Emerging issues in HIV

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About the author:
Dr Peter MacPherson is a Wellcome Trust Clinical Research Fellow and Senior Lecturer at Liverpool School of Tropical Medicine, UK. He holds a PhD from LSTM, an MRes from University of Liverpool, an MPH from Harvard University, and did his undergraduate medical training at the University of Aberdeen.

Peter is based at the Malawi-Liverpool-Wellcome Trust Clinical Research Programme in Blantyre, Malawi, where he leads the Public Health Research Group. His research focuses on the epidemiology of the HIV and TB co-epidemics in sub-Saharan Africa, and on the development and evaluation of interventions to improve case detection and access to treatment. During his present Wellcome Fellowship, Peter is undertaking a number of randomised controlled trials of HIV/TB interventions, including a pragmatic randomised controlled trial of optimised HIV/TB screening using novel diagnostics and linkage to care among adults attending health centres with symptoms of tuberculosis (PROSPECT Study); an intensive TB/HIV household contact tracing intervention; and a male-partner-based index contact tracing study. During his Wellcome Clinical PhD, Peter did a cluster-randomised trial of a novel HIV self-testing and home initiation of treatment intervention among 17,000 adults in urban communities in Malawi.

Peter is an Honorary Consultant in Communicable Disease Control at Public Health England North West.
1. Key concepts

**HIV** (human immunodeficiency virus) is a viral infection of humans that can be transmitted by sexual contact, from mother-to-infant during pregnancy, delivery or breastfeeding, or by injecting drug use.

**AIDS** (acquired immunodeficiency syndrome) refers to the clinical syndrome caused by HIV infection, and is characterised by a weakened immune system that results in increased susceptibility to severe infections, cancers and death. HIV-infection was first recognised among men who have sex with men in Los Angeles, USA, in 1981, but since then has been identified in all continents of the globe. On average, it takes approximately 10-12 years from a person being infected with HIV to them developing AIDS, although other symptoms appear earlier.

**ART** (antiretroviral therapy) refers to the combination of medications (usually three different drugs) that are taken daily and suppress HIV virus replication. Although ART doesn’t cure HIV, taking the correct medication with good adherence allows the immune system to recover, avoid opportunistic infections, and people to regain strength and return to their livelihoods. Increasingly, ART can be given as a single fixed-dose combination single pill once daily with very few side effects. Evidence suggests that people with HIV taking ART can expect a life-expectancy similar to that of HIV-negative individuals.

**HIV viral load** (VL) is a measurement of the number of copies of HIV virus per cubic centimetre of blood. Rates of HIV viral load can reach very high levels (up to $10^7$ copies/cm$^3$) in the 4-6 week period immediately after infection, and as the immune system becomes very weak years after infection. HIV viral load is strongly related to infectivity, with very high levels associated with increased risk of the virus being passed during sexual contact or other exposure. A key aim of ART is to reduce the HIV viral load to an undetectable level in the blood, indicating that viral replication is suppressed. Raised viral load whilst taking ART may indicate treatment failure, resistance to the drugs, or poor adherence.

2. Epidemiology of HIV

Globally in 2016, an estimated 37 million people were living with HIV infection, with the countries Eastern and Southern Africa (53% of all infections) disproportionately affected.

Rates of new HIV infections have declined substantially from a peak of 1.9 million in 2005 to 1.0 million in 2016. However, some groups have shown greater declines in new infections than others. In particular, women have higher treatment coverage and better adherence to ART than men, and rates of death from AIDS-associated illnesses were 27% lower among women than men in 2016.

In Southern and Eastern Africa, reductions in HIV deaths have been rapid, and strongly linked to the roll-out of ART programmes since the early 2000s. Between 2004 and 2016, there was a 62% decline in the number of deaths attributable to HIV infection in this region. Reductions in HIV deaths have also been observed in the Caribbean, North America, West and Central Europe, and Western and Central Africa. However, declines have been more gradual in Latin
America, and there have been worrying recent increases in the Middle East and North Africa and in Eastern Europe and Central Asia.

Recent increases in new HIV infections have been seen among key population groups at increased risk of infection, including men-who-have-sex-with-men (MSM), transgender people, sex workers and people who inject drugs.

3. 90-90-90 targets

UNAIDS has defined targets for ending the AIDS epidemic, known as the 90-90-90 targets.

These are that by 2020:
- 90% of people living with HIV should have been tested and made aware of their status;
- 90% of people diagnosed with HIV should be taking ART;
- 90% of people taking ART should have a suppressed HIV viral load.

Modelling suggests that if these targets are achieved, the global number of new infections would be reduced to less than 500,000 per year.

By the end of 2016, substantial progress had been made towards achieving the 90-90-90 targets. Globally, an estimated 70% of people with HIV knew their status, 77% were taking ART and 82% were virally suppressed. A number of countries in sub-Saharan Africa, including Botswana, Rwanda and Malawi have reported that they are close to achieving the 90-90-90 targets.

However, substantial work remains to be done. Although globally we are on track to have 30 million people taking ART by 2030, rates of new infection are not falling quickly enough, suggesting a more differentiated approach to identifying and treating hard-to-reach groups is needed.

The HIV care cascade is a key advance in understanding care, treatment and prevention gaps, and analysis of a country’s or a region’s cascade can provide insights into how to best improve HIV care systems.

The global HIV care cascade, 2016
4. Recent advances in HIV treatment and prevention

HIV testing services

HIV testing is the entry point to comprehensive care and prevention. WHO recommends that all individuals at risk of HIV receive an HIV test annually (or more frequently if ongoing exposure) and when they come into contact with a health provider. However, a substantial HIV testing gap remains, with only half of adults in sub-Saharan Africa reporting having had a test within the previous 12 months. Men have particularly low rates of HIV testing.

In addition to improving HIV testing services within health centres—which many people struggle to access, or only do so once their illness is advanced—a broad mixture of HIV testing services are required to meet the needs of local populations. This should include high-quality community-based HIV testing initiatives such as mobile campaigns, door-to-door testing programmes, school-based HIV testing, workplace-based HIV testing, and event-based HIV testing (such as associated with sporting events, or on national testing days). Evidence shows that extensive pre-test counselling is detrimental, and WHO now recommends that only very brief counselling should be provided, except in exceptional cases.

In recent years, HIV self-testing—defined as someone performing and interpreting their own HIV test, perhaps supported by a family member, friend or health worker—has become widely available, driven by convenient oral fluid and blood-based kits. Data from a number of large studies in Africa, Asia, Europe and the Americas shows that HIV self-testing programmes can achieve high rates of coverage and are extremely popular with testers because of their low cost, convenience and confidentiality.

It is critical that following an HIV test, comprehensive programmes are in place to link people to either HIV treatment or prevention services. Too often individuals are not successfully linked to the care that they require, increasing risk of death, and of passing infection to others. Interventions such as home-based ART initiation can improve rates of linkage.

HIV treatment as prevention

Over the last decade, a number of mathematical models and observational studies have provided evidence to suggest that achieving high population levels of ART coverage could result in substantial reductions in new HIV infections and deaths. By rapidly identifying people with HIV and reducing their viral load to an undetectable level, their viral load will become “undetectable” and they will be substantially less likely to transmit infection to others. This “test and treat” strategy is known as treatment as prevention.

The HPTN052 study—a study where people living with HIV were randomly allocated to start ART immediately, or were delayed until their immune system had weakened—showed that the risk of HIV infection among their partners decreased by 93% when people living with HIV started ART immediately. This was a landmark study, showing that ART can provide highly effective and durable HIV prevention, and WHO recommended in 2013 that all individuals with HIV, regardless of immune system levels, should be initiated onto ART.
Additionally, further studies have shown that people who are immediately initiated onto ART have substantially lower rates of opportunistic infections, cancers, and death.

At least four large randomised studies are evaluating the population effects of universal HIV testing and immediate ART initiation strategies on rates of new infections and are expected to report results shortly.

**HIV treatment as prevention (TASP)** therefore appears to be by far the most effective intervention that we have, both for preventing new infections, and for improving the health of people living with HIV. However, key challenges will include: sustaining high levels of HIV testing and linkage to treatment; reaching key populations and marginalised groups; and sustained health system support.

**Pre-exposure prophylaxis**

Pre-exposure prophylaxis (PrEP) refers to an intervention where HIV-negative individuals who are at increased risk of HIV infection take a daily or intermittent (e.g. before sexual contact) dose of ART. Several large randomised control trials have shown that, among a variety of populations, including men-who-have-sex-with-men, transgender individuals, sex workers and people who inject drugs, substantial reductions in new HIV infections can be achieved with PReP.

Key challenges with PrEP include ensuring that those most likely to benefit from PReP (especially marginalised groups and key populations) are able to access services, and ensuring high quality risk reduction counselling, adherence and support.

**Voluntary male medical circumcision**

Uncircumcised men are at increased risk of HIV infection due to the high numbers of cells receptive to infection in the foreskin of the penis. Three large randomised trials done in sub-Saharan Africa have conclusively demonstrated that voluntary medical male circumcision (VMMC) can reduce men’s relative risk of HIV infection by around 40%. Although efforts have been made to implement VMMC in high HIV prevalence countries, sustaining services has been challenging.
5. Questions to guide readings

1. What mixture of HIV prevention interventions should be prioritised for the setting in which you work?
2. How can marginalised and key populations be supported in accessing HIV testing, treatment and prevention services?
3. How can health services sustain high quality delivery of HIV care and prevention services in the face of expanding demand, new interventions, and financial pressure?
4. What role do education and behaviour change interventions have in the TASP era?

6. Readings


Geng, E.H. & Havlir, D.V. (2017). The science of rapid start—From the when to the how of antiretroviral initiation. *PLOS Medicine*, 14(7), e1002358. doi:10.1371/journal.pmed.1002358


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