

## Opinion

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# Test and Start for People Living With HIV and Who Use Drugs in Low and Middle Income Countries

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**ABSTRACT**

“Test and Start” implements the World Health Organization (WHO) recommendation of “treat all” by providing anti-retroviral treatment to persons newly diagnosed with HIV infection, at the time of their diagnosis. This HIV treatment algorithm is derived from recent international clinical trials and the recent international HIV treatment guidelines by WHO, recommending all people living with HIV be provided anti-retroviral treatment. This “treat all” recommendation removes any and all limitations for receiving anti-retroviral treatment for all people living with HIV, including people who use drugs. However, there are a limited number of “Test and Start” programs that have focused on the barriers to anti-retroviral treatment for people who use drugs. With an increasing number of low and middle income countries developing guidance for “Test and Start” programs, this articles identified four elements that support access to and successful initiation of the early initiation of anti-retroviral treatment for people living with HIV, who use drugs. The elemental services are: outreach with social services, screening for and management of substance use disorders, comprehensive primary care and differentiated care in anti-retroviral treatment. Together these services can provide a supportive foundation for “Test and Start” programs for people living with HIV, who use drugs.

**KEYWORDS:** ART for all; Drug use; Substance use disorder treatment; HIV infection; Alcohol use; Test and Start.

**WHEN TO START ANTIRETROVIRAL TREATMENT AND INTERNATIONAL TREATMENT GUIDELINES**

Clinical trials and studies assessing the efficacy and uptake of antiretroviral treatment have formed the basis for both international and national HIV treatment guidelines on the use of drugs for treating and preventing HIV infection.<sup>1-4</sup> The most recent international treatment guidelines by the WHO recommend, for the first time, that all people living with HIV be provided anti-retroviral treatment.<sup>1</sup> This “treat all” recommendation removes any and all limitations for receiving anti-retroviral treatment for all people living with HIV, including people who use drugs. Past treatment guidelines on when to start anti-retroviral treatment, relied on findings from early clinical trials of treatment naive people living with HIV, by comparing the initiation of anti-retroviral treatment during chronic infection at CD4 levels at or between 200-350 cells/mm<sup>3</sup>.<sup>4,5</sup> The findings of these studies showed a statistically significant reduction in death when starting anti-retroviral treatment at higher CD4 counts. There was also a reduction of the risk of death and co-morbidities, such as tuberculosis, when starting anti-retroviral treatment at times earlier in infection at higher CD4 counts. Studies also showed that starting anti-retroviral

treatment at the initiation of care at higher CD4 counts, rather than deferring to start at a CD4 count of 250 cells/mm<sup>3</sup>, reduced the risk of disease progression. Based on these findings, the CD4 threshold to start anti-retroviral treatment in most national guidelines was raised to 350 cells/mm<sup>3</sup> by 2012 and later 500/mm<sup>3</sup> around 2009-2013.<sup>4,6,7</sup>

International guidelines have gone further and recommended treating all HIV-infected adults regardless of their CD4 count.<sup>1</sup> This most recent step has been justified by the results of three clinical trials, HPTN 052, Temprano ANRS 12136 and START. The HPTN 052 study was a Phase III randomized clinical trial at 13 international sites that evaluated both whether antiretroviral treatment can prevent the sexual transmission of HIV in serodiscordant couples, as well as, the optimal time to begin anti-retroviral therapy in order to reduce illness and death among people living with HIV. The study showed that that starting anti-retroviral therapy early reduced HIV transmission by 93% over the course of the entire study.<sup>8</sup> The TEMPRANOANRS 12136 study showed, with a 2×2 factorial design of four treatment strategies, patients who started early anti-retroviral treatment with CD4 counts of ≤800 cells/mm<sup>3</sup> in a resource limited setting had a substantially lower risk of death and HIV related disease or co-morbidities, such as tuberculosis.<sup>9</sup> The Strategic Timing of Antiretroviral Treatment (START) study was a global clinical trial in six geographic regions that randomized patients with CD4 counts of >500 cells/mm<sup>3</sup> to either immediate or delayed initiation of anti-retroviral treatment. The immediate treatment groups showed a greater than 50% decrease in death or AIDS related event/co-infection compared to the delayed treatment group.<sup>10</sup> Taken together, these hallmark studies recruited over 8,000 patients in 37 countries and showed a roughly 50% reduction in severe morbidity in the early treatment groups. The trials outcomes were comparable and complementary in demonstrating that earlier initiation of treatment with anti-retroviral treatment is most beneficial to promote excellent clinical outcomes, i.e. reduced morbidity and co-infections, as well as, promoting retention in long term care. As a result of the latter trial, the “treat all” recommendation is now commonly called “Test and START”, an approach that begins the initiation of anti-retroviral treatment immediately after a diagnosis of HIV infection in an effort to improve health outcomes for people living with HIV.<sup>11</sup>

#### PEOPLE WHO USE DRUGS, LIVING WITH HIV AND ANTI-RETROVIRAL TREATMENT

People who use drugs are at high risk for HIV infection and are frequently disengaged from the healthcare system, thereby limiting their access to HIV services.<sup>12</sup> Screening for drug use, including alcohol consumption, is an important recommendation in international guidelines to promote the management of clinical issues that are barriers to HIV diagnosis and treatment.<sup>13</sup> Screening people living with HIV, who use drugs and inject illicit drugs, allows health care providers to address harmful alcohol use and stimulant use which can enhance the risk of sexual transmission of HIV or injection risk of HIV transmission, through injection opioid use and stimulant injection of amphetamine-type

stimulants.<sup>14-17</sup> Thus, alcohol, opioid and stimulant-use disorders are important co-morbidities for people living with HIV in the era of “treat all” as part of the medical management of HIV infection.<sup>17-22</sup> However, substance use disorders are not routinely screened for in HIV care settings although highly prevalent in people who use drugs and seeking care. Opioid use disorders, in particular, are recognized as a significant HIV risk factor for people who inject drugs and has been shown to be the largest contributor to disability-adjusted life years (DALYs) for people living with HIV who use drugs.<sup>16,17,23-25</sup>

Addressing substance use disorders are fundamental components of personal health and well-being as defined by the WHO.<sup>26</sup> Substance use disorders can be addressed in a health care setting with interventions, such as screening and brief interventions with recovery management to reduce harmful use, as well as, by therapies such as cognitive-behavioral therapy (CBT)/ Motivational Enhancement Therapy (MET), or through pharmacotherapy and medical management.<sup>27-32</sup> For people living with HIV with opioid dependence, treatment with Medication Assisted Treatment (MAT) in HIV primary care improves the HIV-related outcomes of mortality, quality of life, retention in care, and anti-retroviral treatment adherence.<sup>33</sup> WHO notes that substance-use disorders are highly prevalent, globally, and burdensome to society; but the gap between providing needed treatment and that which is locally available to reduce the burden of disease remains very wide.<sup>34</sup> WHO guidelines underscore the importance of HIV care settings that can provide the opportunity to screen for and manage common substance-use disorders through a range of care and treatment options that include counseling and pharmacotherapy (MAT). The guidelines additionally urge that that these services are part of national HIV/AIDS programs and integrated into primary care programs for people living with HIV.<sup>23,34</sup> Implementation and integration of HIV primary care to address substance-use disorders, including screening, diagnosis and treatment of substance use disorders, particularly the use of MAT for opioid dependence, can substantially impact public health and the HIV epidemic.<sup>35,36</sup>

People who use drugs face barriers to accessing anti-retroviral treatment for HIV infection resulting in not only less receipt of anti-retroviral treatment but also poorer clinical outcomes when provided anti-retroviral treatment late in care.<sup>37-39</sup> For people who inject drugs, access to anti-retroviral treatment is very low with only one in three reported to receive treatment.<sup>38</sup> For those being released from incarceration back into the community, only one in ten may be receiving anti-retroviral treatment.<sup>40</sup> However, the integration of substance abuse treatment and HIV primary care can enhance the access to anti-retroviral treatment for people who use drugs, as well as, enhance the efficacy of anti-retroviral treatment for people who inject drugs.<sup>41,42</sup> Medication assisted treatment has been shown to increase recruitment in anti-retroviral treatment programs, increase treatment coverage, increase retention in care and adherence to anti-retroviral treatment regimens and increase viral suppression.<sup>42</sup> Together, medication assisted treatment and anti-retroviral treatment have been shown to reduce all

cause mortality for people living with HIV who inject drugs.<sup>43</sup> When integrated into incarceration settings, medicated assisted treatment and anti-retroviral treatment improves HIV treatment outcomes for those being released into the community, can provide a bridge to community-based services post release, and promote better clinical outcomes during the post release period.<sup>44-46</sup>

### TEST AND START FOR PEOPLE WHO USE DRUGS

Test and Start implements the WHO recommendation of “treat all” by providing anti-retroviral treatment to person newly diagnosed with HIV infection, at the time of their diagnosis. HIV policy watch reports that globally nine countries recommend the “Test and Start” strategy while a lower number of low and middle income countries, including Thailand, Malawi and Botswana, have a national policy that recommends anti-retroviral viral treatment regardless of CD4 count, including key populations.<sup>47</sup> Most recently, Tanzania has been added to the growing list.<sup>48</sup> This policy is important for people who use drugs since studies have shown that key populations, people who inject drugs, sex workers, men having sex with men, transgendered people and prisoners, are at high-risk for use and abuse of illicit drugs and alcohol and HIV infection.<sup>49</sup> A national policy supportive of “Test and Start” is an important first step in the implementation of “Test and Start” national programs. What can then follow are initial projects for feasibility and the development of standard operating procedures. The landmark clinical trials could help with standard operating procedures.<sup>50-52</sup> However, a closer look at the clinical protocols show that for the HPTN 052 study a history of drug use was an exclusion criteria; for the TEMPRANO study only psychiatric illness, anxiety and depression, were addressed; and while the START trial included injection drug users, it only randomized 64 participants, 1.4% of the study enrollment. This limited enrollment precluded a sub-analysis of the people who used drugs in this study.<sup>10</sup> These study designs show both the challenges to recruiting people who use drugs into HIV clinical trials, as well as, the limited information that can be utilized from clinical trials in developing standards of practice for people living with HIV, who use drugs.<sup>53</sup>

However, the Present’s Emergency Plan for AIDS Relief Scientific Advisory Board has provided recommendations regarding “Test and Start” and women’s treatment programs have begun to implement “Test and Start”.<sup>54-56</sup> The recommendations support the implementation of “Test and Start” initially in high volume clinics in urban areas in concert with clinical protocols that prioritize the sickest patients, as well as, provide continued access and retention for those receiving anti-retroviral treatment. Other recommendations include the importance of health care worker training and education and a public health education program for people living with HIV, peer educators, community health workers and differentiated care as part of anti-retroviral treatment.<sup>54</sup> Patient education about the health benefits of early initiation of anti-retroviral treatment is important, with a pilot “Test and Start” program in Uganda showing that asymptomatic patients questioning the need for medication.<sup>55</sup> Health service barriers to receiving anti-retroviral treatment

should be reduced with community initiated differentiated anti-retroviral treatment at point of HIV testing/diagnostic sites with patient access to comprehensive care. Thus, people living with HIV are met with care and treatment based on where they are in the course of infection and with a full array of services to meet their needs. The recommendations also support evidence-based guidelines for rapid start of anti-retroviral treatment for persons with opportunistic infection, tuberculosis and those who are pregnant.<sup>54,56</sup> Clear approaches and management of comorbidities and non-communicable diseases, such as substance use disorders is necessary. In the Uganda program, harmful alcohol consumption was perceived to be a barrier to early anti-retroviral treatment due to poor adherence.<sup>55,57</sup> In a high resource setting, a “Test and Start” program has shown that patients who inject drugs are less likely to obtain viral suppression.<sup>58</sup> In a resource limited setting, barriers to early initiation of anti-retroviral treatment for people living with HIV who inject drugs were identified as delays in receiving testing and clinical test results, off-site HIV clinics (non-integrated services and sites), stigma, lack of knowledge of the benefits of early treatment, initiation of treatment only when feeling ill, and dysfunctional care and treatment setting due to limited staff turnover.<sup>59</sup> Thus, there is a clear need to manage substance use disorders and the barriers to early initiation of anti-retroviral treatment in “Test and Treat” programs for people living with HIV, who use drugs.

Treatment of substance use disorders, particularly opioid use disorders, as part of HIV primary care promotes good clinical outcomes.<sup>21,22,60</sup> Medication assisted treatment for opioid dependence increases access to anti-retroviral treatment, anti-retroviral coverage, adherence to anti-retroviral treatment and retention in care, viral suppression, reduces viral transmission and mortality.<sup>21,60</sup> Screening for and management of alcohol use disorders in HIV care or anti-retroviral clinics results in an increase medication adherence and retention in care and treatment, a reduction of HIV transmission and morbidity and mortality, as well as, enhanced quality of life.<sup>22</sup> Thus, incorporating screening for and management of substance use disorders in “Test and Start” programs that target people who use drugs would promote the attainment of good clinical outcomes. Screening for and management of substance use disorders in people who use drugs allows for the development of patient stability from which further treatment of comorbidities, such as HIV infection, can result with improved clinical outcomes. Thus, “Test and Start” for people who use drugs would benefit from screening and management of drug and alcohol use/dependence as an early step in initiation of services.

For people living with HIV, who use drugs, a “Test and Start” program with the following services support the needs of people who use drugs: outreach with social services, screening for and management of substance use disorders, comprehensive primary care and differentiated care in anti-retroviral treatment (Table 1). Peer based outreach is critical to meet people who use drugs where they are in the community.<sup>61-63</sup> These peer groups can comprise community counselling teams, who are people who use drugs in recovery, family members affected by drug use and health care staff. These groups have drug scene credibility, local

Element	Activities that "Support Test and Start"
Outreach with Social Services	peer education of people who use drugs, provision of HIV prevention interventions, social support; screening for drug use and brief interventions, point of care for HIV rapid testing; prevention of overdose mortality
Substance Use Disorder Treatment	screening for and management of substance use disorders, medication assisted treatment for opioid dependence and alcohol dependence, point of care for HIV rapid testing; recovery support
Comprehensive Primary Care	Patient centered screening and management of co-infections and co-morbidities, confirmatory HIV testing
Anti-Retroviral Treatment	Differentiated care and tailored anti-retroviral treatment that allows for an enabling environment for people who use drugs

Table 1: Elements of "Test and Start" for people who use drugs.

knowledge and connectivity, and a level of medical competence to perform screening and brief interventions to reduce harmful substance use. With basic training in addiction counselling these groups can organize self-help groups, recovery communities and provide an alternative to law enforcement.<sup>62</sup> These individuals can also act as peer navigators promoting access to screening for substance use disorders and entry into treatment for substance use disorders and primary care.<sup>64</sup> An enabling, non-discriminatory environment in primary care for people who use drugs can be enhanced utilizing peer and community-based health care workers.<sup>65</sup> Community based care delivery models that are patient-centered models of care can facilitate people living with HIV, who use drugs to access and be retained on anti-retroviral treatment, promote adherence to medications and improve survival rates.<sup>66,67</sup> Differentiated care in anti-retroviral treatment provides tailored care so that people who use drugs with suppressed viral load visit the HIV clinic less frequently and focus on their treatment for substance use disorders; HIV clinic staff then focus attention on people who use drugs with unsuppressed viral load and the barriers these individuals face to achieve adherence and good clinical HIV outcomes.<sup>68</sup> Together outreach with social services, screening for and management of substance use disorders, comprehensive primary differentiated care and anti-retroviral treatment comprise a package of services that can comprise a "Test and Start" program for people living with HIV, who use drugs.

## CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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