

Community consensus statement on the use of antiretroviral therapy in preventing HIV transmission

Introduction to the statement

1. This is a community consensus statement on the use of antiretroviral therapy (ART) to reduce the risk of HIV transmission from people living with HIV. It does not cover the provision of antiretroviral drugs to people who are HIV negative to reduce their risk of acquiring HIV (pre-exposure prophylaxis, PrEP). It is also not specifically about access to ART in general.
2. This statement is issued with the underlying principle in mind of safeguarding the health and wellbeing of people living with HIV, whether they choose to take ART or not. It supports the human rights, dignity and self-determination that enable people to make the choices that most benefit their health and wellbeing and that of their partners.
3. HIV prevention should not be viewed as an aim of ART that is separate from the overall health and wellbeing of the person taking it. The provision of ART for prevention purposes should never violate individuals' rights to health, self-determination, consent or confidentiality.
4. This statement is a specific community response to a number of HIV treatment guidelines^{1,2,3,4,5} and policies⁶ issued in the last few years that have addressed treatment as prevention as part of their remit. There has been divergence of recommendations and opinion in this area within guidelines, partly due to divergence of opinion about the implications for human rights, public and individual health and resources of providing ART for reasons of prevention.
5. This statement is not issued to supplant these guidelines and policies but to establish some guiding principles. It is issued within the broader framework of the Greater Involvement of People Living with AIDS (GIPA),⁷ HIV Leadership and of the Positive Health, Dignity and Prevention policy framework established by GNP+ and UNAIDS.⁸
6. This statement was originated by the European AIDS Treatment Group in collaboration with NAM/Aidsmap.com. It was developed via an online consultation, a community meeting in September 2013, and further consultation with key opinion leaders in the HIV community. It is now offered for sign-on and endorsement by individuals and organisations in the community of people living with and affected by HIV.

Statement

7. There is conclusive evidence^{9,10,11} that effective ART considerably reduces an individual's risk of transmitting HIV through vaginal sex, and convincing epidemiological and limited direct evidence that this applies to anal sex and needle sharing as well.^{12,13,14,15,16} (See appendix two for a summary of our current state of knowledge.)
8. These findings strengthen the evidence base for previous declarations on the potential for prevention of ART.¹⁷ They present great opportunities but also challenges for individuals living with HIV.
9. ART has the potential to relieve people living with HIV of the burden of guilt, anxiety and fear of criminal liability at the prospect of transmitting HIV to others. A community manifesto issued in 2008 said that treatment as prevention "favours quality of life and – even more – social integration of people with HIV."¹⁸ A sign-on community statement issued in 2011 said that earlier initiation of ART "is a powerful, potentially cost-saving tool that can help end the AIDS epidemic."¹⁹ Some surveys have shown that people living with HIV rate no longer being able to transmit the virus as among the most important advantages of a hypothetical cure for HIV infection.^{20,21}
10. However, using ART as prevention also has implications for human rights, resource allocation, and the planning and integration of HIV care and treatment. The 2011 statement cited above²² added: "Biomedical, structural and behavioral interventions need to be delivered in the context of a community-centered mobilization for health and rights".
11. On an individual level, taking ART for life is a decision that most people will need time to consider and which they should not feel pressured into. ART for prevention has potential long-term side-effects, and once started will probably need to be taken for life. In addition, ART, unlike other methods including condoms, cannot prevent most other sexually transmitted infections (see endnote).²³
12. In many countries, the vulnerable populations that need ART most have the worst access to HIV services²⁴ in part due to criminalisation²⁵ and stigma.²⁶ The prevention benefits of ART cannot be realised until these are addressed.
13. The potential to use ART as a public health measure could potentially lead to people with HIV being or feeling coerced into taking an HIV test or ART. This is of particular importance to people belonging to stigmatised populations who may be, or fear being, exposed or endangered by such programmes. There must therefore be safeguards against pressure, coercion or legal threats, in the name of public health, to people who do not yet wish to take ART. We oppose any public health measures, implemented or proposed, that are based on compulsory HIV testing or treatment.²⁷
14. On an individual level, providers should be alert to the possibility of coercion by partners or others and establish that the person living with HIV wishes to take ART of her/his own free choice. This may be a particular issue in situations of gender-based violence or coercion.
15. ART for people who test HIV positive should not be adopted as the sole component of HIV prevention programmes. It should not supplant, or weaken access to, existing methods of proven effectiveness. Scientific studies of biomedical HIV prevention methods have all integrated ART with other proven HIV prevention methods; treatment access programmes must be designed similarly. These methods include the provision and promotion of male and female condoms and lubricant, the provision of sterile injecting equipment, voluntary medical male circumcision, risk-reduction counselling and motivational programmes, and social support programmes to help people minimise their sexual risk.

16. The recognition of the efficacy of effective biomedical prevention methods, and their integration into existing programmes, may be an opportunity to refresh, rethink or challenge community norms that are not sufficiently protective, are difficult or impossible to sustain for some people, or are counterproductive. Typically these norms have required 100% adherence to a strategy such as condom use or sexual abstinence before marriage, or define condomless sex as unsafe in all contexts.
17. Equally, however, it is important that programmes that extend access to ART are carefully thought through and designed so that existing methods and community norms that safeguard people's sexual health and wellbeing are not negatively affected, especially in situations where populations maintain high adherence to existing methods that could be potentially eroded. Examples include high levels of sterile equipment use by people who inject drugs and condom use by sex workers.
18. The provision of ART cannot stand alone as a prevention method. Access to voluntary HIV counselling and testing, access to free or affordable HIV care, access to effective and tolerable ART and access to support for consistent adherence are necessary conditions for the effective use of ART as treatment or as prevention.
19. ART as prevention presents opportunities and challenges regarding the supply of drugs and healthcare system capacity and resource prioritisation. The cost of ART must decrease further if it is to be provided to all who fall within the 2013 WHO treatment guidelines and to those who may wish to use it for prevention outside those guidelines.^{28,29} As ART is associated with higher rates of retention in care³⁰ and viral suppression,³¹ wider use, especially accompanied by falls in price, may be cost-effective, and even cost saving.³²
20. Providing ART for prevention must not in any way impede efforts to make ART available as treatment to anyone who needs it for clinical benefit.³³ They must both be part of a general programme whose aim is to improve the physical and emotional health and social position of people with HIV and their partners.
21. Patient readiness is crucial to support the high levels of adherence necessary to suppress HIV. We recommend adoption of the patient readiness paradigm, as outlined in the EACS treatment guidelines.³⁴ For people with high CD4 counts, readiness should be explored early and should not be deferred until CD4 criteria for clinical need are reached.
22. Many people with HIV remain unaware of the prevention benefits of ART. We recommend the adoption of the BHIVA and EAGA statement³⁵ that healthcare providers should inform all patients of the potential prevention benefits of ART. We also recommend provision of patient materials suitable for different ages, knowledge levels and ethnicities explaining the prevention benefits of ART.
23. The prevention benefits of ART are even less well known among people who are HIV negative but vulnerable to HIV.³⁶ The current partners and potential partners of people with HIV need accurate and clear information on the effect of ART in reducing the likelihood of HIV transmission and providers need training to give this. This needs to be done in a way that they can use to strengthen their ability to stay free of HIV infection rather than undermine it, and to take responsibility for their and their partners' sexual health.
24. Most models predict that ART by itself will not end the HIV epidemic.³⁷ Expanding access to ART as prevention must not endanger access to other proven prevention methods or to reduce investment in research into new methods. Providing ART to people with HIV, however, not only saves lives but may also be a necessary component of what it takes, ultimately, to end the HIV epidemic.

Appendix one: unmet research needs

There remain many areas of uncertainty and lack of evidence that make choices about ART as prevention more difficult. The highest-quality evidence for ART as prevention comes primarily from studies of heterosexual serodiscordant couples and mothers and babies.³⁸ Research is needed in several areas including:

1. **Anal sex.** See appendix two for a summary of what we know about the effect of ART on transmission of HIV via anal sex. Although there is a considerable amount of observational evidence, and a small amount of direct evidence, that ART must be reducing transmission via anal sex to a similar degree as it does in transmission via vaginal sex, we do not yet have evidence from randomised controlled trials that would quantify its effect. Large studies of gay men and heterosexuals who have anal sex is urgently needed and we welcome the fact that two are currently ongoing.^{39,40}
2. **Needle and drug equipment sharing.** As we note in appendix two, there is population-level evidence that ART provision may be helping to reduce incidence among people who inject drugs,⁴¹ but we need more research in this population to distinguish between the effect of ART and the effect of other prevention measures and support.
3. **Network effects.** HIV transmission is not an attribute of individuals: it is an attribute of pairs and networks of individuals. Research suggests that the degree of connectivity among populations may make a crucial difference to the speed and extent of the spread of HIV and other sexually transmitted infections (STIs) in that population. More research is needed on whether ART can break transmission chains and what this suggests about the best way to non-coercively prioritise particular groups that might maximally benefit from ART.^{42,43,44,45}
4. **STIs and infectiousness.** While there is clear evidence⁴⁶ that STIs significantly increase the risk of HIV transmission and acquisition among people not taking ART, more research is needed on whether the same applies to people taking fully suppressive ART (see endnote).⁴⁷ At present the data we have is somewhat conflicting and any additional risk STIs add to the likelihood of HIV transmission by people taking ART has not been accurately quantified.
5. **Clinical risks and benefits of ART for people with high CD4 counts.** There is disputed evidence as to whether clinical benefits of ART outweigh the risks for people with CD4 counts over 500 cells/mm³ or even 350 cells/mm³.⁴⁸ We welcome the START Study⁴⁹ and may need further research to establish the risk/benefit ratio at higher CD4 counts.
6. **Risk compensation.** As the BHIVA/EAGA statement in the UK notes, ART is at least as efficacious as 100% attempted condom use in reducing HIV transmission^{50,51} but its effects may be negated by increases in risk behaviour.^{52,53} We therefore need implementation research in different populations to monitor possible changes in behaviour and risk consequent to the more widespread use of ART as prevention.
7. **Combination programmes.** We need more individually- and cluster-randomised research to assess the efficacy of comprehensive 'combination-prevention' programmes not based solely on condoms or ART alone^{54,55} and carried out in varied populations.^{56,57}
8. **Implementation research.** HIV prevention is always an example of the maxim "Think global, act local". While findings from scientific research will continue to be essential in guiding HIV prevention programmes, and in providing evidence as to the most and least effective methods and mix of methods, HIV prevention is too dependent on individual, demographic and cultural differences ever to be something that is applicable as a 'one size fits all' approach. Every co-ordinated HIV programme should include, and be funded to include, a programme of implementation research that feeds iteratively into the programme and informs and modifies it as necessary as it is carried out.

Appendix two: a summary of the current evidence on the efficacy of treatment as prevention

This section looks at the evidence for the biological and cohort-level efficacy of treatment as prevention: it does not look at the effectiveness of different ways of using ART as part of a co-ordinated HIV prevention strategy.

Transmission via vaginal sex. A number of observational studies^{58,59} had already established that transmission of HIV from people on suppressive ART appeared to be a rare event. In 2011, the HPTN052 study looked at HIV transmission (almost entirely) within heterosexual couples of different HIV status, comparing transmission from the HIV-positive partners taking immediate ART with the HIV-positive partners not taking ART until the guidelines of the time recommended.⁶⁰ The study found a 96% reduction in the likelihood of transmission from partners on ART. There were two transmissions from participants allocated to ART (one of them during the open-label extension of the study) but subsequent analysis indicated that both must have transmitted HIV around the time they started ART and were unlikely to have been virally suppressed at the time.⁶¹ It is also of note that out of a total of 39 HIV transmissions in the study, 11 (28%) did not come from the regular partner who was in the study but from an outside source.

Transmission via anal sex. We do not have the same standard of evidence for the effect of ART on transmission via anal sex. Two randomised controlled trials, the PARTNER study⁶² and the Opposites Attract study,⁶³ are currently looking at this question and early results from the PARTNER study are due in the first half of 2014. Nonetheless there is a combination of strong direct and circumstantial evidence that suggests that ART very significantly reduces the likelihood of HIV transmission.

- **Direct evidence.** A couple of studies have been done that phylogenetically match transmission pairs of gay men. In one in Brighton,⁶⁴ 41 'likely transmitters' were identified in a clinic cohort of whom only three were on ART, yielding a 92% lower incidence in transmission from people on ART. However, two of these probably had a detectable viral load at the time of transmission, leaving one unexplained (97% lower incidence). In another in San Francisco,⁶⁵ only 2 out of 23 gay men who were a transmitting partner were on ART; neither had an undetectable viral load around the time of transmission.
- **Epidemiological evidence.** Observational and modelling studies indicate that in countries with high levels of people on ART, a majority of infections come from people who are undiagnosed, many of them in acute HIV infection, and most of the rest from people not taking ART.^{66,67} A UK study (ref 66) has estimated that, in gay men, 62% of infections come from the undiagnosed and only 5% of infections come from someone who is taking ART. This is despite the fact that gay men with HIV spend much longer periods of time living with chronic infection than they do undiagnosed. If HIV transmission via anal sex by a person on suppressive ART was at all likely, we would see a far higher proportion of infections coming from people with chronic infection and on ART.
- **Case studies.** There are only two cases published in the literature that appear to show HIV transmission between two gay men where the positive partner had an undetectable viral load. One was in the Brighton study cited above,⁶⁸ in which the date of transmission was very uncertain. The other was a case from Germany in 2008 in which a man with a consistently undetectable viral load apparently infected his partner some time between 2002 and 2004.⁶⁹ It is very difficult to be certain about cases like this, as there needs to

be both a known date of transmission and a viral load test very near that date in order to establish the viral load at the time of transmission. Nonetheless, the rarity of such case reports suggests that transmission via anal sex from a partner with a suppressed viral load is very uncommon.

- **Seminal and rectal viral load.** It has been suggested that transmission by someone with an undetectable plasma viral load might be more likely in anal sex. Because transmission is more likely in anal sex, partners may need to be more completely virologically suppressed. However, concordance between plasma and seminal or rectal viral loads appears to be greater than it is between plasma and vaginal viral loads. In one study only 4% of men with a blood plasma viral load under 400 copies/ml had detectable HIV in their semen. Other studies have found figures of about 4 to 7% discordance but even where detectable, seminal viral loads have generally been below 500 copies/ml, a figure suggesting a considerably reduced chance of transmission.^{70, 71, 72, 73, 74} Although rectal viral loads need more study, one study found that 2% of men with an undetectable blood plasma viral load had detectable HIV RNA in rectal secretions.⁷⁵
- **Transmission per exposure.** One study from Sydney⁷⁶ has been cited as demonstrating that ART does not reduce the chances of HIV transmission via anal sex. In this study, gay men had a per-contact risk of HIV infection via anal sex that was as high in the era of ART as it was in the pre-ART era. However, this could be the case if a reduction in acquisitions from partners in chronic infection was offset by an increase in the likelihood of transmission from partners in acute or early HIV infection.

Transmission via sharing needles. We do not have the same amount of epidemiological evidence that ART reduces the chance of infection with HIV by parenteral routes (via injection and other direct-into-the-bloodstream routes). This is partly because stigma and lifestyle has meant that people who inject drugs often have very poor access to ART and partly because access to ART is often accompanied by access to other HIV reduction resources such as needle and syringe exchange and opiate substitution therapy, which are themselves extremely effective methods of reducing HIV infection. The most convincing series of studies of the apparent effect of ART has been that from British Columbia, where a combined programme of safe-injection materials and resources for people who inject drugs and access to ART for those with HIV has been strongly correlated both with a fall in the average viral load among members of this population and a fall in new HIV diagnoses in the same group.^{77, 78} Although it concerned pre-exposure prophylaxis (PrEP) given to HIV-negative people who inject drugs, the Bangkok study of tenofovir PrEP in people who inject drugs⁷⁹ showed that antiretroviral drugs could reduce parenteral HIV infections to the same degree as they did sexual infections.

The effect of sexually transmitted infections. There is abundant evidence that both bacterial and viral sexually transmitted infections (STIs) raise the HIV viral load of individuals not taking ART, increase viral shedding in the genital tract, and raise the likelihood of both transmission and acquisition of HIV on an individual and population level,^{80, 81, 82, 83, 84} though all but one of a number of studies found that presumptive treatment of STIs as a prevention method had no effect on HIV incidence rates.^{85, 86, 87, 88, 89} There is conflicting evidence as to whether STIs raise viral load or increase episodes of viraemia and viral shedding in people on fully-suppressive ART. If they do, this appears to happen only in a minority of people and rarely raises viral loads to a level that would imply significant infectiousness.

In women, one well-designed study in Kenya found that in 142 women living with HIV who were on ART and acquired an STI, STI acquisition was associated with the development of a detectable HIV viral load in five women (3.5%) and that the median vaginal viral load was 115 copies/ml (maximum 820 copies/ml).⁹⁰

In men, there is conflicting evidence as to whether STIs in men on ART raised seminal viral load. In one study⁹¹ urethritis due to bacterial STIs raised the risk of a detectable seminal viral load (median 200 copies/ml, maximum 2560 copies/ml) by 29 times, but in a more recent longitudinal study⁹² no association was found between STIs and a detectable seminal viral load in people on ART. In another study,⁹³ however, 10% of men living with HIV who were taking ART with undetectable blood plasma viral loads had detectable virus in their semen, though the median viral load was only 126 copies/ml. However, a detectable seminal viral load was not associated with infection with an STI (by bacterial or viral STIs) but only by infection with the extremely common but asymptomatic herpes-family viruses CMV (cytomegalovirus) and EBV (Epstein-Barr virus).

In terms of rectal viral load, this is an under-researched area, but in the most recent study, while finding that 38% of men in a group of 80 gay men had detectable HIV in rectal fluids,⁹⁴ found this was far more likely in the 26% of men who were not on ART, and that the acquisition of a new STI was not correlated with detectable HIV in rectal fluids or with an increase in viral load in those whose viral load was already detectable.

Population effects. It seems logical that increasing the proportion of people living with HIV who are taking ART would lead to fewer transmissions, but in practice this is both very difficult to prove and may be confounded by behavioural and demographic changes. In developed-world situations, strong correlations have been observed between community viral load and a fall in HIV diagnoses in both the British Columbia studies cited above^{95, 96} and in a longitudinal cohort study in San Francisco.^{97, 98} However, in the case of the British Columbia study, it is difficult to distinguish between the effect of treatment and of the safer injecting equipment and safe injection rooms offered to drug users at the same time (HIV diagnoses in gay men were not so strongly correlated with treatment access), and in the case of San Francisco, falls in new diagnoses were not significantly correlated with actual declines in incidence as measured by incidence assays. This means that behavioural or demographic causes cannot be ruled out.

Stronger evidence for the success of ART's preventive effects may have come from studies in Africa, where high prevalence means that whole-population effects can be more reliably evaluated. In a study in South Africa, the scale-up of ART in a district in KwaZulu Natal was correlated very closely with falls in HIV incidence: interestingly, a 'plateau effect' seemed to be reached once more than 40% of the HIV-positive population (including undiagnosed people) was on ART.⁹⁹ This study has been critiqued, however, because the relationship between ART scale-up and incidence seems 'too good to be true', with every 1% increase in the proportion of people in ART accompanied by a 1% fall in incidence.

A 'test and treat' study from Uganda found significant correlation between the proportion of the entire HIV-positive population of a district and their average viral load,¹⁰⁰ but so far this has not been analysed to see if there is a correlation with falls in incidence. As well as behavioural and demographic changes, there may be biological reasons other than viral suppression through ART for declines in HIV incidence in certain populations: for instance, studies primarily in southern Africa¹⁰¹ have uncovered evidence that HIV's replicative capacity may be declining in some areas as it acquires resistance mutations to human HLA genes.

References

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- ³ WHO guidelines - www.who.int/hiv/pub/guidelines/arv2013/en/index.html
- ⁴ EACS guidelines - www.eacsociety.org/Portals/0/Guidelines_Online_131014.pdf
- ⁵ BHIVA guidelines - www.bhiva.org/documents/Guidelines/Treatment/2012/120430TreatmentGuidelines.pdf
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