SECTION 3

3

Care for mothers and babies

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KEY MESSAGES

- Gender inequality and women's unique biology make them especially vulnerable to HIV-infection.
- Breastfeeding is not detrimental to the health of women living with HIV.
- Universal HIV treatment, care and support provides the means to cut new infection rates and scale up prevention of vertical transmission to the next generation.
- Women need protection from HIV infection, access to contraception and HIV-testing.
- Mothers living with HIV need access to ARVs, and care and support for themselves and their babies.
- Exclusive breastfeeding for six months, with an appropriate antiretroviral regimen (ART) and continued breastfeeding with adequate complementary foods to up to 24 months or beyond is the safest feeding option, leading to maximum HIV-free survival in most low-income settings.
- The introduction of lifelong treatment for all pregnant women living with HIV is an opportunity to prevent (or reduce) paediatric HIV-infection and rethink how we provide services for the long-term retention in care of infants and children as well as mothers.
- The extremely low risk of postpartum transmission with exclusive breastfeeding when mothers living with HIV with an undetectable viral load are adherent to their antiretroviral regimens (ARVs) permits support for exclusive breastfeeding in resource-rich settings.
- In the absence of any intervention, in countries where extended breastfeeding is the norm, some 35% of children of mothers living with HIV will themselves become infected during pregnancy, labour, birth or breastfeeding. About 90% of HIV-infection in infants and children occurs as a result of such transmission.
- In generalised epidemic settings, infants and children with unknown HIV status who are admitted for impatient care or attending malnutrition clinics should be routinely tested for HIV.

3.1 HOW HIV AFFECTS WOMEN'S LIVES

Inequities in HIV care and support

Biology alone does not explain the vulnerability of young women and adolescent girls to HIV, which is also due to gender inequality and power imbalances (UNAIDS, 2015).

- Women often have little choice about contraception;
- In many countries the rate of girls contracting HIV is still much higher than boys at the same age. They are twice as likely as men to become infected through unprotected sex (De Cock et al., 2000);
- Women are often unable to negotiate condom use and are more likely than men to be subjected to non-consensual sex (UNAIDS, 2011a);
- They are less likely than men to receive treatment for other sexually transmitted infections, or they receive treatment later, increasing their risk for HIV infection (UNAIDS, 2011a);
- However, since 2010, the reduction in AIDS-related death among adult women (with a 33% decrease) has been greater than in adult men (with a 15% decrease) (UNAIDS, 2016b).

How HIV affects women in society and the communities in which they live

Marriage and motherhood

The gender gap in relation to treatment drives the impact of the HIV epidemic. Normally men delay initiation of HIV treatment, with reduced adherence to treatment in comparison to women. This in turn impacts the preventive effects of treatment, and results in men accounting for 58% of adult AIDS related death (UNAIDS, 2016c).

On the other hand, a woman may be the first person in the family to find she is HIV-infected. HIV usually enters a family through her sexual partner, often the baby's father, and the single largest risk factor for many women is being married. Couples are less likely to use condoms during pregnancy and a new HIV infection often occurs at this time, i.e. during late pregnancy .Transmission of HIV to the unborn baby and through breastmilk is more likely during the early period of infection, when there is more virus in the woman's blood (Johnson et al., 2012; Drake et al., 2014).

Fear of disclosure and stigma

Stigma and reluctance to disclose her status may mean that a woman avoids being tested for HIV, or declines treatment. If mixed or shared feeding is common, she may be afraid to exclusively breastfeed in case people ask questions. Expressing and heat-treating breastmilk would also be very difficult unless a mother's family knows why she is doing it (Little et al., 2012).

Social circumstances and discrimination

HIV infection can make a woman ill, compromising her capacity to work, reducing her income and ability to buy food, and her nutrition and immunity. Poor nutrition in turn undermines her adherence and response to ARVs and hastens the development of AIDS-related illnesses.

Women whose partners die of AIDS may be blamed for their husbands' illness, leading to discrimination and abandonment. Their lower status in the family and community make it less likely for them to have access to health care including ARVs. Many women may have decisions made for them by husbands or by women of higher status in the family.

Mothers may have limited choices about infant feeding; both artificial feeding and exclusive breastfeeding may expose their HIV+ status, subjecting them to stigma.

Some countries still have immigration restrictions on entry, stay and residence in relation to HIV. The Joint Programme of the United Nations continues to support countries such as Republic of Korea, Moldova and Mongolia to review and remove restrictions related to HIV (UN, 2015).

Women's reproductive aspirations and choices

With increased likelihood of child survival in the context of HIV, increasing numbers of women living with HIV on every continent wish to have children. In developed countries pregnancy rates among these women are rising (French et al., 2012; Huntington et al., 2013) and they are expressing the wish to give birth vaginally, as well as to breastfeed (Walls et al., 2010; Greene et al., 2015).

Women living with HIV can safely and effectively use most contraceptive methods and access to family planning will help them to make the best reproductive choices. However, ARVs can decrease or increase the bioavailability of steroid hormonal contraceptives (Patel et al., 2010).

Notwithstanding initiatives to limit unwanted pregnancies as a means of reducing vertical transmission to infants, women living with HIV increasingly want to fulfil their desire to have children.

The special risk of pregnancy

In a systematic review and meta-analysis of research published from 1980 to 2013, Drake et al. (2014) found that pregnancy and the postpartum period are times of particular HIV risk, with rates similar to "high risk" cohorts. Pregnant women living in regions where HIV infection is common should be:

- offered repeat HIV testing (using sensitive methods to enhance early detection of infection) during pregnancy and in the postpartum period to detect incident HIV infections.
- promptly referred to HIV care and treatment.
- counselled on the need to use condoms to prevent transmission during this period of their lives.

3.2 INTERVENTION AND TREATMENT FOR WOMEN LIVING WITH HIV

Infant feeding interventions employed to reduce/eliminate the risk of perinatal transmission of HIV

Current early interventions to prevent HIV transmission during birth

Although the risk of transmission of HIV in untreated mother-baby pairs within 24 hours of labour and delivery is as high as it is during 24 months of breastfeeding, practical concerns have determined the focus of prevention of mother-to-child (PMTCT) programmes.

- Current early interventions to prevent HIV transmission during birth in industrialised countries:
  - Routine caesarean section delivery to reduce the risk of peri partum transmission.
  - Vaginal delivery in case of viral load <50 copies mm^3 (Wax, 2006; De Ruiter et al., 2008; Havens et al., 2009).
  - Antiretroviral prophylaxis and therapy.
  - Complete avoidance of breastfeeding.
  - In the US, women are only advised against vaginal delivery if they have a viral load exceeding 1000 copies/mm^3 (Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission, 2017).

- Current early interventions to prevent HIV transmission during birth in developing countries:
  - Vaginal birth with interventions such as vaginal lavage.
  - Avoidance of invasive practices such as premature rupture of membranes and routine episiotomy.
  - Avoidance of foetal electrode.
  - Avoidance of oral suctioning of the infant after birth (Mofenson, 1994; Landesman et al., 1996; De Ruiter et al., 2008).
  - Caesarean section has not been readily available or routinely offered in developing, high HIV-prevalence countries due to cost constraints and concerns about the high risk of infection.

Birth practices

Recent research indicates that when women living with HIV receive adequate combination ART to achieve a viral load below 50 copies/ml (considered undetectable), then having a vaginal delivery does not increase the risk of HIV transmission ((BHIVA & NAM, 2013)). In the US, women are only advised against vaginal delivery if they have a viral load exceeding 1000 copies/ml (Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission, 2017).

Postnatal prevention ARV

Different approaches to postnatal ART

In developing countries, postnatal prevention has taken two different approaches:

- Triple drug combination ART (also known as Highly Active Antiretroviral Therapy (HAART) to the breastfeeding woman to maximise her health and suppress HIV viral load in blood and breastmilk; or
- ARV prophylaxis for the breastfeeding infant.

Prior to 2010, NVP for breastfed infants was recommended as an alternative prophylactic strategy for mothers with moderate to high CD4 cell counts who did not require long-term HAART for their own health, administered as follows (Becquet & Ekouevi, 2011):

- maternal zidovudine prophylaxis from the second trimester of pregnancy until delivery; and
- daily oral nevirapine to the breastfed infant until all breastfeeding has ceased.

Since 2010, either maternal and/or infant prophylaxis has been recommended to be continued until one week after all breastfeeding had ceased (WHO et al., 2010).

Concerns have been expressed about the long-term risks to healthy, uninfected infants, of unnecessary ART prophylaxis administered over many months (BHIVA & CHIVA et al., 2011; Palombi et al., 2011b).The HPTN 046 trial results (Coovadia et al., 2012) confirm that long-term infant NVP offers no additional benefit for infants born to mothers receiving HAART.

A recent modelling paper computes that if mothers receive HAART while breastfeeding, the monthly postnatal transmission risk is assumed to be reduced by 80%. If the mother does not receive HAART while breastfeeding, but the infant receives extended nevirapine prophylaxis, the rate of transmission is estimated to be reduced by 60% (Johnson et al., 2012).

Long-term maternal ARV interventions

In the USA and Europe, where women living with HIV have been treated with a combination of ARVs from early in pregnancy, longer treatment duration has been found to be significantly more effective than shorter regimens in reducing viral load, reducing the risk of transmission during pregnancy and delivery to as low as 1-2% (Townsend et al., 2008a).

For breastfeeding mothers, a combination of ARVs used earlier in pregnancy had greater efficacy in preventing transmission than the same combination starting during labour and delivery. Maternal HAART has been shown to reduce postnatal HIV transmission four-fold compared to sdNVP, even in times of severe socio-economic crisis (Thistle et al., 2011).

- Viral load at enrolment and shorter duration of HAART before delivery have been significantly associated with infant infection, whereas extended maternal or infant treatment or prophylaxis showed reduced postnatal HIV transmission through breastfeeding (Zash et al., 2017) even up to 12 months (Ngoma et al., 2011) or up to 24 months (Ngoma et al., 2015).
- The Kesho Bora Study Group (2011) and other trials (Chasela et al., 2010; Shapiro et al., 2010), found that maternal triple ARV prophylaxis starting from the second trimester of pregnancy until all exposure to breastmilk ends, significantly reduces transmission of HIV to infants exposed to HIV through breastmilk.
- A paper by Chibwesha et al. (2011) showed that the full effectiveness of ART in preventing vertical transmission was only achieved by maternal adherence to ART for at least 13 weeks prior to

delivery, which results in an undetectable viral load. The study found that women on ART for <4 weeks had a 5.2-fold increased odds of transmission.

Between 2010 and 2014 antiretroviral recommendations for pregnant women evolved. In 2010 the following recommendations were made for all pregnant women in need of ART for their own health, i.e. those with a CD4 count of <350 cells/mm^3 (WHO, 2010a):

- ART was recommended for women known to be living with HIV, and their infants, for their own health, to improve their survival and to reduce HIV transmission through breastfeeding, beginning in early pregnancy and, for the first time, continuing throughout the breastfeeding period.
- Many women continued to receive sub-optimal drugs such as single-dose Nevirapine as the main HIV prophylaxis. It was recommended that this must be phased out as a matter of priority.
- Infants found to test HIV-positive were recommended to start immediate ARV therapy, even if asymptomatic.
- The benefit of ART for the health of the woman was stated to outweigh any potential risks for the well-being of the foetus and of potential drug toxicity, drug resistance and additional cost.

In April 2012 WHO updated the 2010 guidance (WHO, 2012c) recommending that:

- Triple-therapy ARVs should be provided to the pregnant woman starting from the antenatal period.
- Maternal ART should be continued for life.

ART recommendations for pregnant and breastfeeding women

Universal and lifelong ART

Most countries are moving to adopt universal ART for all pregnant women and breastfeeding women living with HIV. The benefits of lifelong ART, Option B+, for pregnant and breastfeeding women include (WHO, 2016c):

- improved maternal and infant health outcomes.
- lower rates of vertical HIV transmission.
- the potential for reduction of horizontal transmission.

Providing all pregnant women with lifelong ART regardless of CD4 count/disease stage (WHO, 2016c) could be the most effective option to prevent both HIV transmission and resistance, assuming adherence and retention are successfully maintained. This strategy is more likely to achieve sustained undetectable HIV viral load, does not involve ART interruptions, is simpler to implement, and is cost-effective (Paredes et al., 2013).

Anticipating that earlier treatment could avert an additional 3 million deaths and prevent 3.5 million more new HIV infections by 2025, and reduce vertical transmission of HIV to between 2 and 5%, consolidated treatment guidelines were issued by WHO in June 2013 (WHO, 2013a) and up-dated in July 2016 (WHO, 2016c).

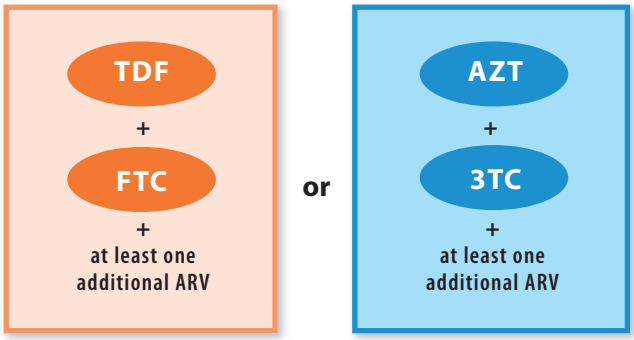
Globally, mounting evidence (Goosby, 2013) supports earlier treatment (known as Option B+) as the next step for a combination prevention intervention that:

- prevents HIV transmission to infants.
- minimises transmission to uninfected sexual partners.
- averts orphanhood.
- protects maternal health.

Concerns about safety of ART regimens during pregnancy

A study from Botswana shows that certain antiretroviral treatment regimens in pregnancy may have adverse birth outcomes (Zash et al., 2017). The study suggests the ART mechanism at the placenta level, for instance, ZDV-3TC-NVP and ZDV-3TC-LPV-R may be linked to adverse birth outcomes such as stillbirth, preterm birth, neonatal death and very preterm birth compared to infants exposed to TDF-FTC-EFV.

Summary of recommended ART combinations for pregnant women living with HIV-1 to reduce the risk of HIV vertical transmission – according to the US Department of Health and Human Services and the British HIV Association (Siemieniuk et al., 2017):



Source: Siemieniuk et al. (2017)

TABLE 1: Summary of current preferred ART regimens for adults, pregnant or breastfeeding women

First-line ART	Preferred first-line regimens	Alternative first-line regimens
Adults	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + DTG[1] TDF + 3TC (or FTC) + EFV_{400}[1,2] TDF + 3TC (or FTC) + NVP
Pregnant or breastfeeding women	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + NVP

[1] Safety and efficacy data on the use of DTG and EFV_{400} in pregnant women, people with HIV/TB coinfection and adolescents younger than 12 years of age are not yet available.

[2] EFV at lower dose (400 mg/day)

3TC lamivudine, AZT zidovudine, DTG darunavir, EFV efavirenz, FTC emtricitabine, NVP nevirapine, TDF tenofovir

Source: WHO (2016c)

ART recommendations for breastfeeding women

It has been shown that exclusive breastfeeding is much safer than mixed feeding, and should be encouraged even in settings where ART for either the mother or infant is not readily available, but that HAART could drastically reduce the risk of transmission of HIV through breastfeeding (Slater et al., 2010).

Appropriate long-term ARV maternal/infant treatment and/or prophylaxis while breastfeeding and beyond has the potential to:

- reduce viral load and improve the health of HIV-positive mothers in the short-term.
- extend the life-span of women living with HIV to almost normal.
- reduce vertical transmission of HIV during pregnancy, birth and breastfeeding for 24 months.
- reduce the risk of horizontal transmission in serodiscordant couples where one partner is not HIV-infected.

Duration and adherence to ART

The effectiveness of full ART in preventing vertical transmission by HIV-infected individuals is achieved by:

- strict adherence to ART.
- early initiation and lifelong ART (WHO, 2016c), e.g. 13 weeks duration of ART to lower viral levels to undetectable (Chibwesha et al., 2011).

The existing emphasis on maternal interventions has meant that follow-up of their infants is often poor, especially when they stop breastfeeding between 12 and 24 months.

The introduction of lifelong treatment for all pregnant women living with HIV is an opportunity to rethink how services are provided for the long-term retention in the care of infants and children as well as mothers (Sugandhi et al., 2013).

According to a study on "Retention in care under universal antiretroviral therapy for HIV infected pregnant and breastfeeding women ('Option B+') in Malawi", each year over a million infants are born to HIV-infected mothers and lack of follow-up may affect as many as half of all mothers and infants in PMTCT programmes" (Tenthani et al., 2014).

Implementing current guidelines – a win-win situation

Underpinning current guidance is up-to-date research which shows that appropriate ARV regimens for women living with HIV in all epidemic settings:

- improve their health.
- prevent vertical HIV transmission.
- prevent HIV transmission from a woman to her sexual partner.
- allow a couple to live a normal life-span.
- reduce their infectivity to their babies during pregnancy, birth and breastfeeding.

These findings finally permit modification of previous PMTCT initiatives where women were provided with ARVs during pregnancy, delivery and breastfeeding, only to have this life-saving medication withdrawn as soon as the baby was born. Today there is firm evidence to show that with lifelong ART, it is no longer necessary for mothers living with HIV to relinquish breastfeeding as an important and satisfying way of mothering their babies.

Current recommendations for a return to breastfeeding with maternal ART and infant prophylaxis have been carefully compiled based on accumulating evidence over the last decade. They have been designed to enhance the health and survival of both pregnant and breastfeeding women living with HIV and their HIV-exposed infants. For the first time, elimination of postnatal transmission, even in resource-limited settings, is an achievable goal only awaiting implementation.

3.3 BENEFITS OF BREASTFEEDING FOR MOTHERS

When a mother breastfeeds, she decreases her risk of developing (Victora et al., 2016):

1. Diabetes (both gestational as well as type 2)
   - Breastfeeding may also reduce the mother's risk of type 2 diabetes later in life. The longer the duration of breastfeeding, the lower the incidence of diabetes.

2. Overweight and obesity
   - A longer duration of breastfeeding may contribute to reducing the risk of postpartum weight retention under non-HIV circumstances, although evidence is not conclusive;
   - Studies suggest that breastfeeding up to a 6-month postpartum period is not detrimental for postpartum weight among well nourished HIV-infected mothers at intermediate-disease stage. In the absence of breastfeeding or after weaning, triple antiretroviral prophylaxis is associated with weight gain among women with high BMI, even after cessation of prophylaxis. (Cames et al., 2014; Chetty et al., 2014).

3. Osteoporosis
   - Cross-sectional studies indicate that women with many children and a long total period of lactation have similar or higher bone mineral density and similar or lower fracture risk than their peers who have not given birth and not breastfed.

4. Breast cancer, ovarian cancer and uterine cancer
   - There is a consistent protective effect against breast cancer, with a 4.3% reduction per 12 months of breastfeeding in the better controlled studies;
   - There is suggestive evidence of a protective effect of breastfeeding against ovarian cancer.

5. Hypertensive and cardiovascular diseases
   - Formula feeding mothers have higher BP levels in the initial postpartum period. They are also at increased risk of developing hypertension, hyperlipidaemia, and cardiovascular disease later in life.
   - More breastfed children and longer duration of breastfeeding were associated with lower risk of hypertension in postmenopausal women, and degree of obesity and insulin resistance moderated the breastfeeding-hypertension association.

6. Maternal depression
   - A qualitative review of 48 studies showed clear associations between breastfeeding and reduced maternal depression, but it is more likely that depression affects breastfeeding than the opposite.

7. Reduced child spacing
   - Consistent effect on prolonging lactational amenorrhoea, especially for exclusive or predominant breastfeeding.

3.4 HEALTH CARE AND NUTRITION REQUIREMENTS FOR WOMEN LIVING WITH HIV

Care for the mother's health and nutrition when living with HIV

- Good general health and nutrition support for the mother living with HIV helps her to experience fewer side-effects from her ART medications, to have a stronger immune system and to care for her baby. There is little evidence of harm to the mother's health if she continues breastfeeding. In fact, research indicates that there are advantages to women's health due to breastfeeding, such as increased birth spacing, protection from breast and ovarian cancer, type 2 diabetes, osteoporosis, and heart disease. Studies from high income countries also show reduced risk of maternal depression and weight retention (Victora et al., 2016);
- Services in the community which are close to where women live, should be available to assist uninfected women to remain HIV-negative. This is especially important during pregnancy or lactation, to avert the high risk of vertical HIV infection to infants during a new maternal infection (Johnson et al., 2012);

- Mothers whose status is unknown should be offered HIV testing periodically (WHO, 2016c);
- Mothers who are HIV-uninfected should be counselled about ways to prevent HIV infection and about the strategies available such as condom use, to help them remain uninfected. Every man and woman needs to know that unprotected sex can expose them to HIV infection, and babies would be in turn be exposed to HIV infection;
- Sexually transmitted infections (STIs) family planning service (WHO, 2016c) can be integrated within HIV care settings;
- Tuberculosis treatment services can be included in the PMTCT package;
- Where HIV testing is not available, and if, for this or any other reason, mothers do not know their HIV status, then breastfeeding is the recommended feeding method in all populations, since avoiding breastfeeding for all infants would increase overall child mortality;
- A severely ill woman living with HIV or AIDS with a CD4 count of <200 cells/mm^3 is more likely to have higher levels of virus in her breastmilk and to transmit the infection to her baby through all routes. ARVs can help to reduce her viral load and keep her CD4 cell count high. With higher CD4 cell counts, i.e. >500 cells/mm^3, the risk of transmission is lower. Guidelines released in June 2013 recommend that countries use HIV viral load as the preferred approach to ART monitoring (Doherty et al., 2013). The WHO 2013 consolidated guidelines recommend commencing ARVs for all HIV-infected pregnant women beginning in the first trimester and continuing this therapy for life (WHO, 2012c). Furthermore, according to the WHO 2016 consolidated guidelines, all efforts should be made to reduce the time between HIV diagnosis and ART initiation (WHO, 2016c).
- A woman newly diagnosed with HIV in late pregnancy or in the early postpartum period can be offered the option of feeding her own heat-treated expressed breastmilk to her baby pending sufficient duration of ARV therapy to reduce her viral load.

Key information to decrease the potential of transmitting or acquiring HIV include:

- reducing the number of sexual partners.
- ideally having a sexual relationship with only one partner who is faithful and monogamous.
- additional screening for STIs such as hepatitis B and syphilis (WHO, 2016c).
- using a condom correctly, including the option of a female condom (Femidom), for every occasion of sexual intercourse.
- HIV-prevention counselling for HIV-negative pregnant women in early pregnancy and in the early postpartum period (WHO et al., 2011).
- ART for an HIV-infected partner.
- male circumcision (NIAID, 2006).
- home testing to improve participation of males and children, and reduce the possibility of stigmatisation.
- mandatory HIV testing (CDC, 2017a).

Nutritional requirements for women living with HIV and ways to improve nutritional status

General nutritional requirements

Good nutrition is very important for long-term health and well-being. Studies have found that people living with HIV who have a healthy diet and good nutritional status can better tolerate HIV drugs, maintain a healthy weight, and feel better overall (The Well Project, 2016). Good nutrition depends on many things, including:

- what type of food you eat and how much.
- how you digest and absorb nutrients.
- how different parts of your body use these nutrients.

HIV-related changes in any of these factors can affect your nutritional status. Over time, this can lead to a variety of nutritional problems, including:

- weight loss.
- muscle wasting (loss of muscle).
- high levels of fats and sugars in the blood.
- not enough vitamins and minerals.
- many of these HIV-related problems can be avoided, or managed, by eating the right foods.

A healthy diet is a key part of any HIV treatment plan. A diet is simply any food and drink that you consume regularly. Your diet should give you the nutrients you need to:

- fight weight and muscle loss.
- keep energy levels high.
- help you get what you need from medications you take.
- minimise the negative impact of HIV drugs.

Ways to improve nutritional status

Maintain a healthy weight

Eat more complex carbohydrates (also called starches). Complex carbohydrates are a good source of energy, and often contain more fibre and other nutrients than simple carbohydrates. Complex carbohydrates include whole grains, beans (legumes), starchy vegetables like corn and potatoes, and brown rice.

Fight muscle loss

Eat More Protein. Protein (along with physical activity) helps your body build and maintain muscles. During times of infection, protein stored in muscles can get burned as a fuel source. Eat at least three servings of protein every day. Foods high in protein include lean meats, fish, cottage cheese and yogurt, eggs, beans, chickpeas, soybeans, and nuts.

Maintain gut health

Consume enough fibre, water, fruits, and vegetables. Foods high in fibre can help keep your bowel movements regular and support gut health. These include oats, lentils, chickpeas, beans, fruits and vegetables, prunes and apricots. Water (8-10 8-oz cups a day, or about two litres) helps you digest and eliminate waste. Drinking more water can help you avoid dehydration and constipation, and reduce the side effects of medications.

3.5 RISK FACTORS FOR TRANSMISSION OF HIV TO INFANTS

When does transmission of HIV to infants occur?

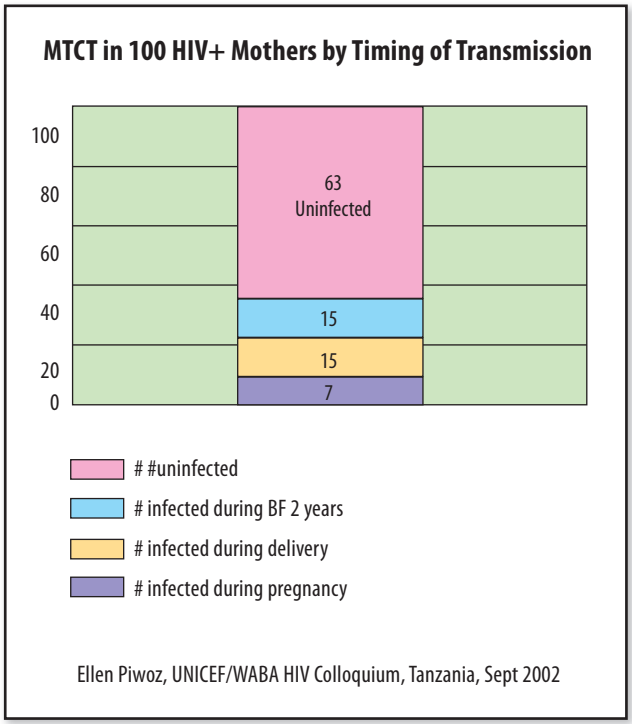
With no interventions, such as not giving any ARV drugs or avoiding breastfeeding, ~30-40% of infants born to HIV-positive mothers may be infected during:

- pregnancy.
- birth.
- after birth, during breastfeeding (Luzuriaga & Mofenson, 2016).
- after birth, by HIV-positive adults feeding infants premasticated foods (Maritz et al., 2011).

Knowing the facts on HIV transmission to infants

Even without any intervention, most babies are not infected. More than half of infants of HIV-positive mothers who become infected themselves (approximately 15 to 25% of all exposed infants) are infected before and during birth; somewhat less than half (5 to 20% of all exposed infants) will become infected through breastfeeding (De Cock et al., 2000). See Figure 1 for details.

FIGURE 1: Relative contribution of each route of transmission of HIV to infants and Young children, 2002



Source: Piwoz (2002)

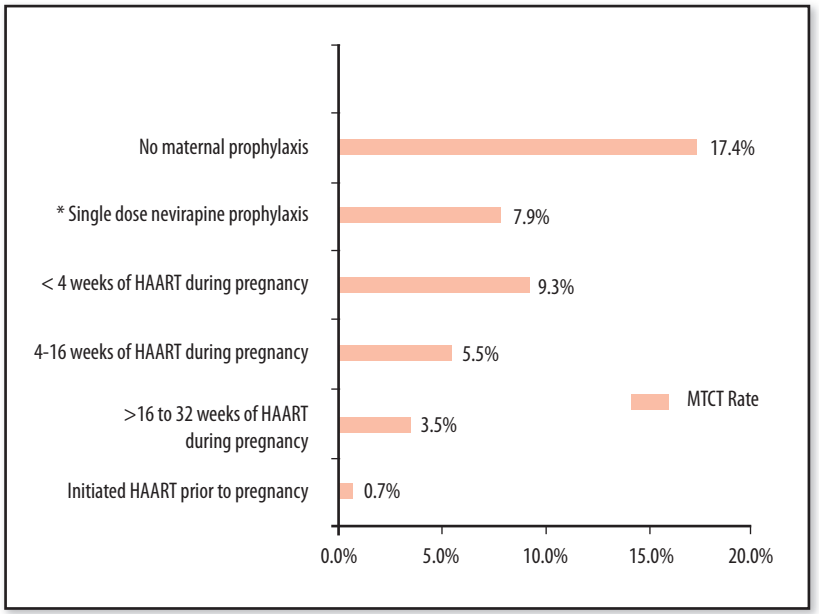
Factors which increase the risk of vertical transmission – during pregnancy, labour, birth and breastfeeding

During pregnancy

The risk is increased if the woman:

- is already HIV-infected, but remains untreated (Hoffman et al., 2010), as shown in Figure 2.
- has a high viral load, e.g. >3500 copies/mm^3 and/or low CD4 count (<200 cells/mm^3) (Garcia et al., 1999).
- becomes newly infected/seroconverts during pregnancy (Johnson et al., 2012).

FIGURE 2: Risk of vertical transmission (infant HIV DNA positive at 4-6 weeks) among women receiving ART before or during pregnancy compared with those receiving single-dose nevirapine or no maternal prophylaxis



Source: Hoffman et al. (2010)

During labour and birth

Birth practices for untreated mothers which increase the risk of vaginal secretions infecting the baby during delivery (Mofenson, 1994; Landesman et al., 1996; De Ruiter et al., 2008)

- rupture of membranes for more than 4 hours.
- assisted delivery with vacuum extractor or forceps.
- episiotomy, or other breaks in the woman's skin.
- foetal monitoring that breaks the infant's skin.
- suctioning the newborn or other early infant oral surgical procedures e.g. division of ankyloglossia.

Definition of High-risk infant (WHO, 2016c)

- Infants born to women with established HIV infection who have received less than four weeks of ART at the time of delivering; or
- Infants born to women with established HIV with viral load >1000 copies/mL in the four weeks before delivery, if viral load measurement is available; or
- Infants born to women with incident HIV infection during pregnancy or breastfeeding, or
- Identified for the first time during the postpartum period, with or without a negative HIV test prenatally.

3.6 INFANT TESTING AND ACCESS TO CARE

Early infant screening

The optimal timing of testing to diagnose HIV infection in infants depends upon:

- when infection occurs (in utero, intra partum or postpartum during breastfeeding).
- test performance.
- mortality risk by age.
- retention in the testing and treatment cascade.

A definitive diagnosis of HIV infection among children younger than 18 months can only be confirmed with virological testing. Simplified testing technologies open the possibility of earlier infant diagnosis and treatment. HIV-exposed Infants should have virological testing at 4 to 6 weeks or at the earliest opportunity thereafter, and ART should be initiated without delay in those testing positive (WHO, 2014a).

For infants who have negative virological testing results, the definitive diagnosis of HIV infection should be determined when HIV exposure (usually through breastfeeding) ends. At this time, serological testing should be used (WHO, 2014a).

In a South African study of 883 mothers and their infants it was found that 81.3% of HIV-infected infants who died were infected by 3 weeks of age. Of infected infants, 28% died before 6 weeks and 56.7% died by 12 weeks. A greater focus on prevention of early infection, earlier screening for HIV infection and access to ART for infected infants is needed (Chopra et al., 2010).

Guidance to reduce the number of children newly infected

The remaining challenge is to eliminate new HIV infections among children and reduce maternal death. In order to achieve the global goal of reducing the number of children newly infected, 90% of pregnant women need to receive measures such as primary

prevention of HIV, access to family planning and linking pregnant women and children with HIV treatment and care (UNAIDS, 2010c).

In 2008, results from two randomised clinical trials demonstrated that providing daily NVP to the breastfeeding infant offered protection against HIV infection (Kumwenda et al., 2008; SWEN study team, 2008). However, once NVP was withdrawn, transmission risk returned unless mothers were receiving HAART.

With increased duration of prophylaxis, extended NVP administered to breastfeeding infants for 6, 14 or 28 weeks was shown to result in reduced postnatal transmission at 6-9 months, though results varied greatly among the trials:

- To 6 weeks - 6.9% (SWEN study team, 2008).
- To 14 weeks - 5.2% (Kumwenda et al., 2008).
- To 28 weeks - 1·1% (Coovadia et al., 2012).

A study showed very low rates of transmission (1.4% and 1.5%) when infant ART prophylaxis with either Kaletra or 3TC was provided for 12 months (Nagot et al., 2012).

HIV Drug Resistance (HIVDR)

There have been concerns about the emergence of viral resistance in women interrupting ARV drugs, particularly NVP. Resistance can have important clinical implications after the demonstration that women previously exposed to single-dose nevirapine (NVP) and harbouring resistant mutations had an inferior virological response. Research conducted on women receiving ART for 6 months in Malawi to prevent postnatal MTCT found that overall, the risk of developing resistant mutations in compliant women was low (Palombi et al., 2011a). In women adhering to a HAART regimen, there is much less risk of resistance developing.

Drug resistance can fuel the AIDS epidemic by compromising HIV treatment success and scale up (Palombi et al., 2011a).

Women can have HIV drug resistance due to previous exposure to PMTCT ARV regimens followed by lack of continuation of adherence to ART (WHO, 2017f).

IMPORTANT! HIV drug resistance is becoming more common. It is important to identify critical areas and implement actions to combat the threat of HIV drug resistance threat (WHO, 2017f).

FIGURE 3: Global goals, plans and strategies aligned with the Global Action Plan on HIV drug resistance

Source: UNAIDS (2017d)

Do maternal antiretroviral drugs transfer to the infant?

Antiretroviral levels in infant plasma, cord blood, and breastmilk reflect recent exposure. Hair concentrations reflect cumulative exposure and can uniquely quantify in utero transfer of maternal medications to the foetus.

Table 2: Factors that can drive drug resistance

What can drive drug resistance (WHO, 2017f; WHO, 2017g)			
Virus	**Patient**	**Clinic**	**Programme**
HIV Subtype Replication capacity Genetic mutations Low potency Drug-drug interaction	Poor tolerability Low genetic barrier to resistance Poor adherence to drugs Stigma and discrimination Barrier to treatment access e.g. cost, travel distance, transport, parental consent	Interrupt drug supply Sub optimum support to treatment adherence Poor treatment retention Limited use of viral load testing Delays in switching in ART failure	Gaps in ART service delivery such as access to viral load testing Drug procurement & supply management No plan or capacity to monitor and address ART programmes

3.7 INFANTS LIVING WITH HIV AND CHILD SURVIVAL

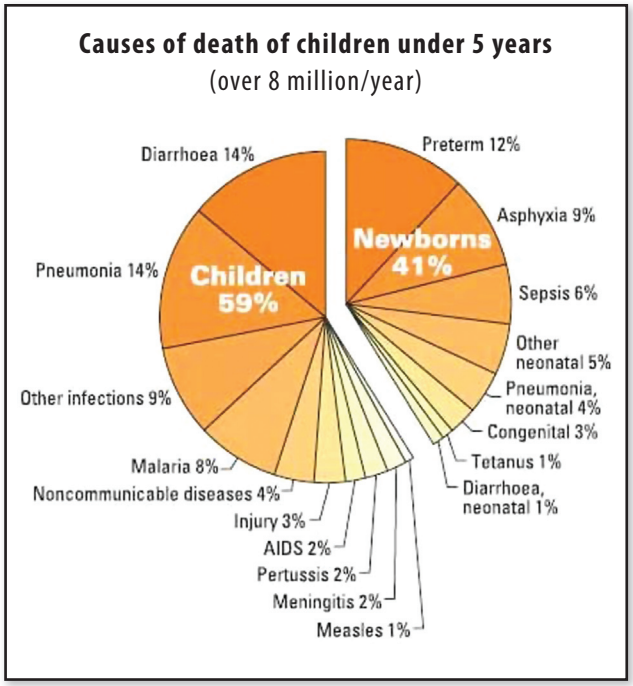
Child survival, a balance of competing risks

Infant feeding and HIV free survival

The most frequent causes of preventable child mortality, against which breastfeeding is protective, are pneumonia, diarrhoeal diseases and under nutrition as an underlying cause (UNICEF et al., 2011).

Programmes designed to prevent HIV transmission to infants have demonstrated that discouraging breastfeeding increases the risk of morbidity and mortality from other childhood illnesses. See Figure 4 for details. Unless safe alternative methods of artificial feeding are available, continuing to promote breastfeeding has been shown to improve HIV-free survival.

FIGURE 4: Global distribution of deaths among children under 5 by cause, 2010

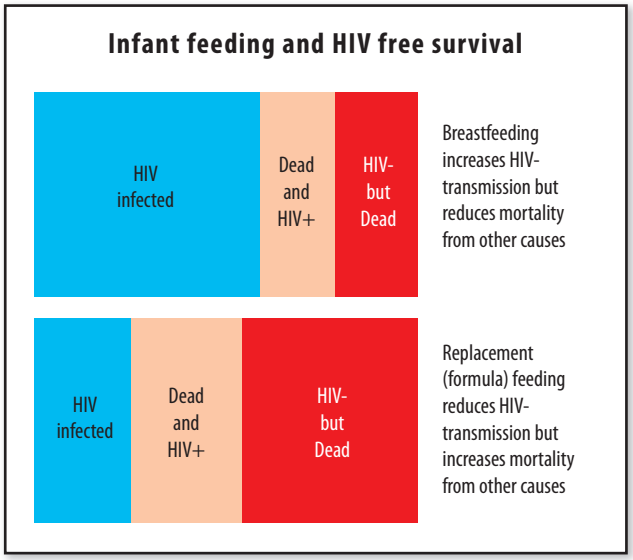


Source: WHO (2010c)

Interventions to prevent HIV transmission

Previously an estimated 300 000 (2%) children died of HIV acquired through breastfeeding and 1.5 million young children died annually because they were not breastfed optimally (WABA, 2007). Thus in 2009, the major focus of global prevention of postnatal transmission of HIV efforts changed its emphasis from promoting breastfeeding avoidance to a new goal of HIV-free survival, meaning that a child is alive and well and has a negative HIV test at a particular time point (WHO, 2009b). See Figure 5 for details.

FIGURE 5: Infant feeding and HIV free survival, 2010



Source: Williams (2010)

The HIV-infected baby

Approximately 20% of babies of untreated mothers living with HIV are born infected. In most circumstances feeding decisions are made prior to knowledge of the child's HIV status. Babies with HIV have an increased risk of acquiring opportunistic infections such as pneumocystis carinii (jirovecii) pneumonia which healthy babies do not get. As well as being a good source of nutrition, breastmilk contains immune factors which provide protection against opportunistic infections, and delay HIV disease progression. Breastfeeding, particularly exclusive breastfeeding, greatly increases the life expectancy of HIV-infected infants (Coutsoudis et al., 2003).

A pooled analysis of 19 children of mothers living with HIV examined their survival according to when HIV infection occurred. It was estimated that 52% perinatally infected children and 26% postnatally infected children would die 1 year after becoming infected versus 4% of uninfected children (Becquet et al., 2012). There has been some success with relactation among women who avoided breastfeeding only to find the infant infected anyway (Nyati et al., 2014).

Recommendation and guidance for baby who is already HIV-infected

Current guidance recommends that mothers of infants and young children known to be infected should be strongly encouraged to exclusively breastfeed for the first six months of life and to continue for two years or beyond (WHO et al., 2010; WHO & UNICEF, 2016).

- In the past it was not easy to quantify the risk of HIV-infection for the breastfed baby because: Breastfeeding itself was often not well defined and frequently of very short duration;
- Little distinction was made between partial or full breastfeeding (Gabiano et al., 1992; The Italian Register for HIV Infection in Children, 1994);
- Testing techniques were insufficiently sensitive to distinguish HIV infection acquired prenatally, perinatally or postnatally (Morrison, 1999a);
- Initial studies comparing overall vertical transmission rates among formula-fed and ever-breastfed infants provided risk estimates between 0-46% (Preble & Piwoz, 2000).

Exclusive breastfeeding provides the perfect food for babies. Breastmilk alone contains sufficient fats, proteins and sugars to enable a baby to grow and thrive for a full six months (Lawrence & Lawrence, 1999). Breastmilk is mostly water (88%) (Linkages project, 2002) and has a low solute load so that a healthy baby does not need extra drinks (Almroth, 1978). Exclusive breastfeeding reduces the risk of infant mortality from other infectious diseases and malnutrition on average by three to six fold in the first six months (WHO Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality, 2000). Exclusive breastfeeding is associated with a three to four fold decreased risk of transmission of HIV compared to non-exclusive (mixed) breastfeeding, due to gut damage caused by other foods and liquids, allowing the virus to be transmitted more easily (Smith & Kuhn, 2000).

How exclusive and continued breastfeeding from 6 to 24 months can maximise infant HIV-free survival

Components of breastmilk which specifically protect against HIV

A study (Friedman et al., 2012) isolated B cell derived antibodies (monoclonal Antibodies CH07 and CH08) from the colostrum of a lactating woman living with HIV. These represent two of the first mucosal-derived antibodies to HIV yet to be reported. They provide protection at mucosal surfaces. This may help explain why most nursing infants of mothers living with HIV are protected from acquiring the virus despite chronic, daily exposure.

- Specific identified protective factors against virus in human milk include: Secretory IgA, IgG, IgM, chondroitin sulphate, β defensins (1-3), lactoferrin, lipids (unsaturated fatty acids and monoglycerides), lysozyme, milk cells, mucin (muc-1; milk fat globulin membrane), ribonuclease and secretory leukocyte protease inhibitor (May & ACLA, 1995);
- The specificity and function of these mucosal antibodies may be distinct from those in plasma (Tuaillon et al., 2009; Permar et al., 2010; Fouda et al., 2011);
- Human milk also contains a glycosamine which is able to inhibit the binding of HIV (gp 120) to CD4, blocking the first step for infection of a target cell. This inhibitory activity was found in colostrum and mature milk samples from both HIV+ and HIV- populations of mothers (Newburg & Yolken, 1992; Newburg et al., 1995);
- One recent study (Wahl et al., 2012) demonstrated for the first time highly reproducible transmission of multiple HIV strains in bone marrow/liver/thymus humanised mice in the oral cavity and GI tract, which can be prevented with antiviral therapy. This research also offered the first in vivo demonstration that human milk can inhibit oral transmission of both cell-free and cell-associated HIV.
- Immunologically active carbohydrates called human milk oligosaccharides (HMOs), the third most abundant component of breastmilk, become concentrated in the mucosal surfaces of the infant's gastrointestinal tract. HMOs are not digestible and act as prebiotics, promoting the growth of desirable bacteria, or probiotics, to protect from HIV transmission. HMOs resemble sugar chains called glycans that are normally found on epithelial cell surfaces and can serve as "decoy" receptors to inhibit HIV binding (Bode et al., 2012).
- Anti-HIV IgG and IgA antibodies have been identified in colostrum from mothers living with HIV, but not from HIV- mothers (Van de Perre et al., 1993).
- It has been suggested that HIV-1 IgM in breastmilk could be protective against postnatal transmission of the virus in three ways (Van de Perre et al., 1993; Morrison, 1999a; Morrison, 1999b):
  - by compensating for a defective secretory IgA response and behaving in a similar way by directly coating viral particles,

- IgM antibodies are strong potentiators of complement-mediated cytotoxicity, of which at least nine components have been identified in human milk, and
- specific IgM could take part in the lysis of infected cells by a mechanism of antibody-dependent lymphocyte cytotoxicity.
- there are several other components of human milk which likely assist with protection against HIV-infection including bile salt-stimulating lipase (BSSL), tenascin-C, and commensal lactic acid bacteria (Martín et al., 2010; Fouda et al., 2013; Liu & Newburg, 2013).

The protective properties of breastmilk

- Human milk, rich in immunoglobulin-secreting B cells that originate in the gastrointestinal-associated lymphoid tissue (Roux et al., 1977; McDermott & Bienenstock, 1979; Tuaillon et al., 2009) has long been known to possess antimicrobial properties which protect newborns from enteric pathogens (Hanson et al., 1989; Morrison, 1999a; Morrison, 1999b; Prameela & Mohamed, 2010).
- The concept of human milk as an effective immunological defence against various pathogens emerged in the 1970s from clinical and laboratory observations made between the late 18th through the mid-20th centuries. The discovery of living leukocytes in human milk in 1970 was the final link to the chain of evidence that culminated in the concept. This was later expanded to include not only antimicrobial but also anti-inflammatory and immune regulatory agents. These agents evolved to compensate for developmental delays in the immune system during infancy. Indeed, that explains the defence by human milk against common infectious diseases in infancy, necrotising enterocolitis in preterm infants, and immune-mediated disorders such as Crohn's disease in later childhood (Goldman, 2007).
- Breastfeeding is superior to infant formula feeding because in addition to the nutritional advantages of breastmilk, it protects against infections through specific and non-specific immune factors, with consequences for metabolism and disease later in life. There is much epidemiological evidence for the benefits of breastfeeding to the human infant against a wide range of illnesses and infections. Other scientific evidence for breastfeeding has demonstrated specific nutritional components that provide immunologic protection and beneficial effects on intestinal flora. Human milk enhances the immature immunologic system of the neonate and strengthens host defence mechanisms against infective and other foreign agents. Mechanisms to explain active stimulation of the infant's immune system by breastfeeding are through bioactive factors in human milk (Oddy, 2001).

Notes:

Notes:

The World Alliance for Breastfeeding Action (WABA) is a global network of individuals and organisations concerned with the protection, promotion and support of breastfeeding worldwide. WABA action is based on the Innocenti Declaration, the Ten Links for Nurturing the Future and the Global Strategy for Infant & Young Child Feeding. WABA is in consultative status with UNICEF and an NGO in Special Consultative Status with the Economic and Social Council of the United Nations (ECOSOC).