Community consensus statement on the use of ARV treatment as prevention

1. This is a community consensus statement on the use and prescription of antiretroviral therapy (ART) to people living with HIV to reduce their risk of transmitting HIV.
2. ART has of course drastically reduced the toll of death and sickness due to HIV infection. There is now, in addition, conclusive evidence from a clinical trial,[1] HPTN 052, that effective ART very considerably reduces an HIV positive person's risk of transmitting HIV through vaginal sex. In this trial, treatment reduced the risk of HIV infection by 96%. There is widespread expert consensus that this reduction in infectiousness applies to anal sex and needle sharing too.[2]
3. The HPTN 052 result and other declarations of the effectiveness of ART as prevention, such as the so-called 'Swiss Statement[3]' in 2008, have presented both enormous opportunities to people with HIV and people working in HIV prevention, but also considerable challenges:
    a. Aside from its public health benefit, ART as prevention has the potential to relieve the burden of guilt, anxiety and fear of criminal liability many people with HIV feel at the prospect of transmitting HIV.
    b. Equally, concerns have been raised by some community activists that using universal ART as prevention as a public health measure could lead to people with HIV being pressured into taking ART, regardless of clinical need.
    c. In addition, access to ART for treatment is still restricted globally and in parts of Europe. In a number of countries the vulnerable communities that need it most have the worst access to HIV treatment and to prevention and testing services, [4] in part due to criminalisation[5] and stigma, [6] and many people still get ill and die from HIV because of lack of access to ART.
    d. In addition to its direct prevention and possible clinical benefits to the patient, the prescription of ART is also associated with much higher rates of retention in care.[7] And yet even in some high-income countries, there is as yet no mechanism for funding the prescription of ART to people who do not meet guideline criteria for treatment. Cost pressures may perpetuate this.
4. For people with HIV, then, advocacy for the provision of ART as prevention has to include and to balance:
    a. Advocacy for the provision of ART to patients who wish or need to take it to reduce their risk of transmitting HIV, even if they fall outside criteria for its provision as treatment;
    b. Advocacy to safeguard the rights of patients who do not need or are not yet ready to take ART for clinical reasons and do not wish to take it for prevention reasons;
    c. Continued advocacy for the right of access to HIV prevention and testing for all affected communities and treatment for people with HIV;
    d. Advocacy and the provision of information on the positive impact and cost-effectiveness to individual and public health of ART as prevention, in order educate funders and health providers of its benefits.
5. The crucial issue that links these four advocacy aims is the safeguarding of patient choice.
6. It is important to ensure that providing ART for prevention will not in any way affect efforts to make ART available as treatment to anyone who needs it for clinical benefit. ART for

prevention and for treatment need not be in competition for resources[8] and should never be set in opposition to each other. Publicising the benefits of ART as prevention can be used to strengthen the case for its wider provision as treatment.

7. In the case of people who do not want ART as prevention, however, there need to be safeguards against health providers using coercion, pressure, future denial of ART if the patent refuses it now, or legal threat to persuade them to take ART. These safeguards are particularly important if, as is the case in the US, a recommendation that all people with HIV should be prescribed ART on diagnosis is adopted.[9]
8. Even in the case of clinical need, patient readiness to take ART is crucial in order to support the high levels of adherence necessary to suppress HIV, and we welcome and recommend the adoption of the patient readiness paradigm, as outlined in the EACS treatment guidelines,[10] as a model to follow.
9. We recommend that in the case of patients with high CD4 counts, readiness to take ART is explored well in advance of patients reaching CD4 criteria for treatment. If patients express readiness, ART should not be deferred until CD4 criteria are reached.
10. Many people with HIV remain unaware of the prevention benefits of ART or are uncertain of the evidence for it, and we also welcome and recommend the adoption by other guidelines of the BHIVA and EAGA statement in the UK[11] that healthcare providers must inform all patients of the potential prevention benefits of ART, and must prescribe it if, on the basis of that information, the patient asks for it.
11. The prevention benefits of ART are also not widely known among people vulnerable to HIV[12] and need publicising in order to encourage testing and enable people to take steps that may reduce their risk of HIV infection.
12. Most models predict that ART by itself will not end the HIV epidemic but will have to be used in combination with other methods. [13] Expanding access to ARTs as prevention should not be a reason to restrict access to other methods of proven efficacy.
13. There remain many areas of uncertainty and lack of evidence that make the choice of whether to take ART as prevention and/or rely on it as a prevention measure difficult. These include:
    a. Most of the evidence we have about the efficacy of ART as prevention concerns transmission between heterosexuals or via vaginal sex alone, or from mother to baby.[14] There is an urgent need for more research into the use of ART to reduce transmission via:
        i. Anal sex: in this case there is a small amount of evidence[15] suggesting a considerable reduction in risk with the use of ART, but large observational studies in gay men and heterosexuals who have anal sex is urgently needed. We welcome studies such as the PARTNER Study[16] and Opposites Attract study[17] designed to answer this question.
        ii. Needle and drug equipment sharing: in this case there is population-level evidence from British Columbia that ART provision may have reduced incidence in injecting drug users (IDUs),[18] but we again need an observational study of IDUs to assess the reduction in risk offered by ART.
    b. STIs: While there is clear evidence[19] that most STIs significantly increase the risk of both transmission of and infection with HIV on people not taking ART or their partners, there is relatively poor evidence on whether the same increase in risk applies to people taking fully-suppressive ART.[20]

c. Clinical risk/benefit of ART in people with high CD4 counts: There is poor, and disputed, evidence as to whether ART offers any clinical benefit, over the risk of side effects, to people with CD4 counts over 500 cells/mm^3 or even 350 cells/mm^3.[21] In this respect we welcome the Start Study,[22] which is designed to answer this question for CD4 counts over 350cells/mm^3, but we may need further studies to establish the risk/benefit ratio at higher CD4 counts.

d. 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.[23] [24] Concern remains however about the epidemiological consequences if people on ART and their partners were to reduce their use of condoms or increase partner numbers or risk behaviours because they feel safer from infection.[25] [26] We therefore need:

   i. Implementation research in different populations to monitor possible changes in behaviour and risk attendant on the more widespread use of ART as prevention or as PrEP;

   ii. More research to assess the efficacy of comprehensive 'combination-prevention' not based solely on condoms or ART alone; an example is the PopART study[27] currently taking place in Zambia and South Africa, [28] though different contexts would require different study designs.

e. We also strongly support the continued supply and promotion of condoms as a method of proven efficacy in preventing HIV. We emphasise that, unlike ART, they also prevent most of the other STIs that in themselves cause considerable morbidity and some mortality.

14. The lack of available evidence as to the efficacy of treatment as prevention to the groups and in the circumstances mentioned above should not be used as a reason to exclude people from access to treatment as prevention. Instead it should be seen as a call for more action in research in these areas.

15. The advent of ART as prevention faces both providers and recipients of HIV prevention methods and support with a considerable paradigm shift in what HIV prevention actually involves, who should provide it and what methods should receive priority. An ongoing programme of training and information is needed to help HIV prevention workers, advocates and recipients respond optimally to what is likely to be a new era in the prevention of HIV.

References

[1] Cohen MS et al. Prevention of HIV-1 Infection with Early Antiretroviral Therapy. NEJM 2011; 365:493-505.

[2] https://www.gov.uk/government/publications/bhiva-and-eaga-position-statement-on-the-use-of-antiretroviral-therapy-to-reduce-hiv-transmission

[3] Vernazza P et al. *Les personnes séropositives ne souffrant d'aucune autre MST et suivant un traitment antirétroviral efficace ne transmettent pas le VIH par voie sexuelle.* Bulletin des médecins suisses 89 (5). See http://www.saez.ch/docs/saez/archiv/fr/2008/2008-05/2008-05-089.PDF. English translation, including translator's affidavit, available at: http://tinyurl.com/cpyt5n). 2008.

[4] See Harm Reduction International. *The Global State of Harm Reduction 2012: Towards an Integrated Response*. 2012.

[5] The Global Forum for MSM and HIV. *Access to HIV Prevention and Treatment for Men Who Have Sex with Men: Findings from the 2012 Global Men's Health and Rights Study (GMHR).* 2012.

[6] Kalichman SC and Simbayi LC. *HIV testing attitudes, AIDS stigma, and voluntary HIV counselling and testing in a black township in Cape Town, South Africa.* Sexually Transmitted Infections 79:442-447. 2003.

[7] Lazzaretti C et al. *Engagement and retention in care of patients diagnosed with HIV infection and enrolled in the Modena HIV Surveillance Cohort.* Eleventh International Congress on Drug Therapy in HIV Infection, Glasgow, abstract P105 (see abstract here), 2012. See www.aidsmap.com/page/2553463 for similar studies.

[8] Sood N et al. *Treat and treat in Los Angeles: a mathematical model of the effects of test-and-treat for the MSM population in LA County.* Clinical Infectious Diseases, early online publication, doi: 10.1093/cid/cit158. 2013.

[9] US Department of Health and Human Services. *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*, 2013.

[10] See http://www.europeanaidsclinicalsociety.org/images/stories/EACS-Pdf/EACSGuidelines-v6.0-English.pdf, page 10.

[11] See reference 2 above

[12] Lampe F et al. *ART use, viral suppression and sexual behaviour among HIV-diagnosed MSM in the UK: results from the antiretrovirals, sexual transmission risk and attitudes (ASTRA) study.* Eleventh International Congress on Drug Therapy in HIV Infection, Glasgow, abstract O323, 2012.

[13] Phillips AN et al. *Increased HIV Incidence in Men Who Have Sex with Men Despite High Levels of ART-Induced Viral Suppression: Analysis of an Extensively Documented Epidemic.* PLoS One 8(2): e55312.

[14] World Health Organization. Antiretroviral Drugs for Treating Pregnant Women and Preventing HIV Infection in Infants. 2010. See http://whqlibdoc.who.int/publications/2010/9789241599818_eng.pdf.

[15] Fisher M, Pao D, Brown AE et al. *Determinants of HIV-1 transmission in men who have sex with men: a combined clinical, epidemiological and phylogenetic approach.* AIDS 24: 1739–1747. 2010.

[16] See http://www.partnerstudy.eu/

[17] See http://www.oppositesattract.net.au/

[18] Gilbert M, Buxton J, Tupper K. *Decreasing HIV infections among people who use drugs by injection in British Columbia: potential explanations and recommendations for further action.* Office of the Provincial Health Officer, British Columbia. 2011. See www.health.gov.bc.ca/library/publications/year/2011/decreasing-HIV-in-IDU-population.pdf.

[19] See for instance Cohen MS *Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. AIDSCAP Malawi Research Group.* Lancet. 349(9069):1868-73, 1997

[20] Fisher et al (ref 15 above) found a 2.8-fold increased risk of HIV transmission to or from gay men who had STIs, independent of ART status, but this was a small study and more are needed.

[21] See British HIV Association, *British HIV Association guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy.* HIV Medicine (2012), 13 (Suppl. 2), 1–85: page 21.

[22] See http://www.thestartstudy.org.

[23] Weller S, Davis K *Condom effectiveness in reducing heterosexual HIV transmission (Cochrane Review).* The Cochrane Library, Issue 4. Chichester, UK: John Wiley & Sons, Ltd., 2003.

[24] Smith D et al. *Condom efficacy by consistency of use among MSM: US.* Twentieth Conference on Retroviruses and Opportunistic Infections, Atlanta, abstract 32, 2013.

[25] See Phillips AN et al. Ref 13 above.

[26] Abbas UL et al. Potential impact of antiretroviral chemoprophylaxis on HIV-1 transmission in resource-limited settings. PLoS ONE 2(9): e875. doi:10.1371/journal.pone.0000875. 2007.

[27] See http://www1.imperial.ac.uk/medicine/research/researchthemes/infection/infectious_diseases/hiv_trials/hiv_prevention_technologies/popart/

[28] See Phillips AN et al. Ref 13 above.