantially reduced the turnaround time to 45 days.

There are concerns that maternal ART reduces the sensitivity of HIV tests because the viral load is substantially reduced by treatment. As PMTCT services expand and HIV transmission declines, the positive predictive value of a single EID test will also decline. It is therefore essential to improve the efficiency of testing programmes so that turnaround time is minimised and HIV-infected babies are linked to care and treatment as quickly as possible. Community initiatives to identify HIV exposed babies may improve detection rates. De-centralised testing facilities, e.g. point of care EID at birth, will reduce the loss to follow up and ensure that HIV-infected babies receive appropriate care.

Update on HIV-1 research: prospects for a cure

Dr Schooley (USA) presented an update on the prospects of a cure for HIV infection [20]. He explained that the goal of eradicating HIV is necessary because although ART is effective, it must be taken lifelong, has side effects and requires considerable healthcare resources. Treatment as prevention only works if people take ARVs and an AIDS vaccine will not be available in the near future. “The biggest challenge to a cure is to eradicate HIV from the resting memory cells”, Dr Schooley said. These cells form a long lasting pool of latently infected cells, which persists even during ART and can re-initiate HIV replication if ART is stopped.

A functional cure for HIV would mean that the host’s immune system is able to control HIV infection in the absence of ART, while a sterilizing cure would be achieved only if HIV were cleared from the whole body. To date, no effective therapeutic vaccine has been identified that can induce control of HIV replication in a patient, thus achieving a functional cure. A sterilizing cure would only be achieved if latently infected memory cells can be activated, using a highly selective agent, so that the cells die after releasing viral particles or are killed by cytotoxic T cells.

Another approach to an HIV cure would be to induce cellular resistance to HIV. Modified stem cells, e.g. with altered

modified cellular receptors or the ability to produce ‘hostile’ nucleic acids, could replace cells that are vulnerable to HIV infection. They could be introduced into the body by a bone marrow transplant or stem cell infusion.

Dr Schooley cited two examples of HIV cure: the Berlin patient and the Mississippi baby. Although a bone marrow transplant (as in the Berlin patient) might not be an appropriate strategy to cure all patients infected with HIV, treating acutely infected adults or babies born to HIV-infected women within the first 24 hours of life (as in the Mississippi baby) might prevent HIV from invading memory cells. Chronically infected individuals could only be cured if a method of activating and killing all of the HIV-infected latent cells in different compartments within the body could be identified.

Dr Schooley concluded by saying that searching for a cure for HIV infection is a worthwhile endeavour because it may succeed and, even if initial efforts are unsuccessful, investigators will learn about HIV immunobiology and regulation, as well as stem cell biology and genetic approaches to curing other diseases.

HIV co-infections and co-morbidities

Tuberculosis

Increased access to ART has been associated with a decrease in tuberculosis (TB) incidence, prevalence and mortality since 2005 [21]. Initiating early ART at CD4 cell counts ≥ 350 cells/mm³ reduced the risk of TB infection by 47%. There were concerns about the potential to activate latent TB in HIV/TB co-infected people but a review of 12 randomised clinical trials has shown that TB preventive therapy can be administered to HIV-infected people. Treatment was associated with a 32% decrease in the incidence of active TB and reductions in mortality rates.

Continuous isoniazid preventive therapy (IPT) is effective in tuberculin skin test positive (+TST), HIV-infected patients: data from the Botswana trial showed that IPT was associated with a 50% decrease in the risk of TB in patients taking ART. The incidence of TB increased in these patients within 200 days of stopping IPT. Three month courses of isoniazid (INH) or of rifamycin have been compared to six months of IPT and to continuous IPT. All four regimens were associated with a decrease in the incidence of TB over time. However, mass screening and nine months of IPT had no significant effect on TB control in South African gold miners in a cluster randomised trial of 78,744 miners. This was a surprising result, Dr Benson (USA) observed: the TB case rate amongst people taking IPT was reduced by ~70% compared to those not taking IPT. However, when IPT was discontinued after nine months, the rate of TB increased to that observed in miners who had not taken IPT. The outcome was influenced by post-treatment reinfection; ongoing risk due to HIV, silicosis and other factors; and failure to rapidly identify and treat active TB or to clear latent TB. The WHO recommends that adults with unknown or +TST status should receive six months of IPT, irrespective of their degree of immunosuppression, or 36 months of IPT. A new, three month regimen of rifapentine (RPT) plus INH (given as directly observed therapy, DOT) was shown to be as effective as nine months of self-administered INH in a randomised, open

label study. Completion rates were higher in the combination regimen arm than the INH arm: 86% vs. 60%. Similar results were obtained when the two regimens were compared in HIV-infected patients: the TB rate per 100 patient-years was 1.25 in the INH arm vs. 0.39 in the INH/RPT arm. The completion rates were 64% and 89%, respectively. ACTG A5279 is an ongoing, multi-centre, randomised trial that has enrolled 3,000 HIV-infected patients who are +TST/+IGRA (interferon gamma release assay) or reside in a high TB endemic area. They are randomised to receive daily INH/RPT for four weeks or daily INH for nine months and are followed for three years after the last patient has been enrolled. The primary endpoint is time to first diagnosis of TB; enrolment is expected to be complete by the end of 2014.

Multi-drug resistant (MDR-TB) and extremely drug resistant (XDR-TB) TB are a growing healthcare problem. Globally, 3.6% of new TB cases and 20.2% of previously treated TB cases are MDR-TB. Nearly 10% of MDR-TB cases are XDR-TB. Overall, the cure rate for MDR-TB is ~40-60% but it is only 20% for those patients with XDR-TB. Developing new drugs that are easier to take, less toxic and can be administered for shorter periods than current regimens should improve cure rates and decrease the risk of MDR-TB and XDR-TB emerging. A number of new TB drugs have recently been approved (bedaquiline and delamanid) or are in the pipeline (the oxazolidinones, sutezolid and linezolid; an ethambutol analogue, SQ-109; long acting rifamycins; and extended spectrum fluoroquinolones). Studies are ongoing to define their safety and efficacy profiles, as well as to determine if short treatment regimens are effective and feasible for use in drug susceptible cases of TB.

Hepatitis B and C

Hepatitis B (HBV) and C (HCV) infections are increasingly being recognised as a significant healthcare issue in SSA [22, 23]. However, knowledge about HBV and HCV in the community, for example in Zambia, is limited [24]. Routine HBV

screening of HIV-infected patients was recommended in 2010 by the Zambian Ministry of Health: the proportion of patients screened increased from 0.9% during 2007-2010 to 30% in 2012. However, screening rates varied between different healthcare facilities from 0% to 70%. Patients were more likely to be screened for HBV if they were older and had a WHO clinical score of 1 or 2. Approximately 11% of the test results were positive. The HBV vaccine has been routinely available in Zambia since 2005: during 2011-12, 10% of HIV-infected children enrolling for care in Lusaka were screened for HBV infection and 11.6% were positive. The rates were higher in older children (14% in those aged 9-18 years vs. 7% in those aged 0-8 years), suggesting that they may not have been vaccinated.

HBV prevalence rates are $\geq 8\%$ throughout most of SSA [22]. HBV infection is associated with an increased risk of cirrhosis and hepatocellular carcinoma (HCC): individuals with detectable HBV viral loads are at a 3.9 fold increased risk of HCC compared to those with an undetectable viral load [22, 23]. In Gambia, HCC is the most common cancer in men and the second most common cancer in women [22]. Although an effective HBV vaccine is available, coverage in SSA is variable. In areas with good HBV vaccine coverage, the prevalence of HBV fell by 11-15% compared to the rate in the pre-vaccine period. New methods of HBV testing, including rapid diagnostic tests (RDTs), have been developed in order to identify HBV-infected people and enable them to access therapy, thus reducing the risk of liver disease progression and onward transmission of the virus [23]. The WHO recommends HBV screening for HIV-infected patients at enrolment into care; at initiation of ART; at treatment failure; and when switching to a new ARV regimen [3]. ART regimens should contain two drugs that are active against HBV as well as HIV (e.g. TDF/FTC or TDF/3TC) and anti-HBV drugs should also be included in a second line regimen [3, 25]. Contacts of a HIV/HBV co-infected patient should be vaccinated against HBV infection. Dr Andersson (South Africa) pointed out that although TDF is available for the treatment of HIV, it is not available for HBV

treatment in RLS. [25]. She suggested that investing in combined viral hepatitis/HIV clinics could increase access to treatment for both co-infected and mono-infected viral hepatitis patients. Dr Andersson called for advocacy to raise the profile of viral hepatitis on the global health agenda. The PROLIFICA (Prevention of Liver Fibrosis and Cancer in Africa) Study is sensitising people in several communities in The Gambia to the risks of HBV and then testing them for infection using rapid, point of care tests [22]. If patients are found to be HBV positive, they are offered therapy with TDF, which has been approved for the treatment of HBV. The cost per HBV case detected was €92.39.

There is considerable variability in the prevalence of HCV throughout Africa: from 6% in Central Africa to 2.4% in West Africa and 1.6% in East and Southern Africa [22]. Risk factors for HCV infection include social history (illicit drug use, incarceration, past and current sexual activity); medical history (blood transfusion, dialysis, etc.); and any exposure to blood. The long term impact of HCV infection includes a significantly higher risk of death due to hepatic and extra-hepatic diseases than HCV negative patients. In two Zambian studies, 1.2% of a cross sectional sample of 323 hospitalized HIV-infected adults was HCV antibody positive; and only one (0.24%) of 418 adults initiating ART was HCV antibody positive in the second study [24]. Liver biopsies are rarely available in SSA; new, non-invasive, low cost tests such as APRI and FIB-4 have been endorsed by the WHO and may enable better management of patients with suspected liver disease.

Only 5% of the 170 million HCV-infected people worldwide are aware of their infection status: affordable, rapid, point of care HCV tests and portable liver scanners are being developed to facilitate easier and quicker diagnosis of HCV [22, 23]. Dr Pawlotsky (France) reviewed comparative data on three HCV RDTs that use whole blood from a finger-stick. Although the specificities of all three tests were 98.2-100%, their sensitivities ranged from 63.7% (cheapest test evaluated) to 99.4%. (most expensive test evaluated) [23]. The most sensitive test (Oraquick) costs €8-10 each, which is too expensive for RLS, Dr Pawlotsky commented. The

performance of the Oraquick test using crevicular fluid, which is produced by the epithelium of the gingival crevices, has been evaluated. Its specificity was 100% and its sensitivity was 98.2%. Molecular tests for HCV are being validated and may be on the market in the next 2-3 years. Dried blood spots (DBS) have been evaluated as a sample collection method in RLS for HCV viral load measurements. They appear to be a practical method of collecting samples for HCV analysis in this setting and can be sent to central laboratories without requiring special storage conditions. Although the sensitivity of the analysis is lower with DBS than when serum or plasma samples are used, it is acceptable for a qualitative test. Improved HCV diagnosis should enable individuals to learn their HCV status and to access care.

The treatment of HCV infection has undergone a revolution in recent years [26]. It is now possible to cure HCV infection with relatively short courses of interferon-free regimens composed of directly acting antiviral drugs, such as sofosbuvir, simeprevir or daclatasvir. Different regimens are used to treat infections caused by the various genotypes of HCV. Dr Pawlotsky speculated that, from 2015 onwards, the choice of interferon-free combination regimens will increase even more (Figure 8). However, the cost of the new HCV therapies is extremely high: sofosbuvir will cost over US\$ 80,000 for a 12 week course. Gilead has already offered the drug to Egyptian patients at a very large discount and is in negotiation with Indian manufacturers to allow a generic version of sofosbuvir to be made available to 60 developing countries. Dr Pawlotsky pointed out that the main barrier to increased access to treatment is the lack of screening for HCV infection. Investment in HCV screening is necessary to diagnose infected people and enable them to access therapy.

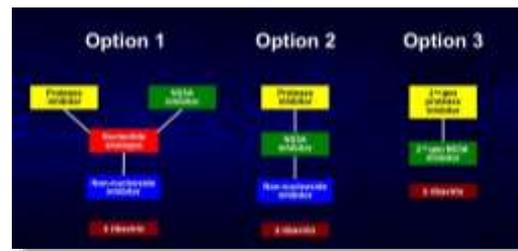


Figure 8: Interferon-free combination options from 2015 onwards

Non communicable diseases (NCDs)

Non communicable diseases (NCDs), such as ischaemic heart disease, stroke, diabetes, etc., are responsible for a high proportion of both mortality and morbidity on a global scale [27]. NCDs are becoming important contributors to DALYs in low and middle income countries: in 1990, ischaemic heart disease was the tenth most important contributor to DALYs; but in 2010, it was the third most important contributor. Stroke and ischaemic heart disease were the third and fifth causes of death in adults aged >30 years in SSA in 2010. High rates of risk factors for NCDs, such as hypertension, obesity, diabetes and smoking, have been identified in people living in SSA but the national governments' responses have been inadequate. In Uganda, baseline data on NCDs are only being gathered now, even though a Programme for the Prevention and Control of NCDs was set up in 2006. Diagnosis and monitoring of NCDs are lacking in Ugandan Health Centres: basic instruments to weigh patients and measure their blood pressure and blood sugar levels are often lacking. Healthcare workers are not trained to manage NCDs. The lack of screening results in a large burden of undiagnosed disease in RLS. Even if Uganda patients are diagnosed and treated for a NCD, retention in care is very poor and drug stock outs are common. Patient records are inadequate. As HIV-infected people live longer, thanks to ART, their risk of suffering from a NCD increases. It might be possible to leverage the care offered at HIV clinics to improve the health of both HIV-infected and – uninfected patients. Lessons learned in HIV testing and care can be applied to NCDs, Dr Kanya (Uganda) suggested; for example, screening large numbers of people for NCD risk factors; and ensuring retention in care and good adherence by

using community support mechanisms. The SEARCH study is a five year evaluation of the Test and Treat strategy for HIV, but it will also investigate if HIV care models can be adapted to establish care for chronic NCDs, such as hypertension and diabetes.

Data from pre-SEARCH pilot studies in South West Uganda have confirmed that the adult HIV prevalence rate is 8%. During a campaign to promote HIV testing, 35% of those tested had never taken an HIV test before. The prevalence of hypertension increased in the study population with age. Nearly one quarter (23%) of the adult population had a blood pressure >140/90 and 12% had a blood pressure >150/100. The majority of patients with very high blood pressure were unaware of their condition, and 61% of those with previously diagnosed hypertension were not taking anti-hypertensive medication. Risk factors for hypertension in this population included age ≥ 60 years; obesity; diabetes; alcohol consumption (men); family history (men); and HIV infection (men). The prevalence of hypertension in men was 34% higher than in women. Linking patients to hypertension care was challenging because of the lack of transportation to the clinic and because patients felt well, despite their hypertension. During the SEARCH pilot studies, 18/80 adults tested (23%) were newly diagnosed with diabetes: 38/62 (61%) were on treatment. Although the SEARCH pilot studies identified effective methods of screening and diagnosing NCDs in the community, they also highlighted the challenges of this approach. The screening campaign sensitised healthcare workers to the burden of undiagnosed NCDs in their communities. However, the clinics were overwhelmed and unable to manage the large number of referred patients because of a lack of staff, medication and resources. Retention in care was poor because of inadequate counselling; no adherence support; and frequent referrals to healthcare facilities which patients found difficult to travel to. Data collection systems were not in place to monitor patients. Dr Kamya concluded that African healthcare systems need to leverage HIV care infrastructure in order to manage patients with NCDs.

Neurocognitive impact of HIV infection and ART

HIV enters the CNS and brain within two weeks of the initial infection: inflammation can be detected in the brain at high levels during acute infection and it persists at lower levels during chronic infection [28]. The majority of the virus is present in the white and deep grey matter of the brain. HIV associated cognitive impairment affects behaviour (e.g. apathy, depression), cognition (memory loss, concentration) and motor function (e.g. gait, tremor). Patients with HIV associated asymptomatic neurocognitive impairment perform everyday tasks as poorly as symptomatic patients do, suggesting that the virus causes damage to the nervous system even if no symptoms are detectable.

Although treatment with ARVs has decreased the risk of dementia in HIV-infected patients, cognitive deficits have been identified in treated patients. In one study conducted in Uganda, 64% of patients (2/3 of whom were taking ART) scored <10/12 on the International HIV Dementia Scale. Poor cognitive function was predicted by negative life events, stress and psychosocial impairment. Persistent neuropsychological deficits were observed in two cohorts of patients (South African and Italian) even though they had been taking ART for one and more than five years, respectively. HIV appears to have a multifactorial and cumulatively damaging effect on the brain. Inadequate penetration of HIV reservoirs by ART may allow virus to persist and continue to damage the nervous system, despite long term therapy. Chronic immune activation and other factors, such as malaria infection or cerebrovascular disease, may also play a role in HIV-associated brain damage. As HIV-infected patients age in RLS, as elsewhere in the world, the risk of co-morbidities that affect the brain increases: these conditions may combine with the adverse effects of HIV on the brain to accelerate cognitive impairment. ART is effective in preventing viral replication and this is essential for the patient's health. However, it does not control HIV-related neuronal damage and cognitive impairment may occur even in the presence of ART.

Satellite symposia

Prior to the start of the Workshop, Janssen Pharmaceutica hosted a symposium entitled *Growing Pains: Developing adequate strategies for HIV care in children and adolescents*. It was chaired by Carolyn Bolton Moore (Zambia). Chewe Luo (Zambia) reviewed the recent changes in the WHO and national guidelines; Elizabeth Obimbo (Kenya) discussed the challenges of paediatric HIV care in SSA; and Marape Marape (Botswana) outlined the options for second and third line paediatric regimens.

AbbVie sponsored a symposium entitled *Optimizing HIV Management in Resource Limited Settings*, chaired by Danjuma Nkami Mbo (Nigeria). Francesca Conradie (South Africa) spoke about men infected with HIV; Mo Archary discussed the management of children with HIV; and Albert Mwangi outlined the potential of viral load monitoring in RLS.

During the meeting, Gilead Sciences hosted a symposium entitled *Tenofovir (TDF) and Truvada® (TVD): A look back and current updates*. Lloyd Mulenga (Zambia) discussed the efficacy and safety of TDF containing ART while Francois Venter (South Africa) reviewed the differences between FTC and 3TC.

MSD (Merck and Co.) hosted a Round Table Discussion, which focused on *Optimizing the use of integrase inhibitors (Adults and Paediatrics) in Sub-Saharan Africa: current and future*. Elly Katabira (Uganda) provided the opening remarks; and Lloyd Mulenga (Zambia) described the introduction of adult and paediatric formulations of raltegravir. Elly Katabira, Lloyd Mulenga and Francois Venter (South Africa) discussed the optimal ways of using HIV integrase inhibitors in the region.

Conclusions

The Workshop closed with the presentation of the prize for the best oral abstract: it was won by Dr NF Clement (Ghana) for her work on non-traditional approaches to reaching MSM with HIV prevention, testing, counselling and care services [18]. Dr Mwangi thanked all of the sponsors (Platinum level: AbbVie, Gilead and Janssen; Silver level: Merck; Supporter: ViiV; Contributor: Mylan; and Others: ANRS and the Kingdom of the Netherlands) and praised the speakers for their stimulating and informative presentations.

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