World Health Organization Guidelines (Option A, B, and B+) for Antiretroviral Drugs to Treat Pregnant Women and Prevent HIV Infection in Infants [1]


To address the international Human Immunodeficiency Virus epidemic, the World Health Organization, or WHO, developed three drug treatment regimens between 2010 and 2012 specifically for HIV-positive pregnant women and their infants. WHO developed the regimens, calling them Option A, Option B, and Option B+, to reduce or prevent mother-to-child, abbreviated MTC, transmission of HIV. Each option comprises of different types and schedules of antiretroviral medications. As of 2018, WHO stated that in Africa alone about 1,200,000 pregnant women were living with untreated HIV. Those women have up to a forty-five percent chance of transmitting HIV to their offspring if they do not receive treatment. Option B+ has decreased the overall maternal mortality rates in many low- and middle-income countries, and numerous studies have supported the notion that it is the most effective of the three regimens for preventing MTC transmission of HIV.

HIV is a virus that attacks the human immune system by infecting a type of immune cell called a CD4 cell, also referred to as a CD4+ T cell, T-cell, T-lymphocyte, or helper cell. CD4 cells fight infections in the body, and because HIV infects and eventually destroys CD4 cells, HIV suppresses the immune system. Eventually, untreated HIV can destroy enough CD4 cells and weaken the immune system to the point that the affected individual is considered to have developed Acquired Immune Deficiency Syndrome, or AIDS. HIV-positive individuals can monitor their HIV through blood tests called CD4 tests. The number of CD4 cells in the person’s blood can inform them and their medical teams the severity of their HIV infection. Medications cannot cure HIV, but they can prevent it from progressing as quickly as untreated HIV, and may prevent HIV transmission from the infected individual to others.

Humans can transmit HIV in different ways, typically involving an exchange of certain bodily fluids, such as blood, semen [6], vaginal fluids, or breast milk. One such mode of transmission is from an HIV-positive pregnant woman to her offspring before delivery, during delivery, or after delivery. Before delivery, transmission can occur in the womb [7]. Normally, the placenta [8] protects the fetus [9] from pathogens like HIV. However, anything that damages or decreases the protective strength of the placenta [8] can cause HIV transmission, such as trauma, blood clotting disorders, or tobacco and other drug usage. A higher viral load may also increase a woman’s chance of transmitting HIV to her fetus [8], which is why health professionals recommend women take antiretrovirals throughout pregnancy [10]. During delivery, transmission can occur because fluids rich in CD4 cells, such as blood and vaginal secretions, are present. Those fluids can infect the neonate through microtears in the skin, which commonly occur during the birthing process. After delivery, transmission can occur during breastfeeding since breast milk contains CD4 cells. According to the United Nations, or UN, without any prevention, the rate of HIV transmission from woman to infant is between twenty and forty-five percent.

WHO developed certain drug regimens to prevent MTC HIV transmission. In 1948, the United Nations founded WHO to facilitate international health services for its Member States. It receives its funding from two sources, which includes set membership fees from its Member States and a variety of voluntary contributions. WHO created the prevention of MTC transmission guidelines as a way to streamline different successful antiretroviral regimens and merge prevention programs from across the world into one universal program. The goal was to successfully standardize a global care plan in order to reduce and prevent new cases of HIV around the world. The outcome of those efforts transpired with the creation of Option A, Option B, and Option B+ regimens. WHO recommended Option A and Option B in 2010. WHO released Option B+ in 2012. All three of the options use combination prophylaxis, which refers to the use of multiple medications taken to prevent an illness.

Since 1996, standard treatment of HIV has been a combination of medications designed to keep the virus suppressed within the affected person. Combination prophylaxis has been available to many people living in developed countries throughout North America and Europe since the 1990s. However, such regimens were not made readily available to people living in many low- and middle-income countries, especially countries in Africa, until the mid-2000s. In 2006, at a UN meeting on HIV/AIDS, Member States agreed to work on a goal of expanding universal access of comprehensive treatment plans, prevention, and care for people, especially those living in low- and middle-income countries, by 2010. In 2003, only around 100,000 HIV-positive people living in Africa were receiving combination treatment. By the end of 2011, that number grew to surpass 6.2 million people, largely due to efforts instituted by WHO. In the midst of many of those efforts, over eighty-five percent of HIV-positive pregnant women were living in Africa. Therefore, many of the efforts put forth by the UN and WHO were aimed at improving access to care and treatment for HIV-positive people in Africa.
In the case of HIV, the regimens consist of three medications called antiretrovirals which help to stop HIV from replicating in the body. Prior to the establishment of combination prophylaxis as a treatment for those living in low- and middle-income countries, preventing MTC transmission of HIV involved non-combination drugs, such as a single dose of nevirapine, or sdNVP, given to the pregnant woman before delivery. While that was effective at preventing transmission during delivery, it raised the risk of both the woman and infant developing drug-resistant HIV following delivery. In a 2007 meta-analysis, researchers found that up to thirty-six percent of women and fifty-three percent of infants treated with sdNVP alone developed detectable NVP resistance within weeks of receiving the medication.

Using multiple antiretrovirals at once prevents HIV from becoming resistant to just one medication, since HIV can change some of its DNA when it replicates itself, which is also known as mutating. However, medications only work if the affected person does not have a strain of HIV that is resistant to that particular treatment. If a person has HIV that becomes resistant to a certain type of medication, that means the medication will no longer work and the person can become sicker as their HIV continues to advance. Therefore, when a person with HIV takes multiple medications, their HIV infection is less likely to become resistant to all three medications as compared to mutating resistance to just one medication. That means that the medication will remain effective, protecting the individual from progressing to develop AIDS. Not only can a person develop drug-resistant HIV over time, but they can also acquire a drug-resistant strain of HIV upon being infected by someone with drug-resistant HIV, meaning an HIV-positive pregnant woman can infect her fetus with a drug-resistant strain. Whereas people diagnosed with HIV in developed countries can often receive a genetic test to determine if their particular strain of HIV is resistant to one or more medications, that same standard of care is often not available for those living in low- and middle-income countries. Therefore, because HIV affects people in low- and middle-income countries at a higher rate, a wider combination of medications are typically more effective when a person cannot receive a test to determine the extent of their medication resistance.

While all WHO-suggested options were meant to prevent the MTC transmission of HIV, they differed based on the type of medication, duration of treatment, and resource demand, such as medication types and amounts or testing requirements. Initially, both Option A and Option B treated pregnant women differently depending on the severity of their HIV infection. If a pregnant woman’s HIV had progressed to the point that her CD4 count was very low, she required drug therapy focused more on treatment than solely preventing HIV transmission to her fetus. If her CD4 count was not clinically as severe, she required drug therapy focused on prophylaxis, meaning that which would prevent her from transmitting her virus to her fetus. For Option A and Option B, women who received the prophylactic medications were not required to extend their medications for life. However, Option B+ was designed to simplify the process and entail the dispensing of the same medications, regardless of the severity of infection, for the duration of the woman’s lifetime rather than when the risk of MTC transmission had diminished. However, it was not until 2012 that WHO released the new guidelines for Option B+. Before then, treatment guidelines were complex and multifactorial, and often required a wide array of resources and education materials for both the healthcare providers and patients.

While no longer recommended since 2013, WHO designed Option A to prevent MTC transmission of HIV in 2010. For the Option A guidelines, HIV-positive pregnant women must first receive a CD4 test to determine their eligibility for lifelong medication. During the test, a medical professional takes a blood sample, typically from a vein in the arm of the patient, to determine her CD4 count. That sort of test requires the presence of equipment and staff members who are educated on how to read and interpret blood samples, which can limit its practicality in resource-limited settings. If the test shows the woman’s CD4 count is below a certain threshold, the woman must begin triple antiretroviral therapy immediately because that test value indicates that she will soon progress to AIDS without medical intervention. WHO recommends patients whose CD4 counts are critically low to continue those medications for life rather than just during and immediately following pregnancy to lower the rates of maternal mortality.

Pregnant women with a CD4 count greater than the aforementioned threshold begin Option A after gestational week fourteen, which prioritizes prophylaxis and decreasing the risk of MTC transmission. Option A requires a mix of different types of drugs given at different points of pregnancy and delivery. With Option A, the woman would begin AZT until delivery. At labor onset, the medical team would give the woman a different medication called single-dose nevirapine, or sdNVP. During the delivery stage of pregnancy, she would then take AZT again along with another medication called lamivudine, often shortened to 3TC. Following delivery, the woman would continue taking AZT and 3TC for seven days.

Some researchers have suggested that Option A is unnecessarily complex due to its use of different amounts and types of medications at different stages of the pregnant woman’s care. The Option A guidelines also advised different medication guidelines for the infant depending on the way the woman chose to feed the infant. If the HIV-positive woman chose to breastfeed the infant, then she would have to give the infant nevirapine up until one week following the final time she breastfed her infant. Instead of breastfeeding, other feeding method options included using formula, animal’s milk, or the use of an HIV-negative wet nurse who could breastfeed the infant instead of the HIV-positive mother. If the woman chose any of those methods to feed the infant, the infant must take nevirapine for four to six weeks post birth. Lending to its complexity, Option A required medical practitioners to become fully educated on when and how to provide the woman and infant different medications at different times depending on the stage of pregnancy and the long-term feeding method. Furthermore, researchers found women were less likely to adhere to the medication regimen upon returning home following delivery due to its complexity. However, according to WHO, many countries initially chose to implement Option A over Option B based on the low medication costs and ease of adding the guidelines to existing guidelines for maternal HIV care.
Option B is a different WHO regimen used to prevent MTC transmission of HIV that WHO also advised in 2010. Option B does not require medical professionals to provide pregnant women with different medications or different doses at varying times throughout the pregnancy. The woman takes the same type of medications and doses at all stages, and all infants are given the same medications regardless of the feeding method the woman chooses. While the treatment is still the same, Option B offers some flexibility on the different medication combinations available, based on access and availability restrictions in differing countries. The only requirement is that the regimen must be a triple-drug therapy, also known as a highly active antiretroviral therapy. Whichever combination therapy the pregnant woman begins, the guidelines advise that she should continue to take that same drug therapy during her pregnancy and delivery and that the doses and medications should not change. If the woman decides to breastfeeding, then she should continue the medications until one week after she chooses to stop breastfeeding. The infant, in Option B, would receive NVP or AZT daily for four to six weeks post birth, regardless of the feeding method the woman chooses.

According to a study conducted in 2014 and published in the *Current HIV/AIDS Report*, Option B is a more effective treatment plan as compared to Option A. Option B is easier for medical professionals to administer since the medications do not change and is easier for the patients as they typically only need to take medications once daily, which makes the patients more likely to adhere to the simpler regimen. Though Option B is more expensive to initially implement, researchers have determined that Option B is less costly than Option A over the course of four years. That is because Option B is more effective than Option A, thereby resulting in fewer new HIV infections that would require more money to treat.

Option B+ is the most recent WHO guideline on the prevention of MTC transmission of HIV, released in 2012. Option B+ is similar to Option B in many ways but does not require a woman to take a CD4 test for immediate eligibility. However, if the woman is HIV-positive, she is advised to begin triple drug therapy immediately, regardless of how many weeks she has been pregnant. Also different with Option B+ is that the woman will receive that same medication regimen for the rest of her life rather than just during and briefly following pregnancy. Some researchers have suggested that the change to recommend medications for the rest of the woman’s life has decreased the overall maternal mortality rate in countries using Option B+ as well. The infant’s medication and dose do not change depending on the woman’s chosen feeding method and the infant receives either NVP or AZT for four to six weeks post birth.

Option B+ best supports many WHO guidelines to test and treat, which means if an individual tests positive for HIV, they will automatically qualify to receive antiretroviral therapy for life. By preventing MTC transmission of HIV, the medication also treats the woman’s own HIV infection regardless of her initial CD4 count. If she continues to take that medication, her HIV level may eventually become undetectable, meaning she will be unable to transmit HIV to anyone, including her offspring and sexual partners. In Option A and Option B, only a woman who is very close to progressing to AIDS qualifies for lifelong treatment based on CD4 blood values. That means that her immune system is already compromised when she begins taking the medication, leaving her more susceptible to other infections since it takes time for her CD4 count to return to a higher amount. If an individual has progressed to AIDS and does not receive treatment, they typically only live for about three years following their AIDS diagnosis. That time estimate further decreases significantly if the individual contracts an infection, like tuberculosis or syphilis.

By 2015, the implementation of Option B+ in countries around the world resulted in over ninety-one percent of the 1.1 million women who received antiretroviral therapy during pregnancy being offered to continue antiretrovirals for the rest of their lives. Option B+ is more readily accessible and applicable to women living in a variety of circumstances. With Option B+, the pregnant woman does not need to obtain a CD4 test prior to beginning medication. Further, Option B+ aligns with the WHO’s test and treat initiative, which focuses on testing individuals for HIV and immediately providing counseling and treatment for that individual. The WHO goal for Option B+ was to bring about global elimination of pediatric HIV, or HIV in children, by 2015.

In 2016, WHO changed its guidelines on HIV management and prevention to recommend that all HIV-positive patients receive antiretroviral medications, regardless of CD4 count. In 2018, 37.8 million individuals were living with HIV. Of that number, 2.8 million were children up to eighteen years of age. However, according to the WHO reports, in 2012 twenty-two countries’ ministries of health in sub-Saharan Africa approved the use of either Option A, Option B, or Option B+ guidelines. Those countries all are reported by the WHO to have a significantly high prevalence of HIV. Of the twenty-two countries, ten adopted Option A, six Option B, and six Option B+. Recent reports as of 2019 by the WHO state that three of the countries who initially implemented Option A are now switching to Option B+. Though more research is necessary on the overall long-term efficacy of Option B+, as of 2021, WHO continues to recommend Option B+ as a means of decreasing the rates of MTC transmission of HIV.

**Sources**


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