ABSTRACT

Background/Rationale: HIV transmission only occurs from people with HIV, and viral load (VL-concentration of HIV) is the single greatest risk factor for all modes of transmission. HAART can lower viral load to nearly undetectable levels. Prevention of mother to child transmission & Post-Exposure Prophylaxis (PEP) offers proof of the concept of HAART interrupting transmission, and observational (among sero-discordant) & ecological studies and modeling work support using HAART for prevention and research is ongoing on their use for Pre-exposure prophylaxis (PrEP). A model by scientists from WHO published in 2008, suggested that expanding antiretroviral therapy to people with CD4 cell count < 350mm3 and beyond could substantially reduce the growth of the epidemic. Some models have predicted substantial reduction in HIV transmission rates all HIV infected individuals are treated with ART, which is reflected by the usage of terms and phrases for this approach (‘test and treat’, testing and linking to care plus’)

Aims and Objectives: To critically examine various studies, explaining the impact of Anti Retro Viral Therapy (ART) on prevention and to discuss it to be potentially used as one of strategies of prevention from HIV/AIDS.

Methods/study design:

Data Source: The scientific literature and eligible materials were surveyed related to the topic of strategy of ‘treatment of AIDS as prevention’.

Data Selection: Building on this conceptual framework, the related observational, ecological studies and modeling works who met the selection criteria of being related to ‘treatment of AIDS as prevention’ and examined the effectiveness strategy of treatment of AIDS as a prevention pill

Data Extraction: Reports were screened and information from eligible studies was abstracted independently and synthesized.

Findings/Results:

1) On an individual level:

ART is a significant component of Prevention of Mother-to-child transmission (PMTCT) interventions -340,000 children were born HIV-free between 2004-2009 because of the preventive effects of ART.

According to PEPFAR estimates ART is effective as post exposure prophylaxis (PEP)

In a case-control study, a 80% reduction in the risk of acquiring HIV in exposed individuals was observed when treated with AZT (a drug used to delay the development of AIDS) alone.

A study of Spanish serodiscordant (one partner HIV-positive and one negative) couples showed that no HIV seroconversions took place in the sexual partners of HAART treated patients.

The use of HAART was independently associated with an 86% reduction in HIV transmission.

A study of 3400 couples in seven African countries found that ART lowered the risk of HIV transmission by an estimated 92% in serodiscordant heterosexual couples.
2) On a population level:
In Taiwan, a 53% reduction in new HIV positive diagnoses was observed between 1997 and 2002 when free access to HAART was introduced.
A population study in British Columbia, Canada showed that the initial ART rollout resulted in an approximate 50% drop in new HIV diagnoses between 1996 and 1999.
In San Francisco, a substantial increase in HIV testing and treatment between 2004 and 2008 was linked to i) a decrease of about one-third in the average viral loads of people living with HIV; ii) a decline of around one-third in HIV incidence and; iii) a decrease in the number of newly reported HIV cases (from 798 new HIV cases in 2004 to 434 newly diagnosed HIV cases in 2008)
During the expansion of ART in British Columbia, Canada, a 50% decline in HIV positive diagnoses among one section of marginalized population --injection drug users (IDUs) was observed after 2007. Furthermore, the proportion of IDUs with a viral load above 1,500 copies/mL (considered as a "high" HIV-1-viral load) fell from about 50% from 2000 to 2004 to about 20% in 2009.

3) There is also one ongoing efficacy trial, called HPTN 052, which has enrolled 1,750 serodiscordant couples (one HIV-positive and one HIV-negative partner) to look at ARV treatment as prevention in a number of countries. It asks whether initiating treatment in the HIV-positive partner can help reduce the risk of sexual transmission of HIV to the HIV-negative partner.

Conclusions: In the studies reviewed, the arguments in favour of preventive ART are: (1) evidence indicates that ART reduces viral replication in a durable way with manageable toxicity (2) the immediate cost of HAART will be compensated by cost-savings from avoided infections (3) intervention could reduce blame, shame and fear, improving social attitude.

Limitations: Using ‘ART as a preventive strategy may present with certain limitations like (1) chances of increased sexual risk-taking (2) development of HIV resistance could lead to failure of protection and transmission of resistant virus, 3) issues of sustainability--funding, outreach, infra structural weaknesses, sudden increase in number of patients to be treated. Whether physicians should counsel their patients to initiate HAART, as a prevention strategy is still unresolved.

Discussion: In the meantime, prevention efforts should focus on: (1) development of prospective clinical trials to confirm the role of HAART in reducing transmission and will be critical to monitor, collate, and analyze data from the full range of research projects and the one current randomized trial HPTN 052 (due to release results in 2013) to develop a sense of how this strategy might be used. It will be equally important to assess the risks and benefits of a test and treat or treatment as prevention approach for HIV (2) identifying HIV infection as early as possible to counsel partners about avoiding risks of infection (3) encouraging partners to always protect themselves, even when the infected partners are being treated successfully (4) infected persons seeking early HAART, as a preventive strategy, should never be denied this intervention. (5) The findings suggest that the benefits of the infections averted would outweigh the initial investments required and most importantly ART is being provided as part of a package of prevention and treatment interventions & not in isolation. (6) Furthermore, this strategy may work better on ‘population level’ than on ‘individual level’ because the ‘undetectability’of Viral load (VL) does mean
only about the virus being too low in the blood for the test to find it and not the total absence of the virus.

**Keywords:** HIV transmission, Anti-retroviral therapy(ART), Viral load(VL), Sero-discordant couples, PMTCT,PEP, PrEP

**Background**

Treatment as Prevention is not a new concept. In the case of an infectious disease, treatment of a patient is primary prevention for his susceptible contacts. By killing the pathogens, in the former, treatment prevents latter from contracting it. Treatment of one condition—renal disease for example, may sometimes may act as primary prevention of another disease—hypertension, in the same individual. Chemoprophylaxis too, is a proven concept in Preventive Medicine as we find examples in case of—Malaria, TB, Meningitis, and more recently Familial Adenomatous Polyposis, particularly when no effective vaccine is available. Post Exposure prophylaxis with vaccines/immunoglobulins against Measles, Hepatitis & Rabies have been another successful strategies, to substantiate the theory of ‘Treatment as Prevention’

Since a case-report identifying AIDS as a disease reported to CDC by an Immunologist, Dr Michel Gottlieb of Los Angeles, USA—as usual presentations of ‘Pneumocystis Carrii’ in some young gay population in MMWR (CDC’s Morbidity and Mortality Weekly Report—of June 5, 1981), we are yet to develop reliable fool proof behavioral or biological methods for prevention of HIV. The great success of Anti-retroviral therapy (ART) too, has been offset by the challenge of treating millions, more so for their whole lives.

Evidence has shown that successful viral suppression through treatment can substantially reduce the risk of vertical, sexual and blood-borne HIV transmission. Prevention of mother to child transmission (MTCT) & Post-Exposure Prophylaxis(PEP) offers proof of the concept of HAART, interrupting transmission, and observational (among sero-discordant) & ecological studies and modeling work support using ART for prevention. Research is ongoing for their use Pre-Exposure prophylaxis (PrEP).

Antiretroviral agents are being used to prevent the sexual transmission of HIV as Pre-Exposure Prophylaxis (PrEP) Post-Exposure Prophylaxis(PEP) or to reduce transmission from infected patients. The latter approach has great promise: because if personal health can benefit from antiretroviral therapy (ART) why not exploit the public health benefit as well.

Anti-retroviral Therapy(ART), now popular, as Highly active antiretroviral therapy (HAART), was first introduced in 1996 and has been shown to substantially reduce AIDS-related hospital admissions and death rates in both developed and developing nations. The HAART regimen is a cocktail of three or four drugs that has shown to be the most effective response to HIV/AIDS. HAART stops HIV replication, resulting in a decline of RNA viral load in the plasma to undetectable levels.

What this means here is that HAART reduces the viral load in both blood and sexual fluids and would therefore reduce the risk of transmission. The potential role of HAART in HIV prevention reflects a new prevention-treatment paradigm in the global response to HIV/AIDS. The idea of using ‘Treatment as Prevention’ came to the forefront in 2006 at the International
AIDS Conference held in Toronto. Since then, this idea has received increasing attention around the world,

The probability of HIV transmission with nearly any type of exposure is directly correlated with viral load. In January 2008, the Swiss Federal Commission, for HIV/AIDS, issued a statement from P. Vernazza, B. Hirshel and E. Bernasconi, that effective ART (Anti-retroviral therapy—defined by < 40 c/ml for > 6 months) eliminates the possibility of transmitting HIV though sexual contact.

Even UNAIDS has come up of “Treatment 2.0” to increase the access and to simplify the treatment regimens in 2010, of whose one of five pillars is “Treatment as Prevention”. During the opening ceremony of the International AIDS Conference, 2010, at Rome, International AIDS Society President Julio Montaner has declared “Consensus has arrived. Treatment and prevention are one thing and they are the way forward.” He went on to assert that Treatment 2.0 strategy “is the most effective way forward to deliver on the universal access pledge,” which has one of 5 important components as ‘treatment as prevention, other four components being a). Creation of a better pill and diagnostics b). Stoppage of cost being an obstacle c). Improvement in uptake of HIV testing and linkage to care d). Strengthening of community mobilization. UNAIDS Executive Director Michel Sidibe has too proclaimed about “Treatment 2.0 in the same conference, as how this strategy radically simplifies treatment to maximize the number of people who can benefit.”

Treating people living with HIV may reduce the sexual transmission of HIV on a population level too. We are familiar with the idea that if someone uses a condom for sex, they can protect themselves and others from getting HIV—this is something an individual is able to do to protect themselves and others.

We know that treatment for HIV can effectively reduce the amount of virus in the blood of someone living with HIV (often to levels that cannot be detected by current viral load tests). For many people this reduction in the amount of virus may reduce infectivity (their ability to transmit the virus). However, we also know that treatment does not eliminate the virus from the body which means that the risk of transmission from one person to another is only potentially reduced and not eliminated. This is why treatment as prevention does not work on an individual level—as efficiently as ‘population level’—the reduction in risk of transmission is not enough to replace conventional methods of prevention, such as practicing safer sex or using clean needles.

However, treatment as prevention may work on a population level. The idea is that if enough people living with HIV are diagnosed and successfully treated, then the result should be a reduction in the average amount of the virus circulating in the community. His reduction in average viral load, over many different exposures to HIV within a population, may result in the occurrence of fewer transmissions. The reduced HIV transmission rate is an effect that only happens when large groups of people living with HIV are successfully treated.

Thus “Treatment as prevention” moves away from the focus on individual prevention efforts toward an approach that focuses on reducing the number of new HIV infections in an entire community or population. This is why experts mainly envision ‘treatment as prevention’ as a population-level approach, which would be undertaken in combination with conventional prevention programs.

Here we shall try to critically examine various studies, explaining the impact of Anti Retro Viral Therapy (ART) on prevention and to discuss its possibility of being
potentially used as one of the strategies of prevention from HIV/AIDS. What does all of this really mean to us? Let us examine first the rationale of using 'ART as Prevention'.

Rationale of using ARV (Anti Retro Virals) for prevention?
"Treatment as prevention" is a term describing the use of antiretroviral drugs that are used to reduce the risk of passing HIV to others. The strategy would function as a secondary benefit of antiretroviral treatment after its primary purpose of improving an individual’s health. The rationale for this approach is that ARVs reduce viral load. Higher viral loads have been linked to increased risk of passing HIV to sexual partners. Treatment as prevention is an emerging area and there are different terms and phrases used to describe this approach, including "test and treat" and "testing and linkage to care plus," which recognizes that voluntary HIV testing and diagnosis is the first step to accessing care.

Methods/study design: As this study basically incorporates multiple deliberations, some of whose results are yet to be available, and, like a ‘commentary, basically examines the value of a strategy,’ so only descriptive statistics were used, wherever applicable.

Data Source: The present study is based on the scientific literatures, and eligible materials which were surveyed related to the topic of use of strategy of ‘treatment of AIDS as prevention’.

Data Selection: Building on this conceptual framework, the related observational, ecological studies and modeling works, who met the selection criteria of being related to ‘treatment of AIDS as prevention’ and examined the effectiveness strategy of treatment of AIDS as a prevention tool.

Data Extraction: Reports were screened and information from eligible studies was abstracted independently and synthesized accordingly.

Findings/Results:
Studies to substantiate the strategy of ‘treatment as prevention’ were found at different levels like:

1) On an individual level:

a) ART is a significant component of Prevention of Mother-to-child transmission (PMTCT) interventions—340,000 children were born HIV-free between 2004-2009 because of the preventive effects of ART,

b) According to PEPFAR (U.S. President's Emergency Plan for AIDS Relief) estimates ART is effective as post exposure prophylaxis (PEP)

c) In a case-control study, a 80% reduction in the risk of acquiring HIV in exposed individuals was observed when treated with AZT (a drug used to delay the development of AIDS) alone.

d) An Observational study of Spanish serodiscordant (one partner HIV-positive and one negative) couples showed that no HIV seroconversions took place in the sexual partners of HAART treated patients. The use of HAART was independently associated with an 86% reduction in HIV transmission.
f) Another observational study of 3400 couples in seven African countries found that ART lowered the risk of HIV transmission by an estimated 92% in serodiscordant heterosexual couples.

2) On a population level:

Ecological studies, which examine two variables at population level, but it is important to keep in mind that ecological studies, while useful, may not tell the whole story.

For example, it is possible that in some or all of these situations, other prevention efforts that may have occurred at or around the same time may have contributed to any decrease found in HIV transmission rates.

It has been found:

a) In Taiwan, a 53% reduction in new HIV positive diagnoses was observed between 1997 and 2002 when free access to HAART was introduced.

b) A population study in British Columbia, Canada showed that the initial ART rollout resulted in an approximate 50% drop in new HIV diagnoses between 1996 and 1999.

c) In San Francisco, a substantial increase in HIV testing and treatment between 2004 and 2008 was linked to (i) a decrease of about one-third in the average viral loads of people living with HIV; (ii) a decline of around one-third in HIV incidence and; (iii) a decrease in the number of newly reported HIV cases (from 798 new HIV cases in 2004 to 434 newly diagnosed HIV cases in 2008).

d) During the expansion of ART in Canada, British Columbia a 50% decline in HIV positive diagnoses among one section of marginalized population --injection drug users (IDUs) was observed after 2007. Furthermore, the proportion of IDUs with a viral load above 1,500 copies/mL (considered as a "high" HIV-1 viral load) fell from about 50% from 2000 to 2004 to about 20% in 2009.

3) Modeling Studies

A modelling study is a hypothetical description of what could happen if a change is made in a population or community. Modelling studies have attempted to explain the relationship between the effect of HAART and viral load on HIV transmission. A model developed by researchers in B.C. (British Columbia) in Canada suggests that, at a population level, HAART may reduce the risk of HIV transmission.

The model predicted that, with increasing numbers of people receiving HAART, there will be fewer transmissions within the population. However, the model suggests that at least 75% of people who are clinically eligible for treatment would have to receive treatment for there to be a substantial reduction in HIV transmission.

It is important to remember that models are only our best guess as to what might happen. They provide little proof that in the real world this will happen.
4) **RCTs**: Randomized controlled trials (RCTs) are the most rigorous form of scientific study. They are the best way to determine whether a cause–effect relationship exists between treatment and outcome. This is because everyone has the same chance of being assigned to a treatment group or a control group and no one knows which group they are in. This means we can be pretty sure that any difference found is due to the intervention or treatment and not because of differences between the groups. There is also an ongoing **multinational randomized clinical efficacy trial**, called **HPTN 052**, with 12 sites in 9 countries, which has enrolled 1,750 serodiscordant couples (one HIV-positive and one HIV-negative partner) to look at ARV treatment as prevention in a number of countries. It asks whether initiating treatment in the HIV-positive partner can help reduce the risk of sexual transmission of HIV to the HIV-negative partner. All participants in the trial receive a basic prevention package including treatment for sexually transmitted infections, condoms, and behavior change counseling.

There may never be a conclusive set of trial data that clarify the HIV risk-reduction benefits of early ARV treatment for all populations. However, it will be critical to monitor, collate, and analyze data from the full range of research projects and the single current randomized trial (due to release results in 2013) to develop a sense of how this strategy might be used. It will be equally important to assess the risks and benefits of a test and treat or treatment as prevention approach for HIV-positive people and look for answers to following questions --

Will rates of coercive or non-voluntary testing go up? Will there be adverse toxicities or additional resistance issues raised by earlier initiation of treatment? Will individuals continue to have the choice about whether to start ARVs? AVAC will continue to explore these and other issues as the research progresses?

5) There is also a **planned feasibility study, HPTN 065**, which is looking at a community-level test, link-to-care and, for those who need it based on current guidelines, treatment approach for HIV prevention in the US. The three-year study will take place in the Bronx, NY and Washington, DC. The study will look at whether this kind of approach is feasible for wide-scale implementation and public health impact -- researchers hope this kind of programming will lead to a decrease in HIV transmissions (through expanded testing, prevention for positives, linkage to care, initiation of treatment and increased treatment adherence).

**Discussion:**

The issue of using ‘treatment as a tool for prevention’ raises certain questions which needs to be answered in the the context of knowledge and information available through this study:

1. **Does HAART affect the rate of HIV transmission?**

   In general, available data are insufficient to draw a firm conclusion about the effects of antiretroviral therapy on HIV transmission. Neither modeling, epidemiology, observational cohort studies, nor retrospective analysis can allow firm conclusions. However, there was
uniform agreement that the effects of antiretroviral therapy on transmission are a critical area for study, and one that is likely to influence the future application of these agents.

A study among serodiscordant couples, as supported by NIH (HPTN 052) is the most powerful way -- and perhaps the only way -- to definitively address this question. However, concerns were raised about details of such a study. For example, subjects with low CD4+ cell counts and high viral burdens are probably most likely to transmit HIV, but such subjects cannot be ethically studied in a randomized trial because of the proven benefit of antiretroviral therapy. Subjects with higher CD4+ cell counts enrolled in such a study will suffer side effects from therapy that may not yet be required for the management of their own disease. It is relatively difficult to enroll couples in research studies. Finally, HIV-negative subjects in long-term stable partnerships may have a degree of acquired immunity that reduces the efficiency of transmission and compromises the interpretation of results.

2. Populations to be benefitted if HAART can reduce transmission?

There was uniform agreement that HIV-infected individuals -- the source of ongoing HIV transmission -- must be included in (and should probably be a major focus of) prevention strategies. Every encounter with such patients is a public health opportunity. However, at present antiretroviral therapy can only recommended for individual health, not for prevention purposes; ie, there are currently no conclusive data to support the routine treatment of people whose health status does not require it, purely to try to reduce transmission.

Nor can people who do receive antiretroviral therapy be reassured about the risk of transmission; in the absence of hard evidence to the contrary, we must assume that people receiving antiretroviral therapy remain infectious.

In settings in which antiretroviral therapy is not available, as is the case for most affected populations, most people have no motivation to learn their HIV status. Pre- and postexposure prophylaxis are likely to be further developed for special populations, but these interventions cannot be expected to have a major impact on the epidemic. The best hope for the development of antiretroviral therapy for prevention lies in continued biological studies of transmission, use of animal models, and mathematical modeling with application of empiric data. Primary HIV infection also demands continued study. If it proves to be a critical source of transmission, and if short-course treatment of primary infection proves to limit the severity of infection and spare immune function, people with primary HIV infection may become a special target group. However, experience to date has indicated immense practical difficulties in identifying individuals with primary HIV infection.

3. Drug Combinations to be used?

Drugs must be selected for the benefit of the individual. However, drugs that are difficult to take should lose favor as their use is more likely to result in drug-resistant mutants. Drugs with longer half-lives and good penetration into the genital tract should be developed, both for individual benefit and for public health reasons. Study of the pharmacology of drugs in women is essential to allow the development of rational policies for PrEP after sexual assault.
4. Are changes in Public Policy necessary now or in the near future?

There are imminent difficulties in bringing HIV-infected subjects into care, and providing them with reliable safer sex counseling. Indeed, proven clinic-based strategies to reduce HIV-transmitting behaviors among patients have been difficult to implement. However, legal strategies to force change in sexual behavior generally cannot be sustained, force HIV-infected subjects into hiding, and are inconsistent with democracy.

Directly observed therapy for HIV infection has been difficult to accomplish, except in small, selected population groups. The training and re-training for HIV care providers about their public health opportunities and responsibilities, and exploration of ways in which providers could be compensated for these activities. Reliable measures of successful interventions must also be developed.

5. Efficacy of strategy of using treatment as prevention at individual level / and population level?

“Viral load (VL)” is a measure of the amount of the virus in the body of someone living with HIV. When someone is successfully treated for HIV with HAART, the blood viral load test reads as “undetectable.” However, this does not mean that the virus is not present; rather, the level of virus in the blood is very low—too low for the test to find it. However, since there is still virus in the body there is still a chance that with every sexual act the individual could transmit HIV to their partner. While a blood viral load test result of “undetectable” means there is a very low level of virus in the blood at the time the test was taken, there are a few things about viral load and testing that underline the complexity of this issue:

First, people who are successfully treated with HAART can experience unexplained temporary increases in viral load. These are known as “blips.” Because blips only last for a short time (usually less than three weeks) they may be missed by routine blood viral load tests (which often take place every three months). In other words, the person with HIV may not know when and if they are experiencing a blip.

Second, the blood viral load test is the only routine test for viral load in Canada. However, sexual transmission of HIV occurs through exposure to other fluids—semenal, anal or vaginal fluids. There is research showing that HIV can be detected in the genital fluids of some people who have undetectable viral load in the blood. Therefore, someone might have an undetectable viral load in blood but not in their genital secretions—which may affect the risk of sexual transmission. However, even if the amount of the virus is similar in blood and genital fluids, it is important to remember that an undetectable reading doesn’t mean the virus is gone.

Finally, sexually transmitted infections (STIs) have also been implicated in causing increases in viral load in genital fluids, which could affect one’s ability to transmit the virus. Compounding this issue is that some STIs can be asymptomatic; meaning those with STIs and their partners may not know they have one and therefore may not be aware that they could be prone to increases in viral load. These factors mean that an individual can never be exactly sure if their viral load is undetectable in all parts of their body. This does not mean that viral load tests are inaccurate; rather, it implies that blood viral load tests do not tell the entire story.
It is important to understand that an individual with an undetectable viral load can still transmit HIV.

There has been cases reported of an HIV transmission in a serodiscordant couples, where the HIV-positive individual was on HAART and had an undetectable blood viral load.

Furthermore, a modeling study predicted a persistent risk for HIV transmission on an individual level. The purpose of this model was to estimate the total number of HIV transmissions in serodiscordant couples where the HIV-positive person was successfully treated with HAART.

In a population of 10,000 serodiscordant couples over 10 years, it was estimated that HIV transmissions might still take place as follows:

- 215 transmissions from an HIV-positive woman to an HIV-negative man;
- 425 transmissions from an HIV-positive man to an HIV-negative woman;
- 3,524 transmissions from an HIV-positive man to an HIV-negative man.

While there is some evidence that treatment as prevention may have an impact on HIV transmission at the level of the population, it will not eliminate all HIV transmissions. For service providers who are working to prevent individual HIV transmissions, this is clearly very important. This information provides a rationale for the need to continue with existing prevention efforts such as condom promotion and distribution.

6 ‘Treatment as prevention or "test and treat" strategies?’

Right now, the decision about whether an individual with HIV starts ARVs (Anti-retrovirals) is based on several factors, including the treatment guidelines in use wherever he or she lives. These guidelines may use factors like the individual's clinical health, infection with other diseases and opportunistic infections, T-cell count, and viral load tests (where available) to make a decision about whether to start ARVs. ARVs are not usually initiated with the goal of reducing the HIV-positive person's risk of passing the virus to others. The one exception is in the case of pregnant or breastfeeding mothers. Some strategies to reduce the risk of infection in infants call for treating

the mother with ARVs, regardless of clinical guidelines, to reduce the risk of passing on HIV to the infant.

The treatment as prevention approach proposes, in some cases, starting people with HIV on ARVs when they are diagnosed, with the goal of reducing the chances that they will pass HIV onto others. The idea behind this strategy is that ARV treatment reduces viral load, and that lowering viral load (below a certain point) may greatly

reduce the risk that a person with HIV will transmit the virus. This is supported by observational studies that show a relationship between low viral loads and reduced risk of transmitting HIV to sexual partners.
Much of this information comes from studies in heterosexual populations. The relationship between lower viral load and reduced risk of transmission has also been observed in some studies of HIV-positive women breastfeeding their HIV-negative children. There is not strong evidence on lower viral load and reduction in transmission to needle-sharing partners. Such a strategy could have an impact on rates of new infections in some settings. However, there are many challenges, including current gaps in coverage of ARVs for people who are clinically eligible for them, low rates of HIV testing, additional scientific questions about the exact relationship between HIV viral load in the blood and risk of transmission, and the lack of consensus around the best time for individuals to begin treatment. The currently enrolling START (Strategic Timing of Antiretroviral Treatment) study is meant to provide guidance on when to start therapy. Until the results become available in around three to four years, it will remain unclear that starting treatment early would definitively benefit health outcomes.

Without this information, advocacy for people to start treatment early for prevention purposes will continue to be debated. These uncertainties require additional research as well as policy and community discussions. This discussion and any future programmatic decisions require additional data and will inevitably need to balance individual benefits of treatment with possible wider-spread public health benefits of prevention.

7. **Main components “treatment as prevention” program?**

   a) **To increase the number of people who know they are HIV-positive:**

   On average it is estimated that one fourth (In Canada 26 % to 24 % in US) of people living with HIV don’t know they have HIV. This means that they are unaware, they have HIV because they haven’t been tested (or tested recently enough to know they are now HIV-positive). Increasing the number of people who know they have HIV is important for several reasons. First, research has shown that when people know they are HIV-positive they are more likely to take steps to protect their partners than when they are unaware. Therefore, increasing the number of people who know they are infected should lead to a reduction in HIV risk behaviours.

   Second, and most importantly for treatment as prevention, increasing testing and thus the number of people who know they are HIV-positive should result in more people accessing care and treatment.

   b) **To increase the number of people with HIV receiving treatment:**

   In order for treatment as prevention to work we need to increase the number of people on treatment. This can be done by increasing the number of people who access care and treatment and increasing the number of people who are clinically eligible for HAART.
Clinical Eligibility

In the mid 1990s anti-HIV treatments, called highly active antiretroviral therapy (HAART) became available for people living with HIV. HAART has been shown to significantly reduce the risk of illness and death as result of HIV. But not everyone needs to be on treatment. The CD4+ count is the main indicator used to determine when someone should start treatment (clinical eligibility). In the past, there was a trend towards delaying the start of HIV treatment until the CD4+ cell count fell quite low, below 200 copies/mm³. However, recent research shows that starting treatment at higher CD4+ counts reduces the occurrences of illness and death. The reason for this is that HIV can cause chronic inflammation, which, over prolonged periods of time, can damage the body. HAART may reduce the level of inflammation caused by HIV, slowing or perhaps even stopping the damage. Based on this new research, current treatment guidelines now recommend that all people living with HIV should start HAART before their CD4+ count falls below 350 cells/mm³ and in certain circumstances they should start at even higher CD4+ counts (500 cells/mm³). In short, the clinical guidelines now suggest that getting on treatment to reduce viral load, even in people with relatively high CD4+ counts, is often the best for the health of people living with HIV. These new guidelines should result in more people living with HIV getting on treatment. In fact, these shifting of clinical eligibility from 250 cells of CD4 to 350 cells of CD4 or even 500 CD4 cells, are pushing us to a stage, where we are thinking of ‘test and treat’, ‘testing and linking to care plus -TLC’ approaches.

Access to treatment

However, clinical guidelines do not tell the entire story. From 2006 to 2010, an extra three million people in low and middle-income countries were put on treatment for HIV. Access to treatment has greatly expanded, rising by a third from 2008-2009. However, the number of people in need of treatment has also increased due to a 2010 change in WHO guidelines, which recommends starting treatment at an earlier stage. This means that of the 33.3 million people living with HIV worldwide the number of people in need of treatment has risen from 10 million to 14.6 million. Under the previous guidelines HIV treatment coverage would have increased from 42% in 2008 to 52% in 2009. However, according to the new guidelines, treatment coverage in low and middle-income countries is 36%. Research also shows that particular groups, especially those who are stigmatized and marginalized, are less likely to access treatment even though HAART is available at no cost to some people living with HIV.

The groups less likely to access treatment include young men who have sex with men, Aboriginal peoples, the homeless, the poor, the mentally ill and people who inject drugs. It is important that barriers such as stigma and discrimination are addressed in order to increase the number of clinically eligible individuals accessing care and receiving HAART.

8. Do ‘treatment as prevention’ has any for community-based programs?

Community-based AIDS service organizations (CSOs) have been at the forefront of HIV prevention since HIV emerged in the communities. The work that has been done has been integral to prevention efforts in countries concerned. With the advent of potential new approaches to HIV prevention, such as treatment as prevention, there may be exciting changes to community-based programming and expansion of the knowledge necessary to prevent HIV transmission within a more complex HIV prevention arena.
‘Message for prevention’

Due to the complexity and less than perfect nature of the science involved in treatment as prevention, service providers need to be aware of what the science is saying. We know that currently there is uncertainty regarding the impact of treatment as prevention at a population level. However, at an individual level this approach does not provide a level of protection that would allow individuals to forego conventional prevention approaches. However, some have misinterpreted the science surrounding this approach and have concluded that people living with HIV can forego condom use. This may be compounded by the increasing media attention being paid to the potential role of treatment as prevention, which may also be misinformed. The risk is that if enough people stop conventional forms of HIV prevention (such as condom use) because they think it is safe to do so, any benefits that might have been gained by this approach could be offset and even overridden, resulting in increasing HIV transmission rates. Talking about risk and assessing risk may become more complicated as a result of this new prevention approach.

Service providers will need to be ready to answer a new battery of questions about HIV prevention from people within their community.

Integration of treatment and prevention programming

Treatment and prevention have always meant two things—with little mixing between the two. However, treatment as prevention combines the two halves and necessitates a more holistic approach to HIV and HIV programming. It pushes treatment into the prevention realm, requiring programmers to figure out how traditional treatment-focused programming could be utilized or adapted to enhance the success of treatment as prevention in reducing HIV infections in the community. As we know, in order for treatment as prevention to work, we need to increase access to testing, care and treatment. Historically these are areas outside the prevention realm that are now essential to ensuring the optimal success of this potential new approach.

Depending on the availability of local services, community-based organizations may have to create new programming or enhance existing programming to ensure optimal access to testing, care and treatment. Examples of such activities are HIV testing campaigns; rapid point-of-care testing; outreach to bring more people into contact with testing services; programs aimed at linking HIV-positive people with care providers; treatment counselling; treatment support programs; and adherence counselling, to name a few.

Combination approach to prevention in community programming:

Combination prevention is now seen as the way forward to preventing HIV transmission. This approach utilizes a strategic combination of HIV prevention approaches to try to ensure that everyone in need has access to prevention messaging and programming when they need it. This means that program planners, with the knowledge of their communities, determine the best-case mix of programming to ensure that the fewest number of people fall through the holes in the safety net they have created by layering many different types of prevention programs.
Since we are introducing another approach to prevention, one that we know is not a magic bullet, it is very important that treatment as prevention be envisioned as yet another potential component to HIV prevention. Program planners will have to figure out how their prevention approaches fit together with treatment as prevention to ensure the best level of protection for people at risk living in their community.

**Protecting the rights of people living with HIV**

Community-based Organizations must continue to be vigilant around the rights of people living with or at risk for HIV. Since the theory of treatment as prevention promotes that the more people who know they have HIV and are on treatment, the better off we are in terms of prevention, there is fear that this could affect the individual rights of people to make their own decisions. Therefore, the community has an important role to play in ensuring that the human rights of people at risk for or living with HIV are safeguarded independent of the potential public health benefits of this approach. In terms of testing, *voluntary* testing must remain the mainstay of testing. Any attempt to increase testing rates should not violate this central ideology. In terms of treatment, the choice to begin HIV treatment must rest solely with the individual living with HIV, and treatment must only be offered when medically necessary. While there may be a public health benefit to having all people on HAART, this benefit should never remove the choice to start therapy from the individual. Furthermore, treatment guidelines should always be made with the interests of the individual as paramount.

**9. Impact on other services**

In addition to programming aimed at increasing testing and treatment, community organizations may have additional demands on them for other services. As discussed, research has found that some marginalized people are not currently accessing treatment. However, many of these people are not well positioned to start treatment due to competing priorities in their life, such as poverty, drug use and homelessness. To better position marginalized people for treatment, an array of issues may have to be addressed, including education, housing, mental health, addictions and many more before treatment issues can be addressed. These issues may place additional burden on community agencies.

**10. Strategy of ‘Treatment 2.0’**

According to UNAIDS, Treatment 2.0 is a radically simplified HIV treatment platform that decreases AIDS-related deaths drastically and could also greatly benefit HIV prevention efforts. Treatment 2.0 seeks to simplify the way HIV treatment is currently provided and scale up access to treatment. Under Treatment 2.0, an additional 10 million deaths could be averted by 2025. The new UNAIDS treatment platform can reduce new HIV infections by one-third if treatment is provided to everyone who needs it. Currently only an estimated 5 million of the 15 million people in need of treatment are accessing life-saving medicines. Treatment 2.0 includes the development of better combination treatment regimens, cheaper and simplified diagnostic tools, and a low-cost community-led approach.
The five pillars of Treatment 2.0 are:
1. Treatment as prevention
2. Creating a better pill and diagnostic
3. Stop cost being an obstacle
4. Improve uptake of HIV testing and linkage to care
5. Strengthen community mobilization

Here, we see ‘Treatment as Prevention’ is an important component of ‘Treatment 2.0, strategy.

11. Funding Implications

The cost of increasing the number of people on therapy could have a large financial impact. There is some concern that this increasing cost could lead to prevention funds, being diverted to finance treatment costs (since treatment is now seen as a form of prevention). The community must fight to ensure that funding agencies do not divert dollars in this manner. It should be noted that preliminary work in this area estimates that there will be substantial financial benefits in the long-run due to a reduction in new HIV transmissions. Policy-makers need to envision a short-term increase in costs for long-term cost savings and keep this in mind when allocating resources.

12. Limitations of ‘strategy of treatment as prevention’:

One study in China consisting of a large subgroup of paid plasma donors (now called former plasma donors in deference to the elimination of the practice) who were inadvertently infected with HIV through flawed procedures, have retrospectively evaluated 1,927 discordant couples for 2 years, 2006-2008.

Eighty-four sero-conversion events were observed in 4.3% of couples with 2 critical twists, distributed equally among subjects on and off ART. These results related to HIV transmission in these couples are important, and cautionary as the transmission events had increased with time of follow-up, regardless of counseling, knowledge, and condom availability and, transmission events occurred with equal frequency in couples regardless of whether the partner was provided free ART. We can conjecture that the failure in these Chinese subjects may have been due to ‘patient variables like – they may have used their drugs poorly and/or developed resistance to therapy or got infected from other sexual partners or may be due to the fact that they were receiving routine health care and were put not under special conditions with (for the most part) frequent visits, laboratory monitoring, and some unique health care resources, as studies reporting the great success of ART in reducing HIV have done. (Wang L, Ge Z, Luo S, 2010). So further research is to be needed and these all studies are to be interpreted with caution.
Conclusion:

The arguments in favour of preventive ART are:

(1) evidence indicates that ART reduces viral replication in a durable way with manageable toxicity

(2) the immediate cost of HAART will be compensated by cost-savings from avoided infections (3) intervention could reduce blame, shame and fear, improving social attitude towards people living with HIV/AIDS.

Using ‘ART as a preventive strategy may present with certain challenges like:

a) Probability of increased sexual risk-taking - There might arise spurt in incidences of increased sexual risk taking activities, as had happened after the discovery of ‘Penicillins, some five decades earlier.

b) Sustainability: The cost of HAART regimens is still a concern, but has been mitigated by the increasing availability of generics and cheaper drug combinations. Funding universal access to treatment faces significant upfront financial challenges but ultimately, it is important to consider that in the long-run, ART the expansion of HAART is potentially cost-averting and a sound global health investment.

c) Outreach: Achieving the desired high HIV detection levels (even in well-resourced countries) will be difficult when stigma, criminalization and human rights abuses act as strong deterrents to testing services. Continued advocacy and awareness campaigns will be needed to increase the number of people tested for HIV.

d) Infrastructural weaknesses: For countries where there is poor health infrastructure, a scale-up of HAART programs will be challenging. Obstacles range from ensuring timely drug rollout and availability, and stringent drug adherence across a treated population. Sustained support from trained health-care workers, effective community involvement, and initiatives to strengthen health care systems including task shifting from doctors to nurses in monitoring first-line ART will be crucial in overcoming these obstacles.

e) Drug Resistance: There is potential that along with the expansion of HAART, there will be an emergence of drug-resistant strains of HIV, especially in resource-poor settings. Drug resistance can arise when adherence to the HAART regimen is disrupted. Disruptions to HAART regimens are often caused by infrastructural forces such as treatment stock-outs, poor transportation systems resulting in obstructed access to health care facilities, and a lack of trained professionals to deliver treatment, care and monitoring. Continuity of supply and increased uptake are important to minimizing this risk.

The amount of ongoing complementary research on role of antiretroviral therapy in HIV transmission is quite remarkable, and is likely to clarify many critical issues. It seems clear that the data are currently insufficient for the purposes of hard-and-fast recommendations. However, guidelines and policies related to antiretroviral therapy ought to address the possibility of HIV transmission from a patient to his/her sexual partners, the state of the art for prevention, and (at a minimum) the present and future importance of the interface of antiretroviral therapy and transmission. In the studies reviewed, Treatment as prevention is a new potential approach to help curb the growth of the HIV epidemic. Despite access to care
and treatment in some developed countries, people are being diagnosed with HIV infection late and some are dying without ever receiving treatment. Any programming to bring people into treatment is long overdue and imperative to ensure that marginalized communities receive the same benefits of health care as the rest of the population. Finally whether physicians should counsel their patients to initiate HAART or not, as a prevention strategy is still unresolved.

References:


12. Janssen R. Serostatus Approach to Fighting the HIV Epidemic (SAFE): A new prevention strategy to reduce transmission. Program and abstracts of the 8th Conference on Retroviruses and Opportunistic Infections; February 4-8, 2001; Chicago, Illinois


17. Donnell D et al. ART and risk of heterosexual HIV-1 transmission in HIV-1 serodiscordant African couples: a multinational prospective study. 17th Conference on Retroviruses and Opportunistic Infections,


25. Fang CT, Hsu HM, Twu SJ, et al. Decreased HIV transmission after a policy of providing
free access to highly active antiretroviral therapy in Taiwan. J Infect Dis. 2004;190:879-885


29. Myron S. Cohen, MD ‘HIV Treatment as prevention : To be or not to be J Acquir Immune Defic Syndr Volume 55, Number 2, October 1, 2010, 137-38


32. CDC :Fact sheets about Pre-Exposure Prophylaxis for HIV Prevention
Figure 1: Expected number of deaths under two hypothetical scenarios: compared with current antiretroviral therapy approaches an additional 10 million lives could be saved under Treatment 2.0.

Figure 2: Incidence of new infections in four different scenarios.
Figure 3: On average, the largest share of treatment costs in low- and middle-income countries is not drug-related.

![Figure 3](image)

Figure 4: Comparison of antiretroviral therapy costs per person-year for early and late treatment initiation. Late treatment initiation for patients with often severe clinical conditions requires significant levels of clinical care. This is avoidable through treatment initiation prior to the development of severe HIV-related disease.

![Figure 4](image)