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Moving toward test and start: learning from the experience of universal antiretroviral therapy programs for HIV-infected pregnant/breastfeeding women

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Abstract

In 2015, the WHO recommended universal antiretroviral therapy (ART) for all people living with HIV after two randomized controlled trials revealed lower rates of mortality and serious illnesses among people living with HIV receiving immediate ART compared with those receiving deferred ART. Many countries in sub-Saharan Africa rapidly adopted this guidance and are implementing 'test and start' programs.

As this work begins, lessons learned from prevention of mother-to-child transmission Option B+ programs can inform decisions for new universal HIV treatment programs. The Option B+ approach involved initiation of lifelong treatment for all HIV-infected pregnant and breastfeeding women. Since its inception in Malawi in 2011 and WHO endorsement in 2012, widespread scale-up of Option B+ prevention of mother-to-child transmission programs in most resource-limited countries has resulted in a dramatic increase in ART coverage for HIV-infected pregnant and breastfeeding women.

Despite the overall success of the Option B+ universal lifelong treatment approach, program and operational research data highlight the need for additional focus on strategies to retain women in care. In this commentary, we highlight program considerations and lessons learned from Option B + implementation experience in resource-limited countries, which may help guide decisions and enhance the quality of general 'test and start' programing.

Keywords

antiretroviral therapy; HIV/AIDS; Option B+; prevention of mother-to-child HIV transmission; universal access

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Conflicts of interest

There are no conflicts of interest.

At the end of September 2015, the WHO issued recommendations for initiation of universal, lifelong antiretroviral therapy (ART) for all people living with HIV (PLHIV), regardless of $CD4^+$ cell count [1]. Two important randomized controlled trials informed WHO's recommendations for universal ART: the Strategic Timing of AntiRetroviral Treatment (START) study [2] and the TEMPRANO ANRS 12136 trial [3]. Both trials revealed lower rates of mortality and serious illnesses among PLHIV receiving immediate ART compared with those receiving deferred ART. Prevention of mother-to-child transmission (PMTCT) programs first introduced universal lifelong ART for HIV-infected pregnant and breastfeeding women (Option B+) 6 years ago, and the approach has been quickly and broadly adopted. Now, as the global community has begun to implement universal ART, or 'test and start', HIV programs may benefit from the experience and hard-won lessons learned in the first several years of Option B+ program expansion.

WHO recommendations for universal ART for all PLHIV signal an important global policy shift, enabling countries to work toward meeting the 90-90-90 targets set by the Joint United Nations Programme on HIV/AIDS. The 90-90-90 targets aim to diagnose 90% of PLHIV, place 90% of those diagnosed on treatment, and achieve viral suppression in 90% of those on ART by 2020 to end the HIV epidemic by 2030 [4]. However, meeting these targets successfully will depend on excellent performance at critical points of the HIV clinical care and treatment cascade, including access to high-quality rapid HIV testing services, support and careful counseling at ART initiation, consistent long-term retention in care, and reliable adherence to ART for durable viral suppression. The 'test and start' approach in PMTCT programs began in 2011 in Malawi. Pragmatic policy-makers in Malawi decided to endorse lifelong ART, which they called 'Option B+' [5] for all HIV-infected pregnant and breastfeeding women to increase the number of these women receiving ART and provide operational simplicity to the existing WHO recommendations for PMTCT [Option A (comprised giving zidovudine (ZDV) to the mother prophylactically during pregnancy, single-dose nevirapine (NVP) to both the mother and the neonate at delivery, maternal ZDV and lamivudine to the mother during the first week *post partum*, and NVP daily to the infant throughout breastfeeding (http://www.who.int/bulletin/volumes/92/3/13-122523/en/)) or Option B (comprised a triple ARV regimen, typically consisting of the recommended first-line ART for the mother during pregnancy and throughout breastfeeding and 6 weeks of daily NVP for the infant, regardless of infant-feeding method (http://www.who.int/bulletin/volumes/92/3/13-122523/en/))] that were based on the woman's $CD4^+$ cell count or WHO clinical staging [6]. In Malawi, Option B+ dramatically increased ART uptake among HIV-infected pregnant and breastfeeding women [7].

The success resulted in rapid WHO endorsement of Option B+ and widespread revision of global PMTCT policies. Between 2011 and 2014, more than 20 countries supported by the US President's Emergency Plan for AIDS Relief (PEPFAR) implemented Option B+ programs; during this time period, the proportion of HIV-infected pregnant and breastfeeding women receiving ART through PEPFAR-supported programs nearly tripled. In fiscal year 2016 alone, more than 730 000 HIV-infected pregnant women in PEPFAR-supported programs received lifelong ART through PEPFAR Option B+ programs (PEPFAR data, 2016). By the end of September 2015, 80% of 144 low-income and middle-income countries reported having adopted universal, lifelong ART for pregnant and breastfeeding

women [8]. With the new ‘test and start’ recommendations from WHO, even more countries are embracing lifelong ART for pregnant and breastfeeding women as well as for all PLHIV. However, even after guidelines are revised, the early Option B+ experience has shown that additional policy and program work will be required.

Access to quality, accurate HIV rapid testing services has been paramount to the expansion of ‘test and start’ for pregnant and breastfeeding women. This includes reliable availability of rapid HIV test kits to allow timely diagnosis and adherence to WHO-recommended testing strategies to prevent misclassification of maternal HIV status. Retesting all clients who have been diagnosed as HIV-positive prior to ART initiation is of particular importance [9]. A false-positive HIV test result could lead to needless lifelong ART for a mother; conversely, a false-negative result could cause potentially preventable vertical HIV transmission to an infant as well as disease progression in the mother. Despite the potential dire consequences of misclassification of HIV status, recent analysis of 48 national testing policies found less than 20% of those policies aligned with WHO-recommended testing strategies [10]. Although retesting prior to ART initiation will minimize misdiagnoses, it does not replace the need for comprehensive quality-assurance programs that include periodic assessment of tester competency, implementation of a proficiency-testing program, ongoing supportive supervision, verification of new rapid test kit lots, and proper record keeping [11].

Although the ‘test and start’ approach of Option B+ has increased uptake of ART among HIV-infected pregnant and breastfeeding women, routine program data have exposed patient retention as a major challenge, thus threatening the long-term individual and public health impact of expanded ART coverage. Loss to follow-up, especially during the first few months of treatment, is of particular concern. In Malawi, analysis of routine program data from over 20 000 women who initiated ART between October 2011 and March 2012 as part of the national Option B+ program revealed that 17% of women were lost to follow-up at 6 months [12]. Loss to follow-up increased over time, with up to 29% of women lost at 12 months [13]. Similar findings have recently been reported from Haiti where analysis of national electronic medical record data from more than 17 000 adult patients initiating ART between October 2012 and August 2014 showed that the risk of attrition from HIV care among Option B+ patients was 63% greater than the attrition among nonpregnant women with similar characteristics, including age, $CD4^+$ cell count, and WHO stage. In the Haiti program, loss to follow-up among Option B+ patients began to appear several months after ART initiation and steadily increased over the 22-month observation period [14].

One of the most troubling findings from Option B+ programs is that many women do not return for antenatal care after receiving the first month’s supply of ART. Of 3225 pregnant and breastfeeding women who initiated ART as part of Option B+ at six large facilities in Malawi between 2011 and 2014, 16% did not return after their first clinical visit [15]. These women were documented as having initiated ART but, in reality, they may represent a category of ART ‘noninitiators’. Tenthani *et al.* found that women in Option B+ programs in Malawi were five times more likely to never return for care after their initial visit than women initiating ART for their own health [12]. Although loss to follow-up data are limited,

other countries such as Rwanda and Uganda have reported high rates of loss to follow-up among pregnant and breastfeeding women initiating ART in PMTCT programs [16,17].

Whether the patterns of noninitiation and loss to follow-up identified in Option B+ programs prove unique to pregnant and breastfeeding women remains to be seen. Pregnant women may confront different situations and pressures in the ‘test and start’ context than nonpregnant women or men. Pregnant women who present to an antenatal clinic expecting only prenatal care may be less prepared to accept a new HIV diagnosis and immediate ART than adults who present to healthcare facilities specifically for HIV testing or for initial HIV care. In antenatal care settings that implement Option B+, the newly diagnosed HIV-infected pregnant woman might undergo HIV testing, learn of her HIV diagnosis, receive ART counseling, start ART, and receive her routine pregnancy counseling and care during the same clinical visit. Although this is necessary to provide maximal prevention of MTCT, mothers who do not return for subsequent visits will not receive the additional counseling needed for optimal adherence.

As PMTCT programs have transitioned to Option B+, ART services have been integrated into routine antenatal care clinics through varied approaches. The result is a diverse set of Option B+ service delivery models, each of which presents its own considerations for patient retention, tracking and monitoring, and evaluation. Women who attend programs that require separate antenatal care and ART clinic visits cope with additional time and logistical barriers. Alternatively, most women who receive ART within antenatal care clinics will be asked to transition to adult HIV care and treatment clinics, requiring navigation of new HIV clinical settings and providers at the cessation of breastfeeding. By contrast, nonpregnant, adult HIV patients can establish and maintain stable care at a given HIV clinic. In addition, pregnant/post-partum women may attend several different PMTCT clinics because of cultural traditions that encourage women to deliver near their mother’s home; this mobility can challenge tracking retention in Option B+ programs. These service delivery model and mobility issues may impose retention challenges that are unique to pregnant and breastfeeding women.

However, other facets of Option B+ implementation may directly apply to the general HIV-infected population and more directly inform ‘test and start’ program scale-up. The START and TEMPRANO trials showed that earlier ART initiation confers personal health benefits for HIV-infected adults with higher $CD4^+$ cell counts, many of whom will be asymptomatic when diagnosed. Patients who feel healthy may resist embarking immediately on lifelong ART; they also lack the incentive of preventing HIV transmission to an unborn child. ART uptake and retention for newly diagnosed HIV patients are likely dependent on the quality of initial and ongoing counseling that they receive; this may be especially true for those who feel well. Data are limited on retention of asymptomatic HIV-positive individuals on ART; studies prior to the ‘test and start’ era have shown that HIV-positive individuals were more likely to be maintained in HIV services after starting ART than while in HIV care but not on ART. Emerging data from early ‘Treat All’ programs show that tailored approaches involving differentiated care and patient support can result in high retention and viral suppression [18,19].

Research to identify factors contributing to loss to follow-up and to identify interventions that improve retention in Option B+ programs would benefit generalized ‘test and start’ programing. Engagement in care is complex, and a variety of factors may influence retention, including interpersonal or community-level barriers (such as stigma or fear of disclosure to a partner or family members), clinic-level issues (such as patient–provider relationships), and structural barriers to care that compete for patient time and resources [20,21]. Emerging themes from early research on loss to follow-up in Option B+ programs suggest that enhanced attention should be directed to certain populations and to key steps in the PMTCT cascade. For example, in Malawi, loss to follow-up is more common among younger patients in Option B+ programs [22], whereas in Haiti, loss to follow-up is more common among those who initiate ART immediately after enrollment in HIV care [14]. Among Option B+ patients, studies suggest that community-based and communication-related interventions may improve retention [23], and service delivery factors, such as initiation of ART on the day of diagnosis and high health facility client–staff ratios, are associated with lower retention rates [24]. These findings may help guide general ‘test and start’ programing. In addition, programs that establish standard procedures for identifying women at risk of loss to follow-up and that implement timely tracking of appointment defaulters will be best poised to retain patients in care.

Universal ART coverage provides the potential for epidemic control, but programatic success – achievement of viral suppression – will depend on accurate HIV diagnosis, high ART uptake, and retention for all PLHIV. Retesting prior to ART initiation is critical to assure the validity of an initial positive HIV test result [11], perhaps making a case for language such as ‘test, confirm, and start’ an apt and quality-driven moniker for the universal ART approach. As universal ART is introduced, operational research will be needed to assess individual and program-level determinants of retention and interventions that work best to achieve long-term retention for PLHIV in both Option B+ and in broader ‘test and start’ programs. As we work to end the HIV epidemic, sharing experiences across public health programs will be vital to ensure that lessons learned from Option B+ inform the implementation and expansion of ‘test and start’ and ensure that the HIV community can come together to optimize outcomes for all families affected by HIV.

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