

2016



GUIDELINE UPDATES ON HIV AND INFANT FEEDING

The duration of breastfeeding and support from health services to improve feeding practices among mothers living with HIV

GUIDELINE

Updates on HIV and infant feeding

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Contents

Abbreviations and acronyms	v
Definitions and key terms	vi
Acknowledgements	viii
Executive summary	1
Scope and purpose	5
The 2010 WHO principles and recommendations on HIV and infant feeding: valid and updated	6
Background	10
Target audience	11
Population of interest	11
Priority questions for review	11
Evidence and recommendations	12
1. The duration of breastfeeding by mothers living with HIV	12
2. Interventions to support infant feeding practices by mothers living with HIV	22
3. What to advise when mothers living with HIV do not exclusively breastfeed	28
4. What to advise when mothers living with HIV do not plan to breastfeed for 12 months	32
Implications for monitoring and evaluation	36
Implications for conflict and emergency settings	37
Methods	39
Evidence retrieval, assessment and synthesis	39
WHO Steering Committee	39
Guideline Development Group	40
External Peer Review Group	40
Managing conflicts of interest	40
Grading the quality of the evidence	40
Decision-making process	41
Dissemination, adaptation and implementation	44
Dissemination	44
Adaptation and implementation	44
Monitoring and evaluating the implementation of the guideline	45
Implications for future research	45
Plans for updating the guideline	45

References	46
Annex 1. Systematic reviews including GRADE tables related to the duration of breastfeeding by mothers living with HIV	51
Annex 2. Systematic reviews including GRADE tables related to interventions to improve infant feeding practices by mothers living with HIV	52
Annex 3. Survey of national health authorities in the 22 priority countries for the Global Plan	53
Annex 4. Guideline Development Group and advisory groups	54
Annex 5. Questions and PICO used as the basis for preparing systematic reviews of the available published evidence	57

Abbreviations and acronyms

AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
ARV	antiretroviral drug
CD4	T-lymphocyte cell bearing CD4 receptor
CI	confidence interval
HIV	human immunodeficiency virus
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
PICO	population, intervention, control, outcome
RR	relative risk
RRRF	relative risk of infant and child mortality associated with replacement feeding compared with exclusive breastfeeding
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
WHO	World Health Organization

Definitions and key terms

Antiretroviral (ARV) drug: the medicine used to treat HIV infection.

Antiretroviral therapy (ART): the use of a combination of three or more ARV drugs for treating HIV infection. ART involves lifelong treatment.

ARV drugs for HIV prevention: ARV drugs for the prevention of HIV transmission and includes ARV drugs given to the mother or infant for preventing mother-to-child transmission of HIV, ARV drugs to reduce the transmission of HIV among serodiscordant couples and ARV drugs to prevent people from acquiring HIV when they are exposed (post-exposure and pre-exposure prophylaxis).

Exclusive breastfeeding: the infant receives only breast milk without any other liquids or solids, not even water, except for oral rehydration solution or drops or syrups of vitamins, minerals or medicines.

HIV: the human immunodeficiency virus. There are two types of HIV: **HIV-1 and HIV-2**. The vast majority of people living with HIV infections globally have HIV-1.

HIV-exposed infant or child: an infant or child born to a mother living with HIV until the infant or child is reliably excluded from being HIV infected.

HIV-free survival: an infant or young child born to a mother living with HIV remains both HIV uninfected (confirmed negative HIV status) and also alive over a defined follow-up period. It is commonly reported at 18 months or 24 months of age.

Mixed feeding: an infant younger than six months of age is given other liquids and/or foods together with breast milk. This could be water, other types of milk or any type of solid food.

Neonate: an infant 0–28 days old.

Postnatal transmission: transmission of HIV to an infant or child after birth. Most postnatal transmission is through the breast milk of a woman living with HIV, but this also includes accidental infection, such as through an infected needle or through child abuse.

Prevention of mother-to-child transmission of HIV: previous WHO guidelines have used the terms “options A, B and B+” to refer to different approaches to preventing the mother-to-child transmission of HIV. The 2013 WHO consolidated guidelines on the use of ARV drugs recommended one of two approaches: (1) providing ART during pregnancy and breastfeeding to women who are otherwise not eligible for ART (option B); or (2) providing lifelong ART to all pregnant and breastfeeding women living with HIV regardless of CD4 count or clinical stage (option B+).

Public health approach: addresses the health needs of a population or the collective health status of the people rather than focusing primarily on individual case management. This approach aims to ensure the widest possible access to high-quality services at the population level, based on simplified and standardized approaches, and to strike a balance between implementing the best-proven standard of care and what is feasible on a large scale in resource-limited settings. For HIV, key elements of a public health approach include simplified drug formularies; large-scale use of fixed-dose combinations; care and drugs provided free of charge at the point of service delivery; decentralization and integration of services, including task shifting; and simplified approaches to clinical monitoring.

Replacement feeding: feeding an infant who is not receiving any breast milk with a diet that provides all the nutrients children need until they can be fully fed on family foods. During the first six months, this should be with a suitable breast milk substitute: commercial infant formula milk. After six months, it should preferably be

with a suitable breast milk substitute and complementary foods made from appropriately prepared and nutrient-enriched family foods given three to five times per day.

Treatment failure: the current WHO virological criterion for treatment failure is a viral load of 1000 copies per ml or more.

Universal access to ART: defined broadly as a high level of access (80% or more of the eligible population) that is affordable. It does not necessarily mean 100% coverage.

Vertical transmission: transmission of HIV that occurs from a mother living with HIV to her infant. This may occur in utero, in the peripartum period or postnatally through breastfeeding.

Viral failure: the inability to achieve or maintain viral suppression below a certain threshold.

Viral suppression: a viral load below the detection threshold using viral assays.

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Executive summary

Background

Breastfeeding is one of the foundations of child health, development and survival, especially where diarrhoea, pneumonia and undernutrition are common causes of mortality among children younger than five years. For these reasons, exclusive breastfeeding for the first six months of life is the recommended way of feeding infants, followed by continued breastfeeding with appropriate complementary foods for up to two years or beyond.

In southern and eastern Africa, where child mortality rates are among the highest in the world, HIV infection is common and a leading cause of death. In these settings, use of commercial breast-milk substitutes and other replacement feeds among infants not exposed to HIV is associated with significantly increased morbidity and mortality. Moreover, the evidence for the long-term benefits of longer duration of breastfeeding for both maternal and child health outcomes, including child development and prevention of noncommunicable diseases, highlights the relevance of supporting breastfeeding in high- and low-income settings alike.

In 2010, WHO for the first time recommended antiretroviral (ARV) drug interventions to prevent postnatal transmission of HIV through breastfeeding. In the same year, WHO revised its guidelines on HIV and infant feeding to recommend a public health approach that advised national authorities to promote and support one feeding practice to all women living with HIV accessing care in public health facilities. Since then, countries have largely implemented the recommendations in the 2010 WHO guidelines on HIV and infant feeding. However, these guidelines had not been updated since then, since little new evidence emerged on either the uptake or impact of the recommendations.

The WHO consolidated guidelines on the use of ARV drugs for treating and preventing HIV infection were updated in 2013 and again in 2016. WHO now recommends lifelong antiretroviral therapy (ART) for everyone from the time when any adult (including pregnant and breastfeeding women) or child is first diagnosed with HIV infection. These revisions to the ARV drug guidelines, recent evidence and programmatic experience and demand for clarification on specific issues created a need to review the HIV and infant feeding guidelines.

Purpose of this guideline

The objective of this guideline is to improve the HIV-free survival of HIV-exposed infants by providing guidance on appropriate infant feeding practices and use of ARV drugs for mothers living with HIV and by updating WHO-related tools and training materials.

The guideline is intended mainly for countries with high HIV prevalence and settings in which diarrhoea, pneumonia and undernutrition are common causes of infant and child mortality. However, it may also be relevant to settings with a low prevalence of HIV depending on the background rates and causes of infant and child mortality.

This guideline aims to help Member States and their partners in their efforts to make informed decisions on the appropriate nutrition actions to achieve the Sustainable Development Goals, the global targets set in the comprehensive implementation plan on maternal, infant and young child nutrition, the Global Strategy for Women's, Children's and Adolescents' Health (2016–2030) and the Global Health Sector Strategy on Sexually Transmitted Infections 2016–2021.

The target audience for this guideline includes: (1) national policy-makers in health ministries; (2) programme managers working in child health, essential drugs and health worker training; (3) health-care providers, researchers and clinicians providing services to pregnant women and mothers living with HIV at various levels

of health care; and (4) development partners providing financial and/or technical support for child health programmes, including those in conflict and emergency settings.

Guideline development methods

WHO developed the present evidence-informed recommendations using the procedures outlined in the WHO handbook for guideline development. The steps in this process included: (i) identification of priority questions and outcomes; (ii) retrieval of the evidence; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations, including research priorities; and planning for (v) dissemination; (vi) implementation, equity and ethical considerations; and (vii) impact evaluation and updating of the guideline. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) method was followed, to prepare evidence profiles related to preselected topics, based on up-to-date systematic reviews.

In November 2014, a WHO Guideline Development Group reviewed the former guidelines on HIV and infant feeding and identified specific questions that should be updated. These questions and clarifications related mainly to one recommendation (number 2) from the 2010 WHO guidelines. All other recommendations and principles in those guidelines remain valid (see summary table below). Four areas were given priority for review:

- the duration of breastfeeding by mothers living with HIV;
- interventions to support infant feeding practices by mothers living with HIV;
- what to advise when mothers living with HIV do not exclusively breastfeed (if a mother living with HIV does not exclusively breastfeed, is mixed feeding with ART better than no breastfeeding at all?); and
- what to advise when mothers living with HIV do not plan to breastfeed for 12 months (if a mother living with HIV plans to return to work or school, is a shorter duration of planned breastfeeding with ART better than no breastfeeding at all?).

The Guideline Development Group also suggested examining the implications of recommendations in two programmatic areas:

- What guidance on infant feeding should be provided to mothers living with HIV and to health authorities in conflict or emergency settings?
- What are the implications of the updated recommendations for monitoring and evaluation?

To develop these recommendations, a WHO Steering Committee and a Guideline Development Group of 21 experts was convened. Based on the evidence reviews, the WHO Steering Committee developed an initial set of draft recommendations. Members of the Guideline Development Group then reviewed and evaluated the quality of the evidence identified through the systematic reviews using the GRADE method and revised and finalized the guideline recommendations and guiding practice statements. Tables 1 and 2 present the final recommendations and guiding practice statements, which were submitted for approval to the WHO Guideline Review Committee.

Available evidence

WHO commissioned independent institutions to conduct systematic reviews of the questions identified in the Guideline Development Group scoping meeting. Experts provided technical support to the guideline process by preparing systematic reviews, developing additional models and drafting evidence summaries and GRADE tables. Guideline Development Group members declared relevant interests, but none was deemed to represent a conflict of interest.

This new guideline does not reflect all WHO recommendations related to HIV and infant feeding but only the areas to which the Guideline Development Group gave priority for updating. The recommendations included in the WHO 2010 guidelines on HIV and infant feeding (see Table 3) remain valid except as noted. Specifically, recommendation 2 from 2010 has been revised in terms of the duration of breastfeeding, as reflected in recommendation 1 in 2016; one other area of guidance has been introduced (recommendation 2 in 2016).

RECOMMENDATIONS

Table 1. The 2016 WHO recommendations on HIV and infant feeding

RECOMMENDATIONS	Strength of the recommendation	Quality of the evidence
<p>1. The duration of breastfeeding by mothers living with HIV^a For how long should a mother living with HIV breastfeed if she is receiving ART and there is no evidence of clinical, immune or viral failure?</p> <p>Mothers living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or longer (similar to the general population) while being fully supported for ART adherence (see the WHO consolidated guidelines on ARV drugs for interventions to optimize adherence).^b</p> <p>The Guideline Development Group agreed that recommendation 1 should be framed by the following statement.</p> <p>In settings where health services provide and support lifelong ART, including adherence counselling, and promote and support breastfeeding among women living with HIV, the duration of breastfeeding should not be restricted.</p> <p>“Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter and continue breastfeeding.”</p> <p>“Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.”</p>	<p>Strong</p>	<p>12 months: low 24 months: very low</p>
<p>^a This recommendation updates the component of the 2010 recommendation on which breastfeeding practices and for how long related to the duration of breastfeeding. The components of the 2010 recommendation regarding breastfeeding practices and stopping breastfeeding remain unchanged and valid.</p> <p>^b WHO-recommended breastfeeding is defined as: (1) initiation of breastfeeding within the first hour of life; (2) exclusive breastfeeding for the first six months of life (that is, the infant only receives breast milk without any additional food or drink, not even water); followed by (3) continued breastfeeding for up to two years of age or beyond (with the introduction of appropriate complementary foods at six months); and (4) breastfeeding on demand – that is, as often as the child wants, day and night.</p>		
<p>2. Interventions to support infant feeding practices by mothers living with HIV Can facility- and community-based interventions improve the quality of infant feeding practices among mothers living with HIV?</p> <p>National and local health authorities should actively coordinate and implement services in health facilities and activities in workplaces, communities and homes to protect, promote and support breastfeeding among women living with HIV.</p>	<p>Strong</p>	<p>High</p>

Table 2. 2016 guiding practice¹ statements

GUIDING PRACTICE STATEMENTS	
1.	<p>When mothers living with HIV do not exclusively breastfeed</p> <p>If a mother living with HIV does not exclusively breastfeed, is mixed feeding with ART better than no breastfeeding at all?</p> <p>Mothers living with HIV and health-care workers can be reassured that ART reduces the risk of postnatal HIV transmission in the context of mixed feeding. Although exclusive breastfeeding is recommended, practising mixed feeding is not a reason to stop breastfeeding in the presence of ARV drugs.</p>
2.	<p>When mothers living with HIV do not plan to breastfeed for 12 months</p> <p>If a mother living with HIV plans to return to work or school, is a shorter duration of planned breastfeeding with ART better than no breastfeeding at all?</p> <p>Mothers living with HIV and health-care workers can be reassured that shorter durations of breastfeeding of less than 12 months are better than never initiating breastfeeding at all.</p>

Plans for updating this guideline

Countries are encouraged to hold key stakeholder discussions to inform decision-making on the use and introduction of the recommendations into national programmes. This guideline will be reviewed in 2019 when WHO will constitute a Guideline Development Group to review the literature and update the recommendations as needed.

¹ A guiding practice statement is made to encourage action or clarify an issue of concern. It addresses an area of suboptimal practice and provides a contingency and guidance to health workers regarding how to respond to a specific challenge.

Scope and purpose

The overall purpose of this guideline is to improve the HIV-free survival of HIV-exposed infants by providing guidance on appropriate infant feeding practices and use of ARV drugs for mothers living with HIV and by updating WHO-related tools and training materials.

The guideline addresses four aspects of infant feeding in the context of HIV:

- the duration of breastfeeding by mothers living with HIV;
- interventions to support infant feeding practices by mothers living with HIV;
- what to advise when mothers living with HIV do not exclusively breastfeed; and
- what to advise when mothers living with HIV do not plan to breastfeed for 12 months.

The guideline informs national policy-makers in health ministries and local programme managers on what may be relevant for national policies and programmes, including health worker training; it provides guidance to health-care providers, researchers and clinicians involved in managing pregnant women and mothers living with HIV at various levels of health care; and it updates development partners that may be providing financial and/or technical support for maternal, newborn and child health programmes. It will also inform revisions to current WHO training and reference materials, including: *Integrated Management of Childhood Illness* (WHO, 2016a); *Infant and young child feeding counselling: an integrated course* (WHO & UNICEF, 2006); *Essential newborn care course* (WHO, 2010a); *Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice* (WHO et al., 2015); and *A training course for community health workers: caring for newborns and children in the community* (WHO, 2015).

This guideline requires appropriately training and developing the capacity of health-care workers, to supply them with the necessary skills and job aids and provide adequate supervision and oversight. Systematic monitoring of the programme will be needed for ensuring success and for identifying and documenting challenges to implementation.

The 2010 WHO principles and recommendations on HIV and infant feeding: valid and updated

The WHO recommendations on HIV and infant feeding from 2010 (Table 3) (WHO, 2010b) remain valid except as noted. This guideline revised only the WHO recommendations related to HIV and infant feeding given priority by the Guideline Development Group.

Table 3. Principles and recommendations from the 2010 guidelines on HIV and infant feeding

PRINCIPLES	Notes
<p>Balancing HIV prevention with protection from other causes of child mortality</p> <p>Infant feeding practices recommended to mothers known to be living with HIV should support the greatest likelihood of HIV-free survival of their children and not harm the health of mothers. To achieve this, giving priority to preventing HIV transmission needs to be balanced with meeting the nutritional requirements of infants and protecting them from non-HIV morbidity and mortality.</p>	Remains valid
<p>Integrating HIV interventions into maternal and child health services</p> <p>National authorities should aim to integrate HIV testing, care and treatment interventions for all women into maternal and child health services. Such interventions should include access to CD4 count testing and appropriate ART or prophylaxis for the woman's health and to prevent the mother-to-child transmission of HIV.</p>	Remains valid
<p>Setting national or subnational recommendations for infant feeding in the context of HIV</p> <p>National or subnational health authorities should decide whether health services will mainly counsel and support mothers known to be living with HIV to either (1) breastfeed and receive ARV drug interventions or (2) avoid all breastfeeding as the strategy that will most likely give infants the greatest chance of HIV-free survival.</p> <p>This decision should be based on international recommendations and consideration of:</p> <ul style="list-style-type: none"> • the socioeconomic and cultural contexts of the populations served by maternal and child health services; • the availability and quality of health services; • the local epidemiology, including the HIV prevalence among pregnant women; and • the main causes of maternal and child undernutrition and infant and child mortality. 	Remains valid
<p>When ARV drugs are not (immediately) available, breastfeeding may still provide infants born to mothers living with HIV a greater chance of HIV-free survival</p> <p>Every effort should be made to accelerate access to ARV drugs for both maternal health and preventing HIV transmission to infants.</p> <p>While ARV drug interventions are being scaled up, national authorities should not be deterred from recommending that mothers living with HIV breastfeed as the most appropriate infant feeding practice in their setting.</p>	Remains valid

PRINCIPLES (CONTINUED)		Notes
	<p>Even when ARV drugs are not available, mothers should be counselled to exclusively breastfeed in the first six months of life and continue breastfeeding thereafter unless environmental and social circumstances are safe for and supportive of replacement feeding.</p> <p>In circumstances in which ARV drugs are unlikely to be available, such as acute emergencies, breastfeeding of HIV-exposed infants is also recommended to increase survival.</p>	
	<p>Informing mothers known to be living with HIV about infant feeding alternatives</p> <p>Pregnant women and mothers known to be living with HIV should be informed of the infant feeding practice recommended by the national or subnational authority to improve the HIV-free survival of HIV-exposed infants and the health of mothers living with HIV and informed that there are alternatives that mothers might want to adopt.</p>	Remains valid
	<p>Providing services to specifically support mothers to appropriately feed their infants</p> <p>Skilled counselling and support in appropriate infant feeding practices and ARV drug interventions to promote the HIV-free survival of infants should be available to all pregnant women and mothers.</p>	Updated to a formal recommendation. See recommendation 2 (2016)
	<p>Avoiding harming infant feeding practices in the general population</p> <p>Counselling and support to mothers known to be living with HIV and health messaging to the general population should be carefully delivered to avoid undermining optimal breastfeeding practices among the general population.</p>	Remains valid
	<p>Advising mothers who are HIV uninfected or whose HIV status is unknown</p> <p><i>Mothers who are known to be HIV uninfected or whose HIV status is unknown</i> should be counselled to exclusively breastfeed their infants for the first six months of life and then to introduce complementary foods while continuing breastfeeding for 24 months or beyond.</p> <p><i>Mothers whose status is unknown</i> should be offered HIV testing.</p> <p><i>Mothers who are HIV uninfected</i> should be counselled about ways to prevent HIV infection and about the services that are available, such as family planning, to help them to remain uninfected.</p>	Remains valid
	<p>Investing in improving infant feeding practices in the context of HIV</p> <p>Governments, other stakeholders and donors should greatly increase their commitment to and resources for implementing the Global Strategy for Infant and Young Child Feeding, the United Nations HIV and infant feeding framework for priority action and the global scale-up of the prevention of the mother-to-child transmission of HIV to effectively prevent infants from becoming infected with HIV postnatally, improve HIV-free survival and achieve relevant goals of the United Nations General Assembly Special Session on HIV/AIDS.</p>	Remains valid

RECOMMENDATIONS		
1.	<p>Ensuring mothers receive the care they need</p> <p>Mothers known to be living with HIV should be provided with lifelong ART or ARV drug prophylaxis interventions to reduce HIV transmission through breastfeeding in accordance with WHO recommendations.</p>	Remains valid
<p>In settings in which national authorities have decided that the maternal and child health services will mainly promote and support breastfeeding and ARV drug interventions as the strategy that will most likely give infants born to mothers known to be living with HIV the greatest chance of HIV-free survival</p>		
2.	<p>Which breastfeeding practices and for how long</p> <p>Mothers known to be living with HIV (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter and continue breastfeeding for the first 12 months of life.</p> <p>Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.</p>	The 2016 guideline revises the recommended duration of breastfeeding and HIV treatment, see recommendation 1 (2016).

RECOMMENDATIONS (CONTINUED)

<p>3.</p>	<p>When mothers decide to stop breastfeeding</p> <p>Mothers known to be living with HIV who decide to stop breastfeeding at any time should stop gradually within one month. Mothers or infants who have been receiving ARV drug prophylaxis should continue prophylaxis for one week after breastfeeding is fully stopped.</p> <p>Stopping breastfeeding abruptly is not advisable.</p>	<p>Remains valid. Nevertheless, lifelong ART is recommended now instead of ARV drug prophylaxis.</p>
<p>4.</p>	<p>What to feed infants when mothers stop breastfeeding</p> <p>When mothers known to be living with HIV decide to stop breastfeeding at any time, infants should be provided with safe and adequate replacement feeds to enable normal growth and development.</p> <ul style="list-style-type: none"> • <i>For infants younger than six months of age:</i> Alternatives to breastfeeding include: <ul style="list-style-type: none"> – commercial infant formula milk if the home conditions outlined in recommendation 5 are fulfilled; or – expressed, heat-treated breast milk (see recommendation 6 below). Home-modified animal milk is not recommended as a replacement food in the first six months of life. • <i>For children older than six months of age:</i> Alternatives to breastfeeding include: <ul style="list-style-type: none"> – commercial infant formula milk if the home conditions outlined in recommendation 5 are fulfilled; or – animal milk (boiled for infants under 12 months), as part of a diet providing adequate micronutrient intake; meals, including milk-only feeds, other foods and combination of milk feeds and other foods, should be provided four or five times per day. All children need complementary foods from six months of age. 	<p>Remains valid</p>
<p>5.</p>	<p>Conditions needed to safely formula feed</p> <p><i>Mothers known to be living with HIV</i> should only give commercial infant formula milk as a replacement feed to their HIV-uninfected infants or infants who are of unknown HIV status when specific conditions are met:</p> <ol style="list-style-type: none"> (a) safe water and sanitation are assured at the household level and in the community; and (b) the mother or other caregiver can reliably provide sufficient infant formula milk to support the normal growth and development of the infant; and (c) the mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition; and (d) the mother or caregiver can exclusively give infant formula milk in the first six months; and (e) the family is supportive of this practice; and (f) the mother or caregiver can access health care that offers comprehensive child health services. <p><i>These descriptions are intended to give simpler and more explicit meaning to the concepts represented by AFASS (acceptable, feasible, affordable, sustainable and safe).</i></p>	<p>Remains valid</p>

RECOMMENDATIONS (CONTINUED)

6.	Heat-treated, expressed breast milk Mothers known to be living with HIV may consider expressing and heat-treating breast milk as an interim feeding strategy: <ul style="list-style-type: none">• in special circumstances, such as when the infant has low birth weight or is otherwise ill in the neonatal period and unable to breastfeed; or• when the mother is unwell and temporarily unable to breastfeed or has a temporary breast health problem such as mastitis; or• to assist mothers in stopping breastfeeding; or• if ARV drugs are temporarily not available.	Remains valid
7.	When the infant is living with HIV If infants and young children are known to be living with HIV, mothers are strongly encouraged to exclusively breastfeed for the first six months of life and continue breastfeeding in accordance with the recommendations for the general population: that is, up to two years or beyond.	Remains valid

Background

Breastfeeding is one of the foundations of child health, development and survival, especially where diarrhoea, pneumonia and undernutrition are common causes of mortality among children younger than five years. For these reasons, exclusive breastfeeding for the first six months of life is the recommended way of feeding infants, followed by continued breastfeeding with appropriate complementary foods for up to two years or beyond (WHO, 2016b). Action is needed at the policy level, in the workplace, in health systems and in the community to provide an enabling environment for women to be able to breastfeed as recommended. The WHO Global Strategy for Infant and Young Child Feeding (WHO, 2003) describes the essential interventions to protect, promote and support breastfeeding. In southern and eastern Africa, where child mortality rates are among the highest in the world, HIV infection is common and is a leading cause of death. In these settings, use of commercial breast-milk substitutes and other replacement feeds among non-HIV-exposed infants is associated with significantly increased morbidity and mortality. Moreover, the evidence for the long-term benefits of longer durations of breastfeeding for both maternal and child health outcomes, including child development and preventing noncommunicable diseases, highlights the relevance of supporting breastfeeding in high- and low-income settings alike.

In 2010, WHO for the first time recommended ARV drug interventions to prevent postnatal transmission of HIV through breastfeeding (WHO, 2010c). Before this, WHO guidance on HIV and infant feeding (UNICEF et al., 2003; WHO et al., 2006) recommended an individualized approach in which women living with HIV would be counselled on feeding options according to their household circumstances. In 2010, WHO adopted a public health approach, recommending that national authorities promote and support one feeding practice for all women living with HIV accessing care in public health facilities. This was a major paradigm shift. The 2010 guidelines also explained how to protect, promote and support breastfeeding in the general population to avoid undermining optimal infant feeding practices in women and mothers not affected by HIV. The updated *HIV and infant feeding: framework for priority action* (WHO, 2012a) provided guidance to governments on key actions to create and sustain an environment that encourages appropriate feeding practices for all infants and young children, including implementation of the International Code of Marketing of Breast-milk Substitutes to protect mothers and communities from unethical marketing practices and commercial pressures, while scaling up interventions to reduce HIV transmission.

Since then, countries have largely implemented the WHO guidelines on HIV and infant feeding in accordance with the 2010 recommendations. These guidelines have not been updated since that time, since little new evidence emerged on either the uptake or impact of the recommendations in the first years following their release. However, the WHO consolidated guidelines on the use of ARV drugs for treating and preventing HIV infection were updated in 2013 and again in 2016 (WHO, 2013, 2016c). WHO now recommends lifelong ART for all from the time when any adult (including pregnant and breastfeeding women) or child is first diagnosed with HIV infection. This undertaking requires long-term planning and coordination by national health authorities and commitment from international agencies to assist with funding and support to health systems. Reducing HIV-related mortality among adults and children and preventing the vertical transmission of HIV to children will require sustainable approaches to assure the supply of ARV drugs and improve counselling and support to individuals to optimize adherence and retention in care.

The revisions to the ARV drug guidelines, recent evidence and programmatic experience and demand for clarification on specific issues created a need to review the HIV and infant feeding guidelines.

Target audience

The target audience for this guideline includes: (1) national policy-makers in health ministries; (2) programme managers working in child health, essential drugs and health worker training; (3) health-care providers, researchers and clinicians providing services to pregnant women and mothers living with HIV at various levels of health care; and (4) development partners providing financial and/or technical support for child health programmes, including those in conflict and emergency settings.

Population of interest

This guideline is intended mainly for countries with high HIV prevalence and settings where diarrhoea, pneumonia and undernutrition are common causes of infant and child mortality. It may also be relevant to settings with a low prevalence of HIV depending on background rates and causes of infant and child mortality. It should assist health workers providing support to mothers living with HIV who may choose to breastfeed even if this is not the primary recommendation of their national and local health authority.

Priority questions for review

In November 2014, a WHO Guideline Development Group (see the list of experts in the acknowledgements) reviewed the 2010 guidelines on HIV and infant feeding and identified specific questions that should be updated based on new evidence and programmatic experience. Four areas were given priority for review:

- the duration of breastfeeding by mothers living with HIV;
- interventions to support infant feeding practices by mothers living with HIV;
- what to advise when mothers living with HIV do not exclusively breastfeed (if a mother living with HIV does not exclusively breastfeed, is mixed feeding with ART better than no breastfeeding at all?); and
- what to advise when mothers living with HIV do not plan to breastfeed for 12 months (if a mother living with HIV plans to return to work or school, is a shorter duration of planned breastfeeding with ART better than no breastfeeding at all?).

Guided by this process and in consultation with the international experts, each question was described in terms of its characteristics: population, intervention, comparison and outcome (PICO). For each priority question, outcomes that were deemed to be either critical or important were evaluated. See Annex 5.

Evidence and recommendations

1. The duration of breastfeeding by mothers living with HIV

In settings where maternal, newborn and child health services promote and support breastfeeding and ART in order to increase HIV-free survival among infants born to mothers living with HIV:

For how long should a mother living with HIV breastfeed if she is receiving ART and there is no evidence of clinical, immune or viral failure?

Background

In 2010, global WHO HIV and infant feeding guidelines were updated to recommend that, in settings in which diarrhoea, pneumonia and undernutrition were still common causes of infant and child mortality, national health authorities should, while providing ARV drugs, promote and support breastfeeding among women and mothers living with HIV (WHO, 2010b). Such mothers were recommended to exclusively breastfeed their infants for the first six months of life, to introduce appropriate complementary foods thereafter and to continue breastfeeding for the first 12 months of life. Mothers living with HIV should then consider stopping breastfeeding at 12 months if they are able to provide a nutritionally adequate and safe diet without breast milk. The guidelines noted that, for women living in food-insecure regions, continuing breastfeeding beyond 12 months may still be important for the child to achieve an adequate diet.

The recommendation to breastfeed until 12 months of age and then consider whether to either stop breastfeeding or continue breastfeeding for longer was based on four considerations.

- The risk of mortality among young children after 12 months of age is lower than the risk in the first 12 months of life. Even though breastfeeding for longer periods has many other health benefits, it has less impact on mortality in this later period (Victora et al., 2016).
- From 12 months onward, it is possible to provide a diet based on family foods that excludes breast milk and is still nutritionally adequate for the growing child. Although breast milk is still valuable, whole cow's milk can be given after six months of age without modifying the milk (WHO, 2005).
- In 2010, it was uncertain whether health services would be able to retain mothers living with HIV in care and consistently provide ART. If a breastfeeding mother living with HIV did not receive ART or did not return to health services, the infant might have some risk of becoming infected with HIV. At that time, few programmatic data were available to inform the Guideline Development Group.
- It was uncertain whether breastfeeding children would have significant adverse health outcomes from longer-term exposure to ARV drugs through breast milk if the mother was taking ART.

For these reasons, the 2010 Guideline Development Group agreed that, in settings in which diarrhoea, pneumonia and undernutrition were common, breastfeeding until 12 months by a mother living with HIV and taking ART was likely to increase the HIV-free survival of infants and young children compared with replacement feeding or shorter durations of breastfeeding. Concerns regarding the potential for misunderstandings related to these guidelines undermining optimal infant feeding practices in women and mothers not affected by HIV resulted in WHO updating *HIV and infant feeding: framework for priority action* (WHO, 2012a), which provided guidance to governments on key action to create and sustain a protective environment that encourages appropriate feeding practices for all infants and young children while scaling up interventions to reduce HIV transmission.

In 2013, WHO (2013) recommended lifelong ART for all mothers living with HIV and, since October 2015, to all adults and children as soon as they are known to be living with HIV (WHO, 2016c) and not just for the women

fulfilling specific clinical or immunological criteria. Based on these recommendations, the current standard of care and organization within health systems are oriented toward providing lifelong ART, including adherence support and counselling for adults and children living with HIV.

The Guideline Development Group noted that the WHO recommendations for mothers in the general population – that is, HIV negative or of unknown status – remain unchanged: mothers should exclusively breastfeed for the first six months, introduce appropriate complementary feeds and continue breastfeeding until 24 months or beyond because of the many benefits for both mother and child (WHO, 2016b).

Summary of the evidence

Two systematic reviews were commissioned for this guideline and contributed to the GRADE (GRADE Working Group, 2016) tables and evidence for this question (GRADE evidence profile, Annex 1a, Table 4).

1. Chikhungu L, Bispo S, Newell ML. HIV-free survival at 12–24 months in breastfed infants of HIV-positive women on antiretroviral therapy: a systematic review (Annex 1a).
2. Chikhungu L, Bispo S, Newell ML. Postnatal HIV transmission rates at age six and 12 months in infants of HIV-positive women on antiretroviral therapy initiating breastfeeding: a systematic review (Annex 1b).

Under additional evidence not included in the GRADE tables, findings are presented of a modelling exercise that was also commissioned for the guideline and examined the effect of ART among mothers living with HIV on infant survival according to different background risk assessments of diarrhoeal mortality.

3. Mallampati D, MacLean R, Ciaranello A. Modelling the impact of maternal antiretroviral drug use and infant mortality (Annex 1c).

Also included in this section are findings of another systematic review (Zunza et al., 2013) that summarizes evidence how exposure to postnatal ARV drugs affects child growth.

4. Zunza M, Mercer GD, Thabane L, Esser M, Cotton MF. Effects of postnatal interventions for the reduction of vertical HIV transmission on infant growth and non-HIV infections: a systematic review. *J Int AIDS Soc.* 2013;16:18865.

The values and preferences of stakeholders outlined in the decision-making tables were informed by a survey of national health authorities of the 22 priority countries¹ for the Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive (UNAIDS, 2011) (see below and Annex 3).

HIV-free survival by duration of feeding practice and ART use

The systematic review by Chikhungu et al. (Annex 1a) addressed the question of HIV-free survival at 12, 18 or 24 months among infants born to women living with HIV who were receiving ART by infant feeding modality (exclusive breastfeeding, mixed feeding or replacement feeding) and duration of maternal ART. The systematic review did not identify any trial that reported directly comparative data from the population of interest: that is, mothers receiving ART who breastfed for 12 months versus 24 months.

The authors identified 18 cohort studies that provided other data to inform the Guideline Development Group: seven of these studies were nested within randomized controlled trials. Most studies were a follow-up of mothers receiving ART for preventing the mother-to-child transmission of HIV, with mothers advised to exclusively breastfeed for six months with rapid cessation thereafter, in accordance with the prevailing global recommendations. In 11 studies in which women initiated ART specifically for the purpose of preventing the mother-to-child transmission of HIV, ART would have been stopped at the cessation of breastfeeding around six months postpartum, in accordance with previous recommendations (WHO et al., 2006). Six studies offered lifelong ART regardless of CD4 count, and four studies supported breastfeeding for 12 months.

¹ Angola, Botswana, Burundi, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Ghana, India, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia and Zimbabwe.

The majority of the cohort studies did not provide details regarding type of feeding: that is, exclusive breastfeeding or mixed feeding in the first six months. The investigators of 10 studies, of whom six responded, were requested to provide additional information. Five confirmed that exclusive breastfeeding was promoted, but feeding practices were inconsistently assessed as part of the study processes, such as self-reporting only. The investigators assumed that some mothers would have exclusively breastfed up to 5 or 6 completed months as recommended, whereas others would have introduced other fluids, milks or solids while breastfeeding: that is, mixed feeding. No study disaggregated transmission rates according to exclusive breastfeeding or mixed feeding where the mother was receiving lifelong ART.

Of the 18 cohort studies, only four had estimates of HIV-free survival by type of feeding; one of these also presented information on HIV transmission by feeding type. One further study compared cumulative transmission rates among children who were either formula-fed from birth or breastfed for less than three months or for three months or longer. Three studies compared transmission or death between breastfed and formula-fed (replacement-fed) infants, and one study provided HIV-free survival separately for children who were mixed-fed and those who stopped breastfeeding early. Eight studies provided HIV-free survival or rates of transmission and mortality from birth; other studies excluded deaths and HIV transmission in the first days or weeks of life and provided only postnatal rates.

Meta-analysis using a random effects model was conducted, but because of the high level of clinical and methodological heterogeneity observed in the data set, the review authors caution about interpreting these results. The pooled estimates of HIV-free survival at 12 and 18 months were marginally higher for infants whose mothers were receiving lifelong ART than for infants whose mothers were receiving ART until six months postnatally only. The pooled estimates for HIV-free survival at 12 months were 89.8% (95% confidence interval [CI]: 86.4–93.1%) for infants whose mothers were receiving ART for six months postnatally (six studies, $n = 2366$) (Alvarez-Uria et al., 2012; Jamieson et al., 2012; Kilewo et al., 2009; Marazzi et al., 2009; Thistle et al., 2011; Thomas et al., 2011) and 91.8% (95% CI: 87.7–95.9%) for infants whose mothers were receiving lifelong ART (three studies, $n = 898$) (Cohan et al., 2015; Thakwalakwa et al., 2014; Tonwe-Gold et al., 2007). Estimates of HIV-free survival at 18 months were 89.0% (95% CI: 83.9–94.2%) for infants whose mothers were receiving ART to six months postnatally (five studies, $n = 1876$) (Cournil et al., 2015; Fowler et al., 2014; Homsy et al., 2010; Kilewo et al., 2009; Thomas et al., 2011) and 96.1% (95% CI: 93.0–99.2%) for infants with mothers receiving lifelong ART (three studies, $n = 1271$) (Ngoma et al., 2015; Okafor et al., 2014; Sagay et al., 2015) (GRADE evidence profile, Annex 1a, Table 4).

HIV-free survival could not be estimated at 24 months because insufficient data were available for women receiving lifelong ART; the pooled estimate for 24-month HIV-free survival for infants whose mothers were receiving ART until six months postnatally (two studies) (Shapiro et al., 2013; Thomas et al., 2011) was 89.2% (95% CI: 79.9–98.5%). In one additional study, based on a mixed group of infants with respect to the mother's ART status (some were receiving ART up to six months postnatally and others were receiving lifelong ART), estimated HIV-free survival at 24 months was 85.8% (95% CI: 81.4–90.1%) (Giuliano et al., 2013).

Data from the individual studies are difficult to interpret due to heterogeneity and wide confidence intervals (especially in the studies with a shorter duration of ART). In general, HIV-free survival estimates were equivalent or higher for the infants of mothers receiving lifelong ART than for infants of mothers receiving ART for a limited period up to six months postnatal.

- Among infants whose mothers were receiving ART for up to six months, HIV-free survival:
 - at 12 months ranged from 85.0% (95% CI: 74.6–91.7%) to 96.0% (95% CI: 91.0–98.0%);
 - at 18 months ranged from 81.6% (95% CI: 73.4–87.7%) to 95.2% (95% CI: 93.2–97.3%).
- Among infants whose mothers were receiving lifelong ART, HIV-free survival:
 - at 12 months ranged from 88.8% (95% CI: 82.6–95.0%) to 95.0% (95% CI: 92.0–97.0%);
 - at 18 months ranged from 87.2% (95% CI: 79.2–92.5%) to 97.8% (95% CI: 94.6–99.1%).

However, the range of individual study estimates and confidence intervals cannot be directly compared, since not all the included studies reported outcomes at both 12 and 18 months. Overall, the Guideline Development

Group agreed that a longer duration of ART for the mother is associated with greater HIV-free survival for the young child.

Two studies reported 24-month HIV-free survival among infants whose mothers were receiving ART up to six months postnatally at 84.3% (95% CI: 80.6–87.3%) (Thomas et al., 2011) and 93.8% (95% CI: 92.9–96.5%) (Shapiro et al., 2013) respectively. In a third study, 24-month HIV-free survival was estimated to be 85.8% (95% CI: 81.4–90.1%) (Giuliano et al., 2013) in a mixed population of children whose mothers were either receiving lifelong ART because of low CD4 count or receiving ART up to six months.

Four studies provided estimates of HIV-free survival by feeding modality; three reported higher HIV-free survival among breastfed infants than formula-fed infants. HIV-free survival among breastfed infants ranged from 82% (95% CI: 73.4–87.7%) [median weaning: five months] to 96% (95% CI: 91–98%) and among formula-fed infants from 67% (95% CI: 35.5–87.9%) to 97.6% (95% CI: 93.0–98.2%).

All studies were graded as low or very low quality because they were observational in design and downgraded for indirectness. The authors urged caution in quoting the pooled estimates because of heterogeneity (GRADE evidence profile, Annex 1a, Table 4).

HIV transmission by duration of feeding practice and ART use

A second systematic review (Chikhungu et al., Annex 1b) summarized HIV transmission rates at six, nine and 12 months among infants born to women who were receiving ART by infant feeding modality in the first six months of life (GRADE evidence profile, Annex 1b, Table 7).

Eleven studies were identified for analysis; four were cohorts nested in randomized controlled trials. In all studies, mothers started ART before or during pregnancy and continued until at least six months postnatally, in accordance with the WHO recommendations at the time. Eight of the 11 studies followed the recommendation of using ART for preventing the mother-to-child transmission of HIV during pregnancy until cessation of breastfeeding at about six months postnatally; three studies provided lifelong ART for all women, and one study provided lifelong ART for women eligible for treatment in accordance with WHO guidelines only. In most studies, mothers were advised to offer exclusive breastfeeding to the child, with rapid weaning after six months; two studies recommended continuing breastfeeding until 12 months. No study provided estimates of transmission rate according to type of feeding – that is, exclusive versus mixed feeding – although two studies reported the feeding practices of infants found to be infected.

Overall HIV transmission at age six months

Six studies reported overall (including peripartum and postpartum) transmission at six months. In the three studies in which pregnant women received ART early from 15 weeks gestation, overall transmission rates were 0.5% (95% CI: 0.2–1.2%), 1.4% (95% CI: 0.5–3.9%) and 1.9% (95% CI: 0.9–4.1%). When pregnant women initiated ART after 30 weeks of gestation, overall transmission rates were 5.0% (95% CI: 3.4–7.4%), 5.0% (95% CI: 2.9–7.1%) and 7.9% (95% CI: 6.2–9.9%). The pooled estimated rate of overall transmission by age six months was 3.5% (95% CI: 1.15–5.93), with substantial heterogeneity ($I^2 = 94.0\%$) (GRADE evidence profile, Annex 1b, Table 7).

Postnatal transmission between 4–6 weeks and six months

Six studies provided estimates of postnatal transmission, excluding peripartum infections diagnosed before 4–6 weeks of age. Among mothers who started ART at the first antenatal visit, estimated postnatal transmission rates ranged from 0.2% (95% CI: 0.0–1.4%) to 3.1% (95% CI: 1.2–7.8%). Among mothers starting ART later in pregnancy, postnatal transmission rates varied from 0.8% (95% CI: 0.3–2.4%) to 2.7% (95% CI: 1.8–4.1%). The pooled postnatal transmission rate by six months of age was 1.08% (95% CI: 0.32–1.85%), with high heterogeneity ($I^2 = 66.4\%$) (GRADE evidence profile, Annex 1b, Table 7).

In addition, one study reported postnatal HIV transmission rates between 3 and 28 weeks by maternal ART exposure: that is, maternal ART, no maternal ART but infants received daily nevirapine and a placebo group: 3.0% (95% CI: 1.7–4.1%), 2.0% (95% CI: 0.8–2.6%) and 5% (95% CI: 3.8–7.4%), respectively.

Overall transmission rates at 12 months

Seven studies provided information on transmission at 12 months, of which five reported overall transmission (including peripartum and postpartum). The pooled estimate for the overall rate at 12 months was 4.2% (95% CI: 3.0–5.5%), with $I^2 = 39.9\%$, indicating moderate heterogeneity (GRADE evidence profile, Annex 1b, Table 7).

Postnatal transmission rates at 12 months

The rates from two studies reporting postnatal transmission between 4–6 weeks and 12 months of age were 1.7% (95% CI: 0.3–4.1%) and 4.0% (95% CI: 3.0–6.0%) with a pooled estimate of 3.0% (95% CI: 0.7–5.2%), with high heterogeneity ($I^2 = 71.2\%$).

Only one study estimated the rate of transmission at 18 months, among infants of mothers on lifelong ART, with a rate of 4.1% (95% CI: 2.2–7.6%).

All studies were rated as having very low quality because of the observational design, indirectness, inconsistency and/or risk of bias.

Although there was substantial statistical heterogeneity between studies in each of the pooled estimates, and the authors (Chikhungu et al.) advised caution when using the absolute pooled estimates, this systematic review provides evidence of reduced postnatal HIV transmission risk under the cover of maternal ART.

Additional evidence not included in the GRADE table

Modelling

A modelling exercise using the Cost-Effectiveness of Preventing AIDS Complications (CEPAC) infant model (Mallampati et al., Annex 1c) projected 24-month HIV-free survival among HIV-exposed, uninfected infants when three key parameters were varied: the relative risk of infant and child mortality associated with replacement feeding compared with exclusive breastfeeding (RRRF – a multiplier of mortality when infants are replacement fed); setting-specific neonatal, infant and under-five mortality rates; and the duration of maternal ART use during breastfeeding (as a proxy for retention in care and medication adherence). The primary goals of the analysis were: (1) to determine the “optimal breastfeeding duration” for each scenario, defined as the duration that maximized HIV-free survival; and (2) to quantify the impact of maternal ART adherence on HIV-free survival. Building on a previous analysis (Ciaranello et al., 2014), the authors incorporated updated HIV transmission data for women receiving ART and neonatal, infant and under-five mortality rates from the 22 Global Plan priority countries (UNAIDS, 2011).

The analysis found the following.

- When the additional mortality risks associated with replacement feeding are high, such as in settings with contaminated water supplies or during diarrhoeal outbreaks, when maternal ART is consistently available, longer durations of breastfeeding, that is, 24 months or more, improve 24-month HIV-free survival. When the risks associated with replacement feeding are lower, then shorter durations of breastfeeding, that is, 12–24 months, result in the highest rates of HIV-free survival as long as maternal ART is consistently available.
- The difference in HIV-free survival between 12 and 24 months of breastfeeding is minimal, usually <1%, as long as women continue to receive ART throughout breastfeeding.
- If mothers are lost from care or stop taking ART before stopping breastfeeding, the 24-month HIV-free survival of their children decreases dramatically. This is because the HIV transmission risks are high when women continue to breastfeed after stopping ART. However, in this scenario, HIV-free survival is very much lower if mothers do not breastfeed at all.
- When the authors simultaneously varied mortality, the relative risk of infant and child mortality associated with replacement feeding compared to exclusive breastfeeding (RRRF) and ART duration, the underlying infant, child and under-five mortality rates were found only to influence optimal breastfeeding duration in scenarios with intermediate RRRF values (RRRF = 4–5). In settings with low to moderate RRRF values

(RRRF \leq 3), the optimal breastfeeding duration is 12 months, and at very high RRRF values (RRRF \geq 6), the optimal breastfeeding duration is 24 months, regardless of the underlying child mortality rates.

The authors found that the 12-month breastfeeding duration recommended in the 2010 WHO HIV and infant feeding guidelines maximizes infant HIV-free survival at 24 months in many settings, even when RRRF or infant, child and under-five mortality rates are low. If programmes in low-RRRF settings recommended 24 months of breastfeeding instead of 12 months, the anticipated reduction in HIV-free survival would be small (<1%), as long as women continue to receive ART throughout breastfeeding. In settings in which RRRF and mortality rates are both high, breastfeeding for 24 months improves HIV-free survival. In all RRRF scenarios, ART adherence throughout the entire breastfeeding period is critical to improve infant HIV-free survival.

Adverse effects of postnatal ART interventions to prevent transmission of HIV through breastfeeding

A systematic review of the adverse effects of postnatal interventions for preventing the mother-to-child transmission of HIV on infant growth and non-HIV infections (Zunza et al., 2013) was updated with literature published up to August 2015. The earlier 2013 review identified three randomized controlled studies with relevant data. Maternal ARV drugs did not significantly adversely affect the growth of infants and children who were breastfed (RR = 1.12; 95% CI: 0.83–1.50). The evidence suggests that breastfeeding may improve the growth and non-HIV infection outcomes of HIV-exposed infants. Extended ARV drug prophylaxis does not appear to increase the risk for HIV-exposed infants for adverse growth or non-HIV infections compared with short-course ARV drug prophylaxis.

The reviewers rated the evidence as moderate quality.

When this review was updated to 2015, the search identified two further observational studies. Thakwalakwa et al. (2014) found that length-for-age and weight-for-height among HIV-exposed infants who were breastfed by mothers receiving ART and also giving the infants quality complementary foods were comparable or better than the historical growth rates reported among the general child population in Malawi. The second report by Parker et al. (2013) found that earlier cessation of breastfeeding among HIV-exposed infants whose mothers received ART was associated with dietary deficiencies, and female infants experienced reduced growth velocity. However, it was unclear whether these effects were related to earlier cessation of breastfeeding or to other HIV-related factors.

Survey of national health authorities of the 22 priority countries of the Global Plan

To learn about the values and preferences of stakeholders regarding infant feeding, WHO conducted a survey among representatives of national health authorities in the 22 priority countries of the Global Plan (UNAIDS, 2011). Most national health authorities in these countries have opted to recommend breastfeeding to mothers living with HIV while providing ART. The findings were presented to the Guideline Development Group and are reported in Annex 3 and also included in the decision-making table (Table 4). The Guideline Development Group considered these findings in their deliberations of the values and preferences of communities and stakeholders that would be affected by the guidelines.

Table 4. Considerations when developing infant feeding recommendations in the context of HIV

SUPPORTING EVIDENCE AND ADDITIONAL CONSIDERATIONS	
	Question
BENEFITS AND HARM	<p>For how long should a mother living with HIV breastfeed if she is receiving ART and there is no evidence of clinical, immune or viral failure?</p> <p>Do the desirable effects (of longer breastfeeding by mothers living with HIV receiving ART) outweigh the undesirable effects?</p> <p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>
VALUES, PREFERENCES AND ACCEPTABILITY	<p>Is there important uncertainty or variability about how much people value the options?</p> <p><input checked="" type="checkbox"/> Major variability <input type="checkbox"/> Minor variability <input type="checkbox"/> Uncertain</p> <p>Is the option acceptable to key stakeholders?</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Uncertain</p>

FEASIBILITY AND RESOURCE USE	<p>How large are the resource requirements?</p> <p><input type="checkbox"/> Major</p> <p><input checked="" type="checkbox"/> Minor</p> <p><input type="checkbox"/> Uncertain</p> <p>Is the option feasible to implement?</p> <p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Uncertain</p>	<p>Health systems must already consider using most of the resources for ART and support for ART adherence, since ART is already recommended, and hence these would not be additional costs.</p> <p>The main additional costs would be for training and developing the capacity of health workers to promote breastfeeding to 24 months or beyond, and these are likely to be modest. In addition, breastfeeding promotion would benefit the entire population and not just a select proportion; thus, the anticipated cost-benefit ratio would be low.</p> <p>These costs should be differentiated from the substantial funds required to implement systems to adequately protect, promote and support breastfeeding across the entire population, including the Baby-friendly Hospital Initiative and monitoring the Code of Marketing of Breast-milk Substitutes.</p> <p>Two countries are already implementing the proposed intervention, and no major challenges are reported.</p>
EQUITY	<p>Would the option improve equity in health?</p> <p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Uncertain</p>	<p>Implementing a recommendation for breastfeeding for 24 months may improve health equity, since the recommendation would then be essentially the same for all populations.</p> <p>Breastfeeding in the general population tends to improve health equity.</p>

RECOMMENDATION 1

Mothers living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or beyond (similar to the general population^a) while being fully supported for ART adherence.

(See the WHO consolidated guidelines on ARV drugs for interventions to optimize adherence).

The Guideline Development Group agreed that recommendation 1 should be framed by the following statement.

In settings where health services provide and support lifelong ART, including adherence counselling, and promote and support breastfeeding among women living with HIV, the duration of breastfeeding should not be restricted.

Recommendation 1 (2016) updates the component of the 2010 recommendation on which breastfeeding practices and for how long that relates to the duration of breastfeeding. The components of the 2010 recommendation regarding breastfeeding practices and stopping breastfeeding remain unchanged and valid.

Mothers living with HIV should exclusively breastfeed their infants for the first six months of life, introduce appropriate complementary foods thereafter and continue breastfeeding.

Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.

Strength of the recommendation	Strong
Quality of the evidence	12 months: low 24 months: very low

^a Breastfeeding as recommended by WHO is defined as: (1) initiating breastfeeding within the first hour of life; (2) exclusive breastfeeding for the first six months of life (that is, the infant only receives breast milk without any additional food or drink, not even water); followed by (3) continued breastfeeding for up to two years or beyond (with introduction of appropriate complementary foods at six months); and (4) breastfeeding on demand – that is, as often as the child wants, day and night.

Justification

The Guideline Development Group unanimously supported removing any restriction on the duration of breastfeeding for mothers living with HIV in the context of full support for ART. All Guideline Development Group members agreed that the likely benefits outweighed the harm even if breastfeeding in the general population has less protective effect against serious morbidity and mortality in the second year of life than in the first 12 months. The Guideline Development Group recognized that, in settings in which health systems support and promote high rates of retention in care and adherence to ART, the risk of postnatal transmission is likely to be low. The Guideline Development Group also recognized that, as programmes become even more robust and efficient in delivering ART services and communities become more aware of the benefits and reliability of ART in protecting against HIV transmission, the balance of risks in favour of prolonged breastfeeding with the provision of ART will be even stronger. In addition, the Guideline Development Group noted the significant benefit of harmonizing guidelines for women living with HIV and the general population. This action will probably decrease the stigmatization associated with infant feeding practices undertaken by mothers living with HIV and also facilitate improved feeding practices in the entire population.

There are no comparative data from HIV-exposed children on the overall gains in HIV-free survival that would be associated with prolonged breastfeeding versus shorter durations of breastfeeding, and programmatic and historical data demonstrate small but continued postnatal transmission through the second year of life. The ART adherence rates among the mothers of these children were, however, unknown. Some Guideline Development Group members commented that poor adherence to ART by mothers living with HIV will always constitute a risk factor for postnatal transmission, whether in the first or second year of life. (See the 2013 WHO consolidated guidelines on ARV drugs (WHO, 2013) for interventions to optimize adherence to ART.)

The Guideline Development Group noted these concerns and reviewed, on several occasions, the decision to make a strong recommendation. Although some Guideline Development Group members favoured a conditional rather than a strong recommendation in recognition of the diversity of settings in which the recommendation will be implemented, consensus was achieved through discussion and revising how the recommendation should be phrased. The decision to make a strong recommendation was based on agreement on what package of interventions would be best for the individual mother–infant pairs. Where health systems reliably provide and support ART, and mothers retained in care consistently adhere to ART, the Guideline Development Group considered that prolonged breastfeeding to 24 months or beyond by mothers living with HIV is the best option for HIV-exposed infants. The Guideline Development Group also noted that the change in global recommendations on ART for all people living with HIV regardless of CD4 count should result in greater investment and improvement in health services to achieve the quality required to assure high rates of retention and ART adherence.

	<p>The Guideline Development Group also noted that, in both the past and current recommendations, women living with HIV are not obligated to adopt a single feeding practice even when recommended by the health services. Similar to all women in everyday life, mothers living with HIV ultimately make decisions about infant feeding practices, including the duration of breastfeeding, according to what is appropriate for their circumstances. The 2010 WHO guidelines on HIV and infant feeding highlighted the need for health services to support mothers living with HIV in their chosen feeding practices even when they are inconsistent with the nationally recommended practices. This principle is still endorsed by WHO and remains relevant to these updated recommendations.</p>
<p>Implementation considerations</p>	<ul style="list-style-type: none"> • HIV and maternal and child health programmes need to give priority to integrating ART services, including adherence counselling and support for infant and young child feeding, in all settings. • These programmes and partner agencies need to ensure training and developing the capacity of health workers so that they can explain the rationale for the recommendation and to ensure that staff members are able to explain the benefits to mothers living with HIV while emphasizing the value and importance of adherence to ART. • These programmes and partner agencies should collect data to monitor the duration of breastfeeding by mothers living with HIV in addition to adherence to ART and the rates of retention in care of mothers and infants. Such data should be used to improve the quality of service delivery at district and local clinics. • Investment and action to protect, promote and support breastfeeding in the general population should remain priorities of health ministries, nongovernmental organizations and other partners in all settings.
<p>Research priorities</p>	<ul style="list-style-type: none"> • How does long-term postpartum exposure to low-dose ARV drugs in breast milk affect the early and late health outcomes, especially growth, renal and bone metabolism and neurodevelopment, of HIV-exposed breastfeeding infants and children whose mothers are taking ART?

2. Interventions to support infant feeding practices by mothers living with HIV

Can facility- and community-based interventions improve the quality of infant feeding practices among mothers living with HIV?

- In countries that promote breastfeeding among mothers living with HIV receiving ART, what are the effective interventions to support optimal breastfeeding?
- In countries that promote replacement feeding among mothers living with HIV, what are the effective interventions to support safe and adequate replacement feeding?

Background

The 2010 WHO guidelines on HIV and infant feeding recommended a public health approach in which national authorities should promote and support one infant feeding practice among mothers living with HIV attending public health facilities, either: (1) exclusive breastfeeding for the first six months followed by introducing appropriate complementary feeding and continued breastfeeding for up to one year, while ARV drugs are provided to either the mother or the infant; or (2) avoiding all breast milk. It was recommended that this decision be taken at the national level following consideration of local HIV and general maternal and child health epidemiology and other health system considerations.

The same guidelines highlighted the principles that skilled counselling and support for infant feeding practices should be available to all pregnant women and mothers. For mothers living with HIV, support for ART adherence should also be provided, and guidance on safe replacement feeding should be carefully delivered to avoid undermining optimal breastfeeding practices among the general population.

Guiding principles included in the 2010 WHO guidelines on HIV and infant feeding (WHO, 2010b)

Providing services to specifically support mothers in appropriately feeding their infants

Skilled counselling and support in appropriate infant feeding practices and ARV drug interventions to promote HIV-free survival of infants should be available to all pregnant women and mothers.

Avoiding harm to infant feeding practices in the general population

Counselling and support to mothers known to be living with HIV and health messaging to the general population should be carefully delivered to avoid undermining optimal breastfeeding practices among the general population.

Safe replacement feeding

Mothers known to be living with HIV should only give commercial infant formula milk as a replacement feed to their HIV-uninfected infants or infants who are of unknown HIV status when specific conditions are met:

- a. safe water and sanitation are assured at the household level and in the community; and
- b. the mother or other caregiver can reliably provide sufficient infant formula milk to support the normal growth and development of the infant; and
- c. the mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition; and
- d. the mother or caregiver can, in the first six months, exclusively give infant formula milk; and
- e. the family supports this practice; and
- f. the mother or caregiver can access health care that offers comprehensive child health services.

These descriptions are intended to give simpler and more explicit meaning to the concepts represented by AFASS (acceptable, feasible, affordable, sustainable and safe).

The updated *HIV and infant feeding: framework for priority action* (WHO, 2012a) provided guidance to governments on key priority actions to create and sustain an environment that encourages appropriate feeding practices for all infants and young children while scaling up interventions to reduce HIV transmission.

Since 2010, evidence has become available from studies and programmatic reports about the effectiveness of health system or other community-based interventions in assisting mothers living with HIV to adhere exclusively to one feeding practice or the other.

At the guideline scoping meeting, Guideline Development Group members considered it important to review these data and guiding principles from 2010 and to consider formal recommendations on support to improve both breastfeeding and replacement feeding practices by mothers living with HIV. Guideline Development Group members noted that infant feeding practices strongly influence the risk of morbidity and mortality among all infants and children. Therefore, as the risk of HIV transmission decreases, the support to mothers living with HIV regarding infant feeding practices is likely to significantly influence HIV-free survival and the long-term health outcomes of HIV-exposed infants and children.

Summary of the evidence

Two systematic reviews were commissioned to inform consideration of these questions.

1. Academy of Nutrition and Dietetics: Handu D, Acosta A, Moloney L, Wolfram T, Ziegler P, Steiber A. Effectiveness of interventions to promote exclusive breastfeeding in women living with HIV who are on antiretroviral therapy living in areas that promote exclusive breastfeeding due to limited resources for safe replacement feeding (Annex 2).
2. Academy of Nutrition and Dietetics: Handu D, Acosta A, Moloney L, Wolfram T, Ziegler P, Steiber A. Effectiveness of interventions to promote safe replacement feeding in women living with HIV that are living in areas that promote replacement feeding (Annex 2; no published studies were identified).

A published systematic review that summarized evidence on the interventions to improve breastfeeding practices in the general population (Sinha et al., 2015) also contributed to the discussions.

3. Sinha B, Chowdhury R, Sankar MJ, Martines J, Taneja S, Mazumder S et al. Interventions to improve breast-feeding outcomes: a systematic review and meta-analysis. *Acta Paediatr.* 2015;104:114-34.

Interventions to improve breastfeeding practices among mothers living with HIV

A systematic review (Academy of Nutrition and Dietetics, 2015, Annex 2) examined the effectiveness of interventions to promote the early initiation of and support for exclusive breastfeeding by women who are living with HIV receiving ART in areas that promote breastfeeding.

A total of 859 citations were identified. Thirteen studies met the inclusion criteria; these were conducted in Cameroon, India, Kenya, Malawi, South Africa, Uganda, the United Republic of Tanzania and Zimbabwe. Of these, one was a randomized controlled trial, seven cohort studies, four cross-sectional studies and one a pre-post study.

Five studies reported exclusive breastfeeding at six months, nine studies reported exclusive breastfeeding at three months, four studies reported early breastfeeding initiation within one hour of birth and six studies reported breastfeeding initiation.

The results from the randomized controlled trial (conducted in South Africa) indicated improved exclusive breastfeeding rates at three months but not of rates of early initiation of breastfeeding. The results from four cohort studies (three of fair¹ quality and one poor quality) reported improved exclusive breastfeeding rates at three months following breastfeeding promotion interventions, two of which were statistically significant.

Two observational studies of low quality reported higher exclusive breastfeeding rates at six months among women who received interventions, and there was a positive dose-response effect between intervention visits and exclusive breastfeeding rates.

Evidence for breastfeeding initiation rates and early initiation is mainly supported by studies of low to very low quality. These six observational studies showed an increase in initiation rates post-intervention; however, none of these studies had comparison or control groups.

¹ The authors of the systematic review used the terms “good, fair and poor” to assess the quality of the evidence.

The review found that breastfeeding promotion and support favourably influenced exclusive breastfeeding and breastfeeding initiation rates. The studies also indicated that frequency of contact was associated with improved exclusive breastfeeding practices – more contacts were associated with higher exclusive breastfeeding rates. Combinations of group education and individual counselling sessions regarding infant feeding, involving fathers and other family members with community health workers and/or trained health-care workers and integrating programmes for preventing mother-to-child transmission of HIV along with access to ART each positively affected exclusive breastfeeding.

No studies reported on the effect of interventions on concurrent improvements in adherence to ART, even though such interventions may have been similar in nature.

Interventions to improve safe replacement feeding by mothers living with HIV

No published studies were identified that provided evidence on promoting and supporting safe and adequate replacement feeding practices by mothers living with HIV.

Interventions in the general population to improve breastfeeding practices

Sinha et al. (2015) evaluated the effect of interventions in the general population on early initiation of, exclusive and continued breastfeeding and any breastfeeding rates when delivered in five settings: (1) health systems and services; (2) home and family environment; (3) community environment; (4) working environment; and (5) policy environment; or a combination of any of the above. A total of 195 articles were included. They found that delivering interventions in a combination of settings led to greater improvement in breastfeeding rates. The greatest improvements in early initiation of breastfeeding, exclusive breastfeeding and continued breastfeeding rates were seen when counselling or education were provided concurrently in home and community, health systems and community and health systems and home settings, respectively. Support of baby-friendly hospital interventions at the health system level was the most effective intervention in improving the rates of any breastfeeding. The authors concluded that improving breastfeeding rates requires delivering interventions in a combination of settings by involving health systems, home and family and the community environment concurrently.

In summary, indirect evidence from populations not affected by HIV demonstrates that exclusive breastfeeding rates and also continued breastfeeding can be improved by interventions at the policy level or health facilities and in communities. In general populations, the best outcomes are achieved when interventions are implemented concurrently through multiple channels. Cost-benefit studies were not identified.

As above, the values and preferences of representatives of national health authorities in the 22 priority countries^a for the Global Plan (UNAIDS, 2011) regarding infant feeding were captured in a survey. The findings are included in the decision-making table (Table 5) and reported in Annex 3.

^a Angola, Botswana, Burundi, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Ghana, India, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia and Zimbabwe.

Table 5. Considerations when developing infant feeding recommendations in the context of HIV

SUPPORTING EVIDENCE AND ADDITIONAL CONSIDERATIONS		
	Question	Can facility- and community-based interventions improve the quality of breastfeeding practices among mothers living with HIV?
BENEFITS AND HARM	<p>Do the desirable effects outweigh the undesirable effects?</p> <p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>	<p>Interventions are likely to improve the quality and duration of breastfeeding and therefore the health outcomes of infants, children and mothers. The data from populations affected by HIV are consistent with the experiences in non-HIV settings.</p> <p>Although the review identified no evidence, the Guideline Development Group considered that similar interventions to mothers living with HIV who are giving replacement feeds would also improve their quality and safety including preventing spill-over effects into the non-HIV population.</p> <p>Although not reported in the systematic reviews, interventions to improve feeding practices among mothers living with HIV are also likely to improve breastfeeding practices in the general population not affected by HIV.</p> <p>The Guideline Development Group considered it likely that properly designed counselling and support interventions could simultaneously improve ART adherence and retention in care among mothers living with HIV.</p> <p>anappropriate increased use of replacement feeds among the general population as a result of HIV-related recommendations and practices among mothers living with HIV.</p>
VALUES, PREFERENCES AND ACCEPTABILITY	<p>Is there important uncertainty or variability about how much people value the options?</p> <p><input type="checkbox"/> Major variability <input checked="" type="checkbox"/> Minor variability <input type="checkbox"/> Uncertain</p> <p>Is the option acceptable to key stakeholders?</p> <p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>	<p>The Guideline Development Group considered that interventions to support improved and safer infant feeding practices are likely to be very acceptable to mothers living with HIV.</p> <p>The survey conducted among national health ministries before the guideline meeting found that health managers uniformly supported interventions to help mothers living with HIV to feed their infants appropriately and safely. Health services already provide some support for infant feeding practices, both to the general population and to mothers living with HIV. However, investment in these aspects of programme support is only very modest.</p> <p>The Guideline Development Group also considered that health authorities and individual health workers would be very supportive of individual mothers and also linking with interventions taking place in communities, even if they were not initiated or coordinated by the health authorities.</p>
FEASIBILITY AND RESOURCE USE	<p>How large are the resource requirements?</p> <p><input type="checkbox"/> Major <input type="checkbox"/> Minor <input checked="" type="checkbox"/> Uncertain</p> <p>Is the option feasible to implement?</p> <p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>	<p>The investment required to improve health worker skills and competencies to support early initiation of, exclusive and continued breastfeeding may be significant.</p> <p>Interventions, such as supervision, may also require significant resources to sustain them over time.</p> <p>However, the initial costs may be offset by long-term health benefits in the entire population (they would be cost-effective). These costs need to be considered when health funds are allocated.</p> <p>Investment should be commensurate with the value of the intervention and health outcome: that is, major resources may be needed but would be fully justified.</p>

EQUITY	<p>Would the option improve equity in health?</p> <p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Uncertain</p>	<p>Breastfeeding is one of the few types of health behaviour that tends to be more frequently practised among poorer communities than high-income populations.</p> <p>Interventions to support and improve feeding practices among mothers living with HIV are likely to improve feeding practices in the entire population and therefore reduce inequity. They are also likely to reduce the negative effects of spill-over^a messages in which mothers in the general population mistakenly adopt practices specific to mothers living with HIV.</p> <p>Improving feeding practices is likely to improve health outcomes most in the more vulnerable populations.</p> <p>Multiple analyses in non-HIV populations have shown that improved breastfeeding tends to improve health equity.</p>
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^a Inappropriate increased use of replacement feeds among the general population as a result of HIV-related recommendations and practices among mothers living with HIV.

RECOMMENDATION 2

In settings where maternal, newborn and child health services promote and support breastfeeding and ART to increase HIV-free survival among infants born to mothers living with HIV.

National and local health authorities should actively coordinate and implement services in health facilities and activities in workplaces, communities and homes to protect, promote and support breastfeeding^a among women living with HIV.

Strength of the recommendation	Strong
Quality of the evidence	High quality of evidence
Justification	<p>Guideline Development Group members emphasized that support for breastfeeding should be consistent across policies and programmes, health facilities and community activities for all women, including mothers living with HIV, to create an enabling environment for this practice. Support is needed not only at initiation and during the exclusive breastfeeding period but also to enable mothers to breastfeed for longer: that is, until 24 months or beyond. Therefore, this recommendation would have benefits across the whole population.</p> <p>The group noted that the public health approach of national authorities promoting a single infant feeding practice among mothers living with HIV has resolved much of the confusion among health workers and communities regarding choice of feeding practice and that a recommendation to counsel and support breastfeeding should not be misunderstood as reverting to individual counselling about initial choice.</p> <p>Although there was no published evidence base regarding support for safer replacement feeding, additional support by skilled health workers can probably make replacement feeding practices safer.</p> <p>Long-term investment and sustained support for health workers at all levels are necessary to ensure continued capacity-building.</p>

^a Breastfeeding as recommended by WHO is defined as: (1) initiating breastfeeding within the first hour of life; (2) exclusive breastfeeding for the first six months of life (that is, the infant only receives breast milk without any additional food or drink, not even water); followed by (3) continued breastfeeding for up to two years or beyond (with introduction of appropriate complementary foods at six months); and (4) breastfeeding on demand – that is, as often as the child wants, day and night.

Implementation considerations	<ul style="list-style-type: none"> • Community and health facility approaches to support improved infant feeding practices include: <ul style="list-style-type: none"> – combining group education with individual counselling sessions; – building the skills and competencies of health workers to deliver infant feeding counselling; – involving fathers and family; – involving community health workers and trained health-care workers; and – integrating programmes for preventing mother-to-child transmission of HIV with access to ART.
	<ul style="list-style-type: none"> • Outcomes are improved by more interventions being implemented concurrently and more frequent points of contact. • National authorities need to create and sustain an enabling environment that encourages appropriate feeding practices for all infants and young children while scaling up interventions to reduce HIV transmission. See the updated <i>HIV and infant feeding: framework for priority action</i> (WHO, 2012a). • Simple, consistent messaging is essential to support breastfeeding in the general population, including mothers living with HIV. Such messaging should address views and concerns related to the previous recommendations. • Health-care providers should be trained to implement national recommendations on infant feeding, including how to identify women who may not be able to breastfeed for medical reasons. • As stated in the 2010 WHO guidelines on HIV and infant feeding, health services need to support mothers living with HIV in their chosen feeding practices even when these are inconsistent with nationally recommended practices. This principle is still endorsed by WHO and remains relevant to these updated recommendations. • In settings in which national authorities recommend replacement feeding to mothers living with HIV, it is likely that similar coordinated support can improve the safety of replacement feeding practices. • WHO/Food and Agriculture Organization (FAO) guidance on safe preparation of powdered infant formula (2007) provides technical information that may be helpful in the context of HIV.
Research priorities	<ul style="list-style-type: none"> • Which communication strategies and capacity development approaches are most effective for improving the skills and competencies of health workers to provide support to mothers living with HIV regarding infant feeding practices and adherence to ART? • Which communication strategies and engagement approaches are most effective at informing communities and giving confidence to mothers living with HIV regarding infant feeding practices and adherence to ART? • In the context of HIV, what support increases exclusive and continued breastfeeding in the general population?

3. What to advise when mothers living with HIV do not exclusively breastfeed

In settings where maternal, newborn and child health services promote and support breastfeeding and ART to increase HIV-free survival among infants born to mothers living with HIV:

If a mother living with HIV does not exclusively breastfeed, is mixed feeding with ART better than no breastfeeding at all?

- Are ARV drugs effective in preventing the postnatal transmission of HIV through breast milk according to feeding modality?

Background

In 2003 and 2006, when no other interventions were available to reduce the risk of postnatal HIV transmission, WHO guidelines on HIV and infant feeding highlighted the increased risk of HIV transmission associated with mixed feeding in the first six months of life compared with exclusive breastfeeding (UNICEF et al., 2003; WHO et al., 2006).

Mixed feeding, also referred to as partial breastfeeding, is less protective against serious childhood illnesses such as diarrhoea and pneumonia than exclusive breastfeeding. This is true for both HIV-exposed and unexposed infants and children (Bahl et al., 2005). For this reason, WHO recommends exclusive breastfeeding for all infants in the first six months of life. Despite this, rates of exclusive breastfeeding globally have remained either static or increased only modestly (Victora et al., 2016). However, although exclusive breastfeeding provides the greatest benefits for both mothers and infants, even any breastfeeding is associated with improved survival and other health outcomes compared with no breastfeeding (Victora et al., 2016).

In 2010, the WHO guidelines presented high-quality evidence that ARV drugs are effective in reducing the risk of postnatal transmission. Studies confirming this outcome promoted and supported exclusive breastfeeding among the mothers living with HIV participating in the research. However, in these studies, transmission outcomes were not disaggregated according to infant feeding modality.

At that time, WHO infant feeding guidelines for HIV-exposed infants combined recommendations to prevent postnatal HIV transmission, that is, maternal or infant ARV drugs, with recommendations to protect against non-HIV morbidity and mortality, that is, exclusive and continued breastfeeding with appropriate complementary feeding. However, health workers were reportedly uncertain whether or not to promote and implement the WHO 2010 recommendation in settings in which rates of exclusive breastfeeding were low.

Recommendation included in the WHO 2010 guidelines on HIV and infant feeding (WHO, 2010b)

In settings where national authorities have decided that the maternal and child health services will principally promote and support breastfeeding and antiretroviral interventions as the strategy that will most likely give infants born to mothers known to be HIV-infected the greatest chance of HIV-free survival.

Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life.

At the scoping meeting, the Guideline Development Group advised WHO to clarify whether ARV drugs are effective in preventing the postnatal transmission of HIV among mothers living with HIV according to feeding mode: that is, both mixed-feeding and exclusive breastfeeding.

Summary of the evidence

Two systematic reviews commissioned for question 1 (duration of breastfeeding) provided evidence in consideration of this question.

1. Chikhungu L, Bispo S, Newell ML. HIV-free survival at 12–24 months in breastfed infants of HIV-positive women on ART: a systematic review (Annex 1a).
2. Chikhungu L, Bispo S, Newell ML. Postnatal HIV transmission rates at age six and 12 months in infants of HIV-positive women on ART initiating breastfeeding: a systematic review (Annex 1b).

The first review (Chikhungu et al., Annex 1a) examined the effectiveness of ARV drug interventions in promoting HIV-free survival among HIV-exposed infants by duration of breastfeeding and also according to early infant feeding practices. The systematic review did not identify any randomized controlled trials that directly compared these populations. The review therefore summarized data from cohort studies that reported HIV transmission rates and HIV-free survival among HIV-exposed infants according to early infant feeding practices. However, none reported differences between exclusively breastfed infants and mixed-fed infants (GRADE evidence profile, Annex 1a, Table 4).

The second review (Chikhungu et al., Annex 1b) summarized HIV transmission rates at six, nine and 12 months among infants born to mothers living with HIV who were receiving ART. The review specifically sought evidence regarding transmission rates among infants according to early infant feeding practices, especially among those who were mixed-fed in the first months of life compared with those who were exclusively breastfed.

No randomized controlled trial was identified that directly compared outcomes among infants who were exclusively breastfed versus mixed-fed – conducting a study of this type would be considered unethical.

Eleven studies were identified that provided potentially relevant data. Six provided estimates of postnatal transmission rates, excluding peripartum infections that were diagnosed before six weeks of age, among mothers living with HIV who were receiving ARV drugs. Seven studies provided similar information on transmission rates at age 12 months, five reported overall HIV transmission rates (including peripartum) and two reported postnatal transmission rates (GRADE evidence profile, Annex 1b, Table 7).

However, none of these studies disaggregated transmission rates by early infant feeding modality (exclusive breastfeeding or mixed feeding) among mothers living with HIV who were receiving ARV drugs; indeed, the majority of reports of these studies did not provide any details of feeding practices: that is, exclusive breastfeeding or mixed-feeding in the first six months. In all studies, mothers were recommended to exclusively breastfeed their infants for six months. Alvarez-Uria et al. (2012) noted that one of the children living with HIV was mixed-fed but did not provide the rate of transmission by feeding modality.

The principal investigators of 10 studies were contacted for additional information regarding how feeding type was assessed and supported during the study. Five confirmed that exclusive breastfeeding was promoted but not assessed as part of the study processes. It was assumed that some mothers would have exclusively breastfed up to five or six months as recommended, but others would have introduced other fluids, milks or solids: mixed-feeding. No study had transmission rates available that were disaggregated according to exclusive breastfeeding or mixed feeding where the mother was receiving lifelong ART.

Transmission rates reported by the respective studies in peer-reviewed literature therefore represented a mix of feeding practices. The Guideline Development Group noted the very low postnatal transmission rates when there were high levels of adherence to ARV drugs and viral loads were low. The Guideline Development Group considered that, although there was no direct evidence, it was very likely that ARV drugs were equally effective at reducing postnatal transmission whether mothers were mixed-feeding or were exclusively breastfeeding.

However, in the general population not affected by HIV, high-quality evidence indicates that predominant and partial breastfeeding are associated with improved health outcomes compared with no breastfeeding (Victora et al., 2016).

Table 6. Considerations when developing infant feeding recommendations in the context of HIV

SUPPORTING EVIDENCE AND ADDITIONAL CONSIDERATIONS		
	Question	If a mother living with HIV does not exclusively breastfeed, is mixed feeding with ART better than no breastfeeding at all?
BENEFITS AND HARM	<p>Do the desirable effects outweigh the undesirable effects?</p> <p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>	<p>Compared with exclusive breastfeeding, mixed feeding is associated with a greater risk of serious morbidity, such as diarrhoea and pneumonia and the related mortality among HIV-exposed infants and children. In the absence of ART, it is also associated with an increased risk of postnatal transmission of HIV.</p> <p>However, compared with non-breastfeeding (replacement feeding) in resource-limited settings, mixed feeding in the first six months of life (more correctly referred to as partial breastfeeding) is associated with reduced morbidity among both HIV-exposed and unexposed infants (WHO, 2010b).</p> <p>ARV drugs significantly reduce the risk of postnatal transmission – and appear to be effective when mothers living with HIV either exclusively or partly breastfeed. They also appear to be equally effective in reducing HIV transmission after six months of age when complementary foods are introduced, based on supportive evidence that ARV drugs reduce the transmission risks in the context of mixed feeding among infants younger than six months of age.</p> <p>However, promoting breastfeeding and ARV drugs when mixed feeding is common may appear to endorse mixed feeding and undermine the principle of exclusive breastfeeding.</p> <p>Clear messaging and supportive interventions in health services and activities in communities can promote and support exclusive breastfeeding in the general and HIV-exposed populations to achieve the best health outcomes (non-HIV-related) for mothers living with HIV and their infants.</p>
VALUES, PREFERENCES AND ACCEPTABILITY	<p>Is there important uncertainty or variability about how much people value the options?</p> <p><input type="checkbox"/> Major variability <input checked="" type="checkbox"/> Minor variability <input type="checkbox"/> Uncertain</p> <p>Is the option acceptable to key stakeholders?</p> <p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>	<p>Breastfeeding is very acceptable to mothers living with HIV when ARV drugs are available. Clear messaging that confirms the effectiveness of ARV drugs in reducing postnatal transmission in the context of all feeding modalities would further increase acceptability and confidence.</p> <p>Clarifying that exclusive breastfeeding is promoted to reduce non-HIV-related morbidity and mortality would provide insight for the rationale and also help to promote exclusive breastfeeding.</p> <p>Clarifying the effectiveness of ARV drugs in reducing the risk of postnatal transmission is similarly likely to give added confidence to health workers. However, similar to mothers living with HIV, clear explanations and communication are needed in addition to training.</p>
FEASIBILITY AND RESOURCE USE	<p>How large are the resource requirements?</p> <p><input type="checkbox"/> Major <input checked="" type="checkbox"/> Minor <input type="checkbox"/> Uncertain</p> <p>Is the option feasible to implement?</p> <p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>	<p>There are minimal additional resource implications. Training and capacity development costs for health workers would be the most immediate requirement. An investment to improve counselling services to mothers living with HIV could also serve to improve services to the general population.</p> <p>Clarifying evidence and optimal infant feeding practices among health workers would be very feasible, as would implementation by health workers.</p>

EQUITY	Would the option improve equity in health? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain	<p>The intervention may improve health equity, since any breastfeeding, especially in the poorest populations, reduces the risk of serious morbidity and mortality not related to HIV.</p> <p>Improving feeding practices is likely to have the greatest positive impact on the health outcomes of the more vulnerable populations.</p>

GUIDING PRACTICE STATEMENT¹

Mothers living with HIV and health-care workers can be reassured that ARV treatment reduces the risk of postnatal HIV transmission in the context of mixed feeding. Although exclusive breastfeeding is recommended, practising mixed feeding is not a reason to stop breastfeeding in the presence of ARV drugs.

Strength of the recommendation	Not applicable
Quality of the evidence	Very low
Justification	<p>The Guideline Development Group unanimously agreed that this should not be a recommendation but instead should be presented as a guiding practice statement. Although the Guideline Development Group was confident of the efficacy of ARV drugs in reducing postnatal transmission even when mothers living with HIV are mixed feeding, the importance and value of exclusive breastfeeding for non-HIV-related health outcomes is such that no recommendation should be perceived as endorsing non-exclusive breastfeeding of infants in the first six months of life.</p> <p>However, the group considered that it is equally important to clarify the efficacy of ARV drugs in reducing postnatal HIV transmission even when mothers are mixed feeding and that, although not optimal, mixed feeding while the mother is taking ART is better than not breastfeeding at all.</p>
Implementation considerations	<ul style="list-style-type: none"> Implementing recommendations for mothers living with HIV should be contextualized first by the optimal infant feeding practice recommended for all mothers and infants: to exclusively breastfeed for six months and then introduce appropriate complementary foods and continue breastfeeding for 24 months or beyond. When implementing recommendations for mothers living with HIV, national health authorities need to clearly communicate the hierarchy of what is ideal and how recommendations for mothers living with HIV are specific to their circumstances. Programmes should develop clear messaging to avoid misunderstandings among health workers, mothers living with HIV and the general population. If this is not achieved, infant feeding practices and health outcomes among children could be substantially harmed.
Research priorities	<ul style="list-style-type: none"> How to improve exclusive breastfeeding rates among mothers living with HIV who are receiving ARV drugs

¹ A guiding practice statement is made to encourage action or clarify an issue of concern. It addresses an area of suboptimal practice and provides a contingency and guidance to health workers regarding how to respond to a specific challenge.

4. What to advise when mothers living with HIV do not plan to breastfeed for 12 months

In settings in which maternal, newborn and child health services promote and support breastfeeding and ART to increase HIV-free survival among infants born to mothers living with HIV:

If a mother living with HIV plans to return to work or school, is a shorter duration of planned breastfeeding with ART better than no breastfeeding at all?

- What is the HIV-free survival of infants breastfed for durations less than 12 months compared with breastfeeding for 12 months?

Background

In 2010, WHO guidelines on HIV and infant feeding were updated to recommend that, in settings in which diarrhoea, pneumonia and undernutrition were still common causes of infant and child mortality, national health authorities should, while providing ARV drugs, promote and support breastfeeding among women and mothers living with HIV (WHO, 2010b). Such mothers were recommended to exclusively breastfeed their infants for the first six months of life, to introduce appropriate complementary foods thereafter and to continue breastfeeding for the first 12 months of life.

The recommendation was informed by evidence that breastfeeding in the first 12 months was associated with significantly lower mortality risks for infants. Studies had also reported low rates of postnatal HIV transmission associated with ARV drugs being given to lactating mothers living with HIV or HIV-exposed breastfeeding infants. Since then, studies in non-HIV populations have shown health benefits to mothers and infants with longer durations of breastfeeding.

Recommendation included in the 2010 WHO guidelines on HIV and infant feeding (WHO, 2010b)

In settings where national authorities have decided that the maternal and child health services will principally promote and support breastfeeding and antiretroviral interventions as the strategy that will most likely give infants born to mothers known to be HIV-infected the greatest chance of HIV-free survival:

Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life.

However, in both HIV-affected populations and in the general population, some women choose to breastfeed for durations less than 12 months or are unable to breastfeed for 12 months or more, because they go back to work or school and do not benefit from sufficient breastfeeding protection, promotion and support at the workplace.

Although longer durations of breastfeeding are generally considered better for the infant, the Guideline Development Group advised WHO to clarify whether, if a mother living with HIV plans to return to work or school, a shorter duration of planned breastfeeding with ART is better than no breastfeeding at all. The Guideline Development Group considered that the most relevant evidence to inform this decision would be the rates of HIV-free survival among infants breastfed for durations less than 12 months compared with breastfeeding for 12 months.

Summary of the evidence

One systematic review commissioned for question 1 (duration of breastfeeding) provided evidence in consideration of this question.

1. Chikhungu L, Bispo S, Newell ML. HIV-free survival at 12–24 months in breastfed infants of HIV-positive women on ART: a systematic review (Annex 1a).

The review (Chikhungu et al., Annex 1a) examined the effectiveness of ARV drug interventions to promote HIV-free survival among HIV-exposed infants according to early infant feeding practices, including the duration of breastfeeding in the first 12 months of life. The review summarized data from cohort studies that reported HIV transmission rates and HIV-free survival among HIV-exposed infants according to the duration of breastfeeding versus non-breastfeeding and by ART exposure. Four studies provided estimates of HIV-free survival by feeding modality; three reported higher HIV-free survival among breastfed infants than formula-fed infants (GRADE evidence profile, Annex 1a, Table 4). HIV-free survival among breastfed infants ranged from 82% (95% CI: 73.4–87.7%) [median weaning: five months] to 96% (95% CI: 91–98%) and in formula-fed infants from 67% (95% CI: 35.5–87.9%) to 97.6% (95% CI: 93.0–98.2%). All studies were graded as low or very low quality. (Additional details on this review are cited in the evidence summaries for questions 1 and 3 above).

The Guideline Development Group also noted the standing recommendations in the WHO 2010 guidelines on HIV and infant feeding that were informed by outcome data from infants according to feeding practices among mothers living with HIV who were not receiving lifelong ART (WHO, 2010b). The evidence that informed those recommendations highlighted:

- **Exclusive breastfeeding in the first six months of life was also associated with reduced mortality over the first year of life in HIV-exposed infants compared with mixed feeding and replacement feeding in both research and programme settings, especially if inappropriately chosen by mothers.**
- **Infants given replacement feeds after a period of breastfeeding also suffered increased serious infections, including diarrhoea and pneumonia, growth faltering and death (Arpadi et al., 2009; Creek et al., 2010; Homsy et al., 2010; Kafulafula et al., 2010; Kagaayi et al., 2008; Onyango-Makumbi et al., 2010; Phadke et al., 2003).**

Additional supporting evidence:

- **High-quality evidence from non-HIV settings that mixed feeding and non-breastfeeding are associated with increased morbidity and mortality.**

In the general population not affected by HIV, high-quality evidence indicates that predominant and partial breastfeeding are associated with improved health outcomes compared with no breastfeeding.

Table 7. Considerations when developing infant feeding recommendations in the context of HIV

SUPPORTING EVIDENCE AND ADDITIONAL CONSIDERATIONS		
	Question	If a mother living with HIV plans to return to work or school, is a shorter duration of planned breastfeeding with ART better than no breastfeeding at all?
BENEFITS AND HARM	<p>Do the desirable effects outweigh the undesirable effects?</p> <p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>	<p>In the context of maternal ART, low-quality evidence shows that the HIV-free survival of infants born to mothers living with HIV who are breastfed is better than for infants who are never breastfed.</p> <p>Data from low- and middle-income settings before the scaling up of ART for mothers living with HIV (in accordance with the 2010 WHO recommendations) demonstrated increased mortality and morbidity, including growth faltering, among infants of mothers living with HIV who were never breastfed or who stopped breastfeeding early. Among these infants, breastfeeding was never initiated or the duration of breastfeeding was limited to reduce the risk of postnatal transmission of HIV. In 2010, this evidence supported the principle that any breastfeeding is better than no breastfeeding at all. Comparable data from mothers receiving ART during the past five years were not identified.</p> <p>When mothers living with HIV are receiving ART, the rationale for never initiating or reducing the duration of breastfeeding is even weaker, and programmes may focus their support on longer durations of breastfeeding.</p> <p>Further, in populations not affected by HIV, morbidity and mortality are significantly increased among infants who are never breastfed compared with infants who are exclusively or predominantly breastfed. A dose-related effect is also reported: longer durations of breastfeeding are associated with better health outcomes among both mothers and infants. Even early initiation of breastfeeding in addition to short durations of breastfeeding result in health benefits for neonates and young infants and for older children.</p> <p>More closely aligning the recommendations for mothers living with HIV with those for mothers without HIV is likely to improve practices across all populations.</p>
VALUES, PREFERENCES AND ACCEPTABILITY	<p>Is there important uncertainty or variability about how much people value the options?</p> <p><input type="checkbox"/> Major variability <input checked="" type="checkbox"/> Minor variability <input type="checkbox"/> Uncertain</p> <p>Is the option acceptable to key stakeholders?</p> <p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>	<p>A recommendation would be likely to be acceptable to mothers. Clear messaging that confirms the effectiveness of ARV drugs with all breastfeeding durations would further increase acceptability and confidence.</p> <p>For mothers returning to work or school, efforts and support could be focused on plans and support to enable them to continue breastfeeding, similar to mothers who do not have HIV.</p> <p>A recommendation would be likely to be acceptable to health workers as long as it is accompanied by guidance on supporting breastfeeding among working mothers or mothers returning to school.</p> <p>In the survey of health ministry officials (Annex 3), they considered clarifying the value of even short durations of breastfeeding to be advantageous. The value of harmonizing recommendations between mothers living with HIV and mothers in the general population was highlighted.</p>
FEASIBILITY AND RESOURCE USE	<p>How large are the resource requirements?</p> <p><input type="checkbox"/> Major <input checked="" type="checkbox"/> Minor <input type="checkbox"/> Uncertain</p> <p>Is the option feasible to implement?</p> <p><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain</p>	<p>There are minimal additional resource implications, but training and capacity development would be required.</p> <p>However, support would be needed for breastfeeding at work – although this is also necessary for all mothers at work, not just those living with HIV.</p> <p>Implementing this recommendation would be feasible.</p>

EQUITY	<p>Would the option improve equity in health?</p> <p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Uncertain</p>	<p>This may improve health equity, since any breastfeeding, especially in the poorest populations, reduces the risk of non-HIV-related serious morbidity and mortality.</p>

GUIDING PRACTICE STATEMENT¹ 2

Mothers living with HIV and health-care workers can be reassured that durations of breastfeeding of less than 12 months are better than never initiating breastfeeding at all.

Strength of the recommendation	Not applicable
Quality of the evidence	Low
Justification	<p>The Guideline Development Group considered the evidence from the systematic reviews that indicated that infants of mothers living with HIV benefited more from some breastfeeding than breastfeeding never being initiated at all. However, the Guideline Development Group did not want to make a formal recommendation in case it appeared to endorse shorter durations of breastfeeding being better than longer durations. The group felt that a guiding practice statement would respond to day-to-day realities and give sufficient guidance to deal with current situations.</p> <p>Members of the Guideline Development Group emphasized that infants living with HIV are vulnerable and need breastfeeding the most, so this is one motivation to keep breastfeeding as long as possible. Where early infant testing is carried out, delivering the results should prompt a discussion on feeding, even in countries where formula feeding is the norm.</p> <p>Accountability of community and service providers could help achieve the type of support needed for continued breastfeeding; however, national policy ensuring adequate maternity leave and maternity benefits will be required as a long-term solution for both non-HIV-affected and HIV-affected populations.</p>
Implementation considerations	<ul style="list-style-type: none"> • In all settings, implementing recommendations for mothers living with HIV should be contextualized first by the optimal infant feeding practice recommended for all mothers and infants: to exclusively breastfeed for six months, then introduce appropriate complementary feeds and continue breastfeeding for 24 months or beyond. • When implementing recommendations for mothers living with HIV, national health authorities need to clearly communicate the hierarchy of what is ideal and how the recommendations for mothers living with HIV are specific to their circumstances. • Programmes should develop clear messaging to avoid misunderstandings among health workers, mothers living with HIV and the general population. If this is not achieved, infant feeding practices and health outcomes among children could be substantially harmed.
Research priorities	<ul style="list-style-type: none"> • How to support mothers living with HIV who are receiving ARV drugs to breastfeed for longer in circumstances such as when they return to work or school

¹ A guiding practice statement is made to encourage action or clarify an issue of concern. It addresses an area of suboptimal practice and provides a contingency and guidance to health workers regarding how to respond to a specific challenge.

Implications for monitoring and evaluation

A subgroup of the Guideline Development Group discussed possible implications of the proposed recommendations on how national and local authorities monitor and evaluate HIV programmes and programmes for preventing the mother-to-child transmission of HIV. The subgroup reported back to the full Guideline Development Group. The following points summarize the discussions and suggestions of the full Group.

The Guideline Development Group first considered what information and data would be needed for future guideline revisions, including:

- which countries took up the guidelines and how they were adapted;
- nationally representative data on:
 - the rates of retention in care at minimum at 12 and 24 months postpartum among mothers living with HIV and their infants or young children;
 - the duration and type of breastfeeding among mothers living with HIV – ideally disaggregated by urban and rural populations;
 - the HIV transmission rates among infants and children disaggregated by the timing of infection;
 - the infant and child mortality rates disaggregated by HIV exposure and infection status;
 - the maternal mortality rates by HIV status;
 - the rates of ART coverage and viral load of mothers living with HIV at the time of first antenatal care booking;
- routine programme data regarding:
 - infant and maternal nutrition status disaggregated by HIV exposure and infection status;
 - ART coverage among women living with HIV at time of first antenatal care booking;
 - the prevalence among young children of diarrhoea and other serious morbidity, especially morbidity related to undernutrition; and
- the skills and competencies of health workers regarding infant and young child feeding and training courses attended:
 - number of training or skill-building courses conducted;
 - skill assessments;
 - the acceptability of training and capacity development and the roles expected among health-care workers.

The Guideline Development Group formulated some key principles for data collection and use.

- Use existing datasets where available, such as:
 - vital statistics and laboratory data;
 - household surveys (especially in settings with a high prevalence of HIV) and cohort phone follow-up (especially in settings with a low prevalence of HIV); and
 - sentinel surveys if needed.
- Use data for decision-making in local services; this would help to justify the cost of collecting data. In addition, data collection approaches should:
 - link to service delivery; and
 - not divert resources from treatment.

Implications for conflict and emergency settings

A subgroup of the Guideline Development Group considered the implications for supporting infant and young child feeding in conflict and emergency settings. The subgroup reported back to the full Guideline Development Group. The following points summarize the discussions and suggestions.

The Guideline Development Group noted the wide range of challenging settings in which the updated recommendations would be relevant, including acute, protracted and recurrent conflict and emergency settings. The Group noted that emergencies commonly disrupt and overwhelm the routine systems of support at all levels including drug supply, the availability and capacity of health workers and authorities and of communities to respond. Physical and health system disruptions undermine optimal breastfeeding and complementary feeding, and these are compounded by the stress of mothers and families.

Because data collection is complex, evidence is lacking on how best to support and guide infant feeding practices in emergencies. Nevertheless, considering the balance of risks of feeding options and the impact on child survival is paramount. For example, Jakobsen et al. (2003) reported that, during the first three months of the war in Guinea-Bissau in 1998, children 9–20 months of age who were no longer breastfed were six times more likely to die than were children still breastfeeding.

HIV adds specific challenges and considerations to infant and young child feeding.

- Crises change risk profiles, and the relative risks and acceptability of various feeding practices among mothers and communities therefore need to be re-evaluated. In such settings, the acceptable, feasible, affordable, sustainable and safe criteria for determining the appropriateness of use of replacement foods may still be useful.
- The prevailing policy on HIV and infant feeding may not be in accordance with international recommendations on infant and young children in emergency settings.
- ARV drug supplies may be disrupted, or no ARV drugs may be available at all.
- Girls and women may be especially vulnerable and at additional risk of HIV infection.
- The fear of HIV transmission among families may result in inappropriate responses, including recommendations to avoid breastfeeding in the absence of testing and the distribution of infant formula.

The Guideline Development Group considered that WHO should develop specific guidance on HIV and infant feeding in emergencies to address issues including:

- integrated responses that consider health, HIV, preventing the mother-to-child transmission of HIV, infant and young child feeding, etc.;
- emergency preparedness by national authorities, including community responses;
- key infant and young child feeding emergency principles that apply and should be integrated into situations in which HIV is a concern;
- managing the interruption of supplies of ARV drugs; and
- consistent, accurate communication.

Next steps

The Guideline Development Group acknowledged that addressing the complexities of HIV and infant feeding in emergencies was beyond the scope of the current technical consultation in terms of time, scope of the evidence presented and the profile of participants present. Members proposed that WHO convene a meeting specifically on HIV and infant feeding in emergencies with participants to include United Nations agencies, operational nongovernmental organizations working in nutrition and health, government representatives and nutrition and health agencies. Such a meeting should seek to clarify programmatic issues and develop a framework and key principles regarding infant feeding and HIV in emergencies to help put the current HIV and infant feeding guidance into practice. The meeting should seek to collaborate with and learn from the HIV community and other sectors. In the absence of formal research evidence, case studies could be developed to inform thinking and direction, with consideration of qualitative research (such as the CERQual [Confidence in the Evidence from Reviews of Qualitative Research] approach). An important output of such a meeting would be to identify evidence gaps and set priorities for research questions to address. The meeting would inform the update of the operational guidance on infant and young child feeding in emergencies (IFE Core Group, 2007) endorsed by the World Health Assembly being updated in 2016.

Methods

The process outlined in the *WHO handbook for guideline development* (WHO, 2012b) was followed. This included: (1) identifying priority clinical questions and outcomes; (2) retrieving the evidence; (3) assessing the quality of evidence and synthesizing the findings; (4) formulating recommendations, including future research priorities; and (5) planning for dissemination, implementation, impact evaluation and updating the guideline.

The GRADE method was followed to prepare evidence profile tables related to preselected topics, based on up-to-date systematic reviews. The Guideline Development Group comprised content experts, methodologists and representatives of potential stakeholder groups. Some of these experts participated in a WHO technical consultation held in New York City, United States of America, on 17–18 November 2014 to scope questions for the systematic reviews and guideline update.

The full Guideline Development Group met in Geneva, Switzerland on 21–23 October 2015, to review and discuss the evidence, draft the recommendations and agree on their strength, taking into consideration: (1) the desirable and undesirable effects of this intervention; (2) the quality (confidence in estimates of effect) of the available evidence; and (3) the values and preferences related to the intervention as well as to outcomes and specific contextual factors that pertain to various settings. The cost of the options available to health-care workers in various settings was not formally assessed because of lack of primary data in the literature or elsewhere, but the cost and resource implications were considered as part of a general discussion by the Guideline Development Group.

An additional group of external experts and stakeholders reviewed the proposed recommendations following their drafting. All Guideline Development Group members submitted declarations of interest forms before each meeting and also made verbal declarations of interest at the beginning of meetings.

Evidence retrieval, assessment and synthesis

The evidence retrieval process for the priority questions followed the standard outlined in the *WHO handbook for guideline development* (WHO, 2012b). The acknowledgements provide a list of reviewers. A protocol for each systematic review was developed and included the search terms and strategy and the populations, interventions, comparators and outcomes used to define the inclusion and exclusion criteria. The detailed search strategy for each priority question was agreed on after a series of discussions with the WHO Steering Committee and lead investigators of each review. Each review includes a flow diagram showing the numbers of studies excluded and included. Medline and EMBASE databases were used to identify peer-reviewed publications. The Cochrane Central Register of Controlled Trials, the International Standard Randomised Controlled Trial Number Registry and ClinicalTrials.gov were searched for ongoing studies. The quality of the evidence for each priority question was assessed using the GRADE method (GRADE Working Group, 2016). The quality of the evidence for treatment interventions was graded as high, moderate, low or very low based on the definitions in the *WHO handbook for guideline development* (WHO, 2012b). The GRADE tables were prepared using the GRADE profiler software (GRADEPro), when appropriate. The reviews are available through URLs as in Annexes 1a, 1b, 1c and 2 and will be published. Based on these reviews, the WHO Steering Committee proposed an initial set of draft recommendations.

WHO Steering Committee

A Steering Committee, with members from the Department of Maternal, Newborn, Child and Adolescent Health, Department of Nutrition for Health and Development and the Department of HIV, has overseen the guideline review process. The acknowledgements list the WHO staff members on the Committee.

Guideline Development Group

WHO convened a 21-member Guideline Development Group consisting of internationally recognized experts in terms of content, methods and regional representation. The acknowledgements list the members. Members were tasked with reviewing and evaluating the quality of the evidence identified through the systematic reviews using the GRADE method (described below) and revising and finalizing the guideline recommendations.

External Peer Review Group

Members of the External Peer Review Group were asked to review the recommendations developed by the Guideline Development Group to ensure that there were no important omissions, contradictions or inconsistencies with scientific evidence or programmatic feasibility and to assist in clarifying the language, especially in relation to implementation and how policy-makers and programme staff might read them.

No additional recommendations were invited from the External Peer Review Group. The WHO Steering Committee collated the queries raised by the External Peer Review Group and discussed them with the chairs to resolve any inconsistencies or contradictions raised.

The acknowledgements list the members, from various countries and disciplines, with their affiliations.

Managing conflicts of interest

All members of the Guideline Development Group, systematic review teams and members of the External Peer Review Group were required to sign and submit a declaration of interests prior to their participation in the meetings. The WHO Steering Committee reviewed the declarations before the Guideline Development Group meeting to determine whether any of the proposed members had a conflict of interest that might have precluded or limited his or her participation. Although the WHO Steering Committee did not identify any conflicts of interest requiring any action, the potential conflicts of interest declared by the Guideline Development Group members are summarized next.

Lesley Bamford works at the National Department of Health, South Africa and declared to have a public position regarding breastfeeding, as stated in the Tshwane Declaration. As an employee of the National Department of Health, she explains, defends and advocates such a position. It was agreed that she could participate fully in the deliberations and decision-making on these recommendations.

Louise Kuhn declared her involvement in projects related to oligosaccharides and cytokines in breast milk, early antiretroviral therapy in neonates and follow-up of children living with HIV, which received grants from the National Institute of Dental and Craniofacial Research, the United States National Institutes of Health and the Eunice Kennedy Shriver National Institute of Child Health and Human Development. It was agreed that she could participate fully in the deliberations and decision-making on these recommendations.

Angela Mushavi declared being employed by the Elizabeth Glaser Pediatric AIDS Foundation and seconded to the Ministry of Health and Child Care of Zimbabwe as national coordinator of services for preventing the mother-to-child transmission of HIV and HIV care and treatment for children. In this role, she discusses infant and young child feeding as a child survival strategy and also recognizes and articulates the benefits of breastfeeding, even among women living with HIV. It was also declared that the outcome of this meeting is of importance to the Ministry of Health and Child Care. It was agreed that she could participate fully in the deliberations and decision-making on these recommendations.

Anju Seth declared her role as a co-investigator of a project for the nutritional needs of children made vulnerable by HIV funded by UNICEF. At the time of this meeting, the project was scheduled to be completed by November 2015. It was agreed that she could participate fully in the deliberations and decision-making on these recommendations.

Grading the quality of the evidence

The Guideline Development Group used the GRADE method (GRADE Working Group, 2016) to evaluate the quality of the evidence. The GRADE method is a widely used, standardized approach for characterizing the quality of evidence and distinguishing between the quality of the evidence and the strength of the recommendations.

(WHO, 2012b). GRADE tables summarize details about the studies included in the systematic review, including study outcomes, limitations (risk of bias), possible inconsistency, indirectness, imprecision and other factors that might affect judgements of the quality of the evidence. Guideline Development Group members then used the information to define the overall quality of the evidence as very low, low, moderate or high as defined below.

Table 8. Definition of the quality of the evidence using the GRADE method

QUALITY	DEFINITION	IMPLICATION
High	The Guideline Development Group is very confident that the true effect lies close to that of the estimate of the effect.	Further research is very unlikely to change confidence in the estimate of the effect.
Moderate	The Guideline Development Group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.	Further research is likely to have an important impact on confidence in the estimate of the effect and may change the estimate.
Low	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the true effect.	Further research is very likely to have an important impact on confidence in the estimate of the effect and is unlikely to change the estimate.
Very low	The Guideline Development Group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.	Any estimate of effect is very uncertain.

In general, evidence based on randomized controlled trials is given a high-quality rating, and evidence from observational studies is given a low-quality rating. These initial ratings may be adjusted by the following factors:

- study limitations or considerations on the risk of bias such as concealment, blinding, attrition and detection bias;
- consistency: whether the results from the studies are similar and in the same direction of effect;
- directness: whether the population, intervention or comparator are the same as for the clinical question the guideline is considering;
- precision: whether data arise from a large sample with high event rates as represented in the breadth of confidence intervals; and
- reporting or publication bias: whether the underlying beneficial or harmful effect is systematically underestimated or overestimated because of the selective publication of studies or selective reporting of outcomes.

In non-randomized studies, additional adjustment factors include dose–response gradients, the directional effect of plausible bias and the magnitude of effect.

The authors of one systematic review (Annex 1a) also developed a modified Newcastle-Ottawa Scale to assess the quality of all studies included in the analysis (Wells et al., 2009).

Decision-making process

For each draft recommendation, the WHO Steering Committee presented a synthesis of the evidence, the GRADE tables and the draft null recommendation language. The decision-making tables were drafted, including the benefits and risks of the interventions from a public health perspective; the values, preferences and acceptability to mothers living with HIV and their communities as well as programme managers, policy-makers and health-care providers; and the feasibility of implementing any recommendations (including the resources needed, focusing on national programmes in resource-limited or other settings).

Information from a survey of national health authorities from the 22 priority countries of the Global Plan (UNAIDS, 2011) and from an online survey of other stakeholders was used to inform the values and preferences (Annex 3).

The cost of options available to health-care workers in various settings was not formally assessed because of a lack of primary data in the literature or elsewhere. However, the Guideline Development Group considered the cost implications as part of the general discussion. Comments were therefore restricted to personal experiences and extrapolations from general cost considerations of programmes.

Each Guideline Development Group member was asked to review the material and independently comment on and suggest revisions to the proposed guidance and decision-making tables. They were requested to rank the overall quality of the evidence using the GRADE method (independent of the rating made in the synthesis of the evidence), the balance of benefits versus harm, the values that should be considered in making a recommendation and the applicability of any proposed recommendations to the populations for whom they are intended. Finally, they were asked to assess what strength each recommendation should be given based on the criteria provided in Table 9.

Table 9. Criteria for assessing the strength of recommendations

STRENGTH OF THE RECOMMENDATION	RATIONALE
Strong	<p>The Guideline Development Group is confident that the desirable effects of adherence to the recommendation outweigh the undesirable effects.</p> <p>With strong recommendations, the guideline communicates the message that the desirable effects of adherence to the recommendation outweigh the undesirable effects. This means that, in most situations, the recommendation can be adopted as policy.</p>
Conditional	<p>The Guideline Development Group concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects. However, the recommendation is only applicable to a specific group, population or setting or where new evidence may result in changing the balance of risk to benefit or where the benefits may not warrant the cost or resource requirements in all settings.</p> <p>Conditional recommendations are made when there is greater uncertainty about the benefits versus risks, values and preferences, feasibility and acceptability and cost, or if local adaptation has to account for a greater variety in values and preferences or when resource use makes the intervention suitable for some locations but not for others. This means that substantial debate and involvement of stakeholders are needed before this recommendation can be adopted as policy.</p>
No recommendation	Further research is required before any recommendation can be made.

The Guideline Development Group used a consensus-building process to finalize the recommendations. Once participants expressed their opinions and suggestions on a recommendation, the chairs and the WHO Steering Committee summarized this information. This summary was presented to the Guideline Development Group members to gauge the degree of consensus and where differences existed. The chairs of the Guideline Development Group facilitated discussions among Guideline Development Group members until there was consensus on the language of each recommendation, the quality of the evidence and the strength. If consensus could not be reached, the Guideline Development Group had agreed at the beginning of the meeting that a simple majority vote would determine a contested decision.

WHO staff members did not express personal opinions on the data, in the discussions or in the decisions on language, the strength of the recommendations or the quality of the evidence. Throughout the meeting, WHO staff members articulated the principles and guidelines of the WHO decision-making process.

The Guideline Development Group reached agreement on all the recommendations following revisions of the text. The recommendations on the duration of breastfeeding by mothers living with HIV were discussed extensively to achieve consensus on the strength of the recommendation. Voting was only used as a straw-poll method to evaluate consensus, and no decisions were required to be subjected to a final vote.

The Guideline Development Group declined to make a recommendation in all cases, but instead formulated guiding practice statements using the same methods.

The WHO Steering Committee circulated the draft recommendations to an External Peer Review Group, which made several suggestions to improve the document. The WHO Steering Committee reviewed all suggestions and incorporated the comments as appropriate following discussion and agreement with the chair and co-chair of the Guideline Development Group. No new recommendations were considered in this round of comments. The Guideline Development Group approved the final version.

Dissemination, adaptation and implementation

Dissemination

The current guideline will be posted on the WHO website, including the child health, HIV and nutrition websites (http://www.who.int/maternal_child_adolescent/, <http://www.who.int/HIV/>, <http://www.who.int/nutrition/>), the WHO e-Library of Evidence for Nutrition Actions (eLENA) (<http://www.who.int/elena/>) and social media.

The recommendations in this guideline will be disseminated through a broad network of international partners, including WHO country and regional offices, health ministries, WHO collaborating centres, other United Nations agencies and nongovernmental organizations. They will also be published on the WHO website as well as the websites of partner agencies. To ensure that the guideline reaches users most likely to benefit from it, WHO will organize meetings among key stakeholders in settings with a high prevalence of HIV and make presentations in international AIDS and infant feeding conferences. As needed, assistance will be provided to adapt the guideline to national contexts.

The Guideline Development Group specifically commented that it would be important to clarify what changes were included in the recommendations and to comment on what had not changed. They also commented that communities need to be supported in understanding the recommendations and that this would involve simplifying messages. As part of this, coordinating with other health programmes will be essential, including HIV programmes on ARV drugs as well as general maternal and child health programmes.

Adaptation and implementation

The first steps in implementation after the final approval of this guideline will be to revise all WHO publications that deal with the populations of pregnant women, mothers and infants for whom there may be implications. These include WHO training and reference materials such as: *Integrated Management of Childhood Illness* (WHO, 2016a); *Infant and young child feeding counselling: an integrated course* (WHO & UNICEF, 2006); *Essential newborn care course* (WHO, 2010a); *Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice* (WHO et al., 2015); and *Caring for the newborn at home, and Caring for newborns and children in the community: training courses for community health workers* (WHO, 2015).

WHO will work with health ministries and established partners who are involved with training and capacity development related to HIV and infant feeding and supervision of health workers at first-level health facilities. The successful introduction of evidence-informed policies related to supporting infant feeding practices by mothers living with HIV into national programmes and health-care services depends on well planned and participatory consensus-driven processes of adaptation and implementation. These processes may include developing or revising existing national guidelines or protocols based on this document and also undergraduate and in-service teaching curricula.

Individual countries are expected to adapt the recommendations to suit the local social, cultural and economic contexts. Countries will be encouraged to hold key stakeholder discussions to inform the decision-making on using and introducing the recommendations into national programmes. Frameworks for assisting policy-makers, such as DECIDE (Developing and Evaluating Communication Strategies to Support Informed Decisions and Practice based on Evidence) (DECIDE Project Office, 2016), will be shared. The recommendations contained in the present guideline should be adapted into locally appropriate documents to meet the specific needs of each country and health service.

An enabling environment should be created for the use of these recommendations, including relevant national policies and changes in the behaviour of health-care practitioners to enable the use of evidence-informed practices.

Local professional societies may play important roles in this process, and an all-inclusive and participatory process should be encouraged. WHO's Department of Maternal, Newborn, Child and Adolescent Health, Department of Nutrition for Health and Development and Department of HIV have substantial experience with introducing WHO guidelines and tools into national programmes.

Within this context, programme managers will need to ensure that adequate quantities of required ARV drugs are available to health workers and mothers living with HIV. These drugs would normally be provided through existing health system supply chains.

Monitoring and evaluating the implementation of the guideline

Monitoring and evaluation should be built into the implementation process to provide important lessons for uptake and further implementation. For monitoring and evaluating their impact on the quality of care, priority should be given to the strong recommendations.

The implementation of this guideline should involve national child health programmes collecting and reporting data on pregnant women and mothers living with HIV and their exposed newborns. Putting this into practice may require reviewing existing patient monitoring systems, including reporting tools, to ensure that the conditions are adequately addressed.

Key areas that require monitoring include but are not limited to:

- infant feeding practices by mothers living with HIV, including the duration of breastfeeding;
- ART coverage among mothers living with HIV; and
- growth among the infants and children being breastfed by mothers living with HIV who are taking ART.

The WHO Department of Maternal, Newborn, Child and Adolescent Health, Department of Nutrition for Health and Development and Department of HIV will monitor the implementation of the guideline in collaboration with WHO regional and country offices using indicators such as the number of requests from countries for technical assistance in implementing the guideline as well as requests to WHO headquarters and regional offices for monitoring and evaluation in countries applying the guideline. In addition, the Department of Maternal, Newborn, Child and Adolescent Health, Department of Nutrition for Health and Development and Department of HIV will monitor the number of downloads of the guideline publication from the WHO website and those of partners and other stakeholders as well as the number of hard copies of the guidance requested and distributed through the WHO document centre.

Implications for future research

Several specific clinical and programmatic research questions were identified as part of the discussions on individual recommendations; these are included in the summary table for each recommendation – see the individual recommendations. In addition, implementation research will inform and assist the adoption of policy and implementation.

Facilitating policy adoption and putting in place an enabling environment for implementation will require dialogue with policy-makers and other stakeholders at country level. Programme managers will require technical support for developing and implementing operational plans in programme settings from experts with experience in delivering these interventions. Small-scale demonstration projects may support designing and scaling up training and capacity development and implementation at the country level.

Plans for updating the guideline

This guideline will be reviewed in 2019. At that time, the WHO Steering Committee will constitute a Guideline Development Group to review the literature and update the recommendations as needed. In the interim, the WHO Steering Committee will continue to monitor any new studies, interim research results or reports of adverse events associated with this policy implementation that become available. If relevant new information requires urgent changes to the recommendations before 2019, a Guideline Development Group will be constituted at that time in accordance with the procedures of the WHO handbook for guideline development (WHO, 2014).

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Annex 1.

Systematic reviews including GRADE tables related to the duration of breastfeeding by mothers living with HIV

- 1a. Chikhungu L, Bispo S, Newell ML. HIV-free survival at 12–24 months in breastfed infants of HIV-positive women on ART: a systematic review. Commissioned for the guideline review.

http://www.who.int/maternal_child_adolescent/documents/hiv-infant-feeding-2016/en/

- 1b. Chikhungu L, Bispo S, Newell ML. Postnatal HIV transmission rates at age six and 12 months in infants of HIV-positive women on ART initiating breastfeeding: a systematic review. Commissioned for the guideline review.

http://www.who.int/maternal_child_adolescent/documents/hiv-infant-feeding-2016/en/

- 1c. Mallampati D, MacLean R, Ciaranello A. Modelling the impact of maternal ARV use and infant mortality. Commissioned for the guideline review.

http://www.who.int/maternal_child_adolescent/documents/hiv-infant-feeding-2016/en/

Annex 2.

Systematic reviews including GRADE tables related to interventions to improve infant feeding practices by mothers living with HIV

2. Academy of Nutrition and Dietetics: Handu D, Acosta A, Moloney L, Wolfram T, Ziegler P, Steiber A. **Effectiveness of interventions to promote exclusive breastfeeding in women living with HIV that are on antiretroviral therapy living in areas that promote exclusive breastfeeding due to limited resources for safe replacement feeding.**

http://www.who.int/maternal_child_adolescent/documents/hiv-infant-feeding-2016/en/

Annex 3.

Survey of national health authorities in the 22 priority countries for the Global Plan

http://www.who.int/maternal_child_adolescent/documents/hiv-infant-feeding-2016/en/

Annex 4.

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Additional data and information

The following research teams kindly supplied information and analyses about their studies in addition to that published in the peer-reviewed literature.

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Annex 5.

Questions and PICO used as the basis for preparing systematic reviews of the available published evidence

1	Question	For how long should a mother living with HIV breastfeed if she is receiving ART and there is no evidence of clinical, immune or viral failure? What is the HIV-free survival of HIV-exposed infants according to feeding practices when mothers are taking ARV drugs?	Importance
	Population	Infants of mothers living with HIV	Critical
	Intervention	Breastfeeding and maternal ARV drugs	
	Comparison	Not breastfeeding or early cessation of breastfeeding No maternal ARV drugs	
	Outcome	HIV transmission and HIV-free survival between birth and 24 months	
2	Question	Can facility- and community-based interventions improve the quality of breastfeeding practices among mothers living with HIV?	Importance
	Population	Mothers living with HIV receiving ARV drugs	Important
	Intervention	Support and counselling delivered by facility-based or community-based health workers or peers (people living with HIV in the same community)	
	Comparison	Standard care without support	
	Outcome	<ul style="list-style-type: none"> • Exclusive breastfeeding (three months and six months) • Initiation of breastfeeding • Early initiation of breastfeeding (within one hour of birth) • Safe replacement feeding 	
3	Question	If a mother living with HIV does not exclusively breastfeed, is mixed feeding with ART better than no breastfeeding at all? Are ARV drugs effective in preventing the postnatal transmission of HIV through breast milk according to feeding modality?	Importance
	Population	Infants of mothers living with HIV receiving ARV drugs	Critical
	Intervention	Exclusive breastfeeding	
	Comparison	Mixed feeding	
	Outcome	HIV transmission and HIV-free survival	
4	Question	If a mother living with HIV plans to return to work or school, is a shorter duration of planned breastfeeding with ART better than no breastfeeding at all? What is the HIV-free survival of infants breastfed for durations less than 12 months compared to breastfeeding for 12 months?	Importance
	Population	Infants of mothers living with HIV receiving ARV drugs	Critical
	Intervention	Breastfeeding for 12 months	
	Comparison	Earlier cessation of breastfeeding	
	Outcome	HIV-free survival	

The Guideline Development Group also suggested examining the implications of updated recommendations on two programmatic areas:

- What guidance on infant feeding should be provided to mothers living with HIV and to health authorities in conflict or emergency settings?
- What are the implications for monitoring and evaluation?

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