UNAIDS/PCB(30)/12.13
15 May 2012

30th Meeting of the UNAIDS Programme Coordinating Board

Geneva, Switzerland
5-7 June 2012

UNAIDS Thematic Segment
Background paper

Combination Prevention: Addressing the urgent need to reinvigorate HIV prevention responses globally by scaling up and achieving synergies to halt and begin to reverse the spread of the AIDS epidemic

Executive Summary

The decline in AIDS-related deaths, due to an increase in treatment uptake, over recent years has not been matched by successes in prevention, with five new infections for every three people starting treatment. The number of new HIV infections varies widely within and between countries and across different populations.

The international community has committed to achieve universal access to HIV prevention, treatment, care and support, to halt and reverse the spread of HIV and contribute to the achievement of the Millennium Development Goals. This commitment was reinforced in 2011 with the adoption of the Political Declaration on HIV/AIDS: Intensifying our efforts to eliminate HIV/AIDS at the United Nations General Assembly High Level Meeting (HLM) on HIV.

'Know your epidemic, know your response' has become accepted as a fundamental approach in the response to AIDS. Central to this is the ability to consider the local context of each epidemic. A breakthrough in global HIV prevention which will send the epidemic into decisive decline will require strategic scaling up of combination approaches, targeted to the epidemiology of specific HIV epidemics.

Combination prevention programmes refer to a portfolio of biomedical, behavioural and structural activities applied in accordance with the epidemiologic and demographic profile and needs of different populations. Combination programmes bring unique challenges both for implementation and evaluation as they entail multi-faceted, context-dependent actions, whose impact is achieved as a result of the mix of programme activities. Simpler and discretely-delivered programmes, for example many biomedical interventions, are often easier to implement and evaluate, than behavioural and structural approaches whose impact may depend on more hard-to-measure variables.

To reach a significant and sustained reduction in the number of new HIV infections, countries must move away from a commodity approach which has considered programme elements in isolation and adopt a more focused response, scaling up combined programmatic approaches that address both short and long term impacts and both immediate risks and underlying causes of risk.

Those involved in the HIV response must call on tailored and innovative methods to ensure effective, evidence-based operational monitoring and evaluation and mutual accountability mechanisms between all stakeholders.

Key Features of Combination Prevention Programmes:

- tailored to national and local needs and contexts,
- a combination of biomedical, behavioural and structural interventions
- full engagement of affected communities, promoting human rights and gender equality;
- operates synergistically, consistently over time, on multiple levels—individual, family and society;
- invests in decentralized and community responses and enhances coordination and management;
- flexible—adapt to changing epidemic patterns and can rapidly deploy innovations.

Source: Combination HIV Prevention: Tailoring and Coordinating Biomedical, Behavioural and Structural Strategies to Reduce New HIV Infections. Geneva: Joint United Nations Programme on HIV/AIDS (UNAIDS), 2010

List of contents

I. Introduction and purpose of this background paper

1. The aim of this background paper is to set the scene for the thematic day on Combination Prevention, complementing information provided during the planned sessions.

2. The background paper contains the following:

- An overview of the state of the epidemic and progress in the global HIV response, highlighting the international commitments on HIV prevention set out in the Political Declaration on HIV/AIDS 2011;
- Best evidence on combination prevention and how different epidemic settings require a specific combination of HIV prevention programmes;
- An examination of how countries can identify and reach their prevention goals, with examples of successful combination prevention programmes;
- How to scale-up the response in order to reduce as many new infections as possible by doing the right things correctly and at a scale to have a decisive and sustained impact;
- A discussion of the importance of monitoring and evaluation in combination prevention programmes; and
- An annex to the background paper considers in depth the issues of HIV and co-infections in people who use drugs.

II. Epidemic update

- **34 million people living with HIV globally in 2010**
- **6.6 million people receiving antiretroviral therapy in low and middle income countries as of the end of 2010**
- **2.7 million people (including 390,000 children) became HIV-positive in 2010**
- **25% drop in new infections between 2001 and 2009**

3. By the end of 2010 an estimated 34 million people [estimate range: 31.6 million–35.2 million] were living with HIV. During the period 2000-2010, the number of deaths due to AIDS-related causes fell from an estimated 2.2 million [2.1 million–2.5 million] in the mid-2000s to 1.8 million [1.6 million–1.9 million] in 2010.[1] These figures are a testament to the impact of improved access to antiretroviral therapy, particularly in the last two to three years. At the end of 2010, over 6.6 million people in low- and middle-income countries were receiving antiretroviral therapy, an increase of 27% from December 2009.[1,2] In 2010 alone, 700 000 AIDS-related deaths were averted by scale-up of access to treatment.[1]

4. However, the pace of HIV prevention is lagging: prevention programmes are not focused on the right group of people, the coverage is too small and the quality of prevention programmes is often poor. For every three people starting treatment in 2010, there were five people newly infected.[3] A total of 2.7 million people acquired HIV in 2010.[2] To reach the goal of zero new infections, there must be renewed focus on prevention.[1,4]

5. UNAIDS characterizes HIV epidemics[a] as concentrated, low-level, generalized and hyperendemic. These distinctions between epidemic types are intended to point to the different population dynamics which characterize different epidemic situations. A concentrated epidemic (such as that in the Americas, Europe, the Middle East, Asia and Australasia) is defined as one in which the virus has spread among sub-populations reaching prevalence of over 5%, while in the general population it is less than 1%. A low-level epidemic is one in which HIV prevalence is less than 1% in the general population and less than 5% in any subpopulation, whereas generalized epidemics (e.g. those in large parts of southern Africa and parts of east Africa) are self-sustaining via heterosexual transmission with prevalence above 1%, and above 15% in a hyperendemic generalized epidemic.[5,6]

6. HIV epidemics are more complex than these epidemiological categories. Epidemics can shift over time, with concentrated epidemics evolving into generalized epidemics. Within generalized epidemics there can also be concentrated epidemics at a higher level in specific settings like urban areas or in specific populations. There are also regions, such as the Caribbean, Central and Western Africa, and parts of the Pacific region, where the epidemic is mixed. In these parts of the world there is a generalised epidemic as well as high transmission rates among sub-groups or key populations, significantly affecting certain geographic areas and specific population groups.

7. Globally the proportion of people living with HIV is evenly divided between men and women. However, there are regional differences. In Latin America and Asia Pacific men outnumber women. In sub-Saharan Africa and the Caribbean, women are disproportionately affected, at 59% and 53% of the total, respectively in 2010.[12] An estimated 42 000 to 60 000 pregnant women died due to AIDS-related causes in 2009.[5] A combination of factors- lack of sexual and reproductive health services, violence and fear of violence, inadequate educational opportunities and gender inequity and related poverty- conspire against women and girls to increase risk and restrict access to HIV prevention, treatment and care.[2,3]

8. The impact of HIV on children is devastating — there were 390 000 new infections among children in 2010.[1,2] Young people aged 15–24 stand at the forefront of the HIV epidemic and accounted for 42% of all new HIV infections among people aged 15–49 in

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[a] **Generalized epidemic**

- HIV is established in the general population.
- A high proportion of transmission occurs outside the context of commercial sex, injecting drug use or multiple partner male-to-male sex.
- Sex with multiple partners among the general population is at high enough levels to sustain epidemic growth.
- Populations with specific behaviors that increase their risk to HIV infection may contribute to more new HIV infections, even if the number of people with those behaviors is low.

Concentrated epidemic

- HIV transmission has taken root in one or more populations whose behavior puts them at high risk, such as sex workers, clients of sex workers, men who have sex with men and persons who inject drugs.
- HIV is rarely transmitted to people outside of the most at risk populations or their regular sex partners.
- Unless behaviour changes or levels of other risk factors such as sexually transmitted infection prevalence, HIV transmission will continue among the high-risk subpopulations. Transmission will occur most rapidly among persons who inject drugs or engage in unprotected anal sex.
- The size of populations most at risk to HIV and the degree of risk behaviours will determine the number of new infections. Most new infections among the general population can be linked to contact with a sex worker, men who have sex with men and persons who inject drugs.

Low-level epidemic

- HIV has not spread to significant levels in any sub-population, including populations most at risk to HIV, such as sex workers, clients of sex workers, men who have sex with men and persons who inject drugs.
- The spread of HIV is slow and inefficient because there are infrequent and few repeated transmission contacts among high-risk group members. HIV may have only recently been introduced or may not have entered a high-risk group network.

2010.[7] Young women are especially vulnerable to HIV — nearly two-thirds of infections in young people are in young women for a number of reasons including the greater biological susceptibility to HIV infection of young women and because young women are more likely to have older sexual partners than young men. Despite increased efforts to educate young people about HIV, the level of knowledge about HIV among young people in low- and middle-income countries is still low, with only a quarter to a third of young people correctly answering the full set of basic questions about HIV prevention and transmission and many young people lacking access to sexual and reproductive health services and rights.[3]

9. In areas characterized as generalized, concentrated and low-level epidemics, sub-populations that include people who inject drugs, men who have sex with men, transgender people, sex workers, clients of sex workers, prisoners and migrants typically have the highest prevalence of HIV.[2] Men who have sex with men are disproportionately impacted by the HIV epidemic, in comparison to all men in the population, regardless of whether the epidemic is concentrated or generalized.[8] A combination of biological, behavioural and structural factors combine to raise the risk faced by men who have sex with men. An international review of 38 countries found that on average, men who have sex with men were 19 times more likely to be HIV infected than the general population.[9] The figures for men who have sex with men frequently include men who sell sex and transgender people.

10. In the 151 countries where injecting drug use is known to occur, estimates of the number of people who inject drugs range from 11 million to 21 million, and among this population an estimated 3 million [range: 0.8 million to 6.6 million] are living with HIV.[10] Women who inject drugs are particularly vulnerable to HIV as they are more likely to be in riskier situations such as injecting at an early age or being injected by an injecting partner than men and face more barriers to access HIV-related services.[11,12]

11. Even though the vulnerability of women, men, and transgender people to HIV through sex work has been recognized from the earliest days of the HIV epidemic, sex workers still report inadequate access to HIV-related services, and funding for HIV prevention targeted at sex workers accounts for less than 1% of the global total. According to the findings of recent studies, sex workers in low and middle income countries are up to 14 times more likely to acquire HIV than all women of reproductive age, with average HIV prevalence rates between 100% and 32%.[13,14]

12. While the annual global rate of new infections fell by 25% between 2001–2009, there are huge differences in the impact of the HIV response at regional and national levels.[3] The evolution of the HIV epidemic shows that whether it charts the course of a concentrated or generalized epidemic, or evolves from one to the other is determined by a complex combination of individual and community factors. Moreover the legal, social, cultural and economic environments all play a part, and the ability of people and communities to protect themselves from HIV depends on the availability of commodities and services, and the extent to which individual behaviours, risk environments and structural factors can be changed.

III. International commitments on prevention

The Political Declaration on HIV/AIDS: Intensifying our efforts to eliminate HIV/AIDS set ambitious prevention targets for 2015:

- **reduction of sexual transmission of HIV by 50%;**
- **reduction of HIV transmission among people who inject drugs by 50%;**
- **elimination of new HIV infections among children.**

It emphasizes the need for prevention strategies to respond to infection patterns, and to include commodity access, reduction of risk behaviours and creation of an enabling environment.

13. The UNAIDS Programme Coordinating Board's 2010 adoption of the *UNAIDS 2011-2015 Strategy: Getting to Zero* represented a commitment by the international community to achieve universal access to HIV prevention, treatment, care and support.[4] It also signified a commitment to halt and reverse the spread of HIV and contribute to the achievement of the Millennium Development Goals. This determination was reinforced in 2011 with the adoption of the Political Declaration on HIV/AIDS: Intensifying our efforts to eliminate HIV/AIDS at the United Nations General Assembly High Level Meeting on HIV.[15]

14. The Political Declaration set out specific targets for HIV prevention including: i) reduction of sexual transmission of HIV by 50% by 2015; ii) reduction of HIV transmission among people who inject drugs by 50% by 2015; iii) elimination of new HIV infections among children by 2015 and a substantial reduction in AIDS-related maternal deaths. The Political Declaration moreover emphasized the need for a wide range of actions that address the creation of an enabling environment for the AIDS response, and an over-arching commitment "to redouble HIV prevention efforts by taking all measures to implement comprehensive, evidence-based prevention approaches."[15]

15. In particular, these actions encompass the needs of young people, women of childbearing age, promotion and facilitation of safer sex and risk and harm reduction programmes for people who inject drugs. The Political Declaration, recognized that prevention strategies and programmes are often too generic and do not adequately respond to infection patterns and the disease burden. Subsequently the Declaration drew specific attention to sero-discordant relationships and to key populations which epidemiological evidence shows are often at higher risk, specifically men who have sex with men, sex workers and people who inject drugs. Member states at the High Level Meeting emphasized the need to raise public awareness, promote gender equity and address structural factors such as the vital role of the family, targeted deployment of financial resources and the role of enabling legal, social and policy frameworks. They call for deployment of biomedical interventions as soon as they are available and strengthening the evidence base for all forms of HIV prevention interventions.[15]

16. Complementing the UNAIDS Strategy and the HLM Political Declaration are a number of strategies and instruments which have been adopted by UNAIDS Cosponsors and related bodies and serve to reinforce the progress towards HIV prevention within their specific mandates and areas of responsibility. These include the United Nations Educational, Scientific and Cultural Organization's Strategy for HIV and AIDS, with its strategic priorities of building country capacity for effective and sustainable education responses to HIV; strengthened comprehensive HIV and sex education; and advancement of gender equality and protection of human rights.[16] Similarly the

International Labour Organization's 2001 code of practice on HIV/AIDS and the world of work and the subsequent Recommendation concerning HIV and AIDS and the world of work 2010 (No. 200) and follow-up to this Recommendation in 2012 underscore the commitment to workplace responses to HIV prevention, treatment, care and support.[17,18] Likewise, the key role of the health sector was laid out in the World Health Organization's global health sector strategy on HIV/AIDS, 2011-2015.[19,20] UN agencies have also promoted inter-agency coordination and alignment of decisions. For example, the Commission on Narcotic Drugs has called for collaboration among stakeholders in UNODC and UNAIDS to promote better coordination of the HIV response in order to scale up access to comprehensive prevention, care, treatment and support services for people who use drugs.

IV. Defining your epidemic and responding to the next 1000 HIV infections

Effective HIV prevention programmes need to be able to respond to the next 1000 infections. They need to know where and why these infections are occurring, what is the current response, and what are the additional needs to prevent them. Prevention responses will fail unless they consider the social and cultural context in which they are intending to make change.

17. Prevention policies, programmes and activities can only be successful if they are grounded in a thorough understanding of the epidemic they aim to tackle.[2] The concept, 'know your epidemic, know your response' has become accepted as a fundamental step in the response to AIDS. Central to this is the ability to consider the local context of each epidemic.[21] Know your epidemic, know your response is a means for programme planning to be informed by exercises to understand modes of transmission, resource tracking and gap analysis of existing HIV programmes.[22] This information is the cornerstone of developing national prevention strategies that are context-specific.[23,24]

18. Understanding the nature of an HIV epidemic goes beyond HIV prevalence, to ascertain not just what has happened in the past, but where, among whom and why new infections are likely to occur.[25] Modelling of the expected distribution of HIV infections in the coming year according to exposure group is a key tool for programme planning.[26] Modes of transmission studies rely on a wide range of reliable data sources including from Ministry of Health statistics, demographic and health surveys, behavioural surveillance and scientific studies.[27] Using these data to inform the modelling and to understand the sources of HIV infection can identify not just the contribution of different risk groups but can also highlight the gaps in existing monitoring.[28] Lack of reliable data to inform the key model input parameters (including information on key populations and risk behaviour) can jeopardize the reliability of the modes of transmission studies.

19. In addition to knowing the distribution of anticipated new infections, optimal HIV prevention responses need also to know the financial and human costs of the appropriate programmes to prevent these new infections, as well as the size of current allocations to them in order to determine whether and where gaps exist. The National AIDS spending assessment (NASA) is a standardized tool that describes the flow of resources from their origin to the beneficiary populations.[29] It provides detailed information about the resource allocation among programmes and also identifies possible funding gaps, allowing decision makers to incorporate into the strategic planning cycle a more efficient use of resources for HIV prevention.

20. While 'know your epidemic, know your response' has become a well-established approach, the importance of understanding the social, cultural, political and legal environment is rarely fully appreciated.[30] Prevention programmes are unlikely to succeed unless they take the social and cultural context into consideration when they assess where and how they may be able to effect change. To date HIV prevention efforts have had an over-emphasis on individual risk and a commodity approach to HIV interventions. National programmes typically comprise disconnected interventions with little or no coordination between them.[27] This creates inherent weaknesses in the AIDS response due to a lack of coordination and a failure to maximise positive synergies and ameliorate negative synergies or unintended consequences in relation to different programme elements. A combination prevention approach addresses these weaknesses.[27]

Planning an effective HIV prevention response

The key to planning an effective HIV prevention response is knowing who is most affected by HIV, the extent to which HIV is prevalent among the population and different subgroups, and the risk behaviours, laws, policies, and settings that may facilitate the transmission of HIV.

Vital questions in planning an effective national HIV prevention response include:

- Where, among whom and why are new HIV infections happening?
- How fast are infections moving?
- What are the legal, human rights, gender, socioeconomic and cultural drivers of the epidemic?
- Have the most effective and feasible strategies been prioritized for the local context?
- Have the risks of the current strategy been analysed?
- Have the human and financial resources for an effective response been assessed?

Source: Practical Guidelines for Intensifying HIV Prevention. Towards Universal Access. Five steps to HIV prevention planning and implementation: Joint United Nations Programme on HIV/AIDS (UNAIDS), 2008

V. Combination Prevention: what elements does the evidence support?

21. Combination prevention refers to a mix of biomedical, behavioural and structural activities to respond to the needs of different populations in a particular epidemic context.[2,24,31] Combination prevention is evidence-informed. It seeks to deploy right-based and community-owned strategies and brings together the best set of prevention activities to meet the needs and conditions of specific communities and countries. Ideally, combination prevention efforts are generated by a transparent cycle of HIV programming engaging all stakeholders and engendering a sense of common purpose where the needs to include all those affected and to set effective priorities are both met.[27] Combination programmes bring unique challenges as they entail multi-faceted prevention efforts that are sensitive to context. Most importantly, combination prevention efforts must match the local epidemiological landscape.[32]

22. The evidence base for different HIV prevention activities varies widely. For activities which are long-standing, the most important body of evidence is rigorous and routine programme monitoring and evaluation to establish that the activity meets its intended impact. For activities which are being introduced into a programme and where there is existing evidence of efficacy, it is important to establish a case for the plausibility of their

effectiveness in real world situations using a variety of research and evaluation designs and methods with robust counterfactuals (i.e. is there a demonstrated effect/can we plausibly rule out that effect being caused something other than the programme). For new activities where efficacy needs to be demonstrated, it is important to use experimental or quasi-experimental designs where the effects of chance or selection bias can be ruled out.[33,34]

23. Compelling evidence exists for a number of HIV prevention activities which are delivered in different settings and include a mix of biomedical, behavioural and structural elements. The most important activities or clusters of activities which have been found to make a major contribution to the impact of HIV programmes, or whose scale-up would likely have a major impact, are considered in the paragraphs below.

24. **Eliminating new infections among children**: One of the 10 goals of the UNAIDS 2011-2015 Strategy, *Getting to Zero.*[4] This goal was incorporated as a target in the 2011 Political Declaration adopted at the UN General Assembly. The four pillars of programmes to eliminate new infections among children and keep mothers alive are antiretroviral prophylaxis for pregnant women, primary prevention of infections in women, prevention of unintended pregnancies in HIV-positive women and linkages with long-term care and support for women living with HIV and their families. [5,35,36] Prophylactic antiretroviral treatment of pregnant women with HIV can reduce the risk of HIV transmission during pregnancy delivery and breastfeeding to less than 5%, and contraception to prevent unintended pregnancies among women living with HIV is also a successful means of reducing potential new infections of infants.[7,37,38]

25. **Male circumcision**: There is compelling evidence from three randomized controlled trials that **voluntary medical male circumcision** reduces the risk of sexual transmission of HIV from women to men by approximately 60%.[39-41] Since 2007, the World Health Organization and UNAIDS have recommended voluntary medical male circumcision as a component of HIV prevention programmes for all settings where HIV rates are high and where rates of male circumcision are low.[87] As male circumcision provides only partial protection against the acquisition of HIV, it is always recommended as part of a package of HIV prevention activities. As of October 2011, over 1.1 million males had been circumcised for HIV prevention in sub-Saharan countries considered high priority for this intervention.[b] There are indications the rate of growth in adult male circumcision programmes has continued to increase with new numbers of performed male circumcisions scheduled for release at a regional meeting in July 2012. There has also been debate about how to present the protective effect for women, as fewer HIV infections amongst men will result in less exposure to HIV amongst women.[32]

26. **Treatment as Prevention**: Since the advent of highly effective antiretroviral therapy there has been interest in the extent to which suppression of the virus in an HIV-infected person also translates into interrupting transmission of the virus. Data from observational and cohort studies strongly indicated the likelihood that effective treatment also resulted in effective prevention. In 2008 the Swiss National AIDS Commission concluded that people with fully suppressed viral load and in the absence of sexually transmitted infection were sexually non-infectious, that is, they could not pass on the virus.[42] Subsequently in 2011 results of a major clinical trial (HPTN 052) showed that people living with HIV were at least 96% less likely to transmit HIV to their partners if they were receiving antiretroviral therapy.[2,43,44] Ensuring that antiretroviral drugs reach the people who need them is essential, and research is on-going into strategies that increase both uptake and adherence.[37]

[b] PEPFAR Male Circumcision Technical Working Group

27. **Integrated programmes directed at key populations**: Community-based programmes, and **community outreach programmes,** particularly via peer educators, play a crucial role in reaching key populations at higher risk of HIV. The evidence base suggests that structural, biomedical and behavioural interventions combined in one package offer the best strategy to reduce HIV among people who inject drugs. [45-47] The risk of HIV transmission can be reduced by opioid substitution therapy, needle and syringe programmes and antiretroviral therapy, and a combination of all three is required to reduce HIV infections in this population by more than half.[11] Peer educators and community outreach are essential in this process.[46]

28. In an environment where homophobia, stigma and discrimination prevent gay and other **men who have sex with men** (MSM) from disclosing their behaviour and seeking sexual health services, community-based outreach is essential for HIV prevention.[9,48] The most successful community-based outreach programmes are those that rely on peers to disseminate HIV risk reduction information, distribute condoms and facilitate referrals to MSM-friendly HIV testing, treatment and care. Although a number of effective behavioural HIV prevention strategies targeted at gay and other men who have sex with men promote increasing condom use during anal sex, there is consistent evidence that such episodic activities are prone to decay and/or limited in their reach and impact by community and other national/legal norms.[49] There are also emerging biomedical HIV prevention strategies for men who have sex with men, including oral and rectal pre-exposure prophylaxis. (See point 35)

29. Interventions focused at **sex workers** have been found to be cost effective for HIV prevention. This is particularly the case for community-led approaches where sex workers are empowered to make their work, work place and environment safer. Successful approaches attend to the complex sexual and reproductive health needs of female, male and transgender sex workers, including economic empowerment, legal and social support and protection from gender-based violence that sex workers everywhere face. Importantly, the most effective programmes are those where sex workers are involved in programme planning and management as well as on-going data collection and analysis.[46,50] Sex workers operate in a wide variety of settings, but in settings where they can insist on safer sex (condom use), vulnerability to HIV has been shown to be sharply reduced.[13] Arguably, the most direct way to promote condom use in sex work settings is to empower sex workers to enforce it, and to be supported by both clients and the wider society in doing so.[13] Despite limited evidence in support of structural interventions focused on sex work, programmatic experience points to a need for such interventions to combat social, political, and environmental obstacles to HIV outreach in this community.

30. **Condom programming** is a long-standing mainstay of prevention programming efforts. Despite the fact that there is relatively little novel in approaches to increase access to male condoms and create demand for their use, condom use continues to be a key determinant of success in reducing HIV incidence.[51] Female condom programming is a more recent addition to condom efforts, and while success in increasing access to and use of female condoms was slower than many expected, there are now numerous country examples where female condoms contribute a significant proportion of overall condom use, and as further female condom products are developed and unit prices continue to fall, it is likely that this sector will grow.[52]

31. **Behavioural change strategies** are those that aim to reduce the risk of HIV transmission by changing individuals' behaviour and also social norms.[59] Examples of direct targets for behaviour change are prevention programmes that encourage delay in onset of first sexual intercourse, partner reduction and increased use of male and female condoms.[60] They can be implemented at the individual and family level, but also across

social and sexual networks and within institutions, and whole communities.[60] Implemented in isolation, behavioural strategies cannot bring about sufficient change to sustainably reduce HIV transmission on their own but they play a vital part in combination prevention efforts.[60] Effective behaviour change also needs to utilize strategies that operate at social and norm-setting levels, as well as individual level.

32. A meta-analysis of 42 studies found that **behaviour change programmes to increase condom use** are effective to reduce sexual risk behaviour and avert HIV as well as other sexually transmitted infections.[53] Research on changes to HIV prevalence in Malawi, a country at the epicentre of the HIV epidemic, have shown that interventions to change sexual behaviours (namely delayed initiation of sexual activity, reductions in concurrent sexual relationships and increased condom use) can significantly reduce new HIV infections.[54] Similarly, in Zimbabwe, the declines in partner concurrency due to reduced extramarital, commercial and sexual relations which were associated with a sharp reduction in HIV prevalence point to a need for prevention approaches that focus on a combination of partner reduction, condom promotion and evidence-based approaches.[55-57]

33. **Structural HIV prevention** refers to social, economic, political and environmental factors that have a direct impact on HIV risk and vulnerability.[61] There is a lack of both clear definitions of structural interventions and data on their effectiveness. However, it is clear that HIV prevention efforts cannot be successful over the long term unless structural factors are addressed.[61] One suggestive recent example is cash transfers to encourage adolescent schoolgirls in low-income settings to stay in education.[62] A randomized controlled trial in Zomba district, Malawi found that cash transfers, either conditional on school attendance or unconditionally paid to girls' families, was associated with lower rates of HIV. Empowering adolescent girls to be less dependent on older men for presents and petty cash reduces the likelihood of their engaging in risky sexual behavior.[62-66]

Addressing the link between HIV and gender-based violence: the Stepping Stones programme in sub-Saharan Africa[35,58]

Despite the fact that behavioural change has long been considered to be a cornerstone of HIV prevention, there had been relatively little research into behavior change interventions that operate at the level of community or network. In contrast to previous school-based behavior change interventions, the Stepping Stones programme aimed to improve sexual health by using participatory learning approaches to build knowledge, risk awareness, and communication skills and to stimulate critical reflection. Originally developed for adult and teenage community use in Uganda in 1995, Stepping Stones has been adapted and used in over 100 countries globally, including South Africa in 1998, and is one of the most widely used intervention of its kind in the world. (www.steppingstonesfeedback.org)

A cluster randomized controlled trial in South Africa involved a limited version of the programme, with only two younger peer groups, of 1360 men and 1416 women, aged 15–26 years. It sought to assess the impact of Stepping Stones on incidence of HIV and genital herpes and changes in sexual behaviour. There was no evidence that the adaptation lowered the incidence of HIV but the programme was associated with about 33% reduction in genital herpes incidence. The programme significantly improved a number of reported risk-related events in men: men reported less intimate partner violence perpetration across two years of follow-up and less transactional sex and problem drinking at 12 months. However, in women desired behaviour changes were not reported, and those in the programme even reported more transactional sex at 12 months. Increased testing among friends and family, improved mental health of participants and good participant retention throughout the programme were also reported. The results suggested that additional research was needed to better understand underlying processes and improve programme outcomes. A comprehensive response which incorporates the full Stepping Stones programme should also incorporate all four peer groups, the whole array of basic HIV prevention, treatment and care strategies available to women and heterosexual men in generalized epidemic contexts, including STI screening and care, voluntary medical male circumcision and comprehensive peri-natal care.

34. **Approaches to increase the uptake of behavioural and biomedical responses**: Structural approaches that can support or enable uptake of biomedical and behavioural approaches to HIV prevention are critical to ensure an effective response. Stigma and discrimination weaken the ability of both communities and individuals to seek out information on HIV, access HIV services and adopt protective behaviours.[67] Laws that criminalize HIV transmission, sex work, same-sex activity and drug use or harm reduction measures for people who inject drugs all fuel HIV-related stigma and weaken people's ability to access information and services. A legal environment that promotes and protects human rights is essential to optimizing the delivery and uptake of HIV prevention, treatment and care.[68,69]

VI. Potential new HIV prevention activities: pre-exposure prophylaxis

35. In 2010 and 2011, landmark studies were published on the impact of **antiretroviral drugs-based prevention**. Studies of antiretroviral pre-exposure prophylaxis found that it can reduce the risk of HIV- negative people acquiring HIV through sexual transmission. In clinical trials topical tenofovir-containing gel was found to reduce HIV acquisition

among women. There are currently eight trials of pre-exposure prophylaxis with antiretroviral compounds currently underway and several papers have been recently published (see Table 1).[2,37]

Table 1. Summary of recently published studies on topical and oral pre-exposure prophylaxis

Study name	Type and antiretroviral agents used	Study population	Date results release	Study results
CAPRISA 004 *(21)*	Pre-exposure prophylaxis – vaginal tenofovir gel 1%	Women	July 2010	39% overall decrease in HIV acquisition
iPrex *(29)*	Pre-exposure prophylaxis – oral tenofovir plus emtricitabine	Men who have sex with men	November 2010	44% overall decrease in HIV acquisition and 79% decrease in high- adherence group
FEM-PrEP *(30)*	Pre-exposure prophylaxis – emtricitabine and tenofovir	Women	April 2011	Discontinued because of a lack of statistically significant difference
Partners PrEP *(31)*	Pre-exposure prophylaxis – oral tenofovir	Serodiscordant couples	July 2011	62% decrease in HIV acquisition
	Pre-exposure prophylaxis – oral tenofovir plus emtricitabine	Serodiscordant couples	July 2011	73% decrease in HIV acquisition
TDF2 *(32)*	Pre-exposure prophylaxis – oral tenofovir plus emtricitabine	HIV-negative heterosexual men and women	July 2011	63% decrease in HIV acquisition

Source: Global HIV/AIDS Response. Epidemic update and health sector progress towards Universal Access. Joint United Nations Programme on HIV/AIDS (UNAIDS), World Health Organization, United Nations Children's Fund (UNICEF), 2011.

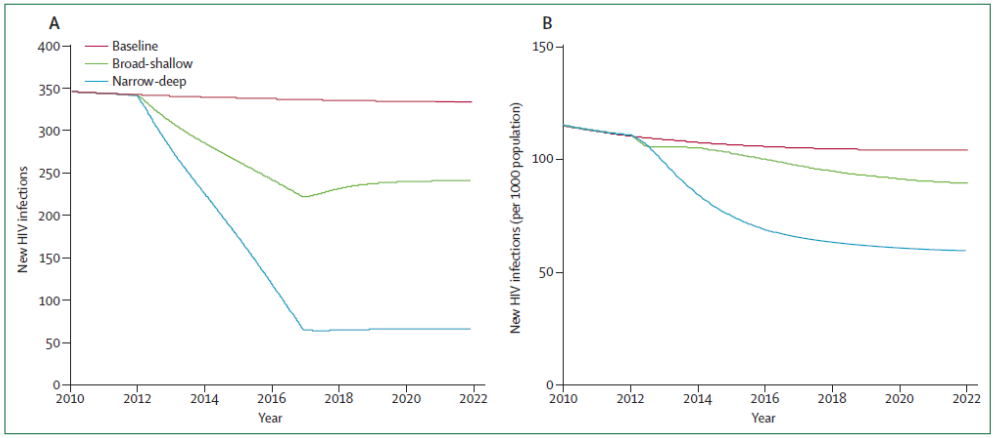
36. A trial among HIV-negative men who have sex with men showed a 44% reduction in HIV acquisition associated with use of daily emtricitabine and tenofovir disoproxil fumarate. However, a study of the same antiretroviral combination among high-risk women was discontinued because there was no difference in infections among the treatment and placebo groups. Thus, wide-scale promotion of pre-exposure prophylaxis for women is considered to be premature.[37]

VII. How we reach the prevention goals: scale-up, depth and community mobilization- scaling up the right combination

37. If a decisive downturn in the number of new HV infections is to be reached, countries must move away from the commodity approach that has characterized the response so far. Taking a one-size-fits-all approach cannot lead to a meaningful and sustainable reduction in the number of new infections. Achieving international commitments on HIV prevention will need not just more investment, but smarter investment, based on scale–up of a more focused response aligned to the local epidemic.

38. To reach the prevention goals, it is necessary to identify what drives epidemics and to identify which activities need to be scaled-up focusing on the areas where new infections are most likely to occur. Once countries have undertaken the process of ‘know your epidemic, know your response’ and identified gaps in coverage, the next step is to scale up activities that can bridge those gaps, using a combined approach that addresses the social, political, economic and legal environments surrounding a specific HIV epidemic. What combination of interventions will have the greatest impact is heavily dependent on the nature of the specific epidemic, and the distribution of risks will determine the priorities for intervention programmes.[59] Figure 1and table 2 show how scaling-up fewer programmes, which are based on an assessment of the state of the epidemic, can lead to important reductions of new HIV infections.

Figure 1. Number of new infections between 2010 and 2022 projected for people who inject drugs in Karachi, Pakistan (A), and the general population in Kwazulu-Natal, South Africa (B)[59]



The baselines assume no further interventions are implemented, the broad-shallow lines show an estimation of a wide range of interventions applied at modest scales, and the narrow-deep lines show an estimation of targeting of a small number of the most effective interventions to high scales, as described in table 2 below.

Table 2. Comparing broad and shallow *vs.* narrow and deep interventions

Comparing Interventions[59]	**broad and shallow *vs.* narrow and deep**	
Modeling of the reduction in new infections in Karachi, Pakistan where injecting drug use is the main mode of HIV transmission	50% coverage of ART, 50% increase in condom use, 15% reduction in casual sex, 40% increase in needle exchange and OST, and 10% use of PrEP	80% coverage of ART and needle exchange and OST
Modeling in KwaZulu-Natal, South Africa, where heterosexual sex is the main route of transmission	10% male circumcision; 40% coverage of ART at CD4 <200 and 10% at CD4 <350; 10% coverage of risk reduction counseling 15% increase in condom among PLWA, 10% microbicide use)	80% coverage of ART at CD4 <200, 70% ART at CD4 <350; 70% male circumcision

39. A large array of different activities at low-scale will probably not be as effective as having fewer yet more context-specific and focused prevention activities/interventions implemented in at a large enough scale to have an impact on reducing the number of new infections.

40. **Scaling-up interventions to reduce sexual transmission of HIV**
Sexual transmission is the cause of more than 5000 new infections every day and also intersects with other modes of transmission, namely new infections in children through the infection of mothers via sexual intercourse with infected male partners, and drug use-associated sex work.[70] Thus, scaling up HIV prevention in this area is crucial. HIV prevention responses need to include programmes directed both at whole populations (particularly in generalized epidemics and essentially in hyper-endemic contexts) as well as tailored and intensive efforts addressing key populations at higher risk. To reach the target of a 50% reduction in the number of new HIV infections under resources constraints it will be necessary for the international community to focus on the most

affected countries; encourage communities to take ownership and leadership of initiatives within a national AIDS response framework; and facilitate responses that address the real epidemic and its underlying drivers by breaking the silence around sex and sexuality.[70]

WHO has based on extensive research, identified 9 steps to assist country programmers to scale-up health programmes.

Step 1: **Planning actions to increase the scalability of the innovation:** clarifying the innovation in question, and assessing what attributes and actions required to successfully scale it up.

Step 2: **Increasing the capacity of the user organization to implement scaling-up** including opportunities for economies of scale, particularly in resource-constrained settings.

Step 3: **Assessing the environment and planning actions to increase the potential for scaling-up success**. Maximize opportunities and minimize constraints.

Step 4**: Increasing the capacity of the resource team to support scaling up**. The people behind a scale-up are a much wider range of players than those who first developed the innovation.

Step 5: **Making strategic choices to support vertical scaling up**. Scaling-up requires an understanding not only of policy but also of related political processes.

Step 6: **Making strategic choices to support horizontal scaling up.** Expansion or replication of an innovation requires processes to be adapted to different environmental contexts.

Step 7: **Determining the role of diversification.** An example is introducing programmes targeting adolescents in a service strengthening innovation for women.

Step 8. **Planning actions to address spontaneous scaling up.** Spontaneous scale-up can occur when a particular innovation addresses a clearly felt need or as a result of a specific event drawing attention to a need

Step 9. **Finalizing the scaling-up strategy and identifying next steps.** This requires a review, summary and detailed operational planning.

Source: Nine steps for developing a scaling-up strategy: World Health Organization (WHO), ExpandNet, 2010

41. Although the key programmatic activities for roll-out of **voluntary medical male circumcision** programmes in priority countries in Eastern and Southern Africa were already in place by the end of 2010, and new devices are now being developed for voluntary medical male circumcision, there has still only been limited progress towards the target of 80% of men aged 15–49 undergoing male circumcision.[2] The estimated number of male circumcisions required to reach 80% coverage ranges from 40 000 in Ethiopia to over 4.2 million in Uganda.[71]

42. **Young people.** Scaling up comprehensive sexuality education for young people relies on buy-in from parents and teachers, and also complex bureaucratic changes and coordination between different sectors/ministries, including education, health and often youth. More than other interventions, there may be no social consensus about the need for scaling up because of inadequate political commitment and because of cultural and political sensitivities surrounding teaching young people about sex before marriage.[8,72] Thus, scaling-up sexuality education may require a longer time-frame than other programmes. Programmes must occur within existing systems and policies, with clarity about the aims and the roles of different players. Sustainability and availability of resources should be included in plans for resource mobilization and strategies must adapt to changes in the political environment.

43. Prevention efforts to reach **young women and girls** in southern Africa have focused on some general programmatic areas such as raising awareness, HIV education and information dissemination, the reduction of socio-economic vulnerability, service provision and life skills development.[73] However, the evidence suggests that this has failed to sufficiently turn the epidemic around for young women and girls. Instead, scale-up of evidence-informed combination prevention activities are required. Recommended actions include community mobilization for HIV prevention, expanded access to essential sexual and reproductive health and prevention services, and closer linkages between the two. There must also be sufficient technical and financial resources for implementation of national strategies and strengthened country capacity for epidemiological and behavioural surveillance.[73]

44. **Gender inequality.** Gender-based violence, an indicator of gender inequality, drives the risk and vulnerability to HIV infection by disempowering women and girls from controlling their sexual lives. Intergenerational and age-disparate sexual relationships, combining with lack of education and economic power also amplify the particular biological risks and vulnerabilities of women and girls.[73] Community-based participatory learning approaches can be effective in changing social gender norms, including violence, when HIV and violence prevention programming are paired with community mobilization and engaging men to challenge harmful gender norms. A landmark study in South Africa recently suggested that nearly one in seven cases of young women acquiring HIV could have been prevented if the women had not been subjected to intimate partner violence.[88]

The Refentse Model for **Post-Rape Care**

This model used in South Africa is a multi-sectoral approach to post-rape care. Relatively inexpensive changes significantly improved service quality and health outcomes, with one-stop lab tests, voluntary counselling and testing services around the clock, and nursed-dispensed post-exposure prophylaxis. Integrating services reduced delays in access PEP and collecting medico-legal evidence and resulted in improvements in care, the quality of clinical history and exams, provision of pregnancy testing and emergency contraception; STI treatment; HIV counselling and testing; PEP; trauma counselling, and referrals. This intervention was relatively inexpensive: when one-off development costs were excluded, the incremental cost per case was US$58.

Source: Kim J, Mokwena L, Ntlemo E, Dwane N, Noholoza A, Abramsky T, Marinda E, Askew I, Chege J, Mullick S, Gernholtz L, Vetten L, Meerkotter A. Developing an Integrated Model for Post-rape care and HIV Post-exposure Prophylaxis in Rural South Africa. NY: Population Council, November 2007

45. **Community mobilization and scale-up.** Community mobilization is critical to scale-up of combination prevention efforts. Communities are best placed to know their needs, and in particular people living with HIV must be at the forefront of community-based efforts.[74] Community-based organizations and community health workers can play a key role in task-shifting to address service bottlenecks, but care must be taken to ensure that task-shifting to volunteers does not exacerbate gender inequalities, a pervasive obstacle to community mobilization, by unfairly burdening women. [75-77] Community mobilization can be crucial to building partnerships and links with service providers in other health areas such as sexual and reproductive health and rights, and maternal, newborn and child health.[74]

46. **Scale-up prevention programmes for people living with HIV.** Scale-up of efforts to promote positive health dignity and prevention for people living with HIV must occur

within a human rights framework and incorporate advocacy; evidence of good practice; dissemination of the positive health, dignity and prevention concept; policy dialogue; planning for operational guidelines and subsequent implementation within national strategic frameworks and HIV policies. The objective of Positive Health, Dignity and Prevention entails a combination approach to HIV prevention that is community-driven, sustainable and empowers people living with HIV and their partners reinforces mutually accountability.[47,78] It is also essential to address the sexual and reproductive health and rights of the diversity of people living with HIV, from young people embarking on new relationships, to couples tackling negative attitudes from health care providers when they wish to conceive, and the sexual health priorities of men who have sex with men.[35]

47. **Integration of HIV and other services.** The integration of HIV services with other health services as well as other development sectors is crucial to maximizing scarce resources.[59] There is a strong logical case for integration of sexual and reproductive health services such as family planning, maternal and infant care and management of sexually transmitted infections with HIV prevention treatment, care and support because of key linkages between the two fields.[35] Similarly, the high rates of co-infection with tuberculosis and HIV are propelling countries towards integrated treatment, resulting in more efficient and powerful responses (see Annex).[79] There is also increased recognition of how the AIDS response can generate better results for other health programmes. One example is the joint action by UNAIDS, the U.S. President's Emergency Plan for AIDS Relief, the George W. Bush Institute and the Susan G. Komen for the Cure foundation to launch the "Pink Ribbon Red Ribbon" initiative, which will expand prevention, screening and treatment for cervical cancer in sub-Saharan Africa and Latin America using the existing HIV prevention platform.[79]

VIII. Monitoring and evaluation

48. The Political Declaration on HIV/AIDS explicitly commits to "effective, evidence-based operational monitoring and evaluation and mutual accountability mechanisms between all stakeholders to support multisectoral national strategic plans for HIV and AIDS." This is necessary in order for the commitments in the Political Declaration to be fulfilled, and requires the active involvement of people living with HIV as well as those affected by and vulnerable to HIV, other relevant civil society and private sector stakeholders.[15]

49. Data from more and more countries show that HIV prevention has measurable population benefits, although the evidence base for specific programmes is varied and incomplete. There is an urgent need to continue to accumulate credible evidence about what is working and what is not to avert HIV infections in particular populations and settings. In addition to scaling up HIV prevention interventions with known effectiveness, programme planners have to be prepared to innovate in implementing HIV prevention strategies of uncertain effectiveness.

50. Evaluation is the only way to understand the programme's effects within the specific social and structural context and know how to improve on them. [33,34] Yet, evaluation of combination prevention is fraught with challenges. There is a paucity of reliable tools for measurement of HIV incidence, and intermediate indicators such as changes on sexually transmitted infection rates, may not be reliable.[33] Furthermore, reported changes in sexual behaviour may not equate to reduced transmission of sexually transmitted infections.[56] Randomized controlled trials (RCTs) are widely used as the most reliable way of eliminating selection bias when assessing whether an intervention has a treatment effect, or whether it has no effect or its effects are the results of chance or some factor extraneous to the treatment. Yet RCTs have had at best mixed success in evaluating public health interventions, even in the case of community RCTs whereby the

community is the unit of intervention.[33,56] Using HIV incidence as an outcome measure is problematic because of the difficulty of measuring it in cases where there are low levels of HIV incidence, such that there would need to be unreasonably large sample sizes to power RCTs. There is also a danger that behavioural, social and contextual components of combination prevention interventions are excluded from RCTs due to the requirements of experiment design.[33]

51. Instead of focusing on randomized controlled trials with a focus on probability design, it may be more effective to instead rely on plausibility design, which has a lower level of certainty, but can triangulate different data sources from diverse evaluation approaches to prove that an intervention's success is plausible. Such triangulation of different data sources has enabled Avahan, a large-scale sex worker programme in India, to engage in an unprecedented level of programme monitoring and evaluation.[33,81,82]

52. Combining behavioural and modelling studies with high-quality sentinel surveillance data sources can provide an assessment mechanism for scaled-up interventions.[56] There are also innovative evaluation approaches already in use in the social sciences that have not yet been well-explored in the field of HIV, such as participatory monitoring and evaluation, utilization-focused evaluation and social network analysis.[83,84]

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Annex

HIV and co-infections among people who use drugs

Prepared by the World Health Organization HIV department as background for the UNAIDS Thematic Session of the 30th Programme Coordinating Board, June 2012

HIV and Co-infections

HIV infection has moved from being an untreatable disease to one that is manageable and can be treated with antiretroviral therapy (ART). However, for people co-infected with HIV and other pathogens, specifically hepatitis B virus (HBV), hepatitis C virus (HCV) and tuberculosis (TB), the management of HIV is hampered by lack of access to treatment for their co-infection. Prevention and management of these co-morbidities are crucial to sustain the successes achieved in HIV care.

Viral hepatitis and HIV

It is estimated that 350 million people are chronically infected with HBV; and 130-170 million people are chronically infected with HCV.[i,ii] Co-infection with HBV and/or HCV with HIV is increasingly recognized as a major public health problem. In certain regions, up to 10% of all people living with HIV (PLHIV) are co-infected with chronic hepatitis B; and 25% are co-infected with chronic hepatitis C.[iii]

The prevalence of HBV and HCV is high among people who inject drugs (PWID). It is estimated that 1.1 million PWID have HBV and 10 million have HCV.[iv] Although HBV is preventable by vaccination, the rate of vaccination among people who inject drugs is low. In addition, although both chronic HBV and HCV can be effectively treated and, sometimes cured, very few PWID access treatment because of the high cost and other barriers to accessing the health system. While people who inject drugs are most affected by viral hepatitis in many regions, there are currently no global WHO clinical or programmatic guidelines.

TB and HIV

The risk of developing TB is estimated to be between 20-37 times greater in PLHIV than among those without HIV infection. In 2009, there were 9.4 million new cases of TB, of which 1.2 million were among PLHIV.[v]

TB also disproportionately affects PWID. The prevalence of TB among PWID ranges from 13 to 67%.[vi] Between 3 to 92% of PWID are also infected with HIV.[vii, viii] Studies and surveillance data show that PWID living with HIV have a 3-6 fold increased risk of developing TB compared to PLHIV who have never injected drugs.[ix]

HBV, HCV and TB

Co-morbidity with HBV and HCV is common among HIV-infected TB patients who are PWID.x In a study from Thailand among TB patients, 9% of all patients were co-infected with HBV and 31% were co-infected with HCV.[xi] Infection with HCV was strongly associated with injection drug use.[xii]

Next steps

Although guidelines for managing HBV and HCV infection have been developed in high and middle-income countries, there is a lack of global guidance for resource-limited settings. Limitations include the high cost of treatment and lack of access to routine screening and diagnostic tools (e.g. viral load measurement, genotyping), and monitoring of drug resistance. New diagnostic tools for TB infection should be evaluated and validated among PWID. Optimal antiretroviral and anti-tuberculosis regimens, including the use of rifabutin,

combined with opioid substitution therapy such as methadone, needs to be defined to minimize pill burden, side effects, drug interactions and the risk of narcotic withdrawal.[xiii]

A TB advocacy guide for drug users, developed by the International Network of People who Use Drugs (INPUD) and HIT-Liverpool, with support from WHO and UNAIDS, will be presented at this forthcoming PCB break-out session on HIV and co-infections among PWID.

The WHO HIV department is currently in the process of developing a set of recommendations that will focus on the prevention of HBV and HCV among PWID. These recommendations are near completion and will also be presented at the forthcoming PCB breakout session. Treatment of HIV and hepatitis co-infection will be covered in the consolidated ART guidelines, due to be released in 2013.

The WHO Global Hepatitis Programme has initiated the development of the HCV treatment guidelines, and will later develop recommendations on surveillance of viral hepatitis in resource limited settings.

In addition, several other organisations are implementing activities focused on addressing HIV and comorbidities in PWID including other UN agencies such as UNODC and non-governmental organisations such as the Eurasian Harm Reduction Network (EHRN).

Conclusions

There is a critical need to assess the true burden of co-infection with HIV and HBV, HCV and/or TB; and identify barriers for the delivery of integrated prevention, diagnosis and treatment services. Likewise, there needs to be a better understanding of optimal strategies to treat co-infections. This includes the use of new HIV antiretroviral medicines, anti-TB and hepatitis antiviral medicines that are in the development pipeline.[xiv]

Co-infection with HIV and HBV, HCV and/or TB poses a great challenge in providing quality care for PWID. Addressing this challenge requires an organized response that integrates HIV care with the management of drug dependence and of co-infections, such as HBV, HCV and TB.

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