BHIVA guidelines on the management of HIV in pregnancy and the postpartum period 2025

Writing group members

Laura Byrne (Chair)	St George's University Hospitals NHS Foundation Trust, London
Charlotte-Eve Short (Vice-chair)	Chelsea and Westminster NHS Foundation Trust, Imperial College London and Imperial College Healthcare NHS Trust, London
Alasdair Bamford	Great Ormond Street Hospital for Children NHS Foundation Trust, London
Daniel Bradshaw	UK Health Security Agency
Emily Cheserem	North Middlesex University Hospital, London
Emily Clarke	Liverpool University Hospitals NHS Foundation Trust
Ana de Oliveira	UK Community Advisory Board
Sarah Dermont	Infectious Diseases in Pregnancy Screening (IDPS) Programme, NHS England
Yvonne Gilleece	Brighton and Sussex Medical School and University Hospitals Sussex NHS Foundation Trust, Brighton
Joris Hemelaar	University of Oxford and Oxford University Hospitals NHS Foundation Trust
Portia Jackson	HIV Pharmacy Association
Hermione Lyall	Imperial College Healthcare NHS Trust, London
Kim MacLeod	Manchester University NHS Foundation Trust and St Mary's Hospital, Manchester
Janine Mcgregor-Read	UK Community Advisory Board
Eleni Nastouli	University College London Hospitals NHS Foundation Trust and University College London
Helen Peters	Integrated Screening Outcomes Surveillance Service, UCL Great Ormond Street Institute of Child Health, London
Luciana Rubinstein	London North West University Healthcare NHS Trust
Shema Tariq	UCL Institute for Global Health and Central and North West London NHS Foundation Trust
Yee Suh Teh	Oxford University Hospitals NHS Foundation Trust
Imina Ugbekile	St George's University Hospitals NHS Foundation Trust, London
Steven Welch	University Hospitals Birmingham NHS Foundation Trust

Correspondence: Laura Byrne, St George's University Hospitals NHS Foundation Trust, London.

Email: guidelines@bhiva.org

Contents

1 Introduction

These clinical guidelines have been produced to help ensure women/birthing parents living with human immunodeficiency virus (HIV) are supported to maintain optimal health for themselves during pregnancy and the postpartum period, and the health and wellbeing of their infant(s). Pregnancy and the postpartum period are a time of joy and excitement for most parents and it is important to emphasise that the majority of women/people living with HIV in the UK engage well in care during pregnancy, resulting in the very low rates of vertical transmission.

The understanding of how to improve the health and wellbeing of people living with HIV continues to evolve at pace, with recent paradigm shifts in antiretroviral therapy (ART) including two-drug regimens, long-acting injectable therapy and novel drug classes and agents. However, even though more than half of adults worldwide living with HIV are women, women/people who are pregnant or lactating and those who could become pregnant have been routinely excluded from pre-licensing ART trials. Most new antiretroviral agents are approved for use in adult populations without dosing and safety data in pregnancy [1]. This has been identified as a global health inequality and there are now major efforts to ensure that pregnant women/people living with HIV are 'protected through' rather than 'protected from' research [2].

Despite this, since the last guidelines update there have been several robust clinical trials in pregnant women living with HIV which have added valuable evidence of antiretroviral efficacy and safety in pregnancy and lactation. In the UK, vertical transmission rates of HIV remain very low, and uptake of antenatal HIV testing remains very high. In this latest version of the guidelines, we have attempted to ensure that women/people who are or who may become pregnant can access the best available ART for their own health, while highlighting where pregnancy safety and efficacy data are, and are not, available. Although the situation is improving, there is still a clear and urgent need for a wider variety of neonatal preparations as current options, particularly in the case of maternal viral resistance, are limited.

These guidelines have been designed to be as accessible, informative and practical as possible. The writing group considered issues reflecting day-to-day practice and queries. For some situations the evidence remains limited, but we recognise that there is a need to provide guidance despite this, to ensure pregnant women/people living with HIV can access an equal standard of personalised care wherever they choose to give birth.

The principle that underpins these guidelines is that the health and wellbeing of women/people living with HIV during pregnancy and the postpartum period goes beyond an undetectable viral load. Pregnancy can bring physical, social and psychological challenges, particularly in the context of marginalisation and existing long-term conditions, such as HIV. We have stressed the importance of holistic care, with an emphasis on effective multidisciplinary team (MDT) working. If expertise is not available locally, we strongly encourage the formation of local networks to share knowledge and experience. We have kept the evidence summaries concise and relevant to the current treatment era, rationalising some of the older data in previous iterations of these guidelines.

The guidelines are not intended to be prescriptive or restrictive; we recognise that situations will arise in which the optimum management may deviate from these recommendations, and that new data will emerge to better inform practice.

Of note, the term 'HIV' refers to HIV-1 throughout these guidelines, unless HIV-2 is specified.

1.2 Key changes in the current guidelines

New sections

- Preconception counselling, acknowledging that discussions about ART safety need to start *before* conception.
- HIV screening in pregnant women/people, which expands on current NHS Infectious Diseases in Pregnancy Screening (IDPS) programme guidelines.
- Infant feeding. This is one of the areas about which we receive the most queries, and we hope this new expanded guidance will enable more women/people living with HIV to feel confident in their feeding choices, and better enable the HIV MDT to support individuals making these choices and manage situations in which things do not go according to plan.

Revised sections

- The ART section of the guidelines has been extensively revised, taking into account the recommendations in the latest British HIV Association (BHIVA) adult antiretroviral treatment guidelines [3] and adapting these in light of additional pregnancy data.
- Managing HIV-2 in women/pregnant people has been updated in line with the BHIVA HIV-2 guidelines [4].
- The hepatitis co-infection section has been updated with new data particularly on the use of tenofovir alafenamide (AF) in pregnancy.
- Guidance for the obstetric management of pregnant women/people living with HIV remains largely similar to the management of those without HIV, however we have added additional recommendations to the obstetric management section for assessing the risk of fetal growth restriction and preterm birth (PTB) in those living with HIV.
- The postpartum care section has been revised and updated.
- In the section on management of infants born to women/people living with HIV, we have simplified the infant postnatal prophylaxis (PNP) guidance to two pathways: for low-risk and high-risk infants.

1.3 Scope and purpose

The overall purpose of these guidelines is to provide guidance on best clinical practice for the treatment and management of women/people living with HIV in the UK during pregnancy and the postpartum period, and of their infants. The scope includes guidance on:

- The use of ART in women/people who may become pregnant;
- The use of ART for the health and wellbeing of pregnant women/people and to prevent vertical transmission of HIV;
- Supporting the social and emotional wellbeing of women/people during pregnancy and the postpartum period;
- The obstetric management of women/people living with HIV;
- Infant feeding and PNP for infants born to women/people living with HIV.

The guidelines are written for clinicians directly involved in and responsible for the care of women/people living with HIV during pregnancy or the postpartum period and their infants, community advocates responsible for promoting the best interests and care of pregnant women/people and their infants, and people living with HIV (for whom a non-technical summary is also available).

1.4 Methodology

1.4.1 Guideline development process

BHIVA fully revised and updated the Association's guideline development manual in 2021 [5]. Full details of the guideline development process, including BHIVA's conflict of interest policy, are outlined in the manual. BHIVA has adopted the modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for the assessment, evaluation and grading of evidence and development of recommendations (see Appendix 1) [6,7].

The guidelines were commissioned by the BHIVA Guidelines Subcommittee; the Subcommittee nominated the Chair and Vice-chair of the writing group, who then nominated experts in the field to join the writing group based on their knowledge, expertise and freedom from conflicts of interest (the conflict of interest statements of members of the writing group are available and a summary has been published with these guidelines on the BHIVA website). In addition, BHIVA members were invited to volunteer as guideline authors, again based on their knowledge, expertise and freedom from conflicts of interest.

The scope, purpose and guideline topics were agreed by the writing group. Questions relating to each guideline topic were drafted and an independent systematic literature review undertaken. Details of the search questions and strategies are outlined in Appendix 2. The literature searches for the 2024 guidelines covered the period from July 2016 to the date of the search (between August 2022 and January 2023), and included abstracts from selected conferences (between January 2020 and September 2022). For each topic and question, evidence was identified and evaluated by writing group members with expertise in the field. Using the modified GRADE system (see Appendix 1), members were responsible for assessing and grading the quality of evidence for predefined outcomes across studies and developing and grading the strength of recommendations. All writing group members received training in the use of the modified GRADE criteria before assessing the evidence.

Due to the lack of data from randomised controlled trials in several important areas in pregnancy and lactation (e.g. mode of delivery and breast/chestfeeding), the writing group was unable to assign high grades in these areas. Therefore recommendations have been made based on best practice and best available evidence.

In addition to graded recommendations, good practice points (GPPs), which are recommendations based on the clinical judgement and experience of the writing group, have been included. GPPs emphasise an area of important clinical practice for which there is no significant research evidence, nor is there likely to be any. They address an aspect of treatment and care that is regarded as such sound clinical practice that healthcare professionals are unlikely to question it and where the alternative is deemed unacceptable. It must be noted that GPPs are not an alternative to evidence-based recommendations.

The guidelines were published online for public consultation and external peer review was commissioned, comments from which resulted in minor revision prior to final approval by the writing group.

1.4.2 Involvement of people living with HIV

BHIVA views the involvement of people living with HIV and community representatives in the guideline development process as essential. The writing group included two representatives appointed through the UK Community Advisory Board (UK-CAB) who were involved in all aspects of the guideline

development process. In addition, community groups were invited to participate in the draft guideline consultation process and have reviewed and commented on the guidelines. Involvement of and consultation with those with lived experience of HIV in pregnancy and during infant feeding has been crucial to ensure that these guidelines are acceptable and accessible, that they address priority areas of those living with HIV, and that language is appropriate and does not contribute to stigma or cause harm.

1.4.3 Dissemination and implementation

The following measures have been or will be undertaken to disseminate and aid implementation of the guidelines:

- E-publication on the BHIVA website and in the journal *HIV Medicine*;
- Non-technical summary;
- E-learning module for continuing professional development;
- Educational slide set to support local and regional educational meetings;
- National BHIVA audit programme.

1.4.4 Inclusive language

Gender-inclusive language has been used throughout the guidelines where possible, acknowledging that while the majority of people experiencing pregnancy identify as women, it is important to ensure our language is appropriate, sensitive and inclusive for gender-diverse pregnant people living with HIV. We have chosen an additive approach, taking into account the importance of maintaining a woman-centred approach and advocating for women's rights. We have therefore used phrases such as 'pregnant women/people', 'mother/birthing parent' and 'breast/chestfeeding' as much as possible. This is in line with the use of language by other major organisations such as the Royal College of Obstetricians and Gynaecologists. When summarising research findings, we have used the terms that the authors have used to define their study population so as to maintain accuracy. We continue to use person-first language as we did in the 2018 guidelines, according to the People First Charter (https://peoplefirstcharter.org/) and as advocated by other authors [8,9].

1.4.5 Guideline updates and date of next review

The guidelines will be fully updated in 2029. However, the writing group will continue to consider new information from high-quality studies and publish interim updates to the current guidelines before the full revision date if the recommendations need updating to ensure continued best clinical practice.

1.5 Supporting women/people living with HIV during pregnancy and the postpartum period

It is important that women/people living with HIV are informed by the HIV antenatal MDT during pregnancy and the postpartum period of the additional support that is available through peer mentoring and resources to support infant feeding decisions.

The 4MNetwork (4mmm.org) is an example of a holistic, person-centered peer mentor service aimed at pregnant women/people and mothers/birthing parents. This service is led by trained Mentor Mothers living with HIV who provide psychosocial support and information to new mothers/birthing parents across the UK.

Pregnant women/people and new parents living with HIV may benefit from the information and support on infant feeding available on the online platform 'Feeding a baby when living with HIV', which is part of the University of Oxford's Health Experiences Insights (hexi) website (https://hexi.ox.ac.uk/Feeding-a-baby-while-living-with-HIV/overview) and includes videos of interviews with women living with HIV who have breastfed and/or formula fed their infants.

The NOURISH-UK team has also produced an aid to support mothers'/parents' decision-making, and this is available with BHIVA infant breast/chestfeeding leaflets on the BHIVA website (https://www.bhiva.org/pregnancy-guidelines).

1.6 References

1. Colbers A, Mirochnick M, Schalkwijk S *et al*. Importance of prospective studies in pregnant and breastfeeding women living with human immunodeficiency virus. *Clin Infect Dis*. 2019; **69**: 1254–1258.

2. Lyerly AD, Beigi R, Bekker LG *et al*. Ending the evidence gap for pregnancy, HIV and co-infections: ethics guidance from the PHASES project. *J Int AIDS Soc* 2021; **24**: e25846.

3. Waters L, Winston A, Reeves I *et al*. BHIVA guidelines on antiretroviral treatment for adults living with HIV-1 2022. *HIV Med* 2022; **23 Suppl 5**: 3–115.

4. Reeves I, Cromarty B, Deayton J *et al*. British HIV Association guidelines for the management of HIV-2 2021. *HIV Med* 2021; **22 Suppl 4**: 1–29.

5. British HIV Association. *British HIV Association (BHIVA) Guideline Development Manual*. October 2022. Available at: https://bhiva.org/wp-content/uploads/2025/01/Guideline-Development-Manual.pdf (accessed March 2024).

6. GRADE Working Group. *Grading the quality of evidence and the strength of recommendations*. Available at: www.gradeworkinggroup.org (accessed June 2024).

7. Guyatt GH, Oxman AD, Kunz R *et al*. Going from evidence to recommendations. *BMJ* 2008; **336**: 1049–1051.

8. Dilmitis S, Edwards O, Hull B *et al*. Language, identity and HIV: why do we keep talking about the responsible and responsive use of language? Language matters. *J Int AIDS Soc* 2012; **15 Suppl 2**: 17990.

9. Watson S, Namibia A, Lynn V. The language of HIV: a guide for nurses. *HIV Nursing* 2019; **19**: BP1–BP4.

2 Summary of recommendations

From Section 4.2 Managing women/people who decline HIV screening in pregnancy

- We recommend that pregnant women/people who decline HIV screening in pregnancy should be managed by an antenatal screening ID MDT, with emphasis on providing support to understand the benefits of HIV testing, both for their own health and that of their infant, and ensuring that any additional communication needs are met (Grade 1D).
- The antenatal screening ID MDT should offer a face-to-face appointment with the HIV team and/or sexual health advisor to discuss the benefits of testing for both women/birthing parents and their infants (GPP).
- We recommend that infant HIV antibody testing and HIV RNA/DNA polymerase chain reaction (PCR) testing at birth should be offered by the antenatal screening ID MDT if all HIV screening in pregnancy has been declined. It should be made clear that HIV antibody testing is a proxy for maternal/parental HIV status and will inform the administration of PNP to reduce the risk of vertical transmission and to provide advice on safe infant feeding (Grade 1D).
- If infant HIV testing at birth is declined, the antenatal screening ID MDT should continue dialogue with the family and continue to recommend that HIV RNA/DNA PCR testing is completed to exclude infection (GPP).
- We recommend that the infant's general practitioner (GP) should be informed in writing if the mother/birthing parent has declined HIV screening in pregnancy and at birth, and infant testing has not been completed (i.e. if the infant has an unknown HIV status). The mother/person with parental responsibility should be informed that this will happen (Grade 1D).
- The woman/birthing parent should be offered a follow-up appointment with a sexual health advisor to discuss maternal/parental HIV testing in the postnatal period (GPP).

From Section 4.5 Preventing HIV acquisition during pregnancy and infant feeding from a partner living with HIV

- We recommend that postexposure prophylaxis (PEP) after condomless receptive vaginal or anal sex for women/people during pregnancy or breastfeeding is not required if their partner living with HIV meets the U=U criteria, as per the British Association for Sexual Health and HIV (BASHH) PEP guidelines (Grade 1A).
- We recommend that consent should be sought from partners with HIV to obtain confirmation that they meet the U=U criteria, including the result of their last viral load test, by either the ID MDT or the partner's HIV clinician (Grade 1D).
- If the conditions for U=U are not met, or viral load results are not available, we recommend that the couple should be advised to use condoms for sexual intercourse until such time that the conditions are met; in addition, retesting of pregnant or breastfeeding women/people and PEP and/or pre-exposure prophylaxis (PrEP) for them and/or PEP for their infant should be considered according to a risk assessment by the ID MDT and according to existing national guidelines [9-11] (Grade 1D).

From Section 6.1 The antenatal HIV MDT

- We recommend that antenatal HIV care should be delivered by an MDT (Grade 1D).
- We recommend that HIV clinics with relatively few women/people who are pregnant should ensure there is a mechanism for MDT discussion of cases and establish links with larger units for further support (Grade 1D).
- All those who are newly diagnosed or not currently engaged in HIV care (not attended for HIV care ≥12 months) should be seen within 2 weeks of the referral by maternity services [3] (GPP).
- We recommend that all pregnant women/people living with HIV should be offered peer support (Grade 1B).
- The antenatal HIV MDT should include at least an HIV specialist, obstetrician, specialist midwife, paediatrician and peer mentor (GPP).

From Section 6.2 Supporting emotional and psychological wellbeing

- We recommend that a full mental health history and assessment of antenatal depression and anxiety be undertaken at antenatal booking, and later in pregnancy if needed, as per National Institute for Health and Care Excellence (NICE) guidelines for the general pregnant population [13] (Grade 1D).
- If screening indicates a mental health concern, we recommend that women/people should be referred to their GP and/or local perinatal mental health service and offered peer support (Grade 1D).

From Section 6.3 Supporting social wellbeing

- We recommend that all pregnant women/people living with HIV should be asked about their social situation at antenatal booking (or soon after) and later in pregnancy if indicated as per NICE guidance for the general pregnant population [24] (Grade 1D).

From Section 6.4 Screening for domestic abuse in pregnancy

- All pregnant women/people living with HIV should be asked about domestic abuse at the antenatal booking appointment, or at the earliest opportunity when they are alone as per NICE guidance for the general pregnant population [24] (Grade 1D).

From Section 6.6 Pregnancy care in specific populations living with HIV

- We recommend that the antenatal HIV MDT and all other professionals involved in the care of women/people living with HIV during and after pregnancy deliver anti-racist, gender-inclusive, person-centred care (Grade 1D).

From Section 7.1 Sexual health screening

- We recommend sexual health screening for all women/people who are newly diagnosed with HIV in pregnancy (Grade 1B).
- For those individuals already engaged in HIV care and who become pregnant, we suggest that sexual health screening is carried out as early as possible in pregnancy and repeated at 28 weeks where there may be ongoing risk (Grade 2C).
- We recommend that genital tract and sexually transmitted infections (STIs) should be treated according to BASHH guidelines [3] (Grade 1B).
- We recommend that national guidance for immunisation of pregnant women/people should be followed (Grade 1B).

From Section 8.1 What ART to start in women/people who may become pregnant and continue in those who are pregnant

- We recommend that women/people who are planning to conceive are prescribed a regimen in line with current BHIVA adult treatment guidelines [1] for which conception safety data and reassuring pharmacokinetic data are available (see Table 8.1) (Grade 1C).
- We recommend that women/people conceiving on an effective ART regimen should continue this treatment, with some exceptions (see Table 8.2) (Grade 1B).
- Where uncertainty around these risks of a current non-recommended regimen is acceptable to individuals who become pregnant and strong preference given to continuation of a current non-recommended regimen, they should be supported with additional 1- to 2-monthly viral load measurement with or without therapeutic drug monitoring (TDM) as appropriate (see Section 8.5) (GPP).

Table 8.1 Recommended ART for women/people starting treatment who are planning to conceive

Antiretroviral agents for which conception safety and reassuring pharmacokinetic data are available (Grade 1C)	
Regimen/agent	**Details**
Nucleoside reverse transcriptase inhibitor (NRTI) backbone	
Tenofovir disoproxil (DX) or tenofovir AF with emtricitabine	
Abacavir with lamivudine	If no active HBV infection, HBV immune, HLA B*5701 negative and 10-year cardiovascular disease risk <10%
Preferred anchor agent	
• Dolutegravir	Reassuring conception safety data available from multiple sources; data on pregnancy outcomes from RCTs available
• Raltegravir 400 mg twice daily	Raltegravir 1200 mg once daily may be prescribed in those planning to conceive but must be switched to raltegravir 400 mg twice daily once they are pregnant

• Darunavir with ritonavir	Darunavir/cobicistat can be initiated in those planning to conceive but cobicistat must be switched to ritonavir as soon as they become pregnant
Alternative anchor agent	
• Bictegravir	Limited pharmacokinetic and pregnancy outcome data so should only be used if benefits outweigh risks. If continuing in pregnancy, consider additional viral load monitoring
• Rilpivirine	Not recommended if viral load >100,000 copies/mL or CD4 count <200 cells/mm^3. Take with food. Note important drug–drug interaction with proton pump inhibitors and other acid-lowering drugs which are routinely given during caesarean section
• Efavirenz	Non-preferred regimen due to side effect profile; may be used to manage drug interactions with tuberculosis treatment and can be switched postpartum
• Atazanavir with ritonavir	Boosted atazanavir is no longer recommended as first-line ART in the BHIVA adult ART guidelines and should be reserved for those who need a protease inhibitor (PI) and cannot take darunavir. Atazanavir/cobicistat can be initiated in those planning to conceive but cobicistat must be switched to ritonavir as soon as they become pregnant

Table 8.2 Advice on continuing specific regimens/agents with limited human safety, efficacy and/or pharmacokinetic data in pregnancy

Regimen/agent (alphabetical order)	**Evidence**	**Advice**
Abacavir/zidovudine/ lamivudine fixed-dose combination	Adequate human safety and pharmacokinetic data. No longer a recommended option for ART due to toxicity profile and efficacy	No longer available in the UK
Bictegravir	Limited pharmacokinetic and pregnancy outcome data exist to recommend in pregnancy	Discuss risks/benefits and consider switch to a regimen in Table 8.3. If continuing, consider additional viral load monitoring
Cabotegravir plus rilpivirine long-acting injectable	Limited pharmacokinetic, safety and viral efficacy data in pregnancy	Consider switching to oral three-drug regimen in Table 8.3. Continuation or initiation without additional oral agents may be considered in complex cases with MDT discussion and increased viral load monitoring. There is no evidence on optimum dosing regimens in pregnancy; we recommend 4-weekly dosing during pregnancy in the absence of data, with consideration of TDM
Cobicistat	Pharmacokinetic data demonstrate reduced drug levels and thus	Cobicistat used as a pharmacological booster should be switched to ritonavir as soon as possible in pregnancy

	cobicistat should NOT be used as a booster in pregnancy	
Darunavir/ritonavir	Evidence of reduced drug levels with darunavir once-daily dosing	Use darunavir 600 mg plus ritonavir 100 mg twice-daily dosing if initiating in pregnancy (see Section 8.2)
Doravirine	Limited pharmacokinetic data. Insufficient human data available to establish safety in pregnancy	Discuss risks/benefits and offer switch to a regimen in Table 8.3; if continuing, consider additional viral load monitoring
Enfuvirtide	No adequate human data and pharmacokinetics have not been described. Does not cross the placenta	No longer available in the UK
Etravirine	Very limited teratogenicity data. Pharmacokinetic data show an increase in levels during pregnancy	Recommend switch to a three-drug regimen in Table 8.3
Fostemsavir	No pharmacokinetic data. Insufficient human data are available to establish risk to pregnancy outcomes	May be considered in complex cases with MDT discussion
Ibalizumab	No pharmacokinetic, safety or efficacy data in pregnancy	May be considered in complex cases with MDT discussion
Lenacapavir	No pharmacokinetic, safety or efficacy data in pregnancy	May be considered in complex cases with MDT discussion
Lopinavir/ritonavir	Adequate human safety and pharmacokinetic data. Some evidence of association with PTB and small for gestational age neonates	Discuss risks/benefits and offer switch to a regimen in Table 8.3
Maraviroc	No pharmacokinetic data. Insufficient pregnancy safety data	Recommend switch to a three-drug regimen in Table 8.3
PI monotherapy	Minimal transplacental transfer of PIs	Recommend intensify to a three-drug regimen in Table 8.3
Raltegravir	Pharmacokinetic data only available for 400 mg twice-daily regimen	Use 400 mg twice daily in pregnancy
Oral two-drug regimens		
Dolutegravir plus lamivudine, rilpivirine or darunavir/ritonavir	Safety and pharmacokinetic data for individual drugs exist but not in combinations with fewer than three agents in pregnancy	May be considered with discussion of limited data with pregnant woman/person and HIV MDT with increased viral load monitoring. Note important drug–drug interaction between rilpivirine and proton pump inhibitors or other acid-lowering drugs which are routinely given during caesarean section
Darunavir/ritonavir or atazanavir/ritonavir plus	Safety and pharmacokinetic data for individual drugs exist but not in	Recommend intensifying to a three-drug regimen in Table 8.3

lamivudine or emtricitabine	combinations with fewer than three agents in pregnancy	

From Section 8.2 ART dosing in pregnancy

- We do not recommend routine dose alterations for antiretrovirals during pregnancy if used at standard adult licensed doses with the following exceptions (Grade 1C):
  - Darunavir/ritonavir should be administered as 600 mg/100 mg twice daily if initiated in pregnancy; once-daily dosing can be continued if the woman/person conceived on darunavir/ritonavir and remains virologically suppressed;
  - Raltegravir should be administered as 400 mg twice daily if initiated or continued in pregnancy.
- We suggest that switching to standard dosing throughout pregnancy or regular TDM should be considered if a woman/person continues an off-licence non-standard dosing regimen (Grade 2C).

From Section 8.3.1 Regimens for first-line ART in pregnancy

Recommended and alternative first-line ART choices in pregnancy are shown in Table 8.3

Table 8.3 Choice of first-line ART when starting treatment in pregnancy

Regimen	Details	Grade
Recommended as initial treatment for most pregnant women/people		
Dolutegravir plus emtricitabine/tenofovir DX	First choice in the absence of renal or bone concerns	1A
Dolutegravir plus emtricitabine/tenofovir AF	Association with weight gain should be discussed Consider baseline weight if in overweight range	1A
Dolutegravir/lamivudine/abacavir	Ensure HLA B*5701 negative Estimated 10-year risk of cardiovascular disease should be <10% Ensure no active HBV infection Ensure immune to HBV Association with weight gain should be discussed Consider baseline weight if in overweight range	1C
Alternative regimens that may be preferred in certain clinical situations		
Rilpivirine plus emtricitabine/tenofovir DX or emtricitabine/tenofovir AF or lamivudine/abacavir	Not recommended if viral load >100,000 copies/mL or CD4 count <200 cells/mm^3 Take with food	1C
Raltegravir 400 mg twice daily plus emtricitabine/tenofovir DX or emtricitabine/tenofovir AF or lamivudine/abacavir	May be considered if evidence of liver dysfunction prevents use of dolutegravir	1B
Darunavir 600 mg plus ritonavir 100 mg twice daily plus emtricitabine/tenofovir DX or emtricitabine/tenofovir AF or lamivudine/abacavir	Twice-daily dosing if initiating in pregnancy (or known resistance)	1C
Efavirenz plus emtricitabine/tenofovir DX or emtricitabine/tenofovir AF or lamivudine/abacavir	Non-preferred regimen due to side effect profile; may be used to manage drug interactions with tuberculosis treatment and can be switched postpartum	1A

From Section 8.4 When to start ART in pregnancy

- We recommend that all pregnant women/people should start ART as soon as possible during pregnancy (Grade 1B).
- We recommend that ART should be started in the first trimester, especially if the viral load is >100,000 copies/mL and/or CD4 count is <200 cells/mm^3 (Grade 1C).
- If the pregnancy is complicated by significant nausea and vomiting that impacts the ability to adhere to treatment, the aim should be to establish consistent ART by 18–20 weeks' gestation (Grade 1C).
- We recommend that all pregnant women/people should have commenced ART by week 24 of pregnancy at the very latest (Grade 1C).

From Section 8.5 Laboratory monitoring of ART in pregnancy

New diagnosis in pregnancy:

- For pregnant women/people who are newly diagnosed with HIV, we recommend investigations as per the BHIVA routine investigation and monitoring guidelines [76], as well as those routinely performed in the general antenatal clinic (Grade 1D).

Stable virological suppression in pregnancy:

- In women/people who conceive and are virologically suppressed on ART in pregnancy, we recommend that an HIV viral load test should be performed every 2 months, at 36 weeks and at delivery (Grade 1C).
- We recommend that CD4 cell count should be measured at baseline in the first trimester for all women/people who conceive and are virologically suppressed on ART in pregnancy. Repeat tests are only indicated if the baseline CD4 count is <350 cells/mm^3 as per BHIVA routine monitoring guidelines [76] (Grade 1D).
- We suggest more frequent viral load monitoring and TDM can be considered for non-standard regimens (GPP).

Starting or switching ART in pregnancy:

- For women/people who commence or switch ART in pregnancy, we recommend that HIV viral load tests and toxicity monitoring should be performed at 2 weeks after commencing new ART, then monthly until undetectable, and then at least once every 2 months, at 36 weeks and at delivery (Grade 1C).
- We recommend that HIV resistance testing (including integrase resistance) should be undertaken prior to initiation of treatment, including in treatment-experienced women/people (Grade 1D).
- If starting ART with a high-genetic barrier to resistance (dolutegravir-based or darunavir/ritonavir-based regimens), it is reasonable to commence before genotypic resistance test results are available (Grade 1B).
- We suggest that more frequent viral load monitoring and TDM can be considered for non-standard regimens (GPP).

- We recommend liver function tests (LFTs) at 2–4 weeks after starting or switching ART, and at the time of each routine antenatal visit (Grade 1C).

Incomplete virological response in pregnancy:

- We recommend that HIV resistance testing (including integrase resistance) should be attempted for any pregnant woman/person with an incomplete virological response (less than a 1-log drop at 4 weeks post-initiation) or failure to suppress to <200 copies/mL (Grade 1C).
- TDM is not routinely recommended for pregnant women/people with an incomplete virological response but can be considered on an individual basis (Grade 1C).

From Section 8.6 HIV-2

- We recommend case discussion with experts with experience of managing HIV-2 for all women/people (Grade 1D).
- We recommend that pregnant women/people with HIV-2 are treated with tenofovir DX plus emtricitabine AND either twice-daily dolutegravir 50 mg or twice-daily darunavir/ritonavir 600 mg/100 mg (Grade 1C).
- We recommend that tenofovir AF plus emtricitabine can be used as an alternative backbone; abacavir plus lamivudine can be used if avoidance of tenofovir DX or tenofovir AF is necessary, subject to the caveats listed in Table 8.3 (Grade 1C).
- We recommend raltegravir 400 mg twice daily as an alternative third agent if avoidance of both dolutegravir and darunavir/ritonavir is necessary (Grade 2C).

From Section 8.7.1 Presenting late in pregnancy (>28 weeks) not on ART

Recommendations for choice of ART for late-presenting pregnant women/people not on ART are summarised in Table 8.4.

Table 8.4 Recommended regimens for pregnant women/people presenting late in pregnancy not on ART

Regimen	Details	Grade
Preferred regimen for pregnant women/people presenting late not on ART		
Dolutegravir/emtricitabine/tenofovir DX	First choice in the absence of renal or bone concerns	1A
Dolutegravir/emtricitabine/tenofovir AF		1A
Dolutegravir/lamivudine/abacavir	Ensure HLA B*5701 negative Ensure no active HBV infection Ensure immune to HBV Ten-year cardiovascular disease risk <10%	1C
Alternative regimens		
Darunavir 600 mg plus ritonavir 100 mg twice daily plus emtricitabine/tenofovir	Higher concentrations at this dosage (see Table 8.3 and Section 8.2)	1C

DX or emtricitabine/tenofovir AF or lamivudine/abacavir		
Raltegravir 400 mg twice daily plus emtricitabine/tenofovir DX or emtricitabine/tenofovir AF or lamivudine/abacavir	May be considered if evidence of liver dysfunction	1B

From Section 8.7.2 Presenting in labour or after spontaneous rupture of membranes (SROM) (term and pre-term)

- We recommend commencing triple ART immediately with tenofovir DX/emtricitabine plus dolutegravir 50 mg (Grade 1B).
- We recommend the following additional agents to be given at labour (any gestation) to preload the fetus:
  - An additional oral dose of tenofovir DX 245 mg immediately (Grade 1D) AND
  - Oral nevirapine 200 mg immediately (Grade 1B) AND
  - Intravenous zidovudine for the duration of labour (Grade 1C).

From Section 8.7.3 Management of pregnant women/people with viraemia on ART

- In the event that a woman/person has initiated ART during pregnancy and does not have a suppressed plasma viral load to <50 copies/mL, we recommend the following (Grade 1C):
  - Review adherence (including a full exploration of potential impacting factors) and drug–drug interactions;
  - Perform a resistance test if appropriate;
  - Consider TDM;
  - Optimise the regimen.
- In the event of detectable viral load at 36 weeks' gestation, we recommend the following (Grade 1C):
  - Review adherence and resistance testing to guide therapy;
  - Optimise the regimen which should include dolutegravir (unless significant resistance);
  - Consider intensification to a four-drug regimen such as the addition of darunavir/ritonavir to a dolutegravir-based regimen;
  - Perform weekly viral load testing;
  - Directly observed therapy should be considered.

- In the event of detectable viral load at delivery, we recommend the following (Grade 1C):
  - Optimise the regimen which should comprise three active drugs including dolutegravir; can consider intensification to four drugs;
  - Include double-dose tenofovir DX* and single-dose nevirapine;
  - Liaise closely with obstetric colleagues aiming for a caesarean section and consider intravenous zidovudine if the latest HIV viral load is >1000 copies/mL (see Section 10.11).

*If a woman is taking ART containing tenofovir AF, a double dose of tenofovir DX 245 mg should be administered in labour.

From Section 9.1.3 Investigation and monitoring

- On diagnosis of new HBV infection, we recommend the following (Grade 1C):
  - Confirmation of viraemia with quantitative HBV DNA, HBV 'e' antigen and 'e' antibody testing;
  - Hepatitis A virus (HAV) immunity, HCV and hepatitis D virus (HDV) testing;
  - LFTs, bilirubin, serum albumin, platelet count and clotting tests;
  - Assessment of hepatic inflammation/fibrosis.
- We recommend that LFTs should be repeated at 2 and 4 weeks after commencing ART to detect the presence of hepatotoxicity or immune reconstitution inflammatory syndrome (IRIS), and then monitored regularly throughout pregnancy and the postpartum period (Grade 1C).

From Section 9.1.5 Antiviral treatment

- We recommend that tenofovir DX or tenofovir AF plus lamivudine or emtricitabine should form the backbone of an ART regimen in treatment-naïve patients with wild-type HIV/HBV and no contraindication to any of these drugs (Grade 1B).
- We recommend against using lamivudine or emtricitabine as the only active drug against HBV in ART because of the likelihood of emergent HBV resistance (Grade 1B).
- We recommend that ART active against both HBV and HIV should be continued postpartum in all women/people with HIV/HBV co-infection (Grade 1B).

From Section 9.1.7 Obstetric management of HIV/HBV co-infection

- We suggest against routine caesarean section for the purpose of reducing vertical transmission of HBV (Grade 2A) when all suggested immunoprophylaxis is followed.

From Section 9.1.8 Management of neonates born to women/people with HIV/HBV co-infection

- We recommend that infants born to women/people with HIV/HBV co-infection should be managed with HBV vaccination with or without HBIG (Grade 1D).

From Section 9.2.2 Diagnosis and monitoring

- On diagnosis of new HCV infection in pregnant women/people living with HIV, we recommend confirmation of HCV viraemia with quantitative analysis of RNA and genotype, and assessment of hepatic inflammation/fibrosis and liver function and concomitant liver disease should be performed (Grade 1C).
- In pregnant women/people with HIV/HCV co-infection, we recommend that LFTs should be repeated at 2 and 4 weeks after commencing ART to detect the presence of hepatotoxicity or IRIS and then monitored regularly throughout pregnancy and the postpartum period (Grade 1C).

- All pregnant women/people with HIV and newly diagnosed HCV, or those with detectable HCV RNA and HIV, should be managed jointly with an experienced clinician, and those with advanced cirrhosis should be managed in a tertiary centre with a hepatologist (GPP).
- The following investigations are indicated (these should also be available for women/people diagnosed preconception) (GPP):
  - HCV markers: HCV antibody (confirmed by a second test), HCV RNA (viral load) and genotype;
  - Other hepatitis viruses: HAV IgG to assess immunity, HBsAg, anti-HBc and anti-HBs.

From Section 9.2.3 Antiviral treatment

- We suggest that women/people of reproductive potential with both HIV and HCV wishing to become pregnant should be prioritised for direct-acting antiviral (DAA)-based HCV therapy prior to conception (Grade 2D).
- We recommend that all women/people with HIV/HCV co-infection with HCV viraemia in pregnancy should be referred for postpartum HCV treatment (Grade 1A).
- We recommend that ART should be continued postpartum in all women/people with HIV/HCV regardless of HCV viraemia, fibrosis stage or CD4 cell count (Grade 1A).

From Section 9.2.4 HBV vaccination

- We recommend vaccination against HBV in non-immune women/people with HIV and HCV co-infection after the first trimester, unless already immune, as per the BHIVA immunisation guidelines [58] (Grade 1C).

From Section 9.2.5 Mode of delivery

- We suggest vaginal delivery can be planned if the woman/person is on effective ART for HIV with an undetectable HIV viral load irrespective of HCV viral load in the absence of obstetric complications (Grade 2C).

From Section 9.3 HAV vaccination

- We recommend HAV vaccination for all HAV non-immune women/people with HIV and HBV and/or HCV after the first trimester, unless already immune as per the BHIVA immunisation guidelines [58] (Grade 1A).

From Section 10.1 Antenatal management

- We recommend the combined screening test for fetal aneuploidies and non-invasive prenatal testing (NIPT) following a high-risk screening result, as this has the best sensitivity and specificity and will minimise the number of women/people who may need invasive testing (Grade 1A).

From Section 10.2 Invasive prenatal testing

- We recommend that invasive prenatal diagnostic testing should not be performed until after the HIV status of the woman/person is known (Grade 1C).

- We recommend that if not virally suppressed, the invasive diagnostic test or procedure should be delayed until viral suppression is achieved; if an invasive procedure cannot be delayed, there should be a multidisciplinary discussion with the obstetric and HIV teams about the timing of the procedure and intensification of the ART regimen with the suggestions in Section 8.7.2 (Grade 1D).

From Section 10.4 External cephalic version (ECV)

- We suggest that ECV can be offered at term to women/people living with HIV on ART with a plasma viral load <50 copies/mL (Grade 2D).

From Section 10.5 Fetal surveillance

- We recommend referring pregnant women/people living with HIV to a clinician with an interest in PTB prevention if additional risk factors for PTB are present (Grade 1C).
- We recommend that HIV infection (treated or untreated) should be considered a moderate risk factor in the risk assessment for fetal growth restriction (Grade 1C).

From Section 10.6 Management of term SROM

- We recommend that delivery within 24 hours should be the aim in the case of prelabour SROM at term (Grade 1C).
- For prelabour SROM at term and when the most recent HIV viral load is <50 copies/mL, we recommend immediate induction or augmentation of labour with a low threshold for treatment of intrapartum pyrexia (Grade 1C).
- For prelabour SROM at term and when the most recent viral load is 50–399 copies/mL, we recommend a caesarean section; however, the mode of delivery decision should take into account the actual viral load, trajectory of the viral load, length of time on treatment, adherence, obstetric factors and the views of the woman/person (Grade 1C).
- For SROM at term and when that most recent viral load is ≥400 copies/mL, we recommend an urgent (category 2) caesarean section (Grade 1C).
- For prelabour SROM at term and a viral load >50 copies/mL, we recommend that attempts should be made to optimise the ART regimen to reduce the risk of vertical transmission while facilitating delivery (see Section 8.7) (Grade 1C).
- We recommend that viral load should be assessed on admission with term prelabour SROM but immediate management decisions should be based on the most recent available viral load result (Grade 1C).

From Section 10.7 Management of preterm prelabour rupture of membranes (PPROM)

- We recommend that where PPROM occurs, HIV viral load should be assessed on admission. Decisions should be made based on the most recent available viral load, taking into account the actual viral load, trajectory of the viral load, length of time on treatment, adherence, obstetric factors and the views of the woman/person (Grade 1C).
- We recommend that when PPROM occurs at ≥35 weeks' gestation (Grade 1D):

- Timing and mode of birth should be discussed among the MDT with careful consideration of the ongoing clinical assessment and preferences of the woman/person;
- In most women/people, the management of PPROM will be the same as that of term SROM, except that those at 35–37 weeks' gestation will require group B streptococcus prophylaxis in line with national guidelines [37];
- Conservative management of PPROM can be considered until 37 weeks' gestation for women/people who have been on ART for longer than 10 weeks and where the two most recent maternal/parental HIV viral loads are <50 copies/mL at least 4 weeks apart, during pregnancy. This requires multidisciplinary discussions, regular clinical assessment and a robust management plan;
- If conservative management is chosen, erythromycin should be given as per the RCOG Green-top Guideline on PPROM [38].

- We recommend that when PPROM occurs at <35 weeks' gestation (Grade 1D):
  - Where HIV viral load is >50 copies/mL, ART should be optimised as per management advice in Section 8.7;
  - There should be a multidisciplinary discussion about the timing and mode of delivery. For those at 34 weeks' gestation it may be beneficial to expedite delivery if the woman/person is a known group B streptococcus carrier. Where delivery is expedited at <35 weeks' gestation, group B streptococcus prophylaxis is required in line with national guidance;
  - Corticosteroids should be administered in accordance with national guidance;
  - Erythromycin should be given in accordance with national guidance on PPROM.

From Section 10.8 Preterm labour

- We recommend for women/people in preterm labour that viral load should be assessed urgently on admission and ART optimised if the viral load is >50 copies/mL (see Section 8.7) (Grade 1C).
- We recommend that corticosteroids should be administered in accordance with national guidelines, taking ART into account (Grade 1A).
- We recommend that intravenous antibiotics for group B streptococcus prophylaxis should be administered in labour according to national guidelines (Grade 1C).
- We recommend that intravenous magnesium sulphate for neuroprotection should be administered in accordance with national guidelines (Grade 1A).
- We recommend that tocolysis may be used to allow administration of steroids or antiretrovirals or to arrange transfer to a unit with appropriate neonatal intensive care facilities (Grade 1C).

From Section 10.9 Mode of delivery

- We recommend that a decision regarding recommended mode of delivery should be agreed with the pregnant woman/person after review of the last measured plasma viral load, which is usually the plasma viral load measured at 36 weeks (Grade 1C).

- Following the agreement on mode of delivery, we recommend that a birth plan is clearly documented in the medical notes of the pregnant woman/person (see https://bhiva.org/clinical-guideline/pregnancy-guidelines/). This should be drafted before the third trimester and finalised by 36 weeks' gestation (Grade 1D).
- We recommend that planned vaginal delivery should be supported where HIV viral load is <50 copies/mL in the absence of obstetric contraindications (Grade 1C).
- We recommend that vaginal birth after caesarean section (VBAC) can be offered where HIV viral load is <50 copies/mL (Grade 1C).
- We recommend planned caesarean section where HIV viral load is 50–399 copies/mL, taking into account the actual viral load, the trajectory of the viral load, length of time on treatment, adherence, obstetric factors and the views of the woman/person (Grade 1C).
- We recommend caesarean section where HIV viral load is ≥400 copies/mL (Grade 1C).

From Section 10.10 Timing of birth

- We recommend that where induction of labour or prelabour caesarean section is undertaken and plasma viral load is <50 copies/mL, the usual obstetric considerations should apply regarding timing of delivery (Grade 1C).
- We recommend that where caesarean section is undertaken at a viral load of >50 copies/mL to prevent vertical transmission, delivery should be considered from 38 weeks' gestation (Grade 1C).

From Section 10.11 Intrapartum management

- We recommend that women/people are advised to give birth in a facility that has direct access to neonatal care (Grade 1D).
- We recommend that obstetric management in women/people who plan for a vaginal delivery should follow the same guidelines as for those without HIV, apart from duration of ruptured membranes (see Sections 10.6 and 10.7) (Grade 1D).
- We recommend that women/people with no additional risk factors can opt for midwifery-led intrapartum care (Grade 1D).
- There is minimal evidence on vertical HIV transmission risk and delayed cord clamping; however, we recommend that delayed cord clamping should be supported if the viral load is <50 copies/mL (Grade 1D).
- There is minimal evidence to support water birth; however, we recommend that women/people who choose a water birth should be supported to achieve this if the viral load is <50 copies/mL (Grade 1D).
- We recommend intravenous zidovudine infusion through labour and/or delivery, which should be discontinued following cord clamping, for (Grade 1C):
    - Women/people who are admitted for planned caesarean section, where HIV viral load is >1000 copies/mL; infusion should be commenced 4 hours prior to the planned caesarean section;
    - Women/people who present in labour or with SROM who are planning vaginal delivery, where HIV viral load is >1000 copies/mL;

- Women/people who present in labour or with SROM who are planning caesarean section where HIV viral load is >1000 copies/mL; infusion should be commenced at presentation but should not delay the caesarean section;
- Untreated women/people with an unknown viral load who present in labour or with SROM irrespective of mode of delivery.

- The use of intrapartum intravenous zidovudine infusion can be considered for women/people on ART with a plasma viral load of 50–1000 copies/mL, along with other interventions recommended in Section 8.7 (Grade 1C).

From Section 11.1 Infant PNP

- In infants at low risk of acquiring HIV, we recommend 2 weeks of zidovudine monotherapy if *all* the following criteria are met in the mother/birthing parent (Grade 1C):
  - ART has been commenced at least 10 weeks prior to delivery;
  - There is evidence of good engagement with maternity, antenatal and HIV services;
  - At least one viral load measurement in the 6 weeks prior to delivery;
  - All viral load measurements in the 10 weeks prior to delivery are <50 copies/mL. Of note, individual risk assessment can be made for viral load between 50 and 200 copies/mL, especially if subsequent viral load is <50 copies/mL.
- In infants at high risk of acquiring HIV, we recommend use of combination PNP if the above criteria for low-risk infants are not met, especially if the mother/birthing parent is known or likely to have a viral load >50 copies/mL on the day of delivery, if there is uncertainty about recent adherence or if the viral load is unknown (Grade 1C).
- We recommend that standard combination PNP should consist of nevirapine for 2 weeks with zidovudine and lamivudine for 4 weeks (Grade 1D).
- We recommend that intravenous ART can be considered for neonates who cannot tolerate oral medication or are at significant risk of necrotising enterocolitis associated with prematurity (Grade 1D).
- We recommend that PNP should be commenced as soon as possible after birth, and at the latest within 4 hours (Grade 1D).
- We recommend that HIV RNA PCR results for both the woman/birthing parent and the infant should be available within 24 hours of samples taken at delivery being received by the laboratory (Grade 1D).
- If at high risk of acquiring HIV (i.e. combination PNP is indicated) and there is a documented history of genotypic resistance in the mother/birthing parent, we recommend that expert advice is sought. If advice is not immediately available, standard three-drug PNP (zidovudine, lamivudine and nevirapine) should be commenced until further advice is provided (Grade 1D).
- When an infant has been started on combination PNP because the criteria for low risk have not been fulfilled, and subsequently the viral load for the mother/birthing parent at delivery is <50 copies/mL, we recommend that simplifying infant PNP to zidovudine alone to complete

2 weeks in total is considered. This decision should be made in discussion with a paediatrician with expertise in prevention of vertical HIV transmission (Grade 1D).

From Section 11.1.8 HIV-2

- We suggest that if a woman/person is known to have HIV-2 infection, the same advice should be followed as for HIV infant PNP but if high risk (combination PNP indicated), nevirapine will not be effective. Expert advice should be sought; if advice is not immediately available, zidovudine, lamivudine and raltegravir should be commenced until guidance is available (see Appendix 4) (Grade 2C).

From Section 11.1.9 PNP duration and PEP during breast/chestfeeding

- We recommend that infant PNP should not usually be given beyond 2 weeks for low-risk infants even if the infant is breast/chestfed (Grade 1C).
- We recommend that infants whose mothers/feeding parents become viraemic during breast/chestfeeding are considered HIV exposed and should be managed according to Chiva guidelines for PEP [61] (Grade 1D).

From Section 11.2 Immunisation

- We recommend that immunisations should be given as per the national schedule outlined in the Green Book [62] (Grade 1C).
- We recommend that rotavirus vaccine is not contraindicated (unless an HIV diagnosis has been confirmed and the infant is severely immunosuppressed) (Grade 1C).
- We recommend that infants at low risk of HIV transmission should receive BCG at the same time and for the same indication as for infants unexposed to HIV (including those who are breast/chestfed) (Grade 1D).
- For infants at high risk of HIV transmission, we recommend that BCG should be deferred until PCR testing is completed at 12 weeks of age and they are known to be negative (Grade 1D).

From Section 11.3 Diagnosing or excluding HIV

For infants at high risk:

- We recommend that molecular diagnostics for HIV infection should be performed on the following occasions (Grade 1C):
  - As soon as possible after birth, during the first 24 hours, prior to hospital discharge by HIV RNA and DNA PCR;
  - At 2 weeks by HIV RNA and DNA PCR (additional testing for high-risk infants only);
  - At 6 weeks by HIV RNA PCR (or DNA PCR instead);
  - At 12 weeks by HIV RNA PCR (or DNA PCR instead).
- We recommend HIV antibody testing to detect seroreversion at 24 months of age (Grade 1C).

For infants at low risk and not breast/chestfed:

- We recommend that molecular diagnostics for HIV infection should be performed on the following occasions (Grade 1C):
  - As soon as possible after birth, during the first 24 hours, prior to hospital discharge by HIV RNA PCR (or DNA PCR; only one test needed);
  - At 4–6 weeks (at least 2 weeks after cessation of PNP) by HIV RNA PCR (or DNA PCR; only one test needed);
  - At 10–12 weeks by HIV RNA PCR (or DNA PCR; only one test needed).
- We recommend HIV antibody testing to detect loss of placentally transferred antibody at 24 months of age (Grade 1C).

For infants at low risk and breast/chestfed:

- We recommend that molecular diagnostics for HIV infection should be performed on the following occasions:
  - As soon as possible after birth, during the first 24 hours, prior to hospital discharge by HIV RNA PCR (or DNA PCR) (Grade 1C);
  - Monthly for the duration of breast/chestfeeding by HIV RNA PCR; following fully informed, shared decision-making, as long as viral load monitoring for the mother/feeding parent is taking place monthly, the interval between infant testing during breast/chestfeeding can be extended to a maximum of 2 months (Grade 1D);
  - At 4 and 8 weeks after cessation of breast/chestfeeding by HIV RNA PCR (or DNA PCR) (Grade 1D).
- We recommend HIV antibody testing to detect seroreversion at 24 months of age, or at a minimum of 8 weeks after cessation of breast/chestfeeding if this is later (Grade 1C).

From Section 11.4 Management of infants diagnosed with HIV and prophylaxis for *Pneumocystis jirovecii* pneumonia

- We recommend that infants with a positive test for HIV should be referred urgently to a specialist centre for management of HIV according to Chiva guidelines/standards (https://www.chiva.org.uk/professionals/clinical-guidelines/) (Grade 1C).
- We recommend that infants should be started on trimethoprim-sulfamethoxazole (co-trimoxazole) prophylaxis from 4 weeks of age if HIV PCR testing is positive at any stage, or if the infant is confirmed to have HIV infection; this should be stopped if HIV infection is subsequently excluded (Grade 1C).
- We recommend that an HIV diagnosis in an infant should be reported to the obstetric unit in which the infant was born to allow investigation of any avoidable factors in transmission (Grade 1D).

From Section 11.5 Management of infants born to mothers/birthing parents with hepatitis co-infection

- We recommend following national guidance for management of HBV in pregnant women/people and for prevention of transmission of HBV to the infant (see also Section 9.1) [70] (Grade 1D).

- We recommend following usual practice for investigation and management of HCV in pregnant women/people (Grade 1D).

From Section 11.6 HIV-exposed HIV-negative children

- We recommend that in light of evidence of possible increased infectious morbidity in children who are HIV exposed and HIV negative, timely routine vaccination should be ensured and GPs, health visitors and secondary care physicians should be made aware of a possible increased risk in order to inform decisions when assessing risk in primary/secondary care (Grade 1D).

From Section 12.1 Infant feeding decision-making

- We recommend a model of shared decision-making, facilitating open and supportive discussions about infant feeding, and tailoring advice to women/feeding parents (and their families where appropriate and with their consent) (Grade 1D).
- Where possible, we recommend that infant feeding should be discussed proactively by the HIV MDT by the end of the second trimester at the latest, and revisited in the third trimester, with the decision documented in the antenatal notes and birth plan (Grade 1D).
- We recommend that the HIV MDT shares HIV-specific sources of information and support, including peer support, with individuals making infant feeding decisions (Grade 1D).

From Section 12.2 HIV transmission via breastmilk/human milk

- We recommend that the HIV MDT should discuss with all pregnant women/people the evidence that U=U does not apply to breast/chestfeeding, and that the risk of transmission is greatly reduced by ART but is not zero (Grade 1B).

From Section 12.3 Formula (and other alternative) feeding and HIV in the UK

- Exclusive formula feeding removes all risk of postpartum HIV transmission to infants, therefore we recommend that women/birthing parents feed their babies with formula milk (or other alternatives outlined below) exclusively to ensure that the risk of HIV transmission to their infants postpartum is zero (Grade 1A).

From Section 12.3.1 Supporting women/people living with HIV to formula feed

- We recommend that women/birthing parents who do not breast/chestfeed should receive support from the HIV MDT because of the possibility of financial, social and psychological repercussions (Grade 1C).
- We recommend that efforts should be made to provide free formula and equipment to minimise vertical transmission of HIV (Grade 1D).

From Section 12.4 Suppression of lactation

- We recommend that women/birthing parents who do not breast/chestfeed their infant, either by choice or because of a viral load ≥50 copies/mL, should be offered cabergoline to suppress lactation (Grade 1C).

From Section 12.5 Breast/chestfeeding and HIV in the UK

- We recommend that women/birthing parents with a viral load <50 copies/mL on ART with good adherence, and who choose to breast/chestfeed, should be supported to do so by the HIV MDT (Grade 1D).
- We recommend that the HIV MDT should inform all women/birthing parents who want to breast/chestfeed about the ongoing low risk of transmission of HIV through breast/chestfeeding even when viral load is <50 copies/mL on ART, the importance of adherence to ART to minimise the risk of transmission and the requirement for extra clinical monitoring for both themselves and their infants (Grade 1B).

From Section 12.5.1 Supporting women/people to breast/chestfeed in the UK

- We recommend lifelong ART for the woman/feeding parent (rather than extended infant PNP) to minimise HIV transmission through breastmilk/human milk and in line with the BHIVA adult HIV treatment guidelines [38] (Grade 1A).
- We recommend that *both* women/feeding parents *and* their infants are reviewed monthly for HIV RNA viral load testing (or HIV DNA for infants) during and for 2 months after stopping breast/chestfeeding (Grade 1D).
- Wherever possible, we recommend that blood monitoring for women/feeding parents and infants should be co-located and undertaken at the same appointment to minimise the risk of missed appointments (Grade 1D).
- We recommend exclusive breast/chestfeeding (i.e. not combining breastmilk/human milk with formula, or other milk or liquids, or with solids or both), especially in infants aged <6 months, except in certain circumstances outlined in Box 12.2 (Grade 1C).
- We recommend that breast/chestfeeding is discontinued before, or soon after, 6 months to minimise the cumulative risk of HIV transmission (Grade 1B).
- We recommend that the HIV MDT should provide clear and accessible written information about breast/chestfeeding to all pregnant women/people and mothers/feeding parents (Grade 1D).

From Section 12.6 Management of detectable HIV viral load during breast/chestfeeding

- In the event of a detectable HIV maternal/parental viral load ≥50 copies/mL while breast/chestfeeding, we recommend that (Grade 1D):
  - Breast/chestfeeding should be discontinued immediately;
  - Women/feeding parents should attend clinic as soon as possible for repeat HIV RNA testing for both themselves and their infant;
  - The infant should start PEP, as per Chiva guidelines [42];

- Further management should be based on the result of the urgent repeat viral load sample.

From Section 12.7 Mixed feeding and HIV

- We recommend that infants receiving breastmilk/human milk from a woman/parent living with HIV should not be given solids before 6 months of age due to the potential increased risk of HIV transmission (Grade 1D).
- For infants aged <6 months, we recommend that breastmilk/human milk and formula milk should only be used concurrently in certain situations outlined in Box 12.2, based on the hydration and nutritional needs of the infant (Grade 1D).
- We recommend that breast/chestfeeding should be stopped in the event of infant gastroenteritis (with discussion with paediatricians if concerns about infant fluid intake), and not resumed thereafter (Grade 1D).

From Section 13.1 ART

- We recommend that all women/birthing parents should be advised to continue lifelong ART postpartum (Grade 1A).

From Section 13.2 Postpartum adherence to ART and retention in care

- We recommend that women/birthing parents should be assessed for risk factors for reduced ART adherence and engagement in HIV care postpartum (see Table 13.1) by the MDT during antenatal care, and those found to be at risk should be supported by care coordination, case management, peer support and the use of technologies as available (Grade 1C).
- We recommend that, prior to discharge after delivery, all women/birthing parents should receive an appointment to see a named member of the HIV MDT within 4–6 weeks and receive an adequate ART supply until this appointment (Grade 1D).
- We recommend that the postpartum review should include an assessment of mental health, adherence to ART, infant feeding, medical and social issues and birth experience, and contraception options should be discussed (Grade 1C).

From Section 13.3 Assessing mental health needs postpartum

- We recommend that women/birthing parents should have their mental health needs assessed during the postpartum period as well as during pregnancy (Grade 1D).
- We recommend that women/birthing parents assessed as having mental health problems should be referred to their GPs and/or appropriate mental health services and offered support from community and/or voluntary groups (Grade 1D).

From Section 13.4 Contraception

- We recommend that contraceptive needs should be discussed with all women/birthing parents, and ART should be optimised to accommodate the contraception choices of women/birthing parents as long as it remains fully active against the viral genotype (Grade 1A).

From Section 13.5 Cervical cytology

- We recommend that cytology should be scheduled 3 months post-delivery as per the NHS guidance [25] for cervical screening (Grade 1C).

From Section 13.6 Support services and interventions

- We recommend that women/birthing parents should have their support needs assessed postpartum and be referred to appropriate services in the trust, the community and/or voluntary groups without delay (Grade 1D).

From Section 13.8 Testing of partners and older children

- We recommend testing of partners and older children at risk of HIV for individuals newly diagnosed with HIV in pregnancy, if not previously tested (Grade 1D).

3 UK prevalence and epidemiology of HIV in pregnancy and risk of transmission

The Integrated Screening Outcomes Surveillance Service (ISOSS; previously known as the National Study of HIV in Pregnancy and Childhood [NSHPC]) [1] is part of the NHS IDPS programme [2] and collects, analyses and reports data on the infections that are screened for in pregnancy: HIV, hepatitis B virus (HBV) and syphilis. All pregnant women/people known to be living with HIV, their infants, and all children living with HIV seen for paediatric care are reported to ISOSS. Of note, the geographical coverage has changed: until 2020 ISOSS covered all reported pregnancies, infants and children with HIV in the UK; since 2021 ISOSS receives reports from England only due to legislative changes affecting data sharing in the devolved nations. Unfortunately, at the time of writing, current data on pregnancy outcomes in those living with HIV in the devolved nations are not available. Further information and resources are available from ISOSS [1]). Longitudinal paediatric HIV surveillance is carried out by the Children's HIV and AIDS Reporting System [3], commissioned by NHS England and running alongside ISOSS.

The UK has met and exceeded the Joint United Nations Programme on HIV/AIDS target since 2017 and a major success has been the low vertical HIV transmission rate, which has been estimated to be less than 0.4% since 2012 [4-6]. This reflects the high uptake of HIV antenatal testing (99.8%) and the impact of the NHS IDPS programme. In 2017 there were around 30,000 women living with HIV in the UK, and of these 93% were diagnosed and 97% were on treatment [7].

The number of new HIV diagnoses in women who are pregnant has declined over the last decade particularly among women from sub-Saharan Africa. The number of pregnancies in women known to be living with HIV has also declined from a peak in the period 2006–2010 of over 1300 per year to below 1000 since 2016. There has been a decrease in the proportion of women from sub-Saharan Africa (from 72.0% in 2014–2015 to 61.5% in 2020), and an increase in the proportion of women from Eastern Europe (4.7% to 6.5% respectively); the most frequently reported countries of origin were Lithuania, Latvia, Romania and Poland [8].

Median age at estimated delivery date is 34 years (interquartile range [IQR] 30–38) [8]. The proportion of pregnancies among women aged over 40 years has been increasing, rising from 1 in 7 pregnancies in 2015 to 1 in 5 pregnancies in 2020. This trend is also seen in the general population, and has implications for pregnancy management given the increased risk of multiple births, stillbirths and chromosomal anomalies in infants born to older women [9].

Recent trends show that there is also a growing cohort of pregnant women with perinatally acquired HIV. The proportion of pregnancies in women with perinatally acquired HIV increased 10-fold from 0.3% (15/5011) in the period 2006–2009 to 3.5% (83/2403) in 2018–2021 [10]. There is some evidence that these women are at greater risk of detectable viral load at delivery, reflecting their often-complex clinical history and adherence and drug resistance issues [11]. Further information about demographic and clinical characteristics and trends are available in the ISOSS annual report [12].

The UK vertical transmission rate among women diagnosed by delivery has declined from 2.1% in 2000–2001 to under 0.4% since 2012, with the transmission rate for births in 2020–2021 at 0.36% (England only) [13], reflecting the impact of the universal offer of antenatal screening (see Section 4), high uptake of earlier and effective ART and optimised clinical care before and during pregnancy, at

birth and in the postnatal period. The number of women diagnosed with HIV before pregnancy has increased consistently with approximately 90% knowing their status among women booked in 2021–2022, compared to 80% in 2010–2011 and 40% in the early 2000s [12]. Most women who were diagnosed with HIV before pregnancy were on ART prior to conception in 2021–2022 (95%) compared to 87% in 2016–2017) [12]. Among women newly diagnosed in pregnancy, median gestational age at ART initiation declined from 21 weeks in 2010 to 16 weeks in 2019, reflecting adherence to evolving guidance on when to start ART in pregnancy [13]. The proportion of women with a first antenatal CD4 count >500 cells/mm^3 was 55% in 2021–2022 while the proportion with a CD4 count <350 cells/mm^3 was 33% (no change over time) [12].

Since 2015 in England, more than 90% of deliveries have been to women with an undetectable viral load (<50 copies/mL) at delivery; 91% of women had an undetectable viral load at delivery in 2021–2022 [12,13]. This reflects the high proportion of women diagnosed before pregnancy and those diagnosed and commenced on ART earlier in pregnancy, as well as more rapid viral load decay with integrase inhibitors (INSTIs) which is particularly valuable in those newly diagnosed late in pregnancy.

In an analysis in the UK and Ireland, crude stillbirth rates in women living with HIV were 29% higher than in the general population, while adjusting for maternal country of origin (however there may be other differences that were not adjusted for between these populations) [14].

In England, the proportion of vaginal deliveries has increased from approximately 10% in the period 2000–2004 to more than 48% in 2020, while elective caesarean sections declined between 2000 and 2020 from around 65% to 28%. The emergency caesarean section rate was 24.5% in 2020, remaining stable since 2000, compared with 18.9% in the general population in the same year [13]. There has been a small increase in the number of women being supported to breastfeed in line with BHIVA guidelines, from 1.5% in 2014–2015 to 5.8% in 2018–2019. These trends reflect changing BHIVA guidance, with a drive towards normalising women's experiences of pregnancy and childbirth, while maintaining safety and balancing a low risk of vertical transmission with autonomy and choice [8].

3.1 Vertical transmission in the UK

Improvements in diagnosis and treatment of HIV during pregnancy have led to a steady reduction in the number of children born with HIV in the UK. The number of UK-born children (aged under 16) diagnosed with vertically acquired HIV declined from 65 in 2006–2007 to less than 5 per year since 2014 [12]. A very small number of vertical transmissions still occur in the UK; the transmission rate in women with an HIV viral load <50 copies/mL at delivery in England was 0.11% in 2017–2018. Thus, currently available evidence does not support the hypothesis that undetectable=untransmittable (U=U) in the context of vertical transmission [15].

ISOSS carries out enhanced data collection for all HIV vertical transmissions among children born in England (in the UK prior to 2021). All reports are reviewed by a clinical expert review panel which establishes the circumstances surrounding the transmission and any contributing factors, with many women experiencing multiple vulnerabilities.

Building on previous audit work [16], it was found that two-thirds of the 156 children with vertically acquired HIV born between 2006 and 2021 were born to women with HIV undiagnosed before or during

labour [13,17,18]. Factors contributing to transmissions from women undiagnosed before or during labour included seroconversion during the pregnancy or breastfeeding period, declining HIV screening in pregnancy and not accessing antenatal care (i.e. unbooked delivery). Among women aware of their diagnosis in pregnancy, factors that affected vertical transmission included poor ART adherence, late booking and undeclared breastfeeding; in at least seven cases no contributing factor could be identified.

More than half of the 48 transmissions (in diagnosed and undiagnosed women) reported to ISOSS since 2014 occurred in infants born to women who experienced complicating issues during pregnancy including safeguarding, mental health, substance use issues and insecure housing, highlighting the social inequalities experienced by women living with HIV. The findings highlight the importance of MDT and multi-agency support throughout pregnancy, 'negative now' messaging (i.e. that a negative HIV result only reflects the absence of HIV at that timepoint) and urgent screening for women presenting unbooked in labour.

3.2 References

1. Integrated Screening Outcomes Surveillance Service. *Integrated Screening Outcomes Surveillance Service – ISOSS. 2024*. Available at: www.ucl.ac.uk/isoss (accessed March 2024).

2. NHS England. *NHS infectious diseases in pregnancy screening (IDPS) programme*. 2023. Available at: www.gov.uk/topic/population-screening-programmes/infectious-diseases-in-pregnancy (accessed March 2024).

3. University College London. *Children's HIV and AIDS Reporting System (CHARS)*. Available at: www.ucl.ac.uk/chars (accessed July 2024).

4. Public Health England. *Trends in HIV testing, new diagnoses and people receiving HIV-related care in the United Kingdom: data to the end of December 2019*. Available at https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/959330/hpr2020_hiv19.pdf (accessed March 2024).

5. UK Health Security Agency. *HIV testing, PrEP, new HIV diagnoses and care outcomes for people accessing HIV services: 2023 report*. 2023. Available at: https://www.gov.uk/government/statistics/hiv-annual-data-tables/hiv-testing-prep-new-hiv-diagnoses-and-care-outcomes-for-people-accessing-hiv-services-2023-report#hiv-care-outcomes (accessed July 2024).

6. Integrated Screening Outcomes Surveillance Service (ISOSS). Obstetric and paediatric HIV surveillance data from England. Available at: https://www.ucl.ac.uk/integrated-screening-outcomes-surveillance/sites/integrated_screening_outcomes_surveillance/files/isoss_hiv_annual_slides_2023.pdf (accessed December 2024).

7. Public Health England. *Women and HIV in the United Kingdom Data to end of December 2017*. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/912615/Women_and_HIV_in_the_UK_2017.pdf (accessed March 2024).

8. Peters H, Bukasa L, Francis K *et al*. *Trends in maternal characteristics and pregnancy outcomes among women living with HIV in the UK: 2014-19*. 2022. Available at: https://www.ucl.ac.uk/integrated-screening-outcomes-

surveillance/sites/integrated_screening_outcomes_surveillance/files/isoss_trends_in_maternal_characteristics.pdf (accessed March 2024).

9. Townsend CL, de Ruiter A, Peters H *et al*. Pregnancies in older women living with HIV in the UK and Ireland. *HIV Med* 2017; **18**: 507–512.

10. Peters H, Francis K, Sconza R *et al*. *Pregnancy characteristics and outcomes of women with vertically acquired HIV in the UK. International Workshop on HIV and Women*. 2022. Available at: https://www.ucl.ac.uk/integrated-screening-outcomes-surveillance/sites/integrated_screening_outcomes_surveillance/files/pregnancy_characteristics_to_women_with_vertically_acquired_hiv_hivwomen_bhiva20april.pdf (accessed July 2024).

11. Byrne L, Sconza R, Foster C *et al*. Pregnancy incidence and outcomes in women with perinatal HIV infection. *AIDS* 2017; **31**: 1745–1754.

12. NHS England. *ISOSS HIV Report 2023*. 2024. Available at: https://www.gov.uk/government/publications/idps-isoss-hiv-outcome-report-2023/isoss-hiv-report-2023#vertical-transmissions (accessed July 2024).

13. NHS England. *ISOSS HIV Report 2022*. 2023. Available at: https://www.gov.uk/government/publications/infectious-diseases-in-pregnancy-screening-isoss-hiv-report-2022/isoss-hiv-report-2022 (accessed July 2024).

14. Favarato G, Townsend CL, Peters H *et al*. Stillbirth in women living with HIV delivering in the United Kingdom and Ireland: 2007–2015. *J Acquir Immune Defic Syndr* 2019; **82**: 9–16.

15. Peters H, Francis K, Bukasa L *et al*. *Preventing vertical HIV transmission in the UK: successes and emerging challenges. Conference on Retroviruses and Opportunistic Infections*. 2021. Available at: https://www.croiconference.org/abstract/preventing-vertical-hiv-transmission-in-the-uk-successes-and-emerging-challenges/ (accessed July 2024).

16. NHS Audit Information Analysis Unit, National Study of HIV in Pregnancy and Childhood, Children's HIV Association. *Perinatal transmission of HIV in England 2002–2005*. 2007. Available at: https://www.ucl.ac.uk/integrated-screening-outcomes-surveillance/sites/integrated_screening_outcomes_surveillance/files/perinatal_transmission_of_hiv_in_england_2002-2005.pdf (accessed December 2024).

17. Peters H, Thorne C, Tookey PA, Byrne L. National audit of perinatal HIV infections in the UK, 2006-2013: what lessons can be learnt? *HIV Med* 2018; **19**: 280–289.

18. NHS England. *ISOSS HIV Report 2021*. 2021. Available at: https://www.gov.uk/government/publications/infectious-diseases-in-pregnancy-screening-isoss-hiv-report-2021 (accessed December 2024).

4 Screening for HIV and preventing HIV acquisition in pregnancy

4.1 IDPS programme

HIV screening is offered and recommended to every pregnant woman/person in the UK to facilitate early detection and treatment of HIV and reduce the risk of vertical transmission. The IDPS programme has supported maternity services and laboratories in the delivery of universal antenatal HIV screening since 2000. Guidance and resources are regularly updated and available at www.gov.uk/government/collections/infectious-diseases-in-pregnancy-screening-clinical-guidance. National uptake of antenatal HIV screening has improved year on year and in England uptake is currently 99.8% across all regions [1]. This, combined with increased coverage of HIV testing outside pregnancy, has helped to improve timely diagnosis and treatment contributing to the sustained low vertical transmission rate [2].

Most HIV screening takes place in the antenatal setting in early pregnancy, however screening may be undertaken opportunistically in other settings (e.g. gynaecology wards or emergency departments) and at any stage of pregnancy, in labour or in the early postnatal period. HIV testing in late pregnancy or urgently for those in labour requires reliable and prompt communication between maternity services, the virology laboratory and the antenatal screening infectious diseases (ID) MDT so that, in the event of a positive result, interventions for the mother/birthing parent and infant are as timely as possible. Urgent screening guidance can be found in the IDPS programme laboratory handbook [3]. Women/people who screen HIV negative should be given the message that they are 'negative now', and repeat testing should be offered if they (i) change their sexual partner, (ii) have a partner who is sexually active with other people, (iii) have a partner diagnosed with a sexually transmitted infection, (iv) inject recreational drugs or (v) undertake sex work.

HIV screening in pregnancy is also an opportunity to highlight the importance of a pregnant women/people knowing their partner's HIV status, and testing of partners should be encouraged as per national HIV testing guidelines [4].

4.2 Managing women/people who decline HIV screening in pregnancy

Recommendations

- We recommend that pregnant women/people who decline HIV screening in pregnancy should be managed by an antenatal screening ID MDT, with emphasis on providing support to understand the benefits of HIV testing, both for their own health and that of their infant, and ensuring that any additional communication needs are met (Grade 1D).
- The antenatal screening ID MDT should offer a face-to-face appointment with the HIV team and/or sexual health advisor to discuss the benefits of testing for both women/birthing parents and their infants (GPP).

- We recommend that infant HIV antibody testing and HIV RNA/DNA polymerase chain reaction (PCR) testing at birth should be offered by the antenatal screening ID MDT if all HIV screening in pregnancy has been declined. It should be made clear that HIV antibody testing is a proxy for maternal/parental HIV status and will inform the administration of PNP to reduce the risk of vertical transmission and to provide advice on safe infant feeding (Grade 1D).
- If infant HIV testing at birth is declined, the antenatal screening ID MDT should continue dialogue with the family and continue to recommend that HIV RNA/DNA PCR testing is completed to exclude infection (GPP).
- We recommend that the infant's general practitioner (GP) should be informed in writing if the mother/birthing parent has declined HIV screening in pregnancy and at birth, and infant testing has not been completed (i.e. if the infant has an unknown HIV status). The mother/person with parental responsibility should be informed that this will happen (Grade 1D).
- The woman/birthing parent should be offered a follow-up appointment with a sexual health advisor to discuss maternal/parental HIV testing in the postnatal period (GPP).

Auditable outcomes

- Proportion of women/people not known to be living with HIV accepting HIV screening in pregnancy.
- Proportion of women/people not known to be living with HIV declining testing, who are referred to the antenatal ID MDT.
- Proportion of women/people not known to be living with HIV initially declining antenatal HIV screening but who are offered and accept infant HIV testing.
- Proportion of GPs informed in writing that an infant has been born to a woman/person who has declined HIV screening in pregnancy and/or at delivery.

Rationale

Although very few pregnant women decline the offer of HIV screening (0.15% between 2020 and 2021; unpublished data from NHS England 2022), a national audit of perinatal HIV acquisition in the UK established this as an important risk factor for vertical HIV transmission: women had declined HIV screening in pregnancy in a quarter of cases of vertical transmission [5]. There are limited data on whether women who decline antenatal HIV screening are at higher risk of having HIV than those who accept. In a published quality improvement project at one maternity unit, the reasons women gave for declining HIV testing were needle phobia, health preferences (i.e. declining all antenatal screening), lack of perception of risk and health concerns about blood tests. Among six women who stated that they did not think they needed the test, two subsequently tested positive for HIV [6]. There is also evidence from a study investigating non-selective opt-out HIV screening in non-pregnant adults in an emergency

department in a high prevalence area in the USA that people who decline opt-out HIV screening may be at higher risk of having HIV [7].

The IDPS programme standards have been informed by the findings from the national audit on perinatal HIV in the UK and since 2016 have recommended that women/people who decline the initial offer of HIV screening in pregnancy should be formally re-offered the test in a face-to-face clinic appointment before 20 weeks' gestation or within 2 weeks if more than 20 weeks' gestation at the time of HIV test decline. This face-to-face meeting with an experienced midwife provides an opportunity to revisit the decision regarding HIV test decline, supported by up-to-date information, and enables screening teams to identify any risk factors for HIV [1]. If HIV testing continues to be declined despite the formal re-offer, there should be a referral to the antenatal screening ID MDT which is responsible for review and further management. A survey of obstetric units found a wide variation in management, with only a fifth of units surveyed stating that they had a specific policy on the management of infants born to women who decline HIV testing in pregnancy [8].

Given the variation in local policies, the writing group recommends that the IDPS pathway should be followed to ensure a standard approach at all maternity units. The mainstay of management is to support women/people to understand the benefits of HIV testing, both for their own health and that of their infant. The recommendations in this section are designed to complement and add to the IDPS pathway.

Pregnant women/people who decline antenatal HIV screening should be managed by an antenatal screening ID MDT. This MDT should comprise a member of the antenatal screening team and/or specialist ID midwife, a consultant in HIV medicine or ID, and a paediatrician with expertise in the prevention of vertical HIV transmission. If this expertise is not available at the booking maternity unit, advice should be sought from a centre with expertise in managing HIV in pregnancy. If a baby is born after HIV testing has been declined in pregnancy, a paediatrician should be made aware to allow ongoing assessment, support and discussion about infant testing with the parents.

4.3 Retesting for HIV in pregnancy

Retesting for HIV in pregnancy is another important consideration. Findings from a recent vertical transmission case review showed that 6 of 13 transmissions reported between 2020 and 2021 occurred where the mother had a confirmed negative antenatal HIV test and subsequently acquired HIV during pregnancy or in the postnatal period while breastfeeding [2]. The review highlighted the need to raise the profile of sexual health among maternity providers.

Updated IDPS programme guidance requires midwives to discuss sexual health with all women at booking and to deliver the 'negative now' message when giving screening results, advising that a negative HIV result only reflects the absence of HIV at that timepoint and that HIV can be acquired at any time after the negative test during pregnancy and in the breastfeeding period. Women are encouraged to report any risk to their midwife who will facilitate retesting [9]. The IDPS programme recommends and offers HIV screening in every pregnancy.

4.4 Antenatal referral pathway

The IDPS pathway requires that antenatal screening coordinators are notified of all positive HIV screening results by the screening laboratory. All women/people who test positive should be given their result by the screening team within 5 working days; a referral is then made to HIV services for new screen-positive cases. The antenatal screening team should remain a point of contact for women/people living with HIV throughout their pregnancy and act as a link between maternity and HIV services. For standards for the MDT management of pregnant women/people who have been diagnosed with HIV, see Section 6.

4.5 Preventing HIV acquisition during pregnancy and infant feeding from a partner living with HIV

Recommendations

- We recommend that postexposure prophylaxis (PEP) after condomless receptive vaginal or anal sex for women/people during pregnancy or breastfeeding is not required if their partner living with HIV meets the U=U criteria, as per the British Association for Sexual Health and HIV (BASHH) PEP guidelines (Grade 1A).
- We recommend that consent should be sought from partners with HIV to obtain confirmation that they meet the U=U criteria, including the result of their last viral load test, by either the ID MDT or the partner's HIV clinician (Grade 1D).
- If the conditions for U=U are not met, or viral load results are not available, we recommend that the couple should be advised to use condoms for sexual intercourse until such time that the conditions are met; in addition, retesting of pregnant or breastfeeding women/people and PEP and/or pre-exposure prophylaxis (PrEP) for them and/or PEP for their infant should be considered according to a risk assessment by the ID MDT and according to existing national guidelines [10-12] (Grade 1D).

Rationale

The UK BASHH PEP guidelines summarise the evidence for treatment as prevention and the evidence behind the U=U criteria [11]. Women/birthing parents who test negative for HIV in early pregnancy may be at risk of HIV acquisition during the remainder of the pregnancy and the breastfeeding period if they have receptive vaginal or anal sex with a partner living with HIV who does not meet the U=U criteria:

- History of good adherence;

- Continuing to take ART as prescribed;
- HIV viral load <200 copies/mL for at least 6 months;
- HIV viral load <200 copies/mL within the last 6 months.

In the national audit of perinatal HIV in the UK for 2006–2013, 23 women had acquired HIV after testing negative early in pregnancy. In this group, one current male partner tested negative, and 17 partners were known to be living with HIV or subsequently tested positive. Of the four men known to have HIV at the time of the pregnancy, two had not disclosed their status [5]. In a subsequent update to the data for pregnancies reported in 2020–2021, six infants who acquired HIV were born to women who seroconverted after an initial negative test; of these, none of the six male partners had been diagnosed with HIV at the time of maternal seroconversion [13]. Strategies to reduce the proportion of late diagnosis in men who have acquired HIV through heterosexual contact [14] are key to reducing the risk of HIV acquisition during pregnancy and infant feeding, as is the work of HIV services to educate those newly diagnosed about reducing the risk of onward transmission and facilitating disclosure to sexual partners.

Where a woman/person is pregnant, has tested HIV negative in early pregnancy and has a partner who is living with HIV, it is essential to know the viral load status of that partner. PEP should be routinely recommended following condomless receptive anal or vaginal sex with an index partner known to be living with HIV with an unknown or detectable HIV viral load or following receptive anal sex with an index partner of unknown HIV status as per UK PEP guidelines [11] and PrEP should be considered where there is ongoing risk [10]. PEP is not required for receptive vaginal or anal intercourse if the partner meets the U=U criteria. In pregnancy and breastfeeding, where the risk of HIV acquisition is to both the pregnant woman/person *and* the infant, it is especially important to establish that these criteria are met. Where the ID MDT deems it necessary, infant PEP can be considered according to the Children's HIV Association (Chiva) paediatric PEP guidelines [12].

4.6 References

1. NHS England. *Antenatal screening standards: data report 2020 to 2021*. 2022. Available at: https://www.gov.uk/government/statistics/antenatal-screening-standards-data-report-2020-to-2021 (accessed March 2024).

2. NHS England. *ISOSS HIV report 2022*. 2023. Available at: https://www.gov.uk/government/publications/infectious-diseases-in-pregnancy-screening-isoss-hiv-report-2022/isoss-hiv-report-2022 (accessed March 2024).

3. NHS England. *Infectious diseases in pregnancy screening programme: laboratory handbook*. 2022. Available at: https://www.gov.uk/government/publications/infectious-diseases-in-pregnancy-screening-programme-laboratory-handbook (accessed June 2024).

4. Palfreeman A, Sullivan A, Rayment M *et al*. British HIV Association/British Association for Sexual Health and HIV/British Infection Association adult HIV testing guidelines 2020. *HIV Med* 2020; **21 Suppl 6**: 1–26.

5. Peters H, Thorne C, Tookey PA, Byrne L. National audit of perinatal HIV infections in the UK, 2006–2013: what lessons can be learnt*? HIV Med* 2018; **19**: 280–289.

6. Kingston M, Thomas Leech A, Stott B *et al*. Stepping up from opt-out: achieving 100% uptake antenatal human immunodeficiency virus testing. *Int J STD AIDS* 2022; **33**: 205–208.

7. Czarnogorski M, Brown J, Lee V *et al*. The prevalence of undiagnosed HIV infection in those who decline HIV screening in an urban emergency department. *AIDS Res Treat* 2011; **2011**: 879065.

8. Byrne L. *Women who decline antenatal HIV testing: a national survey of local policy and practice*. Oral Presentation at CHIVA Parallel Sessions at the BHIVA Autumn Conference, November 2015, London, UK. Available at: https://www.chiva.org.uk/files/2414/4836/7769/LauraByrne.pdf (accessed July 2024).

9. NHS England. *Infectious diseases in pregnancy screening: clinical guidance*. 2022. Available at: https://www.gov.uk/government/collections/infectious-diseases-in-pregnancy-screening-clinical-guidance (accessed March 2024).

10. BHIVA/BASHH guidelines on the use of pre-exposure prophylaxis (PrEP) 2018. Available at: https://www.bhiva.org/file/5b729cd592060/2018-PrEP-Guidelines.pdf (accessed July 2024).

11. UK guideline for the use of HIV post-exposure prophylaxis 2021. Available at: https://www.bhiva.org/file/6183b6aa93a4e/PEP-guidelines.pdf (accessed June 2024).

12. Foster C, Lees AE, Lyall EGH *et al*. 2023. *DDIPost-exposure prophylaxis (PEP) guidelines for infants, children and adolescents potentially exposed to blood-borne viruses.* Available at: https://www.chiva.org.uk/wp-content/uploads/2023/11/CHIVA_PEP_2023-Final.pdf (accessed October 2024).

13. Francis K, Peters H, Bukasa L *et al*. *HIV vertical transmission in England: current challenges*. Available at: https://www.ucl.ac.uk/integrated-screening-outcomes-surveillance/sites/integrated_screening_outcomes_surveillance/files/p043_francis_isoss_hiv_vertical_transmissions_in_england_169.pdf (accessed July 2024).

14. Department of Health and Social Care. *Towards Zero – An action plan towards ending HIV transmission, AIDS and HIV-related deaths in England – 2022 to 2025*. 2021. Available at: https://www.gov.uk/government/publications/towards-zero-the-hiv-action-plan-for-england-2022-to-2025/towards-zero-an-action-plan-towards-ending-hiv-transmission-aids-and-hiv-related-deaths-in-england-2022-to-2025#objective-2-scale-up-hiv-testing-in-line-with-national-guidelines-1 (accessed March 2024).

5 Preconception advice

Women account for a third of people accessing care for HIV in the UK, and the majority of these women are currently of reproductive potential [1]. Pregnancies may be unplanned; according to the most recent National Survey of Sexual Attitudes and Lifestyles survey, the proportion of pregnancies that are unplanned or ambivalent in the UK overall is around 45% [2]. In addition, the vast majority of women living with HIV who become pregnant are already on ART [3]. This means that it is essential that women/people who can become pregnant are counselled on the safety of ART at conception (see Section 8) and prevention of vertical transmission (as well as effective contraception) *before* they become pregnant [4].

There is a very useful patient resource for preparing for pregnancy produced by 4M Mentor Mothers and University College London (https://4mmm.org/resources/preparing-for-pregnancy-while-living-with-hiv/).

Potential drug–drug interactions should be checked for any new medications prescribed prior to or during pregnancy and the postpartum period using the University of Liverpool's HIV drug interactions website (https://www.hiv-druginteractions.org) or by contacting a specialist HIV pharmacist.

5.1 Folic acid supplementation

In the UK, women trying to conceive are recommended to take folic acid supplementation prior to conception and up to 12 weeks of pregnancy to reduce the risk of a neural tube defect (NTD) in their infant [5]. The dose recommended for most women is 400 μg daily. Although no trials have compared high-dose versus standard-dose folic acid for prevention of NTDs [6], a higher dose of 5 mg daily is recommended for pregnant women/people if:

- They or their partner have an NTD;
- They have had a previous baby with an NTD;
- They or their partner have a family history of NTDs;
- They have diabetes;
- They have epilepsy [7];
- They have a body mass index >30 kg/m^2 [8];
- They have had bariatric surgery [9].

Given the current lack of evidence of a significantly increased risk of NTDs in women on ART, the writing group recommends that women/people living with HIV trying to conceive should take folic acid supplementation at the standard 400 μg dose recommended for women with no additional risk factors or the higher dose of 5 mg daily if they have one or more of the above risk factors.

5.2 Optimising health before conception

All women/people who are planning to try to conceive should be signposted to resources with advice on optimising health before becoming pregnant, for example advice from the charity Tommy's (https://www.tommys.org/pregnancy-information/planning-pregnancy/planning-for-pregnancy-tool).

In addition, all women/people should be up to date with vaccinations as recommended in the BHIVA immunisation guidelines [10] (and see Section 7.3).

5.3 References

1. Public Health England. *HIV in the United Kingdom: Towards zero HIV transmissions by 2030*. 2019. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/858559/HIV_in_the_UK_2019_towards_zero_HIV_transmissions_by_2030.pdf (accessed March 2024).

2. Wellings K, Jones KG, Mercer CH *et al*. The prevalence of unplanned pregnancy and associated factors in Britain: findings from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3). *Lancet* 2013; **382**: 1807–1816.

3. NHS England. *ISOSS HIV report 2023*. 2024. Available at: https://www.gov.uk/government/publications/idps-isoss-hiv-outcome-report-2023/isoss-hiv-report-2023#pregnancy-management-in-women-with-hiv (accessed July 2024).

4. British HIV Association. *British HIV Association standards of care for people living with HIV 2018*. Available at: https://www.bhiva.org/standards-of-care-2018 (accessed March 2024).

5. National Institute for Care and Health Excellence. *Maternal and child nutrition. Public health guideline [PH11]*. 2014. Available at: https://www.nice.org.uk/guidance/ph11/chapter/4-recommendations#folic-acid-2 (accessed March 2024).

6. Dwyer ER, Filion KB, MacFarlane AJ et al. Who should consume high-dose folic acid supplements before and during early pregnancy for the prevention of neural tube defects? *BMJ* 2022; **377**: e067728.

7. Royal College of Obstetricians and Gynaecologists. *Epilepsy in pregnancy. Green-top Guideline No. 68*. 2016. Available at: https://www.rcog.org.uk/media/rzldnacf/gtg68_epilepsy.pdf (accessed March 2024).

8. Denison FC, Aedla NR, Keag O *et al*.; on behalf of the Royal College of Obstetricians and Gynaecologists. Care of women with obesity in pregnancy. Green-top Guideline No. 72. *BJOG* 2019; **126**: e62–e106.

9. O'Kane M, Parretti HM, Pinkney J *et al*. British Obesity and Metabolic Surgery Society guidelines on perioperative and postoperative biochemical monitoring and micronutrient replacement for patients undergoing bariatric surgery-2020 update. *Obes Rev* 2020; **21**: e13087.

10. Geretti AM, Brook G, Cameron C *et al*. British HIV Association guidelines on the use of vaccines in HIV-positive adults 2015. *HIV Med* 2016; **17**: s2–s81. Available at: https://www.bhiva.org/vaccination-guidelines (accessed June 2024).

6 Emotional, psychological and social wellbeing in pregnancy

The majority of women/people living with HIV engage well in care during pregnancy, resulting in the very low rates of vertical transmission as outlined in Section 3. Furthermore, pregnancy and parenthood can be a time of excitement and joy for most parents. However, regardless of HIV status, pregnancy, birth and early parenthood can also bring significant physical, social and emotional changes.

The impact of these changes can be amplified by the intersecting challenges of being pregnant and living with HIV. Pregnancy may precipitate new emotional, psychological and social issues and/or exacerbate pre-existing issues [1]. Social factors such as immigration issues and HIV-related stigma have been identified as key contributing factors in cases of vertical transmission of HIV in the UK [2]. Therefore holistic care that addresses physical and psychosocial wellbeing (including maintaining rights, freedom from violence, sexual wellbeing, financial security and mental health) is crucial in preventing vertical transmission, as well as supporting the longer-term health and wellbeing of parents and families. For specific guidance on postpartum care, refer to Section 13.

6.1 The antenatal HIV MDT

Recommendations

- We recommend that antenatal HIV care should be delivered by an MDT (Grade 1D).
- We recommend that HIV clinics with relatively few women/people who are pregnant should ensure there is a mechanism for MDT discussion of cases and establish links with larger units for further support (Grade 1D).
- All those who are newly diagnosed or not currently engaged in HIV care (not attended for HIV care ≥12 months) should be seen within 2 weeks of the referral by maternity services [3] (GPP).
- We recommend that all pregnant women/people living with HIV should be offered peer support (Grade 1B).
- The antenatal HIV MDT should include at least an HIV specialist, obstetrician, specialist midwife, paediatrician and peer mentor (GPP).

Auditable outcomes

- Proportion of women/people with new antenatal HIV diagnosis seen by the HIV MDT within 2 weeks of referral by maternity services.
- Proportion of women/people living with HIV for whom there is a record of an offer of peer support during pregnancy.

Rationale

Women/people living with HIV require support from a range of professionals during pregnancy to safeguard their health, the pregnancy and the health of their baby. Optimal support and counselling around issues such as adjusting to an HIV diagnosis, use of ART in pregnancy, advice on mode of delivery and infant feeding decisions and robust confidentiality processes can impact on engagement with care and adherence to ART. Adherence to ART (and resulting virological suppression) is critical in preventing vertical transmission of HIV and safeguarding the health of the pregnant woman/person.

We recommend that antenatal HIV care is delivered by an MDT to provide appropriate medical management and holistic support; 99% of UK HIV clinics report having an MDT to manage HIV in pregnancy [4]. MDT management may be in the form of a specialist HIV antenatal clinic. Dedicated

clinics may not be feasible in settings with low numbers of pregnant women/people living with HIV, thus robust pathways for the management of HIV in pregnancy are required. These should include identifying members of the antenatal HIV MDT, holding regular MDT meetings to discuss management, and promoting links with a larger unit to provide advice and support when necessary [5].

There is currently no evidence to guide the composition of an antenatal HIV MDT. From clinical experience, we recommend that the antenatal HIV MDT should include at least an HIV specialist, obstetrician, specialist midwife, paediatrician and peer mentor (either within the clinic or via links with a peer support provider). Efforts should be made to involve the GP and health visitor with the consent of the pregnant woman/person. It may also be necessary to involve some of the following professionals: social workers, legal advocates, clinical psychologists, psychiatrists, counsellors, health advisors, Citizens Advice Bureau workers, interpreters, community midwives, pharmacists, adult and paediatric clinical nurse specialists and lactation specialists [6]. Good communication between all those involved in the care of the woman/person is vital in view of the complexity of the issues involved.

Mentor Mother programmes providing peer support to women/people living with HIV during pregnancy are well established in the UK and internationally, with positive multidimensional impacts and improvements in clinical outcomes (e.g. improving health literacy, ART adherence, mental health and social support, and preventing vertical transmission) [7-10]. People who are newly diagnosed with HIV may be particularly reluctant to engage with peer support because of fears around confidentiality; however, the great majority of those who do engage find that it becomes one of the most highly valued interventions in their pregnancy [11,12]. Therefore we strongly recommend that all women/people living with HIV are offered peer support during pregnancy and the postpartum period. Clinics should establish links with Mentor Mother programmes via local HIV community organisations, or by contacting the 4M Network (https://4mmm.org/).

6.2 Supporting emotional and psychological wellbeing

Recommendations

- We recommend that a full mental health history and assessment of antenatal depression and anxiety be undertaken at antenatal booking, and later in pregnancy if needed, as per National Institute for Health and Care Excellence (NICE) guidelines for the general pregnant population [13] (Grade 1D).
- If screening indicates a mental health concern, we recommend that women/people should be referred to their GP and/or local perinatal mental health service and offered peer support (Grade 1D).

Auditable outcome

- Proportion of women/people living with HIV with a documented mental health and social wellbeing assessment at antenatal booking.

Rationale

Women living with HIV have a higher prevalence of comorbid mental health conditions than both men living with HIV and women without HIV [14]. A global survey of nearly 500 women living with HIV found that 82% of respondents reported symptoms of depression [15]. It is recognised that transgender and non-binary individuals experience high rates of poor mental health, socioeconomic deprivation and

discrimination (including within the healthcare system) [16,17].

Women living with HIV are also more likely than those without HIV to have antenatal depression; a 2019 meta-analysis found a mean prevalence of antenatal depression of 36% among women living with HIV, with increased odds compared to women without HIV (odds ratio [OR] 1.42, 95% confidence interval [CI] 1.12–1.80) [18]. Factors associated with antenatal depression in this population include HIV diagnosis in pregnancy [19], HIV-related stigma [20], unplanned pregnancy [21], lower socioeconomic status [21,22], previous depression [23] and previous or current intimate partner violence (IPV) [20-23].

Given the increased risk of poor mental health during pregnancy, and the potential impact on engagement in HIV care, we endorse NICE guidance on recognising mental health issues in pregnancy [24]. We advise screening at antenatal booking using validated tools such as the brief Whooley questions (based on the Patient Health Questionnaire-9; see Box 6.1) [13] and the two-item Generalised Anxiety Disorder scale (GAD-2; see Box 6.2). Mental health screening can be repeated later in pregnancy as indicated.

Box 6.1 Whooley questions to screen for perinatal depression

1. During the past month, have you often been bothered by feeling down, depressed or hopeless?
2. During the past month, have you often been bothered by having little interest or pleasure in doing things?

If the woman/birthing parent answers 'yes' to either of the initial questions, consider asking a third question:

3. Is this something you feel you need or want help with?

Box 6.2 GAD-2 screening for anxiety

1. Over the last 2 weeks, how often have you been bothered by feeling nervous, anxious or on edge?
2. Over the last 2 weeks, how often have you been bothered by not being able to stop or control worrying?

Answers of 'not at all' scores 0; 'several days' scores 1; 'more than half the days' scores 2; 'nearly every day' scores 3.

Anyone answering yes to at least one of the depression screening questions and/or scoring ≥3 on the anxiety screening questions should be referred to their GP or appropriate local perinatal mental health services and peer support encouraged.

6.3 Supporting social wellbeing

Recommendation

- We recommend that all pregnant women/people living with HIV should be asked about their social situation at antenatal booking (or soon after) and later in pregnancy if indicated as per NICE guidance for the general pregnant population [24] (Grade 1D).

Rationale

Nearly half of women living with HIV who responded to a 2018 survey led by the Sophia Forum and Terrence Higgins Trust reported living below the poverty line [25]. In the 2022 Positive Voices report, 70% of women living with HIV stated that they did not always have enough money to cover their basic needs; 35% of people living with HIV reported an unmet social or welfare need with women and transgender and non-binary people living with HIV more likely than men to have unmet needs [26].

This means that many people living with HIV will have issues relating to social welfare such as food and housing insecurity, and financial, legal and immigration issues. Adverse social circumstances are associated with vertical transmission [2] and poor antenatal mental health [21,22]. Therefore, we recommend that all pregnant women/people living with HIV are asked about their social situation at antenatal booking (or soon after), and later in pregnancy if indicated, by a member of the MDT, and that people are referred promptly for appropriate specialist advice and support.

6.4 Screening for domestic abuse in pregnancy

Recommendation

- All pregnant women/people living with HIV should be asked about domestic abuse at the antenatal booking appointment, or at the earliest opportunity when they are alone as per NICE guidance for the general pregnant population [24] (Grade 1D).

Auditable outcome

- Proportion of women/people living with HIV with a documented assessment of domestic abuse at booking.

Rationale

We fully endorse NICE guidelines which recommend that healthcare providers 'Ask the woman about domestic abuse in a kind, sensitive manner at the first antenatal (booking) appointment, or at the earliest opportunity when she is alone' [24]. If domestic abuse is identified, the antenatal HIV MDT should follow local safeguarding pathways [27]. The global prevalence of IPV among women during pregnancy is 28% [28]; there are no data in pregnant transgender and gender non-binary people. The link between gender-based violence and HIV is well established [29]. IPV in pregnancy has negative impacts on the fetus and on the woman/person, as a direct result of physical injury, effects on stress and mental health and in the case of women/people with HIV an increased risk of vertical transmission [27]. As in the general population, women/people living with HIV may be at increased risk of IPV during pregnancy with a lifetime prevalence rate estimated to be 14% in women living with HIV in the UK [30]. A recent meta-analysis found that IPV in pregnancy is associated with both an increased prevalence of depression in women with HIV of 180% and an increase in non-adherence to PNP of 145% [31].

6.5 Managing information about HIV status during pregnancy

Reassurance about confidentiality is extremely important, especially regarding family members and friends who may not know the HIV status of the woman/person but who may be closely involved with the pregnancy. People from communities in which HIV is more common may be concerned about the possibility of certain interventions acting as a marker of HIV such as taking medication during pregnancy,

having a caesarean section and/or avoiding breast/chestfeeding. Discussing potential explanations in advance may help with feeling more prepared and confident in answering unexpected questions. Such explanations could include 'needing to take vitamins' or 'having a breast/chest condition' [32].

The importance of informing appropriate healthcare professionals (such as midwives, GPs, health visitors and paediatricians) about their HIV status should be emphasised to pregnant women/people with HIV, as well as the need for this to be included in the birth plan wherever possible. The process of inpatient care should be explained clearly so that pregnant women/people can be supported to inform ward staff explicitly about maintaining confidentiality about their HIV status, especially around visitors.

Confidence in telling others about their HIV status will vary between individuals, and there may be cultural factors that influence the patterns of telling partners and other members of their social network [6,33]. Telling relevant and appropriate people about their HIV status should be viewed as a process that may take some time [34,35].

There are situations in which someone given a new diagnosis of HIV may be reluctant to share this with a current sexual partner(s). This can give rise to complex professional, ethical, moral and, potentially, legal situations. There is a conflict between the duty of confidentiality to the index patient and a duty to prevent harm to others. Breaking confidentiality in order to inform a sexual partner of someone's positive HIV status is sanctioned as a 'last resort' by the World Health Organization (WHO) [36] and the General Medical Council (GMC) [37]. This is an important decision that should not be taken lightly as it could have the negative impact of deterring others from testing because of the fear of forced imparting of HIV status and undermining of trust in the confidential doctor–patient relationship. Such cases should be managed by the antenatal HIV MDT; it is important to accurately record discussions and management strategies. Timely partner testing during the pregnancy should be encouraged and appropriate support given.

HIV testing of older children potentially at risk of HIV should also be discussed, if not documented previously. In practice, if these children are asymptomatic, testing is often most easily done when the newborn infant is attending paediatric follow-up for HIV diagnostic tests [38].

6.6 Pregnancy care in specific populations living with HIV

Recommendation

- We recommend that the antenatal HIV MDT and all other professionals involved in the care of women/people living with HIV during and after pregnancy deliver anti-racist, gender-inclusive, person-centred care (Grade 1D).

Rationale

Women/people living with HIV face numerous intersecting social disadvantages during pregnancy. Therefore it is important for the antenatal HIV MDT to deliver respectful, inclusive and person-centred care. NICE has published guidelines on antenatal care for pregnant women with complex social factors including alcohol or drug use, recent migrant or asylum seeker status, difficulty reading/speaking English, age <20 years and domestic abuse [39]. Additional challenges may be encountered during pregnancy among the four populations living with HIV considered below.

6.6.1 Women/people from racially minoritised communities

Many pregnant women/people living with HIV in the UK are of Black African ethnicity. Women from racially minoritised communities have a higher maternal mortality rate than White women. Black women in the UK are 3.7 times more likely than White women to die during pregnancy, childbirth or the 6 weeks postpartum; Asian women are 1.8 times more likely to die [40]. Although socioeconomic deprivation is one underlying factor, institutional racism has a larger role. A recent analysis by the charity Five X More found that 27% of Black women thought that their maternity care was poor or very poor; 43% felt discriminated against (mainly due to their race and/or ethnicity) [41]. Women described racially discriminatory language, racially biased assumptions (including about pain tolerance and fertility intentions) and poor awareness among healthcare professionals about clinical complications that Black women may experience in pregnancy and childbirth [41]. These racialised experiences of care during pregnancy and childbirth not only result in an increased risk of death, but also have long-term physical, emotional and psychological consequences.

Antenatal HIV MDTs should be aware of these racial disparities in maternity outcomes and ensure that care provided to all women/people living with HIV during and after pregnancy is anti-racist, centred around the individual and empathic. Pregnant women/people living with HIV who are also racially minoritised may particularly benefit from peer support. Five X More has resources for healthcare professionals (https://www.fivexmore.org/healthcare-professionals) and the public (https://fivexmore.org/6steps) to help reduce inequalities in maternity care.

6.6.2 Women/people with insecure immigration status

Migrant pregnant women/people are a heterogenous group with an increased risk of adverse perinatal outcomes. NICE states that recent migrants, refugees and asylum seekers, and pregnant women who speak or read little or no English, are groups with 'complex social factors' requiring specific efforts to improve access to and engagement with maternity services (such as providing access to interpreters) [39].

Immigration issues are commonly experienced by women living with HIV [25,26]. Treatment for HIV is freely available to anyone regardless of immigration status, and no hospital should refuse HIV treatment to someone living with HIV. All antenatal, intrapartum and postnatal services are required by law to be considered 'immediately necessary', and therefore cannot be denied to an individual, regardless of ability to pay. However, people who are not eligible for free NHS care (including those refused asylum, living in the UK without official immigration status, or with no recourse to public funds) can be billed afterwards for these services.

The Home Office may move people seeking asylum and living in asylum accommodation to different accommodation in another part of the UK, often at short notice, while their application is being processed. UK government guidance sets out a protected period (6 weeks before the estimated date of delivery to around 6 weeks after birth) in which pregnant women/people should only be moved at the request of the applicant or their treating medical practitioners. In the event of dispersal of a pregnant woman/person living with HIV, the antenatal HIV MDT should liaise with local teams in the area to which the individual will be moved, to ensure safe transfer of care.

Furthermore, pregnant women/people may be subject to immigration detention, with the recent removal of the previous 72-hour limit that applied in pregnancy. This means that pregnant women/people may be detained in immigration centres for extended periods; resulting stress, adverse

and unsanitary conditions, and disrupted HIV and antenatal care are likely to lead to poor clinical outcomes [42].

In complex cases of either dispersal or detention, advice should be sought from colleagues, the GMC, the British Medical Association and/or medical defence organisations. Advice can also be sought from organisations such as the Terrence Higgins Trust (www.tht.org.uk), the National AIDS Trust (www.nat.org.uk) and Birthrights (https://www.birthrights.org.uk/), and the Doctors of the World advice line can be contacted (0207 515 7534) for advice on access to healthcare in the UK.

6.6.3 Transgender and gender-diverse people

Transgender and gender-diverse individuals may experience significant challenges navigating clinical services during pregnancy. This is likely to be compounded by also living with HIV, although there are currently no data on pregnancy among transgender and gender-diverse people living with HIV. Pregnancy and birth are commonly seen as exclusively female experiences, and cisgender norms inform the majority of maternity services [43]. Transgender and gender-diverse individuals may experience stigma and discrimination within maternity services, and may also feel excluded [43-45]. Furthermore, they may require specific support regarding contraception, lactation and emotional and psychological wellbeing.

Antenatal HIV services should be explicitly gender inclusive. Some trusts have gender inclusion midwives who can support the antenatal HIV MDT to deliver gender-inclusive care. Box 6.3 illustrates other ways in which gender-inclusive pregnancy care can be delivered.

Box 6.3 Gender-inclusive pregnancy care

- Discussing where it is most comfortable to have midwife appointments
- Emphasising that company and support are welcome at all appointments
- Personalised birth, feeding and parenting preparation at home
- Tour of the hospital facilities where the individual will be giving birth
- Writing a birth plan, including language and pronoun preferences
- Developing an infant feeding plan, which may include breast/chestfeeding (depending on other criteria; see Section 12)

Further guidance can be found at https://invivo.citeline.com/-/media/supporting-documents/gender-inclusive-language-in-perinatal-services.pdf and http://www.birthforeverybody.org/.

6.7 References

1. Johnson M, Samarina A, Xi H *et al*. Barriers to access to care reported by women living with HIV across 27 countries. *AIDS Care* 2015; **27**: 1220–1230

2. Peters H, Thorne C, Tookey PA, Byrne L. National audit of perinatal HIV infections in the UK, 2006–2013: what lessons can be learnt? *HIV Med* 2018; **19**: 280–289.

3. British HIV Association. *British HIV Association standards of care for people living with HIV 2018*. Available at: https://www.bhiva.org/standards-of-care-2018 (accessed October 2024).

4. Raffe S, Curtis H, Tookey P *et al*. UK national clinical audit: management of pregnancies in women with HIV. *BMC Infect Dis* 2017; **17**: 158.

5. Redler K, Hallgren R, Swingler R. Audit of the management of HIV positive pregnant women in a low prevalence setting. *Sex Transm Infect* 2016; **92 Suppl 1**: A89.

6. Wood C, Kumalo P, Ainsworth J *et al*. Disclosure, discordance and decisions: the psychosocial impact of antenatal HIV testing. *International Congress On Drug Therapy in HIV Infection*. November 2002. Glasgow, UK.

7. McLeish J, Redshaw M. 'We have beaten HIV a bit': a qualitative study of experiences of peer support during pregnancy with an HIV Mentor Mother project in England. *BMJ Open* 2016; **6**: e011499.

8. Richter L, Rotheram-Borus MJ, Van Heerden A *et al.* Pregnant women living with HIV (WLH) supported at clinics by peer WLH: a cluster randomized controlled trial. *AIDS Behav* 2014; **18**: 706–715.

9. Kanters S, Park JJ, Chan K *et al*. Use of peers to improve adherence to antiretroviral therapy: a global network meta-analysis. *J Int AIDS Soc* 2016. **19**: 21141.

10. Monroe A, Nakigozi G, Ddaaki W *et al*. Qualitative insights into implementation, processes, and outcomes of a randomized trial on peer support and HIV care engagement in Rakai, Uganda. *BMC Infect Dis* 2017; **17**: 54.

11. Wood C, Ellison G. What have clinicians learnt from working with HIV/AIDS? A medical perspective from London. In: Ellison G, Parker M, Campbell C, eds. Learning from HIV/AIDS. Cambridge, UK, Cambridge University Press, 2003: 105–137.

12. Mandisodza R, Stephens C, Russell J, Byrne L. 'I started to talk, and I didn't want to stop'. Evaluating a peer support group set up to improve the health and wellbeing of pregnant and postnatal women living with HIV. *HIV Med* 2015; **16 Suppl 2**: 12–77. Abstract P57.

13. National Institute for Health and Care Excellence. *Antenatal and postnatal mental health: clinical management and service guidance. Clinical guideline [CG192]*. 2020. Available at: https://www.nice.org.uk/guidance/cg192 (accessed March 2024).

14. Waldron EM, Burnett-Zeigler I, Wee V *et al*. Mental health in women living with HIV: the unique and unmet needs. *J Int Assoc Provid AIDS Care* 2021; **20**: 2325958220985665.

15. Orza L, Bewley S, Logie CH *et al*. How does living with HIV impact on women's mental health? Voices from a global survey. *J Int AIDS Soc* 2015. **18 Suppl 5**: 20289.

16. Tebbe AE, Budge SL. Factors that drive mental health disparities and promote wellbeing in transgender and non-binary people. *Nat Rev Psychol* 2022; **1**: 694–707.

17. Hibbert M, Wolton A, Crenna-Jennings W *et al*. Experiences of stigma and discrimination in social and healthcare settings among trans people living with HIV in the UK. *AIDS Care* 2018; **30**: 836–843.

18. Zhu Q-Y, Huang D-S, Lv J-D *et al*. Prevalence of perinatal depression among HIV-positive women: a systematic review and meta-analysis. *BMC Psychiatry* 2019; **19**: 330.

19. LeMasters K, Dussault J, Barrington C *et al*. "Pain in my heart": Understanding perinatal depression among women living with HIV in Malawi. *PLoS One* 2020; **15**: e0227935.

20. Ngocho JS, Watt MH, Minja L *et al*. Depression and anxiety among pregnant women living with HIV in Kilimanjaro region, Tanzania*. PLoS One* 2019; **14**: e0224515.

21. Peltzer K, Rodriguez VJ, Lee TK, Jones D. Prevalence of prenatal and postpartum depression and associated factors among HIV-infected women in public primary care in rural South Africa: a longitudinal study. *AIDS Care* 2018; **30**: 1372–1379.

22. Ojukwu EN, De Oliveira GC, Cianelli R *et al*. Social determinants of peripartum depressive symptoms among Black peripartum women living with HIV. *Arch Psychiatr Nurs* 2021; **35**: 102–110.

23. Nyamukoho E, Mangezi W, Marimbe B *et al*. Depression among HIV positive pregnant women in Zimbabwe: a primary health care based cross-sectional study. *BMC Pregnancy Childbirth* 2019; **19**: 53.

24. National Institute for Health and Care Excellence. *Antenatal care*. NICE guideline NG201. 2021. Available at: https://www.nice.org.uk/guidance/ng201/chapter/recommendations (accessed June 2024).

25. Sophia Forum and Terrence Higgins Trust. *Women and HIV: invisble no longer.* 2018 Available at: https://www.tht.org.uk/sites/default/files/2018-08/women-and-HIV_report_final_amended.pdf (accessed June 2024).

26. UK Health Security Agency. *Positive Voices 2022: survey report*. Available at: https://www.gov.uk/government/publications/hiv-positive-voices-survey/positive-voices-2022-survey-report#:~:text=Positive%20Voices%20survey%202022%20created,welfare%20needs%20have%20been%20met (accessed July 2024).

27. Kuchukhidze S, Walters MK, Panagiotoglou D *et al.* The contribution of intimate partner violence to vertical HIV transmission: a modelling analysis of 46 African countries. *Lancet HIV* 2024; **11**: e542–e551.

28. Garcia-Moreno C, Jansen HAFM, Ellsberg M *et al*. Prevalence of intimate partner violence: findings from the WHO multi-country study on women's health and domestic violence. *Lancet* 2006; **368**: 1260–1269.

29. Orza L, Bass E, Bell E *et al*. In women's eyes: key barriers to women's access to HIV treatment and a rightsbased approach to their sustained well-being. *Health Hum Rights* 2017; **19**: 155–168.

30. Dhairyawan R, Tariq S, Scourse R, Coyne KM. Intimate partner violence in women living with HIV attending an inner city clinic in the UK: prevalence and associated factors. *HIV Med* 2013; **14**: 303–310.

31. Lin D, Zhang C, Shi H. Adverse impact of intimate partner violence against HIV-positive women during pregnancy and post-partum: results from a meta-analysis of observational studies. *Trauma Violence Abuse* 2023; **24**: 1624–1639.

32. Serovich JM. Helping HIV-positive persons to negotiate the disclosure process to partners, family members, and friends. *J Marital Fam Ther* 2000; **26**: 365–372.

33. Siriwasin W, Shaffer N, Roongpisuthipong A *et al*. HIV prevalence, risk, and partner serodiscordance among pregnant women in Bangkok. Bangkok Collaborative Perinatal HIV Transmission Study Group. *JAMA* 1998; **280**: 49–54.

34. Gielen AC, Fogarty L, O'Campo P *et al*. Women living with HIV: disclosure, violence, and social support. *J Urban Health* 2000; **77**: 480–491.

35. Stein MD, Freedberg KA, Sullivan LM *et al*. Sexual ethics. Disclosure of HIV-positive status to partners. *Arch Intern Med* 1998; **158**: 253–257.

36. World Health Organization. *Gender dimensions of HIV status disclosure to sexual partners: rates, barriers and outcomes*. 2003. Available at: https://iris.who.int/bitstream/handle/10665/42717/9241590734.pdf (accessed July 2024).

37. General Medical Council. *Confidentiality: disclosing information about serious communicable diseases*. 2017. Available at: https://www.gmc-uk.org/professional-standards/the-professional-standards/confidentiality---disclosing-information-about-serious-communicable-diseases (accessed March 2024).

38. British HIV Association, Children's HIV Association, British Association for Sexual Health and HIV. *Don't forget the children: guidance for the HIV testing of children with HIV positive parents.* 2009. Available at: https://www.chiva.org.uk/files/3114/2738/8429/dont-forget.pdf (accessed March 2024).

39. National Institute for Health and Care Excellence. *Pregnancy and complex social factors: a model for service provision for pregnant women with complex social factors*. Clinical guideline CG110. 2010. Available at: https://www.nice.org.uk/guidance/cg110 (accessed June 2024).

40. MBRRACE-UK. *Saving lives, improving mothers' care*. 2022. Available at: https://www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/maternal-report-2022/MBRRACE-UK_Maternal_MAIN_Report_2022_UPDATE.pdf (accessed June 2024).

41. FIVE X More. *The Black maternity experiences survey*. 2022. Available at: https://static1.squarespace.com/static/5ee11f70fe99d54ddeb9ed4a/t/628a8756365828292ccb7712/1653245787911/The+Black+Maternity+Experience+Report.pdf (accessed June 2024).

42. Maternity action. *Imigrant detention of pregnant women*. 2023. Available at: https://maternityaction.org.uk/2023/05/immigration-detention-of-pregnant-women-part-2-of-3-blogs/#:~:text=Before%20the%2072%20hour%20maximum,poor%20quality%20food%20and%20sanitation (accessed June 2024).

43. Bower-Brown S. Trans and/or non-binary (TNB) parents' experiences during the perinatal period. *Hum Reprod* 2022; **37 Suppl 1**: p. i425. Available at: https://doi.org/10.1093/humrep/deac107.465 (accessed August 2024).

44. Besse M, Lampe NM, Mann ES. Experiences with achieving pregnancy and giving birth among transgender men: a narrative literature review. *Yale J Biol Med* 2020; **93**: 517–528.

45. Gedzyk-Nieman SA, McMillian-Bohler J. Inclusive care for birthing transgender men: a review of the literature. *J Midwifery Womens Health* 2022; **67**: 561–568.

7 Infection screening and immunisation of pregnant women/people living with HIV

All those who are pregnant should be offered routine screening tests for HBV and syphilis as well as HIV as part of the infectious disease in pregnancy screening programme [1]. It is also recommended that all people diagnosed with HIV are tested for HBV and hepatitis C virus (HCV) on an annual basis, and more often if at high risk [2].

7.1 Sexual health screening

Recommendations

- We recommend sexual health screening for all women/people who are newly diagnosed with HIV in pregnancy (Grade 1B).
- For those individuals already engaged in HIV care and who become pregnant, we suggest that sexual health screening is carried out as early as possible in pregnancy and repeated at 28 weeks where there may be ongoing risk (Grade 2C).
- We recommend that genital tract and sexually transmitted infections (STIs) should be treated according to BASHH guidelines [3] (Grade 1B).
- We recommend that national guidance for immunisation of pregnant women/people should be followed (Grade 1B).

Auditable outcomes

- Proportion of women/people living with HIV who undergo sexual health screening in pregnancy.
- Proportion of women/people living with HIV who accept vaccination according to national guidance in pregnancy.

Rationale

NICE recommends that all pregnant women should be screened for HIV, HBV and syphilis [4]. The UK National Screening Committee does not currently recommend routine screening for chlamydia, bacterial vaginosis (BV), genital herpes, group B streptococcus and HCV in pregnancy [5-9]. BHIVA guidelines recommend that all those newly diagnosed with HIV should be advised to undergo STI screening (including for chlamydia, gonorrhoea, syphilis, HBV and HCV) and that this should be repeated annually for those with a change in partner since the last screen [2].

STIs such as chlamydia, gonorrhoea, syphilis and trichomoniasis are associated with increased risk of PTB (i.e. <37 weeks' completed gestation) in the general population. Ascending infection causing chorioamnionitis may lead to premature rupture of the membranes and PTB, with causative organisms including *Ureaplasma urealyticum, Chlamydia trachomatis, Neisseria gonorrhoea, Mycoplasma genitalis, M. hominis*, group B streptococcus, *Trichomonas vaginalis*, *Gardnerella vaginalis* and *Bacteroides* spp. [10-13]. Pregnant women/people living with HIV are at greater risk of PTB, despite the use of effective ART [14]. A US study demonstrated that despite 96.9% of pregnant women with HIV taking ART, a concomitant STI doubled the risk of spontaneous PTB [15].

In women without HIV, data regarding the effect of screening and treating for BV on PTB are conflicting. A nested matched case–control study compared data from pregnant women living with HIV with pregnant women without HIV. Those living with HIV had an increased risk of vaginal dysbiosis or BV (OR 2.09, 95% CI 1.30–3.32; *P*=0.002). The incidence of PTB did not differ significantly between the groups (cases 8.7%, controls 10%; *P*=0.887) [16]. Conversely, a study conducted in the post-ART era found that PTB in women living with HIV in the UK occurred with adverse dysbiotic vaginal microbiota. This unfavourable vaginal microbiota was associated with cervicovaginal inflammation in pregnancy, despite restoration of CD4 cell levels [17].

In the UK, screening for group B streptococcus during pregnancy is not recommended, but pregnant women/people at risk should be identified and treated when indicated [18]. There was no significant difference found in the prevalence of group B streptococcus colonisation in pregnant women living with HIV in a US case–control study with 225 participants [19].

For pregnant women/people living with HIV with a concomitant genital infection, an additional consideration is the potential effect on the risk of vertical transmission of HIV. There have been no studies on the impact on vertical transmission of HIV in pregnant women/people with an undetectable viral load and an STI. Vertical transmission of HIV in the presence of an STI could theoretically occur through an increase in the HIV viral load in the genital tract and/or the presence of chorioamnionitis.

We suggest screening for genital tract infections including evidence of BV. This should be done as early as possible in pregnancy and consideration should be given to repeating this at around 28 weeks' gestation. Syphilis serology should be performed on both occasions.

Any infection detected should be treated according to BASHH guidelines [3], considering recommended treatment regimens in pregnancy, followed by a test of cure when required. Partner notification should take place where indicated, to avoid re-infection.

7.2 Herpes simplex virus (HSV)

Studies have demonstrated an association between HIV vertical transmission and HSV-2 co-infection [20], HSV-2 shedding [21-25] and HSV-2 seropositivity [26]; however, there have been no studies in women on combination ART. Studies are mostly historical from before the routine use of combination ART throughout pregnancy, or failed to adjust for ART use, or did not show a correlation. A Ukrainian study, in which 96% of women received antenatal ART, found no evidence that HSV-2 seropositivity was associated with risk of vertical transmission of HIV but was only powered to rule out a 2.25-fold increased risk of vertical transmission of HIV with HSV-2 antibodies [26]. HSV-1 can also cause genital herpes, but there have been no studies assessing the relationship between HSV-1 seropositivity and vertical transmission of HIV.

Pregnant women/people with genital HSV should be managed in line with BASHH/Royal College of Obstetricians and Gynaecologists (RCOG) guidelines for the management of HSV in pregnancy which were extensively updated in 2024 [27]. These guidelines recommend that treatment for those living with HIV in pregnancy should be the same as for pregnant women/people without HIV, except for recognising that those with immunosuppression (which may include people with low CD4 counts) may require increased doses of antiviral agents for a first episode of genital herpes.

7.3 Immunisation in pregnancy

National guidance for immunisation in pregnancy (as per the immunisation against infectious disease guidance in the Green Book and BHIVA guidelines for immunisations in people living with HIV [28,29]) should be followed for pregnant women/people living with HIV. Recommended immunisation supports the health of pregnant women/people during a period when they may be relatively immunosuppressed, and the health of their infant after birth by facilitating transplacental antibody transfer [30]. HIV-negative infants born to those living with HIV are at increased risk of lower respiratory tract disease and hospitalisation compared with HIV-unexposed infants [31]. Although the majority of these vaccines may not be offered in the HIV outpatient setting, clinicians should discuss with pregnant women/people the importance of immunisation as per national guidelines, and support referral for this when required.

- Inactivated influenza vaccine should be offered to all pregnant women/people at any stage of pregnancy [28], including those living with HIV [29], and ideally prior to the annual circulation of influenza virus (usually between October and January).
- Pertussis (whooping cough)-containing vaccine should be offered to all pregnant women/people from 16 weeks of gestation and ideally by 32 weeks in each pregnancy [28], including those living with HIV [29].
- Respiratory syncytial virus (RSV) vaccine should be offered to all pregnant women/people from 28 weeks of gestation and up to delivery in each pregnancy (off-licence after 36 weeks' gestation as this may not offer as high a level of passive protection to the infant) [28], including those living with HIV [29]. For optimal immunogenicity, RSV vaccination should be separated from pertussis, influenza or COVID-19 vaccinations by 2 weeks, unless this poses an unacceptable barrier to vaccination (concomitant vaccination is better than no vaccination).
- All pregnant women/people should be offered a seasonal booster for COVID-19 in line with national guidance for that particular year [28], including those living with HIV [29].
- Measles, mumps and rubella (MMR) and other live vaccines should not be offered routinely in pregnancy as there is a potential risk of infection of the fetus. Pregnant women/people who are not immune to rubella should be offered any outstanding doses of MMR vaccine soon after delivery. Pregnancy should be avoided for 1 month after MMR vaccination.

7.4 References

1. NHS England. *Infectious diseases in pregnancy screening (IDPS): programme overview*. Available at: https://www.gov.uk/guidance/infectious-diseases-in-pregnancy-screening-programme-overview#infections-screened-for (accessed May 2025).

2. British HIV Association. *BHIVA guidelines for the routine investigation and monitoring of adult HIV-1-positive individuals 2016 (2019 interim update)*. Available at: https://www.bhiva.org/monitoring-guidelines (accessed March 2024).

3. British Association for HIV and Sexual Health. *Guidelines*. Available at: www.bashh.org/guidelines (accessed August 2024).

4. National Institute for Health and Care Excellence. *Antenatal care NICE guideline [NG201]*. 2021. Available at: https://www.nice.org.uk/guidance/ng201 (accessed March 2024).

5. UK National Screening Committee. *Antenatal screening programme. Chlamydia (pregnancy)*. 2018. Available at: https://view-health-screening-recommendations.service.gov.uk/chlamydia-pregnancy/ (accessed March 2024).

6. UK National Screening Committee. *Antenatal screening programme. Bacterial vaginosis*. 2014. Available at: https://view-health-screening-recommendations.service.gov.uk/bacterial-vaginosis/ (accessed March 2024).

7. UK National Screening Committee. *Antenatal screening programme. Genital herpes*. 2018. Available at: https://view-health-screening-recommendations.service.gov.uk/genital-herpes/ (accessed March 2024).

8. UK National Screening Committee. *Antenatal screening programme. Group B streptococcus*. 2017. Available at: https://view-health-screening-recommendations.service.gov.uk/group-b-streptococcus/ (accessed March 2024).

9. UK National Screening Committee. *Antenatal screening programme. Hepatitis C (pregnancy)*. 2018. Available at: https://view-health-screening-recommendations.service.gov.uk/hepatitis-c-pregnancy/ (accessed March 2024).

10. Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. *N Engl J Med* 2000; **342**: 1500–1507.

11. Hillier SL, Martius J, Krohn M *et al*. A case-control study of chorioamnionic infection and histologic chorioamnionitis in prematurity. *N Engl J Med* 1988; **319**: 972–978.

12. Czikk MJ, McCarthy FP, Murphy KE. Chorioamnionitis: from pathogenesis to treatment. *Clin Microbiol Infect* 2011; **17**: 1304–1311.

13. Lis R, Rowhani-Rahbar A, Manhart LE. Mycoplasma genitalium infection and female reproductive tract disease: a meta-analysis. *Clin Infect Dis* 2015; 61: 418–426.

14. Portwood C, Sexton H, Kumarendran M *et al*. Adverse perinatal outcomes associated with antiretroviral therapy in women living with HIV: A systematic review and meta-analysis. *Front Med (Lausanne)* 2023; **9**: 924593.

15. Burnett E, Loucks TL, Lindsay M. Perinatal outcomes in HIV positive pregnant women with concomitant sexually transmitted infections. *Infect Dis Obstet Gynecol* 2015; **2015**: 508482.

16. Foessleitner P, Petricevic L, Boerger I *et al*. HIV infection as a risk factor for vaginal dysbiosis, bacterial vaginosis, and candidosis in pregnancy: a matched case-control study. *Birth* 2021; **48**: 139–146.

17. Short CES, Brown RG, Quinlan R *et al.* Lactobacillus-depleted vaginal microbiota in pregnant women living with HIV-1 infection are associated with increased local inflammation and preterm birth. *Front Cell Infect Microbiol* 2021; **10**: 596917.

18. Royal College of Obstetricians and Gynaecologists. *Prevention of early-onset Group B streptococcal disease (Green-top Guideline No. 36)*. Available at: https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/prevention-of-early-onset-group-b-streptococcal-disease-green-top-guideline-no-36/ (accessed March 2024).

19. Morgan JA, Hankins ME, Callais NA *et al*. Group B streptococcus rectovaginal colonization and resistance patterns in HIV-positive compared to HIV-negative pregnant patients. *Am J Perinatol* 2023; **40**: 1573–1578.

20. Sivarajah V, Venus K, Yudin MH *et al*. Does maternal HSV-2 coinfection increase mother-to-child transmission of HIV? A systematic review. *Sex Transm Infect* 2017; **93**: 535–542.

21. Warszawski J, Tubiana R, Le Chenadec J *et al*. Mother-to-child HIV transmission despite antiretroviral therapy in the ANRS French Perinatal Cohort. *AIDS* 2008; **22**: 289–299.

22. Bollen LJ, Whitehead SJ, Mock PA *et al*. Maternal herpes simplex virus type 2 coinfection increases the risk of perinatal HIV transmission: possibility to further decrease transmission? *AIDS* 2008; **22**: 1169–1176.

23. Drake AL, John-Stewart GC, Wald A *et al*. Herpes simplex virus type 2 and risk of intrapartum human immunodeficiency virus transmission. *Obstet Gynecol* 2007; **109**: 403–409.

24. Ouedraogo A, Nagot N, Vergne L *et al*. Impact of suppressive herpes therapy on genital HIV-1 RNA among women taking antiretroviral therapy: a randomized controlled trial. *AIDS* 2006; **20**: 2305–2313.

25. Patterson J, Hitti J, Selke S *et al*. Genital HSV detection among HIV-1-infected pregnant women in labor. *Infect Dis Obstet Gynecol* 2011; **2011**: 157680.

26. Aebi-Popp K, Bailey H, Malyuta R *et al*.; Ukraine European Collaborative Study in EuroCoord. High prevalence of herpes simplex virus (HSV)- type 2 co-infection among HIV-positive women in Ukraine, but no increased HIV mother-to-child transmission risk. *BMC Pregnancy Childbirth* 2016; **16**: 94.

27. Clarke E, Patel R, Dickins D *et al*. Joint British Association for Sexual Health and HIV and Royal College of Obstetricians and Gynaecologists national UK guideline for the management of herpes simplex virus (HSV) in pregnancy and the neonate (2024 update). *Int J STD AIDS* 2024; 9564624241280734. doi: 10.1177/09564624241280734. Online ahead of print.

28. UK Health Security Agency. Immunisation against infectious diseases. The Green Book. 2024. Available at: https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book#the-green-book (accessed October 2024).

29. Geretti AM, Brook G, Cameron C *et al*. British HIV Association guidelines on the use of vaccines in HIV-positive adults 2015. *HIV Med* 2016; **17**: s2–s81. Available at: https://www.bhiva.org/vaccination-guidelines (accessed June 2024).

30. Bengston AM, Sanfilippo AM, Hughes BL, Savitz DA. Maternal immunisation to improve the health of HIV-exposed infants. *Lancet Infect Dis* 2019; **19**: e120–e131.

31. Slogrove AL, Frigati L, Gray DM. Maternal HIV and paediatric lung health. *Paediatr Respir Rev* 2017; **21**: 47–53.

8 Current issues in the use of ART in pregnancy and pregnancy outcomes

The vast majority (89%) of pregnant women/people with HIV in the UK know about their status prior to conception, and 95% are already on ART at conception. The BHIVA adult treatment guidelines continue to recommend lifelong treatment for all people diagnosed with HIV. There is a global consensus that this standard applies to women/people who are pregnant, despite the lack of a licence for use in pregnancy for most antiretroviral drugs. Special considerations are needed for women/people who are pregnant; evidence summaries are provided here on:

- Safety at conception;
- Pharmacokinetics in pregnancy;
- Efficacy in terms of suppressing viral load in pregnancy and viral load decay.

Evidence summaries on the effects of ART and both perinatal and maternal/parental adverse outcomes can be found in Appendix 3.

Here we provide recommendations and the rationale for:

- Starting ART in women/people who may become pregnant;
- Continuing ART in women/people who are pregnant;
- ART dosing in pregnancy;
- What ART to start in pregnancy;
- When to start ART in those not already on treatment;
- Monitoring the response to ART;
- Managing HIV-2;
- Managing specific situations that may arise in pregnant women/people.

8.1 What ART to start in women/people who may become pregnant and continue in those who are pregnant

These recommendations specify which regimens are recommended to be initiated in women/people who may become pregnant, and continued in those who are pregnant, and which regimens may need to be switched for women/people who have conceived on ART.

Recommendations

- We recommend that women/people who are planning to conceive are prescribed a regimen in line with current BHIVA adult treatment guidelines [1] for which conception safety data and reassuring pharmacokinetic data are available (see Table 8.1) (Grade 1C).
- We recommend that women/people conceiving on an effective ART regimen should continue this treatment, with some exceptions (see Table 8.2) (Grade 1B).
- Where uncertainty around these risks of a current non-recommended regimen is acceptable to individuals who become pregnant and strong preference given to continuation of a current non-recommended regimen, they should be supported with additional 1- to 2-monthly viral load measurement with or without therapeutic drug monitoring (TDM) as appropriate (see Section 8.5) (GPP).

Table 8.1 Recommended ART for women/people starting treatment who are planning to conceive

Antiretroviral agents for which conception safety and reassuring pharmacokinetic data are available (Grade 1C)	
Regimen/agent	**Details**
Nucleoside reverse transcriptase inhibitor (NRTI) backbone	
Tenofovir disoproxil (DX) or tenofovir AF with emtricitabine	
Abacavir with lamivudine	If no active HBV infection, HBV immune, HLA B*5701 negative and 10-year cardiovascular disease risk <10%
Preferred anchor agent	
• Dolutegravir	Reassuring conception safety data available from multiple sources; data on pregnancy outcomes from RCTs available
• Raltegravir 400 mg twice daily	Raltegravir 1200 mg once daily may be prescribed in those planning to conceive but must be switched to raltegravir 400 mg twice daily once they are pregnant
• Darunavir with ritonavir	Darunavir/cobicistat can be initiated in those planning to conceive but cobicistat must be switched to ritonavir as soon as they become pregnant
Alternative anchor agent	
• Bictegravir	Limited pharmacokinetic and pregnancy outcome data so should only be used if benefits outweigh risks. If continuing in pregnancy, consider additional viral load monitoring
• Rilpivirine	Not recommended if viral load >100,000 copies/mL or CD4 count <200 cells/mm^3. Take with food. Note important drug–drug interaction with proton pump inhibitors and other acid-lowering drugs which are routinely given during caesarean section
• Efavirenz	Non-preferred regimen due to side effect profile; may be used to manage drug interactions with tuberculosis treatment and can be switched postpartum
• Atazanavir with ritonavir	Boosted atazanavir is no longer recommended as first-line ART in the BHIVA adult ART guidelines and should be reserved for those who need a protease inhibitor (PI) and cannot take darunavir. Atazanavir/cobicistat can be initiated in those planning to conceive but cobicistat must be switched to ritonavir as soon as they become pregnant

Table 8.2 Advice on continuing specific regimens/agents with limited human safety, efficacy and/or pharmacokinetic data in pregnancy

Regimen/agent (alphabetical order)	Evidence	Advice
Abacavir/zidovudine/ lamivudine fixed-dose combination	Adequate human safety and pharmacokinetic data. No longer a recommended option for ART due to toxicity profile and efficacy	No longer available in the UK
Bictegravir	Limited pharmacokinetic and pregnancy outcome data exist to recommend in pregnancy	Discuss risks/benefits and consider switch to a regimen in Table 8.3. If continuing, consider additional viral load monitoring
Cabotegravir plus rilpivirine long-acting injectable	Limited pharmacokinetic, safety and viral efficacy data in pregnancy	Consider switching to oral three-drug regimen in Table 8.3. Continuation or initiation without additional oral agents may be considered in complex cases with MDT discussion and increased viral load monitoring. There is no evidence on optimum dosing regimens in pregnancy; we recommend 4-weekly dosing during pregnancy in the absence of data, with consideration of TDM
Cobicistat	Pharmacokinetic data demonstrate reduced drug levels and thus cobicistat should NOT be used as a booster in pregnancy	Cobicistat used as a pharmacological booster should be switched to ritonavir as soon as possible in pregnancy
Darunavir/ritonavir	Evidence of reduced drug levels with darunavir once-daily dosing	Use darunavir 600 mg plus ritonavir 100 mg twice-daily dosing if initiating in pregnancy (see Section 8.2)
Doravirine	Limited pharmacokinetic data. Insufficient human data available to establish safety in pregnancy	Discuss risks/benefits and offer switch to a regimen in Table 8.3; if continuing, consider additional viral load monitoring
Enfuvirtide	No adequate human data and pharmacokinetics have not been described. Does not cross the placenta	No longer available in the UK
Etravirine	Very limited teratogenicity data. Pharmacokinetic data show an increase in levels during pregnancy	Recommend switch to a three-drug regimen in Table 8.3
Fostemsavir	No pharmacokinetic data. Insufficient human data are available to establish risk to pregnancy outcomes	May be considered in complex cases with MDT discussion
Ibalizumab	No pharmacokinetic, safety or efficacy data in pregnancy	May be considered in complex cases with MDT discussion
Lenacapavir	No pharmacokinetic, safety or efficacy data in pregnancy	May be considered in complex cases with MDT discussion

Lopinavir/ritonavir	Adequate human safety and pharmacokinetic data. Some evidence of association with PTB and small for gestational age neonates	Discuss risks/benefits and offer switch to a regimen in Table 8.3
Maraviroc	No pharmacokinetic data. Insufficient pregnancy safety data	Recommend switch to a three-drug regimen in Table 8.3
PI monotherapy	Minimal transplacental transfer of PIs	Recommend intensify to a three-drug regimen in Table 8.3
Raltegravir	Pharmacokinetic data only available for 400 mg twice-daily regimen	Use 400 mg twice daily in pregnancy
Oral two-drug regimens		
Dolutegravir plus lamivudine, rilpivirine or darunavir/ritonavir	Safety and pharmacokinetic data for individual drugs exist but not in combinations with fewer than three agents in pregnancy	May be considered with discussion of limited data with pregnant woman/person and HIV MDT with increased viral load monitoring. Note important drug–drug interaction between rilpivirine and proton pump inhibitors or other acid-lowering drugs which are routinely given during caesarean section
Darunavir/ritonavir or atazanavir/ritonavir plus lamivudine or emtricitabine	Safety and pharmacokinetic data for individual drugs exist but not in combinations with fewer than three agents in pregnancy	Recommend intensifying to a three-drug regimen in Table 8.3

Auditable outcome

- Proportion of women/people who continue on a regimen not recommended in pregnancy.

Rationale

Women/people, particularly those with the potential to become pregnant, have been routinely excluded from antiretroviral clinical trials. In addition, there has been a long delay between marketing authorisation of a new antiretroviral drug and pregnancy safety data becoming available [2]. Despite the fact that very few antiretrovirals have been licensed for use in pregnancy, there is global consensus that women/people who conceive on effective ART should continue ART throughout pregnancy and then lifelong. Detection of adverse events in pregnancy such as birth defects requires evaluation of a large number of exposures, which only occurs when the antiretroviral drug is introduced into populations including women of reproductive potential, principally in resource-limited settings [3].

The 2022 BHIVA guidelines on antiretroviral treatment for adults recommend the second-generation INSTIs bictegravir or dolutegravir as first-line anchor drugs, combined with tenofovir AF or tenofovir DX plus emtricitabine (dual therapy of a combination of dolutegravir plus lamivudine can be used in patients with baseline viral load <500,000 copies/mL and CD4 count >200 cells/mm^3). Boosted darunavir, doravirine and efavirenz are recommended only in certain circumstances [1]. Women/people

of reproductive potential should be prescribed the best agents on an individual basis, dependent on the efficacy and safety data available, and taking into account their concerns and preferences. In addition, clinicians should counsel women/people of reproductive potential on ART safety at conception and should recommend a regimen with adequate conception safety data prior to pregnancy.

The writing group recommends that women/people conceiving on an effective ART regimen should continue this treatment, providing it is well tolerated and efficacious, unless the regimen contains fewer than three drugs, is boosted with cobicistat or contains one of the agents listed in Table 8.2.

8.1.1 Switching in pregnancy

Switching ART in pregnancy can result in periods of viraemia. One observational study in France demonstrated that 20% of 50 virologically suppressed pregnant women who switched away from rilpivirine-based regimens to alternative regimens developed viraemia (the majority switched to PIs based on current guidance), compared to none of the 19 who continued rilpivirine [4]. Nearly all (94%) of those who developed viraemia were undetectable by delivery and there were no HIV transmissions. Italian surveillance data on ART in pregnancy also identified treatment modification as a risk factor for detectable plasma viral load in the third trimester, albeit from a pre-INSTI era [5].

Therefore, we suggest that switches are made only where there is a compelling reason to do so such as limited or unsupportive safety or pharmacokinetic data in pregnancy, intolerance or toxicity, failure to suppress or preference for a regimen with more robust safety data. Where ART needs to be modified due to virological failure with or without new resistance, this should be done with input from the MDT (see Section 8.7.3).

8.1.2 Evidence for safety at conception

The Antiretroviral Pregnancy Registry (APR; https://www.apregistry.com/) is a pharmaceutical company-sponsored prospective registry which enrols approximately 1300–1700 pregnant women exposed to ART each year, the majority of whom receive care in the USA however the registry also includes UK data. The APR estimates congenital abnormality rates in women exposed to particular antiretroviral drugs in the first trimester and compares these rates to two population-based comparators, the US Centre for Disease Control and Prevention's birth defect surveillance system Metropolitan Atlanta Congenital Defect Program and the Texas Birth Defects Registry. To date, based on data from more than 23,000 live births, the prevalence of birth defects among women with first-trimester exposure to ART is not significantly different to the prevalence among those exposed in the second or third trimesters [6].

As of January 2024, the APR has sufficient (>200) first-trimester exposures for the drugs bictegravir, cobicistat, darunavir, elvitegravir, raltegravir and rilpivirine to detect at least a 2-fold increase in overall birth defects, and no such increase has been found. For abacavir, atazanavir, dolutegravir, efavirenz, emtricitabine, lamivudine, lopinavir, nevirapine, ritonavir, tenofovir AF, tenofovir DX and zidovudine, sufficient numbers of first-trimester exposures have been monitored to detect at least a 1.5-fold increase in risk of overall birth defects and a 2-fold increase in risk of birth defects in the more common classes (cardiovascular and genitourinary systems). No such increases have been detected to date. It is important to note that the APR is not sufficiently powered to detect rare birth defects and as such women/people of reproductive potential should be counselled that although data are available to rule out a 2- or 1.5-fold increase in overall birth defects, these data cannot rule out an increase in rare birth defects such as NTDs.

Evaluating the potential association between a drug and birth defects that can be uncommon to rare requires large numbers of exposures to adequately determine the existence and magnitude of risk. For example, a minimum of 2000 preconception exposures are necessary to rule out a 3-fold increase in NTD risk, given a 0.1% background NTD prevalence [7]. In the Tsepamo study, birth outcomes surveillance was conducted throughout Botswana, covering 70% of all births [8]. This is the largest study of birth defects in babies born to women receiving ART to date, and the only study powered to detect rare abnormalities such as NTDs. Among women on dolutegravir at conception, the prevalence of NTDs was 0.11% (10/9460; 95% CI 0.06–0.19%) compared with 0.11% (25/23,664; 95% CI 0.07–0.16%) among women on any non-dolutegravir ART from conception, 11/14,432 (0.08%; 95% CI 0.04–0.14%) on efavirenz from conception, 4/6551 (0.06%; 95% CI 0.02–0.16%) on dolutegravir started in pregnancy and 108/170,723 (0.07%; 95% CI 0.0–0.08%) among women without HIV. NTD prevalence did not differ between women on dolutegravir and those on any non-dolutegravir ART from conception (0.00% difference, 95% CI –0.07% to 0.10%).

Similarly observational data from Botswana from areas not covered by the Tsepamo study did not show a statistical difference in NTD incidence in women on dolutegravir at conception versus those not on dolutegravir (i.e. on efavirenz or without HIV at conception) [9]. A cross-sectional observational study carried out at the five highest-volume hospitals in all four areas of Eswatini, including 24,812 births, showed that NTD prevalence was 0.08% (95% CI 0.03–0.21%) for women on dolutegravir at conception, 0.08% (95% CI 0.04–0.13%) for women without HIV and 0.15% (95% CI 0.04–0.55%) for women on efavirenz at conception [10].

In a retrospective national cohort study conducted in Brazil, outcomes in 382 women exposed to dolutegravir within 8 weeks of conception and in 1045 women exposed to efavirenz were compared; no NTDs were reported in either group. After study closure, two cases of NTDs among women with periconception exposure to dolutegravir were reported; the authors updated their estimated incidence of NTDs in dolutegravir-exposed women to 0.18% (95% CI 0.05–0.67%) compared with a rate of 0.06% in women without HIV [11].

European birth outcome surveillance data from the DOLOMITE-EPICC study include 326 periconception dolutegravir exposures, resulting in an estimated birth defect rate of 4.6% (95% CI 2.6–7.5) compared to 2.9% for second- and third-trimester exposures (4/140; 95% CI 0.8–7.2); overlapping confidence intervals suggest this difference was not statistically significant [12].

In addition, national surveillance registry data from France reported 703, 57 and 48 exposures to raltegravir, dolutegravir and elvitegravir, respectively, with no NTDs and rates of congenital abnormalities similar to those in the general population [13].

The HPTN 084 open-label extension study evaluated maternal, pregnancy and infant outcomes in women who continued to receive long-acting cabotegravir as PrEP during pregnancy. In 351 pregnancies (334 participants), the incidence of pregnancy-related adverse events per 100 person-years was 43.7 when cabotegravir exposure was during pregnancy (95% CI 30.9–60.0), 52.9 when exposure was before pregnancy (95% CI 24.2–100.5) and 40.0 in those who did not use cabotegravir (95% CI 14.7–87.1). There were no maternal deaths, and there was one major congenital abnormality in the cabotegravir exposure during pregnancy group [14].

ISOSS produces aggregated data tables on antiretroviral exposure and congenital anomalies in the UK on an annual basis for the APR. Individual prospective reports should also be sent to the APR antenatally with postnatal follow-up (forms are available at www.apregistry.com).

8.1.3 Individualised and person-centred care

The choice of therapy should always be discussed in full with every person and be individualised, taking into account the individual's concerns and preferences as well as the evidence base, to foster shared decision-making [15].

8.1.4 Anchor drugs with limited data

If women/people conceive on a regimen including agents with limited pharmacokinetic data such as bictegravir or doravirine, they should be counselled regarding the limited available evidence for its use in pregnancy compared to the regimens recommended in these guidelines and offered a third agent with more robust pharmacokinetic and safety data (see Section 8.2.2). Where uncertainty concerning these risks is acceptable and strong preference is given to continuation of the current non-recommended regimen (see recommendations in Sections 8.2 and 8.3 below), an individual should be supported with additional viral load monitoring every 1 to 2 months with or without TDM, as appropriate. At the time of writing, there remains insufficient evidence to support the continuation of injectable ART or regimens containing the drugs listed in Table 8.2.

8.1.5 Viral load monitoring after switching

Switches in ART should be closely monitored with viral load measurement at 2 weeks post-switch and, if the viral load remains undetectable, every 2 months thereafter (see Section 8.5).

8.2 ART dosing in pregnancy

Recommendations

- We do not recommend routine dose alterations for antiretrovirals during pregnancy if used at standard adult licensed doses with the following exceptions (Grade 1C):
  - Darunavir/ritonavir should be administered as 600 mg/100 mg twice daily if initiated in pregnancy; once-daily dosing can be continued if the woman/person conceived on darunavir/ritonavir and remains virologically suppressed;
  - Raltegravir should be administered as 400 mg twice daily if initiated or continued in pregnancy.
- We suggest that switching to standard dosing throughout pregnancy or regular TDM should be considered if a woman/person continues an off-licence non-standard dosing regimen (Grade 2C).

Rationale

Physiological changes that occur even during the first trimester of pregnancy may affect the kinetics of drug absorption, distribution, metabolism and elimination, thereby affecting drug dosing [16]. In pregnancy, gastrointestinal pH is increased, transit time becomes prolonged, body water and fat increase, and there are accompanying increases in cardiac output, ventilation and hepatic and renal blood flow. Plasma protein concentrations decrease, notably albumin and α1 acid glycoprotein; renal sodium reabsorption increases and changes occur in the metabolic enzyme pathways in the liver, including changes in cytochrome P450. Therefore it is important that pharmacokinetic studies in

pregnant women/people are carried out for all available antiretroviral drugs, and that clinicians consider the available data when a woman/person becomes pregnant.

8.2.1 NRTI backbone

The pharmacokinetic properties of most NRTIs (zidovudine [17], lamivudine [18] and abacavir [19]) are not significantly altered by pregnancy and dose adjustment is not required.

Data on emtricitabine show that while third-trimester concentrations are lower than postpartum the absolute concentrations achieved during pregnancy are adequate and dose adjustment is not required [20,21].

Tenofovir DX

A systematic review showed reduced concentrations of tenofovir DX in the third trimester by approximately 15–25% with increased clearance in the second and third trimesters; however, trough levels were adequate and there was no increase in treatment failure during pregnancy with tenofovir DX-containing regimens [22]. Two studies demonstrated that one double dose of tenofovir DX administered shortly before delivery resulted in plasma concentrations similar to those observed in non-pregnant adults following a standard dose of 245 mg and adequate levels in the neonate [20,21]. Therefore, we do not recommend a dose increase of tenofovir DX during pregnancy but do recommend a double dose of tenofovir DX in the case of incomplete virological response or late presentation at infant delivery (see Sections 8.5 and 8.7.2).

Tenofovir AF

The PANNA study demonstrated that tenofovir AF concentrations were reduced in pregnancy by ~50%, with the active end product tenofovir reduced by ~33% [23]. One of the 20 women in the PANNA study had an area under the curve (AUC) below the therapeutic target for tenofovir AF. Recent data on intracellular concentrations of tenofovir AF from the PrEP-PP PK study conducted in South Africa showed that tenofovir AF levels were approximately 40% lower in the third trimester than postpartum [24].

Conversely, the IMPAACT P1026s study group reported that tenofovir AF concentrations did not significantly differ in the second and third trimesters versus postpartum, however participants received tenofovir AF 25 mg with a cobicistat-boosted PI. In this study, TDM levels of tenofovir AF were comparable to historical data in non-pregnant adults [22].

8.2.2 INSTIs

Bictegravir

There is limited pharmacokinetic data to recommend bictegravir in pregnancy and insufficient data to recommend cabotegravir-containing regimens in pregnancy. Pencolé *et al*. analysed placental transfer of bictegravir an *ex vivo* human cotyledon perfusion model [25]. The placental transfer was found to be low, with median maternal-to-fetal ratios of 7% for bictegravir.

The NCT03960645 open-label study of 33 pregnant women receiving bictegravir with emtricitabine and tenofovir DX demonstrated lower plasma concentrations of bictegravir during the second and third trimesters pf pregnancy compared to postpartum, however all participants maintained virological suppression [26]. The IMPAACT 2026 open-label, Phase 4, prospective pharmacokinetic study which included data for 17 pregnant women receiving bictegravir with emtricitabine and tenofovir DX, five for whom a postpartum sample was available, demonstrated 60% lower plasma concentrations of

bictegravir (AUC over 24 hours [AUCtau]/μg*hour/mL) during the third trimester. Nine of 13 women (69%) had an AUCtau below the prespecified target (<10th percentile). Viral suppression was achieved in all but one participant despite this participant having an AUCtau >10th percentile and all participants had a bictegravir plasma concentration 24 hours post dose above the 95% effective concentration (EC_{95}) [27].

Long-acting cabotegravir

Pencolé *et al*. analysed placental transfer of cabotegravir in an *ex vivo* human cotyledon perfusion model [25]. The placental transfer was found to be low, with median maternal-to-fetal ratios of 10% for cabotegravir.

The HPTN 084 trial evaluating long-acting cabotegravir for PrEP in HIV-negative individuals enrolled 55 pregnant participants in an open label extension nested substudy; initial analyses suggest that cabotegravir concentrations decrease throughout pregnancy [28]. Among the cohort of 50 participants included in the analysis, cabotegravir trough concentrations declined from the first through the third trimester. Median trough concentrations were 2.5 μg/mL in the first, 1.7 in the second, and 1.6 μg/mL in the third trimester. The lower 5th percentile trough concentrations were 1.44, 1.04 and 0.81 μg/mL, respectively. However, when evaluating average cabotegravir trough concentrations within the context of the protocol-specified target concentration of 0.664 μg/mL, 100% of participants in the first and second trimesters and 98% of participants in the third trimester had average trough concentrations above this level.

Long-acting cabotegravir plus long-acting rilpivirine

Crauwles *et al*. assessed the pharmacokinetic tail of rilpivirine following discontinuation in pregnancy and found that it was within the expected range for non-pregnant women [29]. Patel *et al*. described outcomes for 10 live births in women exposed to cabotegravir/rilpivirine (long-acting/oral) in Phase 2/3 trials and compassionate access programmes. Most women (9/10) were switched to an oral regimen in pregnancy; one woman continued 4-weekly long-acting cabotegravir/rilpivirine in pregnancy with low-level viraemia until delivery. There were no perinatal transmissions in this group. Plasma cabotegravir and rilpivirine concentrations during pregnancy were within the range of concentrations observed in non-pregnant women within the treatment programme who discontinued long-acting therapy [30]. *In utero* exposure to long-acting cabotegravir and rilpivirine is likely to persist throughout pregnancy in women/people who conceive on these agents given their very long half-lives.

The findings of a non-clinical pharmacokinetic modelling study suggested that monthly long-acting cabotegravir could maintain antiviral efficacy throughout pregnancy, but that bimonthly administration may require careful clinical evaluation, and long-acting rilpivirine may not adequately maintain antiviral efficacy in pregnancy [31]. Further human data are required.

A retrospective and heterogenous case series of 23 women in the USA who either continued or initiated long-acting cabotegravir/rilpivirine in pregnancy showed high levels of viral suppression at delivery (81% <20 copies/mL and 95% <200 copies/mL) [32].

There are no data on optimal dosing strategies for long-acting cabotegravir/rilpivirine in pregnancy; we recommend 4-weekly dosing in the absence of data, with consideration of TDM.

Dolutegravir

The IMPAACT P1026s study demonstrated that dolutegravir exposure was lower in pregnancy compared to postpartum in the same women on once-daily dosing; however, the median AUC during pregnancy was similar to values seen in non-pregnant adults and trough concentrations in pregnancy were much higher than the dolutegravir 90% effective concentration (EC_{90}) [33]. The DolPHIN-1 trial also showed reduced dolutegravir exposure in the third trimester compared with levels previously reported in non-pregnant adults, however in this study nearly all dolutegravir concentrations were above the protein-adjusted 90% inhibitory concentration (IC_{90}) [34]. Dolutegravir is highly bound to plasma proteins; the PANNA group found comparable free dolutegravir concentrations in pregnancy compared with postpartum, related to lower serum albumin levels in the third trimester [35], suggesting that the impact of the moderate reduction in total (free and bound) dolutegravir is minimal.

Both IMPAACT P1026s and DOlPHIN-1 demonstrated that dolutegravir readily crosses the placenta and that infant elimination is prolonged, with a half-life of more than 2-fold that of historical values in adult control subjects (see ART placental transfer table in Appendix 3).

Elvitegravir/cobicistat

IMPAACT P1026s showed reduced concentrations and higher clearance of elvitegravir/cobicistat during pregnancy compared to postpartum, with only 76% viral suppression at delivery [36]. Similarly, the PANNA study found substantially decreased elvitegravir exposure (77%) in the third trimester of pregnancy [37]. In view of this, elvitegravir/cobicistat use during pregnancy is not recommended.

Raltegravir

Adequate trough concentrations of raltegravir were demonstrated in studies of pregnant women taking raltegravir at a dose of 400 mg twice daily and no significant difference in concentration was found compared to postpartum [38,39]. There are insufficient pharmacokinetic data to recommend raltegravir at a dose of 1200 mg once daily during pregnancy. Pregnant women/people who conceive on raltegravir 1200 mg once daily should be switched to raltegravir 400 mg twice daily.

Raltegravir is highly bound to human serum albumin (approximately 84%); in the RalFe trial it was found that unbound trough concentrations of raltegravir did not significantly decrease during the third trimester [40].

8.2.3 Non-nucleoside reverse transcriptase inhibitors (NNRTIs)

Efavirenz

In a study of 25 pregnant women it was found that efavirenz 600 mg once daily resulted in third-trimester plasma concentrations that were similar to 6- to 12-week postpartum concentrations. Cord blood-to-maternal blood ratio was 0.49 resulting in transplacental concentrations in the therapeutic range [41] (see ART placental transfer table in Appendix 3). Efavirenz may be used in pregnancy without dose modification when used at licensed doses.

Etravirine

A study of the pharmacokinetic properties of etravirine 200 mg twice daily in 15 women found an increase in etravirine exposure during pregnancy but still within the range observed in previous studies of non-pregnant individuals with HIV treated with this dose [42]. Fourteen of 15 women had an undetectable viral load during pregnancy and no vertical transmissions were reported. A second study

from the PANNA group has shown similar results [43]. Etravirine may be used in pregnancy without dose modification when used at licensed doses.

Doravirine

The pharmacokinetic profile of doravirine has not been described in pregnancy, therefore we are unable to recommend the use of doravirine in pregnancy.

Nevirapine

Nevirapine has been extensively investigated in pregnancy and plasma concentrations are similar to those in non-pregnant adults [44,45]. No dose adjustment is required when using licensed doses.

Rilpivirine (oral)

Pharmacokinetic studies of oral rilpivirine have shown reduced exposure in the third trimester by 29–50% [46-48]; however, all women had a viral load <50 copies/mL at delivery and there were no vertical transmissions. Based on this, it is recommended that pregnant women/people can continue rilpivirine-containing regimens (with no dose adjustment) if they are able to take their medication with food to optimise absorption.

Rilpivirine (long-acting injectable)

For information on long-acting injectable rilpivirine, see above: long-acting cabotegravir plus long-acting rilpivirine.

8.2.4 PIs

PIs are highly protein bound and placental transfer in humans appears to be limited. During the third trimester of pregnancy, small reductions in protein binding can significantly increase free drug levels.

Atazanavir/ritonavir

The PANNA study demonstrated a 34% reduction in third-trimester AUC and last measurable plasma concentrations compared with postpartum. However, all drug concentrations measured, including with co-administered tenofovir DX, were above the recommended minimum plasma concentration for wild-type virus [49]. More recent data from an observational study, which analysed intracellular concentrations of ritonavir-boosted atazanavir during pregnancy, demonstrated that intracellular concentrations of the standard dose remained stable during the third trimester [50]. Furthermore, a case note review of 122 women in London receiving atazanavir/ritonavir did not show virological failure during pregnancy despite 83% of women receiving the standard dose of 300 mg/100 mg [51].

Darunavir/ritonavir

Results from five studies of darunavir/ritonavir showed reductions in total darunavir concentrations of between 20% and 50% during the third trimester of pregnancy [52]; the clinical significance of this is uncertain. Unbound concentrations of darunavir were measured in subsets of patients in two of the five pharmacokinetic studies. One of these studies found unbound concentrations to be 11% higher during pregnancy with 600 mg/100 mg twice daily and 13–38% lower with 800 mg/100 mg once daily. Darunavir/ritonavir-based ART dosed at 800 mg/100 mg once daily has not been associated with reduced virological suppression in pregnancy [53]. Higher therapeutic levels were seen at 600 mg/100 mg twice-daily dosing [54].

Ratios of darunavir concentration in cord blood compared to maternal plasma suggest that darunavir does not have high transplacental penetration (see ART placental transfer table in Appendix 3).

If a woman/person conceives on darunavir/ritonavir-based ART and has a fully suppressed viral load on a once-daily regimen, this can be continued. Twice-daily darunavir/ritonavir should be considered if initiating darunavir in pregnancy or where there is known darunavir resistance, or failure to achieve virological suppression; women/birthing parents should be reviewed postpartum for their suitability for switching back to once-daily dosing.

Cobicistat-boosted PIs

Cobicistat-boosted PIs result in low exposures during the second and third trimesters which may be associated with virological failure. This was demonstrated in a study of six pregnant women, recruited from week 18, which found that cobicistat-boosted darunavir (oral darunavir 800 mg/cobicistat 150 mg once daily) levels were lower in the second (56%) and third trimesters (50%) compared with postpartum [55]. A further study of 29 pregnant women also found that darunavir levels were 53% lower in the second trimester and 56% lower in the third trimester, compared to postpartum [56].

There are no data regarding first-trimester cobicistat-boosted PI drug levels, however absence of data does not equate to safety.

Therefore cobicistat-boosted PIs should not be initiated in pregnancy and women/people receiving this combination as part of ART and who become pregnant should be switched to ritonavir as the pharmacokinetic boosting agent of choice as soon as they become pregnant.

8.2.5 Oral two-drug regimens

There is most evidence for ART regimens in pregnancy containing three active drugs. We recommend including at least one agent that crosses the placenta (see ART placental transfer table in Appendix 3). While pregnancy safety data and pharmacokinetic evidence for individual drugs commonly used as components of dual therapy exist, data for their use in combinations with fewer than three agents are limited. At the time of writing, 32 cases of dolutegravir/lamivudine use in pregnancy have been described [57-59]. One small pilot study in Brazil examined viral suppression and transmission rates in 20 women who commenced dolutegravir/lamivudine in pregnancy with a mean baseline viral load of 9514 copies/mL (range 1049–118,455 copies/mL); mean time to suppression was 40.4 days, all women were suppressed at delivery and there were no perinatal transmissions [57]. A retrospective cohort study from Italy evaluated dolutegravir/lamivudine use in pregnancy; of the 11 individuals included in the study, three were ART naïve. Ten women had a viral load <20 copies/mL at delivery and one individual, naïve to ART, had a viral load of 53 copies/mL [58]. An additional case report of dolutegravir/lamivudine use in pregnancy has been published [59]. There were no cases of vertical transmission and no new safety signals identified in any of the reported cases to date.

If a woman/person conceives on dual ART we advise counselling regarding the limited available data, and an additional third active agent should be recommended. However, in complex cases, or where the woman/person prefers to stay on the two-drug regimen, we recommend MDT discussion on a case-by-case basis. In the UK the rate of transmission with the use of three-drug regimens is very low at 0.25%, and in the majority of the few cases where transmission occurs, the woman/person is either undiagnosed or not taking ART consistently throughout pregnancy [60].

8.2.6 Long-acting injectable therapy

There are limited pharmacokinetic data (see Section 8.2.2 and 8.2.3) to support the use of long-acting cabotegravir plus rilpivirine in pregnancy and we recommend that this limited evidence base is discussed with women who conceive on this regimen. Consider switching women to a recommended oral three-drug regimen in Table 8.3. However, the writing group recognises that a pregnant woman/person receiving long-acting cabotegravir plus rilpivirine may have had difficulty with adherence to oral agents and the benefits of staying on long-acting cabotegravir plus rilpivirine may outweigh the risks in some cases. This should be a decision made with the pregnant woman/person and the antenatal HIV MDT and enhanced viral load monitoring should be implemented. There are no data to inform the optimal dosing regimen of long-acting cabotegravir plus rilpivirine in pregnancy; we recommend 4-weekly dosing in the absence of data, with consideration of TDM.

8.2.7 Other agents

The pharmacokinetic profiles of enfuvirtide, maraviroc, fostemsavir, ibalizumab and lenacapavir in pregnancy have not been described. It is noteworthy that enfuvirtide does not cross the placenta [61].

8.3 What ART to start in pregnancy

Although most pregnant women/people are already on ART at conception, there remains a significant minority who are either newly diagnosed in pregnancy or not on consistent treatment despite a diagnosis. In 2022, pregnant women had been newly diagnosed in 11% of pregnancies reported to ISOSS [60]. Historically, with the paucity of safety and pharmacokinetic data, the use of antiretrovirals in pregnancy was limited to the few antiretroviral agents for which there were post-licensing observational data. There is now increasing recognition that the availability of data in pregnancy and indeed the design of randomised controlled trials to explicitly examine outcomes in pregnancy is a global priority, and high-quality prospective outcome data for newer antiretrovirals are now available. The recommendations below refer to women/people with wild-type virus at baseline; when constructing regimens for those with known resistance, regimens should be designed with MDT input (see Section 8.7.3).

8.3.1 Regimens for first-line ART in pregnancy

Recommendations

Recommended and alternative first-line ART choices in pregnancy are shown in Table 8.3.

Table 8.3 Choice of first-line ART when starting treatment in pregnancy

Regimen	Details	Grade
Recommended as initial treatment for most pregnant women/people		
Dolutegravir plus emtricitabine/tenofovir DX	First choice in the absence of renal or bone concerns	1A
Dolutegravir plus emtricitabine/tenofovir AF	Association with weight gain should be discussed Consider baseline weight if in overweight range	1A
Dolutegravir/lamivudine/abacavir	Ensure HLA B*5701 negative Estimated 10-year risk of cardiovascular disease should be <10% Ensure no active HBV infection Ensure immune to HBV Association with weight gain should be discussed	1C

	Consider baseline weight if in overweight range	
Alternative regimens that may be preferred in certain clinical situations		
Rilpivirine plus emtricitabine/tenofovir DX or emtricitabine/tenofovir AF or lamivudine/abacavir	Not recommended if viral load >100,000 copies/mL or CD4 count <200 cells/mm^3 Take with food	1C
Raltegravir 400 mg twice daily plus emtricitabine/tenofovir DX or emtricitabine/tenofovir AF or lamivudine/abacavir	May be considered if evidence of liver dysfunction prevents use of dolutegravir	1B
Darunavir 600 mg plus ritonavir 100 mg twice daily plus emtricitabine/tenofovir DX or emtricitabine/tenofovir AF or lamivudine/abacavir	Twice-daily dosing if initiating in pregnancy (or known resistance)	1C
Efavirenz plus emtricitabine/tenofovir DX or emtricitabine/tenofovir AF or lamivudine/abacavir	Non-preferred regimen due to side effect profile; may be used to manage drug interactions with tuberculosis treatment and can be switched postpartum	1A

Rationale

The preferred first-line regimen is dolutegravir with emtricitabine/tenofovir DX. Emtricitabine/tenofovir AF may also be the chosen NRTI backbone in the case of poor renal function or low or immature bone mass and abacavir/lamivudine is also a reasonable option taking into account the caveats listed in Table 8.3. The evidence for the preferred agents is robust and is summarised below. Alternative agents for which there are sufficient safety data in pregnancy and accompanying considerations are shown in Table 8.3. For pharmacokinetic data in pregnancy for these drugs, see Section 8.2.

8.3.2 Evidence for viral suppression in pregnancy

Dolutegravir versus efavirenz and tenofovir AF versus tenofovir DX

The IMPAACT 2010/VESTED open-label randomised controlled trial was a multicentre study of the safety and efficacy of three ART regimens started in 643 women: dolutegravir/emtricitabine/tenofovir AF, dolutegravir/emtricitabine/tenofovir DX and efavirenz/emtricitabine/tenofovir DX [62]. The safety outcomes included the occurrence of a composite, adverse pregnancy outcome and the occurrence of grade 3 or higher adverse events in participants and their infants. The primary efficacy outcome in this study was the proportion of participants who had viral suppression at or within 14 days of delivery (<200 copies/mL) and the findings demonstrated that dolutegravir-containing regimens were superior (see Section 8.4.2). Using an HIV RNA concentration of <50 copies/mL, 387/407 (95.1%) in the combined dolutegravir group had viral suppression, compared to 160/201 (79.6%) in the efavirenz group (estimated difference 15.5%, 95% CI 9.5–21.4; *P*<0.0001). There were two transmissions, both in the dolutegravir arms, one with a detectable viral load at delivery and the other with a viral load of <50 copies/mL; both transmissions were determined to have occurred *in utero*. Virological efficacy was similar in the tenofovir AF and tenofovir DX arms, whereas the proportion of participants with a composite adverse pregnancy outcome differed between arms (see Appendix 3).

The DolPHIN-1 and DolPHIN-2 studies (see Section 8.4.2 below) compared dolutegravir with efavirenz, plus emtricitabine/tenofovir DX, in late-presenting women commencing ART in the third trimester, and showed that both regimens were effective at preventing vertical transmission but that virological suppression was faster with dolutegravir [34,63]. The 100% efficacy of efavirenz in preventing vertical

transmission in DolPHIN-2 when initiated in the third trimester, despite only 43% of exposed participants achieving plasma virological suppression, demonstrates that preloading the unborn infant across the placenta with pre-exposure ART is an important HIV-prevention strategy in antenatal care.

A meta-analysis by Asif *et al*. of the DolPHIN-1, DolPHIN-2, IMPACT 2010, ADVANCE and NAMSAL trials demonstrated that dolutegravir is superior to efavirenz at achieving viral suppression (OR 2.9, 95% CI 2.54–5.46) in pregnant women, with no significant difference in preventing vertical transmission [64].

Raltegravir versus efavirenz

In the NICHD P1081 trial comparing raltegravir (400 mg twice daily) to efavirenz started in pregnant women (20 to <37 weeks of pregnancy), 144/153 (94%) in the raltegravir group and 129/154 (84%) in the efavirenz group had a viral load <200 copies/mL at or near delivery (absolute difference 10%, 95% CI 3–18; *P*=0.001) [65]. The difference was driven by individuals who started later in pregnancy. The vertical transmission rate was 0.5% for raltegravir (1/190) and 3.3% for efavirenz (6/184); all transmissions were deemed to have occurred *in utero*.

Darunavir/ritonavir

There have been no randomised controlled trials comparing darunavir/ritonavir-based ART with other regimens in pregnancy. One small randomised controlled trial compared raltegravir with lopinavir/ritonavir in individuals presenting late [66]. Meta-analyses of randomised controlled trials and observational studies reporting adverse pregnancy outcomes with different ART regimens have shown no differences between dolutegravir-based regimens and regimens containing darunavir or atazanavir with ritonavir [67].

Rilpivirine (oral)

Rilpivirine may be considered where other third agents are not suitable. There have been no randomised controlled trials comparing rilpivirine-based ART with other agents in pregnancy. It is important to ensure that resistance testing has been performed before commencing rilpivirine in pregnancy and that it is taken with food for the fixed-dose combination or with a meal for the single-agent oral formulation [68].

8.3.3 Regimens that are not recommended because of limited data

There are insufficient pharmacokinetic data on bictegravir and two-drug regimens therefore they are not recommended for initiation in pregnancy.

8.3.4 Regimens no longer recommended

Triple NRTI therapy, zidovudine monotherapy and atazanavir boosted with ritonavir are no longer recommended in pregnancy due to their toxicity profiles and/or efficacy and it is recommended that combination ART does not stop postpartum.

8.3.5 Virological controllers

The writing group acknowledges that the evidence base for the management of viral controllers (also known as elite controllers, and defined as people with a confirmed HIV diagnosis who maintain viral control in the absence of ART with a normal CD4 count) in pregnancy is limited [69,70]. We suggest that viral controllers should be managed as per the BHIVA treatment guidelines [1] and ART should be commenced during pregnancy (if not already on ART) given that pregnancy is a state of relative immune suppression, the uncertainty of viral rebound [71] and the potential risk of transmission [1]. For specialist advice on the management of pregnancy in virological controllers, referral to a national NHS

clinical service can be made (Indeterminate Retrovirus Infection Service run at Imperial College NHS Trust, London: imperial.idris@nhs.net).

8.4 When to start ART in pregnancy

Recommendations

- We recommend that all pregnant women/people should start ART as soon as possible during pregnancy (Grade 1B).
- We recommend that ART should be started in the first trimester, especially if the viral load is >100,000 copies/mL and/or CD4 count is <200 cells/mm^3 (Grade 1C).
- If the pregnancy is complicated by significant nausea and vomiting that impacts the ability to adhere to treatment, the aim should be to establish consistent ART by 18–20 weeks' gestation (Grade 1C).
- We recommend that all pregnant women/people should have commenced ART by week 24 of pregnancy at the very latest (Grade 1C).

Auditable outcome

- Proportion of women/people living with HIV taking ART by week 20 of pregnancy.

Rationale

The current BHIVA treatment guidelines recommend that all people are offered the opportunity to start within 2–4 weeks of diagnosis, and this includes pregnant women/people with HIV. All pregnant women/people living with HIV should also be counselled about the importance of continuing ART lifelong. In addition, a longer duration of ART in pregnancy is associated with viral suppression, and viral suppression at delivery is an important factor in minimising the risk of vertical transmission, alongside preloading of the fetus with ART via placental transfer.

Starting ART in early pregnancy can be complicated by nausea and vomiting of pregnancy, and so a balance sometimes needs to be struck between starting as soon as possible and managing the ability of women/people to take oral tablets consistently, their symptoms and the risk of developing resistance. Here we present the available evidence and recommendations for when to start ART in pregnancy.

Randomised controlled trial data on triple ART initiated in the second and third trimesters are reassuring. In particular, with INSTI-based ART, the majority achieve virological suppression within 4 weeks with no intrapartum transmissions (see evidence summaries below). However, in high-income countries it is possible and desirable to commence ART earlier for maximal benefit to maternal health and increased time of virological control prior to delivery to reduce intrapartum transmission and to potentially reduce both *in utero* and sexual transmission risk. The writing group recommends that ART should be commenced as soon as possible in all women/people. Early ART initiation is especially important with baseline viral load >100,000 copies/mL and/or where the woman/person is at risk of or has presented with an opportunistic infection [72]. ART can be commenced prior to receiving the results of resistance testing and modified, if necessary, based on the results.

Deferring treatment to the start of the second trimester may be necessary if the woman/person is experiencing nausea and/or vomiting of pregnancy (see Section 8.7.4). Most people can expect to achieve viral suppression within 4 weeks with INSTIs, even with a high viral load. The writing group recommends that all women/people should have commenced ART by week 18–20 of pregnancy, before the threshold for fetal viability, to maximise the time to achieve viral suppression by 36 weeks. In women/people with a history of PTB, it is prudent to start ART as soon as possible. All pregnant women/people should have commenced ART by week 24 of pregnancy.

8.4.1 Factors to consider in determining when to start ART

When determining the optimal time to start ART, the following must be considered:

- Maternal/parental health;
- Risk of vertical transmission to the infant as determined by maternal/parental viral load and the time on ART prior to delivery;
- Human safety data with first-trimester exposure to the proposed ART regimen (see Sections 5 and 8.1.2);
- Viral decay with the chosen ART regimen;
- Individual readiness to start;
- Risk of transmission to a partner.

Major determinants of a woman/person suppressing to a viral load <50 copies/mL by the time of delivery are the baseline untreated viral load, the time available to achieve this target and the class of third drug in the ART regimen.

8.4.2. Superior virological responses to INSTIs versus efavirenz-based regimens observed in randomised controlled studies

Rapid virological responses with INSTIs have been confirmed in randomised controlled trials in low-, middle- and high-income settings. In both the DOLPHIN-1 and DolPHIN-2 studies, viral suppression at the 14-day visit was significantly faster with dolutegravir compared with efavirenz [34,63,73].

In the IMPAACT 2010/VESTED randomised controlled study, efavirenz- or dolutegravir-based regimens were started at 14–28 weeks and time to viral load suppression was found to be significantly shorter with dolutegravir but there was no overall difference in rates of intrapartum transmission [62].

The NICHD P1081 randomised controlled study demonstrated shorter time to suppression with raltegravir compared with efavirenz [65]. For meta-analyses of adverse pregnancy outcomes and timing of ART, see Appendix 3 [74].

8.4.3 UK data on virological response to ART from the INSTI era

A UK retrospective cohort study including 221 cases from many of the same centres demonstrated baseline plasma HIV viral load to be the main factor associated with time to suppression, with INSTI use associated with faster first-phase viral half-life decay [75]. The time to reach viral suppression was 27.5 days with INSTIs (raltegravir *n*=11, dolutegravir *n*=6), compared to 51.5 days with NNRTIs (*n*=32) and PIs (n=132), despite cases with INSTI exposure having higher baseline viral loads. Viral suppression at delivery was achieved in 94% of participants receiving INSTIs, 75% on NNRTIs and 86% on PIs. The main factors associated with viral suppression at 36 weeks were lower plasma HIV viral load at 14 days post-initiation and earlier ART initiation. The authors of the study suggested that a 99% reduction (2 log) in viral load should be expected by day 14, regardless of regimen, and absence of this should be a cause

for concern suggesting possible non-adherence or failure; they also noted that all regimens performed well [75].

8.5 Laboratory monitoring of ART in pregnancy

Recommendations

New diagnosis in pregnancy:

- For pregnant women/people who are newly diagnosed with HIV, we recommend investigations as per the BHIVA routine investigation and monitoring guidelines [76], as well as those routinely performed in the general antenatal clinic (Grade 1D).

Stable virological suppression in pregnancy:

- In women/people who conceive and are virologically suppressed on ART in pregnancy, we recommend that an HIV viral load test should be performed every 2 months, at 36 weeks and at delivery (Grade 1C).
- We recommend that CD4 cell count should be measured at baseline in the first trimester for all women/people who conceive and are virologically suppressed on ART in pregnancy. Repeat tests are only indicated if the baseline CD4 count is <350 cells/mm^3 as per BHIVA routine monitoring guidelines [76] (Grade 1D).
- We suggest more frequent viral load monitoring and TDM can be considered for non-standard regimens (GPP).

Starting or switching ART in pregnancy:

- For women/people who commence or switch ART in pregnancy, we recommend that HIV viral load tests and toxicity monitoring should be performed at 2 weeks after commencing new ART, then monthly until undetectable, and then at least once every 2 months, at 36 weeks and at delivery (Grade 1C).
- We recommend that HIV resistance testing (including integrase resistance) should be undertaken prior to initiation of treatment, including in treatment-experienced women/people (Grade 1D).
- If starting ART with a high-genetic barrier to resistance (dolutegravir-based or darunavir/ritonavir-based regimens), it is reasonable to commence before genotypic resistance test results are available (Grade 1B).
- We suggest that more frequent viral load monitoring and TDM can be considered for non-standard regimens (GPP).
- We recommend liver function tests (LFTs) at 2–4 weeks after starting or switching ART, and at the time of each routine antenatal visit (Grade 1C).

Incomplete virological response in pregnancy:

- We recommend that HIV resistance testing (including integrase resistance) should be attempted for any pregnant woman/person with an incomplete virological response (less than a 1-log drop at 4 weeks post-initiation) or failure to suppress to <200 copies/mL (Grade 1C).

- TDM is not routinely recommended for pregnant women/people with an incomplete virological response but can be considered on an individual basis (Grade 1C).

Auditable outcomes

- The proportion of women/people living with HIV who have a viral load measurement within 2 weeks of starting or switching ART.
- The proportion of women/people living with HIV for whom starting or switching ART is required prior to resistance test results being available.
- The proportion of women/people living with HIV for whom CD4 count has been determined within the antenatal period.
- The proportion of women/people who have a viral load measurement at 36 weeks.

Rationale

Performing a viral load test at 2 weeks after commencing new ART allows for a more rapid assessment of virological response and adherence and less than a 2-log drop is predictive of failure to achieve virological suppression at 36 weeks. A viral load test at 2 weeks also enables timely assessment of virological suppression in those who present late (after 28 weeks). For those who are stable on a recommended regimen, 2-monthly viral load measurements are recommended. More frequent viral load monitoring is recommended in individuals on non-recommended regimens including those with limited pharmacokinetic data.

Hepatotoxicity may occur as a result of the initiation of ART and/or the development of obstetric complications such as haemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome, pre-eclampsia, obstetric cholestasis and acute fatty liver. We recommend that LFTs should be performed in women/people commencing or switching ART in pregnancy at 2–4 weeks as per routine initiation of ART in adults [76], and then at the time of each routine blood test. Close liaison with the obstetric team is recommended in the case of any abnormal LFTs.

Due to time constraints for ensuring viral suppression in pregnancy, TDM (which has a long turn-around time) is not routinely recommended but can be considered on an individual basis in the third trimester in pregnant women/people where there are concerns about pharmacokinetics, drug absorption, interactions and/or failure to suppress.

8.6 HIV-2

Recommendations

- We recommend case discussion with experts with experience of managing HIV-2 for all women/people (Grade 1D).
- We recommend that pregnant women/people with HIV-2 are treated with tenofovir DX plus emtricitabine AND either twice-daily dolutegravir 50 mg or twice-daily darunavir/ritonavir 600 mg/100 mg (Grade 1C).

- We recommend that tenofovir AF plus emtricitabine can be used as an alternative backbone; abacavir plus lamivudine can be used if avoidance of tenofovir DX or tenofovir AF is necessary, subject to the caveats listed in Table 8.3 (Grade 1C).
- We recommend raltegravir 400 mg twice daily as an alternative third agent if avoidance of both dolutegravir and darunavir/ritonavir is necessary (Grade 2C).

Rationale

Pregnant women/people with HIV-2 should be treated according to the principles in the BHIVA 2021 guidelines for the management of HIV-2 for non-pregnant adults [77], while also considering the pharmacokinetic and safety data in pregnancy. NNRTIs are not effective anchor agents when treating HIV-2.

8.6.1 Risk of vertical transmission

Vertical transmission of HIV-2 is considerably less common than of HIV-1, varying between 0% and 4% in the absence of any intervention to reduce transmission [78-80]. It is likely that this can be explained by the lower viral loads seen in HIV-2 infection [80]; however, vertical transmission has been reported. Dual infection with HIV-1 and HIV-2 can also occur and it is important to test for this.

There is no systematic evidence to guide the choice of treatment of HIV-2 in pregnancy or for PEP for the infant. Case discussion with experts with experience of managing HIV-2 is recommended for all women. Although the evidence base for the treatment of HIV-2 in pregnancy has not evolved since the last guidelines update, the evidence has evolved for the safety, efficacy and pharmacokinetics of dolutegravir in pregnancy, as discussed above.

8.6.2 Commencing ART for HIV-2 in pregnancy

The limited evidence for the treatment of HIV-2 in non-pregnant adults is summarised in the BHIVA guidelines for the treatment of HIV-2 and so this evidence will not be given in detail here, except to note that NNRTIs are not effective anchor agents for treating HIV-2. The guidelines state: 'No data exist on the optimal dose of dolutegravir in the treatment of HIV-2. However, given the potential for resistance development and limited treatment options, we consider that 50 mg twice daily should be used. If an individual is consistently aviraemic prior to starting treatment, use of the 50 mg once-daily dose can be considered. There are no head-to-head comparisons of darunavir/r with dolutegravir to help decide whether one should be preferred over the other. However, clinicians may wish to take into account the likelihood of better tolerability of dolutegravir as well as the reduced potential for drug–drug interactions' [77].

Given the safety and efficacy data for dolutegravir in treating HIV-1 in pregnancy, the writing group recommends that women/people with HIV-2 who are not on ART at conception are started on a three-drug regimen with two NRTIs plus an anchor agent of twice-daily dolutegravir 50 mg or twice-daily ritonavir-boosted darunavir 600 mg/100 mg, even if the HIV-2 viral load is below the limit of detection prior to the start of ART, due to the uncertainties of third-trimester pharmacokinetics and the lack of evidence for use in pregnancy. Raltegravir 400 mg twice daily can be used if avoidance of both darunavir and dolutegravir is necessary.

As per the BHIVA HIV-2 guidelines for non-pregnant adults [77], the preferred NRTI backbone is tenofovir DX plus emtricitabine or tenofovir AF plus emtricitabine. Abacavir plus lamivudine can be used if it is necessary to avoid both tenofovir DX and tenofovir AF.

8.6.3 Management of women/people on ART at conception with HIV-2 viral load consistently <50 copies/mL

In the situation in which a pregnant woman/person with HIV-2 is on two NRTIs plus darunavir/ritonavir 800 mg/100 mg once daily or dolutegravir 50 mg once daily and has been consistently undetectable prior to pregnancy, once-daily dosing may be continued through pregnancy with frequent (4-weekly) viral load monitoring. A more cautious approach would be to increase to twice-daily dosing during pregnancy, given the concerns around pharmacokinetics in the third trimester and the lack of evidence in pregnancy.

8.6.4 Management of pregnant women/people on ART with a detectable HIV-2 viral load

Where pregnant women/people with HIV-2 who are on ART experience virological failure (>200 copies/mL), they should be managed with the same considerations as described in Section 8.7.3. As resistance can develop more readily in HIV-2 infection, there should be a low threshold for requesting resistance testing.

Women/people with a detectable viral load on a once-daily regimen of two NRTIs plus dolutegravir or darunavir/ritonavir should be switched to a twice-daily regimen and a resistance test should be requested. There should be frequent viral load monitoring to ensure re-suppression.

For women/people with a detectable HIV-2 viral load on a twice-daily regimen containing either darunavir/ritonavir or dolutegravir, the other anchor agent should be added in so that they are on both darunavir/ritonavir and dolutegravir twice daily.

The results of the resistance test should be discussed with an expert with experience in the management of HIV-2.

8.6.5 Infant PNP

For advice on PNP for infants born to mothers/birthing parents with HIV-2, see Section 11.1.8.

8.6.6 Infant feeding

There are no specific data to inform the management of infant feeding in the case of maternal/parental HIV-2. The writing group suggests following the guidance in Section 12 as for women with HIV-1.

8.7 Managing specific situations in pregnancy

8.7.1 Presenting late in pregnancy (>28 weeks) not on ART

Individuals presenting after 28 weeks' gestation should start ART as soon as possible and prior to receiving the results of resistance testing. We recommend a dolutegravir-based three-drug regimen first line with subsequent modification if resistance is identified. In the presence of known prior resistance, an appropriate regimen should be constructed.

The management of late-presenting pregnancies (>28 weeks) is shown in the flow diagram below (Figure 8.1).

Recommendations

Recommendations for choice of ART for late-presenting pregnant women/people not on ART are summarised in Table 8.4.

Table 8.4 Recommended regimens for pregnant women/people presenting late in pregnancy not on ART

Regimen	Details	Grade
Preferred regimen for pregnant women/people presenting late not on ART		
Dolutegravir/emtricitabine/tenofovir DX	First choice in the absence of renal or bone concerns	1A
Dolutegravir/emtricitabine/tenofovir AF		1A
Dolutegravir/lamivudine/abacavir	Ensure HLA B*5701 negative Ensure no active HBV infection Ensure immune to HBV Ten-year cardiovascular disease risk <10%	1C
Alternative regimens		
Darunavir 600 mg plus ritonavir 100 mg twice daily plus emtricitabine/tenofovir DX or emtricitabine/tenofovir AF or lamivudine/abacavir	Higher concentrations at this dosage (see Table 8.3 and Section 8.2)	1C
Raltegravir 400 mg twice daily plus emtricitabine/tenofovir DX or emtricitabine/tenofovir AF or lamivudine/abacavir	May be considered if evidence of liver dysfunction	1B

Rationale

As discussed in Section 8.4.2, the DolPHIN-2 study demonstrated faster viral suppression with dolutegravir compared to efavirenz started late in pregnancy (median gestation 31 weeks) [73].

A small randomised controlled trial (*n*=33) conducted in Brazil comparing raltegravir-based regimens with lopinavir/ritonavir in combination with zidovudine/lamivudine initiated after week 28 of pregnancy (mean gestation 33 weeks) demonstrated significantly higher suppression at delivery with raltegravir (77%) than lopinavir/ritonavir (25%) [81].

8.7.2 Presenting in labour or after spontaneous rupture of membranes (SROM) (term and pre-term)

The pharmacological recommendations for the management of women/people who present in labour and are newly identified to be living with HIV are shown below and Figure 8.1.

Recommendations

- We recommend commencing triple ART immediately with tenofovir DX/emtricitabine plus dolutegravir 50 mg (Grade 1B).
- We recommend the following additional agents to be given at labour (any gestation) to preload the fetus:
  - An additional oral dose of tenofovir DX 245 mg immediately (Grade 1D) AND
  - Oral nevirapine 200 mg immediately (Grade 1B) AND
  - Intravenous zidovudine for the duration of labour (Grade 1C).

Rationale

Immediate ART should be started with once-daily dolutegravir and emtricitabine/tenofovir DX; this can be modified postpartum, if required, based on the genotypic resistance profile and toxicity concerns. Dolutegravir has been shown in multiple studies to cross the placenta [82-84] (see ART placental transfer table in Appendix 3) and is an effective component of triple ART when initiated late in pregnancy [63,73]. Therefore, dolutegravir is recommended in the current guidelines, rather than raltegravir. Nevirapine as a single oral dose (regardless of CD4 count, hepatitis status or prior resistance) should be given immediately, as it crosses the placenta and in 2 hours achieves an effective concentration in the neonate which is maintained for up to 10 days; this is particularly important in a neonate who is unable to take medication orally [44,85]. Nevirapine and dolutegravir should be given even in the context of known maternal/parental resistance to these agents.

The additional dose of tenofovir DX is recommended to preload the infant; of note, tenofovir DX levels are lower and the clearance of tenofovir DX is increased in the second/third trimester.

The above regimen should be given concurrently with intravenous zidovudine for the duration of labour and delivery as per the following schedule:

- Loading dose of 2 mg/kg for 1 hour;
- Maintenance dose of 1 mg/kg for the duration of labour, until the cord is clamped.

Management of untested women/people presenting in labour

Any woman/person who presents in labour or after SROM without a previous documented HIV test must be advised to have an urgent HIV test with a fourth-generation laboratory test (see Figure 8.2). Repeat testing should also be offered to women/people at ongoing risk of HIV infection; the ISOSS 2022 HIV report highlights the importance of pregnant women/people understanding that a negative HIV test refers only to the time at which it was taken: ‘negative now’.

The writing group strongly recommends that all HIV centres should have rapid HIV testing pathways in conjunction with pathology and maternity services, with appropriate staff training provided. The recommendation from the IDPS programme is that tests should be performed urgently, and that samples should be processed ideally upon receipt, and results available at least within 24 hours. Local standard operating procedures should define the process. A reactive test must lead to the initiation of interventions to prevent vertical transmission, even if further confirmatory test results are awaited. The recommended antiretroviral regimen is shown below (see Figure 8.1); the neonate should also be given three-drug PNP (see Section 11).

The writing group does not recommend a point-of-care test first line for individuals with undocumented status as trained staff may not be available when an untested woman/person attends in labour. However, where available, rapid point-of-care tests can still be used to determine HIV status but should be performed in parallel with an urgent fourth-generation laboratory test.

Baseline blood tests including for syphilis and HBV, confirmatory HIV testing, CD4 cell count and HIV resistance should also be performed. In urgent cases, if screening results are not yet available, the clinical team may need to consider treating the pregnant woman/person, if before delivery, and the infant.

If a woman/person does not consent to HIV testing in the first instance, guidance in Section 4.2 should be followed.

Figure 8.1 Management of women/people presenting late in pregnancy (>28 weeks) not on ART

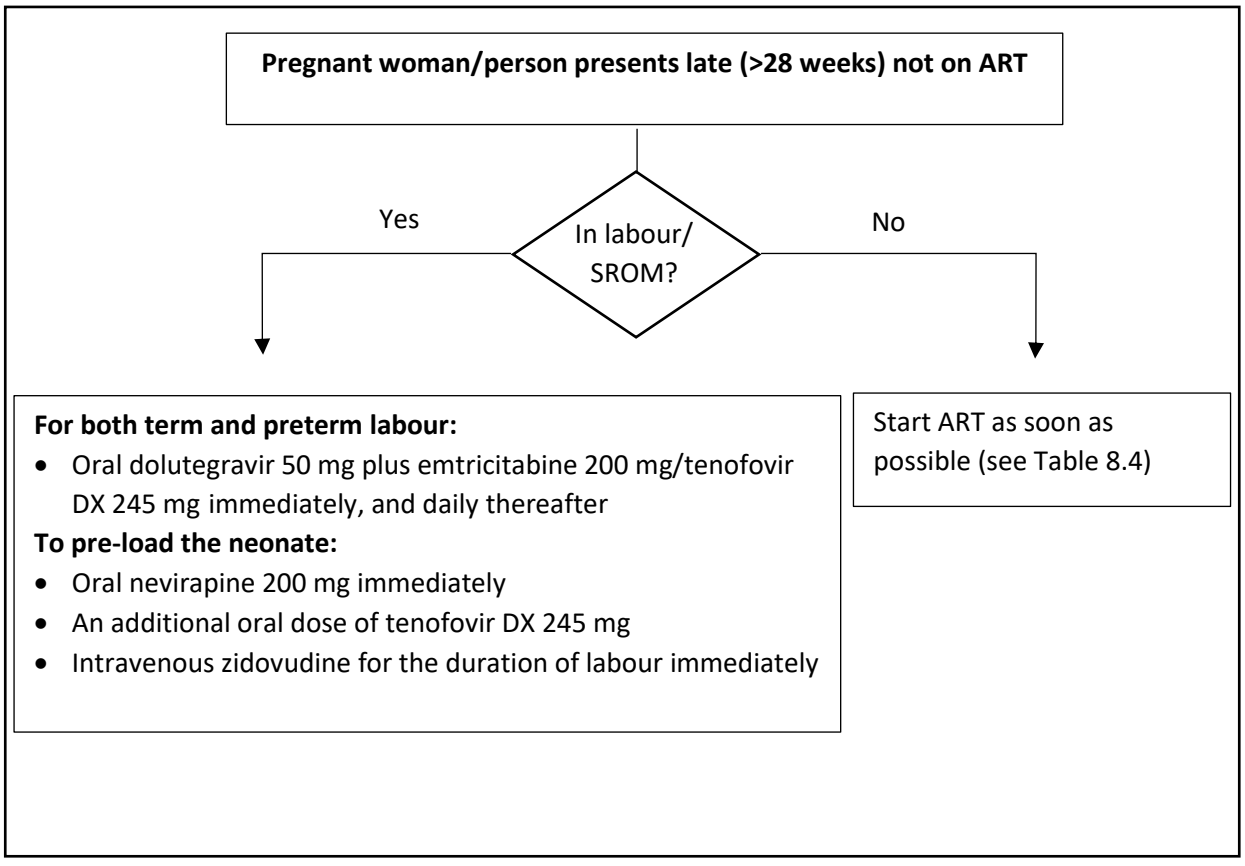
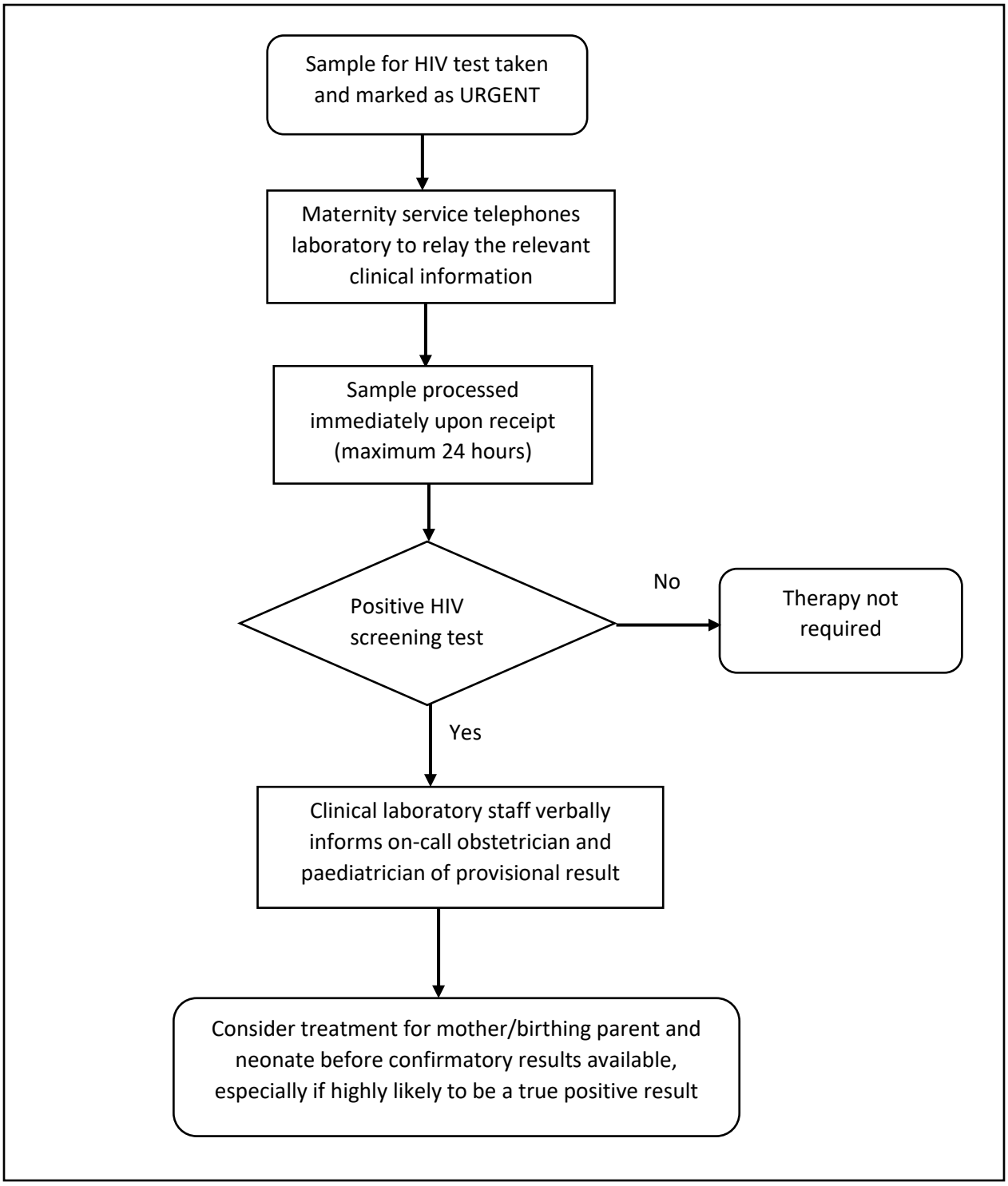


Figure 8.2 Management of untested women/people presenting in labour



8.7.3 Management of pregnant women/people with viraemia on ART

Recommendations

- In the event that a woman/person has initiated ART during pregnancy and does not have a suppressed plasma viral load to <50 copies/mL, we recommend the following (Grade 1C):
  - Review adherence (including a full exploration of potential impacting factors) and drug–drug interactions;
  - Perform a resistance test if appropriate;
  - Consider TDM;
  - Optimise the regimen.
- In the event of detectable viral load at 36 weeks' gestation, we recommend the following (Grade 1C):
  - Review adherence and resistance testing to guide therapy;
  - Optimise the regimen which should include dolutegravir (unless significant resistance);
  - Consider intensification to a four-drug regimen such as the addition of darunavir/ritonavir to a dolutegravir-based regimen;
  - Perform weekly viral load testing;
  - Directly observed therapy should be considered.

- In the event of detectable viral load at delivery, we recommend the following (Grade 1C):
  - Optimise the regimen which should comprise three active drugs including dolutegravir; can consider intensification to four drugs;
  - Include double-dose tenofovir DX* and single-dose nevirapine;
  - Liaise closely with obstetric colleagues aiming for a caesarean section and consider intravenous zidovudine if the latest HIV viral load is >1000 copies/mL (see Section 10.11).

  *If a woman is taking ART containing tenofovir AF, a double dose of tenofovir DX 245 mg should be administered in labour.

Auditable outcomes

- Proportion of pregnant women/people initiating ART without a 2-log reduction in plasma viral load at 2–4 weeks after initiation of ART.
- Proportion of pregnant women/people who initiated ART preconception with a viral load >200 copies/mL during pregnancy (any trimester).
- Proportion of pregnant women/people who require regimen optimisation during pregnancy.
- Proportion of pregnant women/people with a detectable viral load at 36 weeks.

Rationale

Principles of managing incomplete virological suppression in pregnancy

The same principles of management and recommendations apply to pregnant women/people living with HIV with viraemia as for all people with HIV [1]. For a woman/person who conceives on ART that is not fully suppressive or who loses virological control during the pregnancy, the interventions for the management of viraemia recommended in Section 8.7.3 should be considered as soon as possible.

These recommendations also apply for a women/person who has initiated ART in pregnancy and in whom the plasma viral load is no longer declining or indeed has increased. It is important to support adherence, treat nausea, assess mental health and social issues, reinforce patient education, offer peer support and SMS medication reminders, check ART food requirements and assess dosing and drug interactions. Resistance testing should be attempted where plasma viral load is detectable, including integrase resistance. If there are concerns regarding drug absorption or pre-existing evidence for potentially reduced drug concentrations in pregnancy or absence of pharmacokinetic data, TDM should be considered.

Risk factors for virological failure in pregnancy

In the majority of cases, failure to fully suppress is not due to inadequacy of the prescribed therapy but to adherence issues. Barriers to adherence in pregnancy can include hyperemesis, ART tolerability and dosing requirements, poor psychological wellbeing and lack of social support, non-disclosure of HIV status [86], food and housing insecurities, immigration issues [87-89] and intimate partner violence [90].

Risk factors for virological failure in pregnancy include difficulties in engagement with antenatal care with suboptimal ART adherence [91,92], short time on ART or late presentation [92], the presence of drug resistance mutations [93,94], younger maternal age [92,95], vertically acquired HIV [96], low level of education [92] and informal sector employment or unemployment [91,92].

Monitoring of virological response

For those who initiate or switch ART in pregnancy, the writing group suggests viral load measurement at 2 weeks after initiation/switch.

If a woman/person has not achieved a 2-log decrease in plasma viral load at this time, an early repeat test 2 weeks later is suggested (4 weeks following commencing ART). If a 2-log drop in viral load over 4 weeks has not been achieved, all the interventions recommended above should be considered.

Optimisation of the ART regimen in the case of incomplete virological response or resistance

Early consideration should be given to ART optimisation options which would include a switch to an alternative regimen that contains at least two and preferably three fully active drugs with adequate safety data, including one that crosses the placenta (see ART placental transfer table in Appendix 3). The presence of the M184V mutation alone does not preclude the use of emtricitabine/tenofovir DX with dolutegravir [97,98]. Construction of the best regimen should involve review of past and current resistance tests, treatment history, drug interactions with co-administered medication and patient preference, and should be discussed within a specialist MDT [1].

ART optimisation may include increasing drug dosage (e.g. twice-daily darunavir/ritonavir or dolutegravir), particularly in the context of low TDM concentrations and/or documented or suspected resistance. Intensification to a four-drug regimen containing both dolutegravir and darunavir/ritonavir may be appropriate in the presence of resistance, however data are limited to the addition of raltegravir to three-drug regimens in small observational pregnancy studies [99-101]. Data from the VIKING-3 study support the addition of twice-daily dolutegravir to failing regimens in highly treatment-experienced non-pregnant populations with INSTI-resistant virus, which may be extrapolated to pregnant women/people [102]. We acknowledge that very rarely due to triple class resistance, newer drug options may be needed despite the lack of safety data.

Adherence support

Peer mentoring, SMS medication reminders, motivational therapy and addressing tablet phobias through psychological techniques are all useful adjuncts to supporting adherence. On an individual basis, it may be appropriate to explore options for directly observed therapy, which may be virtual, through community nurses or support workers, or even as an inpatient, particularly with failure to achieve virological suppression approaching 36 weeks and where social circumstances are a significant barrier to adherence.

Preterm labour

If treatment failure occurs when the infant is likely to be delivered moderately or severely premature (<34 weeks) and may be unable to take medication enterally, intensification should consist of therapies that readily cross the placenta such as double-dose tenofovir DX, dolutegravir and single-dose nevirapine, as recommended in Section 8.7.2 (see Appendix 3 for table of antiretroviral agents that cross the placenta). See Section 10 for guidance on mode and timing of delivery and additional considerations.

If a woman/person is established on/optimised to a tenofovir AF-containing regimen and has a detectable viral load at delivery at term or preterm, we recommend a double dose of tenofovir DX (i.e. 2x 245 mg tenofovir DX) in addition to their regular tenofovir AF. The rationale for this recommendation is that placental transfer of tenofovir AF is low and 2x 245 mg tenofovir DX ensures transplacental transfer of ART to preload the unborn infant; the risk of maternal adverse effects of the immediate dose of tenofovir DX is low.

8.7.4 Managing ART in the context of nausea and vomiting of pregnancy and hyperemesis gravidarum

Nausea and vomiting of pregnancy is diagnosed when symptom onset is in the first trimester and other causes of nausea and vomiting have been excluded. Hyperemesis gravidarum may be diagnosed when there is protracted nausea and vomiting with the triad of more than 5% pre-pregnancy weight loss, dehydration and electrolyte imbalance. Nausea and vomiting of pregnancy may impact the ability of pregnant women/people to take and absorb antiretroviral agents, leading to variable antiretroviral drug exposure posing a risk of treatment failure and/or development of drug resistance. Clinical management of nausea and vomiting should therefore be proactive and guided by the relevant RCOG guidelines, and should include assessment of severity, prescription of anti-emetics, MDT discussion and inpatient care if required [103].

Consideration should be given to ensuring that women/people experiencing nausea and vomiting of pregnancy are on a regimen with a high-genetic barrier to resistance. If there are prolonged periods of no or very intermittent ART exposure and thus a risk of treatment failure and/or development of drug resistance, the writing group recommends that treatment is interrupted for the minimum time required to overcome the issue and that additional viral load and resistance testing is performed. However, there are no data that specifically address this in pregnancy. In cases of severe and prolonged nausea and vomiting of pregnancy, long-acting injectable therapy could be considered in consultation with an MDT with experience in managing perinatal HIV if the risks are thought to outweigh the benefits.

8.8 References

1. Waters L, Winston A, Reeves I *et al*. BHIVA guidelines on antiretroviral treatment for adults living with HIV-1 2022. *HIV Med* 2022; **23 Suppl 5**: 3–115.

2. Colbers A, Mirochnick M, Schalkwijk S *et al*. Importance of prospective studies in pregnant and breastfeeding women living with human immunodeficiency virus. *Clin Infect Dis*. 2019; **69**: 1254–1258.

3. Mofenson LM, Pozniak AL, Wambui J *et al.* Optimizing responses to drug safety signals in pregnancy: the example of dolutegravir and neural tube defects. *J Int AIDS Soc* 2019; **22**: e25352.

4. Frange P, Tubiana R, Sibiude J *et al*. Rilpivirine in HIV-1-positive women initiating pregnancy: to switch or not to switch? *J Antimicrob Chemother* 2020; **75**: 1324–1331.

5. Floridia M, Ravizza M, Pinnetti C *et al*. Treatment change in pregnancy is a significant risk factor for detectable HIV-1 RNA in plasma at end of pregnancy. *HIV Clin Trials* 2010; **11**: 303–311.

6. The Antiretroviral Pregnancy Registry. *Interim report*. 2024. Available at: https://www.apregistry.com/forms/interim_report.pdf (accessed July 2024).

7. Watts DH. Teratogenicity risk of antiretroviral therapy in pregnancy. *Curr HIV/AIDS Rep* 2007; **4**: 135–140.

8. Zash R, Holmes LB, Diseko M *et al*. Update on neural tube defects with antiretroviral exposure in the Tsepamo Study, Botswana. AIDS 2022. Montreal, Canada. Poster abstract PELBB02. Available at: https://programme.aids2022.org/Abstract/Abstract/?abstractid=12759 (accessed July 024).

9. Raesima MM, Ogbuabo CM, Thomas V *et al*. Dolutegravir use at conception - additional surveillance data from Botswana. *N Engl J Med* 2019; **381**: 885–887.

10 Gill MM, Khumalo P, Chouraya C *et al*. Strengthening the evidence: similar rates of neural tube defects among deliveries regardless of maternal HIV status and dolutegravir exposure in hospital birth surveillance in Eswatini. *Open Forum Infect Dis* 2023; **10**: ofad441.

11. Pereira GFM, Kim A, Jalil EM *et al*.; National Cohort Study of Dolutegravir and Pregnancy Outcomes in Brazil. Dolutegravir and pregnancy outcomes in women on antiretroviral therapy in Brazil: a retrospective national cohort study. *Lancet HIV* 2021; **8**: e33–e41.

12. Thorne C, Aebi-Popp K, Ene L *et al*. Birth outcomes following prenatal exposure to dolutegravir: the Dolomite-EPPICC study. Conference on Retroviruses and Opportunistic Infections. Februrary 2022. Available at: https://www.croiconference.org/abstract/birth-outcomes-following-prenatal-exposure-to-dolutegravir-the-dolomite-eppicc-study/ (accessed July 2024).

13. Sibiude J, Le Chenadec J, Mandelbrot L *et al*. Risk of birth defects and perinatal outcomes in HIV-infected women exposed to integrase strand inhibitors during pregnancy. *AIDS* 2021; **35**: 219–226.

14. Delany-Moretlwe S, Voldal E, Saidi F *et al*. Initial evaluation of injectable cabotegravir (CAB-LA) safety during pregnancy in the HPTN 084 open-label extension. AIDS 2024. Munich, Germany. Abstract 12420. Available at: https://programme.aids2024.org/Abstract/Abstract/?abstractid=12420 (accessed May 2025)

15. Lytvyn L, Siemieniuk RA, Dilmitis S *et al*. Values and preferences of women living with HIV who are pregnant, postpartum or considering pregnancy on choice of antiretroviral therapy during pregnancy. *BMJ Open* 2017; **7**: e019023.

16. Feghali M, Venkataramanan R, Caritis S. Pharmacokinetics of drugs in pregnancy. *Semin Perinatol* 2015; **39**: 512–519.

17. Rodman JH, Flynn PM, Robbins B *et al*. Systemic pharmacokinetics and cellular pharmacology of zidovudine in human immunodeficiency virus type 1-infected women and newborn infants. *J Infect Dis* 1999; **180**: 1844–1850.

18. Moodley J, Moodley D, Pillay K *et al*. Pharmacokinetics and antiretroviral activity of lamivudine alone or when coadministered with zidovudine in human immunodeficiency virus type 1-infected pregnant women and their offspring. *J Infect Dis* 1998; **178**: 1327–1333.

19. Best BM, Mirochnick M, Capparelli EV *et al*. Impact of pregnancy on abacavir pharmacokinetics. *AIDS* 2006; **20**: 553–560.

20. Colbers AP, Hawkins DA, Gingelmaier A *et al*. The pharmacokinetics, safety and efficacy of tenofovir and emtricitabine in HIV-1-infected pregnant women. *AIDS* 2013; **27**: 739–748.

21. Stek AM, Best BM, Luo W *et al*. Effect of pregnancy on emtricitabine pharmacokinetics. *HIV Med* 2012; **13**: 226–235.

22. Brooks KM, Pinilla M, Stek AM *et al*. Pharmacokinetics of tenofovir alafenamide with boosted protease inhibitors in pregnant and postpartum women living with HIV: results from IMPAACT P1026s. *J Acquir Immune Defic Syndr* 2022; **90**: 343–350.

23. Bukkems VE, Necsoi C, Hidalgo Tenorio C *et al*. Tenofovir alafenamide plasma concentrations are reduced in pregnant women living with human immunodeficiency virus (HIV): data from the PANNA Network. *Clin Infect Dis* 2022; **75**: 623–629.

24. Joseph Davey D, Dadan S, Bheemraj K *et al*. Evaluation of pharmacokinetics of tenofovir alafenamide (TAF) and tenofovir disoproxil (TDF) in pregnant and postpartum women in South Africa: PrEP-PP PK study. *Antiviral Res* 2024; **231**: 106014.

25. Pencolé L, Lê MP, Bouchet-Crivat F *et al*. Placental transfer of the integrase strand inhibitors cabotegravir and bictegravir in the ex-vivo human cotyledon perfusion model. *AIDS* 2020; **34**: 2145–2149.

26. Zhang H, Martin H, Lin L *et al.* Pharmacokinetics, safety, and efficacy of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in virologically suppressed pregnant women with HIV. IAS 2023, Brisbane, Australia. Oral abstract 681. Available at: https://ias.reg.key4events.com/key4register/AbstractList.aspx?e=96&preview=1&aig=-1&ai=51111 (accessed August 2024).

27. Powis KM, Pinilla M, Bergam L *et al*. Pharmacokinetics and virologic outcomes of bictegravir in pregnancy and postpartum. Conference on Retroviruses and Opportunistic Infections; February 2023; Seattle, WA, USA. Abstract 783. Available at: https://www.croiconference.org/abstract/pharmacokinetics-and-virologic-outcomes-of-bictegravir-in-pregnancy-and-postpartum/ (accessed August 2024).

28. Marzinke M, Voldal E, Hanscom B *et al*. Evaluation of long-acting cabotegravir (CAB-LA) pharmacokinetics during pregnancy: a sub-study analysis of the HPTN 084 open label extension study. International AIDS Conference 2024. Available at: https://programme.aids2024.org/Abstract/Abstract/?abstractid=12032 (accessed December 2024).

29. Crauwels H, Rice D, Neyens M *et al*. Rilpivirine long-acting pharmacokinetic tail and pregnancy. International Workshop on HIV & Women 2021. Available at:

https://academicmedicaleducation.com/materials/rilpivirine-long-acting-pharmacokinetic-tail-and-pregnancy-10433 (accessed August 2024).

30. Patel P, Ford SL, Baker M *et al*. Pregnancy outcomes and pharmacokinetics in pregnant women living with HIV exposed to long-acting cabotegravir and rilpivirine in clinical trials. *Open Forum Infect Dis* 2021; **8 Suppl 1**: S534.

31. Atoyebi S, Bunglawala F, Cottura N *et al.* Physiologically-based pharmacokinetic modelling of long-acting injectable cabotegravir and rilpivirine in pregnancy. *Br J Clin Pharmacol* 2024 Feb 10. doi: 10.1111/bcp.16006. Online ahead of print.

32. Short WR, Zimmerman M, Aziz M et al. Long-Acting Cabotegravir/Rilpivirine in Pregnancy. Conference on Retroviruses and Opportunistic Infections. March 2025. San Francisco, CA. Abstract 1015. Available at: https://www.croiconference.org/abstract/3441-2025/ (accessed May 2025).

33. Mulligan N, Best BM, Wang J *et al*.; IMPAACT P1026s Protocol Team. Dolutegravir pharmacokinetics in pregnant and postpartum women living with HIV. *AIDS* 2018; **32**: 729–737.

34. Waitt C, Orrell C, Walimbwa S *et al*. Safety and pharmacokinetics of dolutegravir in pregnant mothers with HIV infection and their neonates: A randomised trial (DolPHIN-1 study). *PLoS Med* 2019; **16**: e1002895.

35. Bollen P, Colbers A, Schalkwijk S *et al.*, editors. First report of dolutegravir unbound plasma concentrations during pregnancy in HIV-positive women. 19th International Workshop on Clinical Pharmacology of Antiviral Therapy; 2018; Baltimore, USA. Available at: https://www.natap.org/2018/Pharm/Pharm_10.htm (accessed July 2024).

36. Momper JD, Best BM, Wang J *et al*. Elvitegravir/cobicistat pharmacokinetics in pregnant and postpartum women with HIV. *AIDS* 2018; **32**: 2507–2516.

37. Bukkems V, Necsoi C, Tenorio CH *et al*. Clinically significant lower elvitegravir exposure during the third trimester of pregnant patients living with human immunodeficiency virus: data from the Pharmacokinetics of ANtiretroviral agents in HIV-infected pregNAnt women (PANNA) Network. *Clin Infect Dis* 2020; **71**: e714–e717.

38. Blonk MI, Colbers AP, Hidalgo-Tenorio C *et al*. Raltegravir in HIV-1-infected pregnant women: pharmacokinetics, safety, and efficacy. *Clin Infect Dis* 2015; **61**: 809–816.

39. Belissa E, Benchikh A, Charpentier C *et al.* Raltegravir plasma concentrations on HIV-1 infected pregnant women. Conference on Retroviruses and Opportunistic Infections; February; Seattle, WA, USA 2015.

40. Zheng Y, Hirt D, Delmas S, Lui G *et al*. Effect of pregnancy on unbound raltegravir concentrations in the ANRS 160 RalFe trial. *Antimicrob Agents Chemother* 2020; **64**: e00759-20.

41. Cressey TR, Stek A, Capparelli E *et al*. Efavirenz pharmacokinetics during the third trimester of pregnancy and postpartum. *J Acquir Immune Defic Syndr* 2012; **59**: 245–252.

42. Ramgopal M, Osiyemi O, Zorrilla C *et al*. Pharmacokinetics of total and unbound etravirine in HIV-1-infected pregnant women. *J Acquir Immune Defic Syndr* 2016; **73**: 268–274.

43. Mulligan N, Schalkwijk S, Best BM *et al*. Etravirine pharmacokinetics in HIV-infected pregnant women. *Front Pharmacol* 2016; **7**: 239.

44. Mirochnick M, Siminski S, Fenton T *et al*. Nevirapine pharmacokinetics in pregnant women and in their infants after in utero exposure. *Pediatr Infect Dis J* 2001; **20**: 803–805.

45. Taylor GP, Lyall EG, Back D *et al*. Pharmacological implications of lengthened in-utero exposure to nevirapine. *Lancet* 2000; **355**: 2134–2135.

46. Colbers A, Schalkwijk S, Konopnicki D *et al*. Substantially lower rilpivirine plasma concentrations during pregnancy. *Topics Antivir Med* 2017; **25**: 321s.

47. Osiyemi O, Yasin S, Zorrilla C *et al*. Pharmacokinetics, antiviral activity, and safety of rilpivirine in pregnant women with HIV-1 infection: results of a phase 3b, multicenter, open-label study. *Infect Dis Ther* 2018; **7**: 147–159.

48. Tran AH, Best BM, Stek A *et al*. Pharmacokinetics of rilpivirine in HIV-infected pregnant women. *J Acquir Immune Defic Syndr*2016; **72**: 289–296.

49. Colbers A, Hawkins D, Hidalgo-Tenorio C *et al*. Atazanavir exposure is effective during pregnancy regardless of tenofovir use. *Antivir Ther* 2015; **20**: 57–64.

50. Focà E, Calcagno A, Bonito A *et al*. Atazanavir intracellular concentrations remain stable during pregnancy in HIV-infected patients. *J Antimicrob Chemother* 2017; **72**: 3163–3166.

51. Samuel M, Bradshaw D, Perry M *et al*. Antenatal atazanavir: a retrospective analysis of pregnancies exposed to atazanavir. *Infect Dis Obstet Gynecol* 2014; **2014**: 961375.

52. Khoo S, Peytavin G, Burger D *et al*. Pharmacokinetics and safety of darunavir/ritonavir in HIV-infected pregnant women. *AIDS Rev* 2017; **19**: 16–23.

53. Murtagh R, Else LJ, Kuan KBK *et al*. Therapeutic drug monitoring of darunavir/ritonavir in pregnancy. *Antivir Ther* 2019; **24**: 229–233.

54. Schalkwijk S, Ter Heine R, Colbers A *et al*. Evaluating darunavir/ritonavir dosing regimens for HIV-positive pregnant women using semi-mechanistic pharmacokinetic modelling. *J Antimicrob Chemother* 2019; **74**: 1348–1356.

55. Crauwels HM, Osiyemi O, Zorrilla C *et al*. Reduced exposure to darunavir and cobicistat in HIV-1-infected pregnant women receiving a darunavir/cobicistat-based regimen. *HIV Med* 2019; **20**: 337–343.

56. Momper JD, Wang J, Stek A *et al*.; IMPAACT P1026s Protocol Team. Pharmacokinetics of darunavir and cobicistat in pregnant and postpartum women with HIV. *AIDS* 2021; **35**: 1191–1199.

57. Brites C, Luz E, Nóbrega I *et al*. Efficacy and safety of DRG/3TC for prophylaxis of HIV Perinatal transmission: a pilot study (PREGNANCY). *Open Forum Infect Dis* 2024; **11**: ofae672.

58. Short WR, Patel P, Verdier G *et al*. Role of dolutegravir/lamivudine in the management of pregnant people living with HIV-1: a narrative review. *Infect Dis Ther* 2025; **14:** 59–80.

59. Rohr I, Hoeltzenbein M, Weizsacker K *et al*. Efficacy and safety of 2-drug regime dolutegravir/lamivudine in pregnancy and breastfeeding - clinical implications and perspectives. *J Perinat Med* 2024; **52**: 934–938.

60. NHS England. *ISOSS HIV report 2022*. 2023. Available at: https://www.gov.uk/government/publications/infectious-diseases-in-pregnancy-screening-isoss-hiv-report-2022/isoss-hiv-report-2022 (accessed June 2024).

61. Ceccaldi PF, Ferreira C, Gavard L *et al*. Placental transfer of enfuvirtide in the *ex vivo* human placenta perfusion model. *Am J Obstet Gynecol* 2008; **198**: 433.e1–2.

62. Lockman S, Brummel SS, Ziemba L *et al*. Efficacy and safety of dolutegravir with emtricitabine and tenofovir alafenamide fumarate or tenofovir disoproxil fumarate, and efavirenz, emtricitabine, and

tenofovir disoproxil fumarate HIV antiretroviral therapy regimens started in pregnancy (IMPAACT 2010/VESTED): a multicentre, open-label, randomised, controlled, phase 3 trial. *Lancet* 2021; **397**: 1276–1292.

63. Kintu K, Malaba TR, Nakibuka J *et al*. Dolutegravir versus efavirenz in women starting HIV therapy in late pregnancy (DolPHIN-2): an open-label, randomised controlled trial. *Lancet HIV* 2020; **7**: e332-e9.

64. Asif SF, Baxevanidi E, Venter WDF *et al*. Faster virological suppression with dolutegravir versus efavirenz in pregnancy does not lower the risk of HIV mother-to-child-transmission: A meta-analysis of 5 clinical trials in 1074 pregnant women. *J Int AIDS Soc* 2020; **23 Suppl 4**: OABLB0105. Available at: https://onlinelibrary.wiley.com/doi/10.1002/jia2.25547 (accessed August 2024).

65. João EC, Morrison RL, Shapiro DE *et al*. Raltegravir versus efavirenz in antiretroviral-naive pregnant women living with HIV (NICHD P1081): an open-label, randomised, controlled, phase 4 trial. *Lancet HIV* 2020; **7**: e322–e331.

66. Brites C, Nóbrega I, Luz E *et al*. Raltegravir versus lopinavir/ritonavir for treatment of HIV-infected late-presenting pregnant women. *HIV Clin Trials* 2018; **19**: 94–100.

67. Cowdell I, Beck K, Portwood C *et al*. Adverse perinatal outcomes associated with protease inhibitor-based antiretroviral therapy in pregnant women living with HIV: A systematic review and meta-analysis. *EClinicalMedicine* 2022; **46**: 101368.

68. Electronic Medicines Compendium. *Edurant 25 mg film-coated tablets.* Available at: https://www.medicines.org.uk/emc/product/4968/smpc#gref (accessed July 2024).

69. Gabagaya G, Rukundo G, Amone A *et al*. Prevalence of undetectable and suppressed viral load in HIV-infected pregnant women initiating Option B+ in Uganda: an observational study nested within a randomized controlled trial. *BMC Infect Dis* 2021; **21**: 907.

70. Byrne L, de Alwis O, Toby M *et al*. Managing the pregnancies of HIV elite controllers: what are we doing? *HIV Med* 2012; **13 Suppl 1**: 1–11.

71. Short C-ES, Byrne L, Hagan-Bezgin A *et al*. Pregnancy management in HIV viral controllers: twenty years of experience. *Pathogens* 2024; **13**: 308.

72. Greig J, Bamford A, Chadwick D *et al*. British HIV Association guidelines on the management of opportunistic infection in people living with HIV: Considerations in pregnancy 2024. *HIV Med* 2024; **25 Suppl 3**: 3–19.

73. Malaba TR, Nakatudde I, Kintu K *et al*. 72 weeks post-partum follow-up of dolutegravir versus efavirenz initiated in late pregnancy (DolPHIN-2): an open-label, randomised controlled study. *Lancet HIV* 2022; **9**: e534-e543.

74. Sexton H, Kumarendran M, Brandon Z *et al*. Adverse perinatal outcomes associated with timing of initiation of antiretroviral therapy: systematic review and meta-analysis. *HIV Med* 2023; **24**: 111–129.

75. Alagaratnam J, Peters H, Francis K *et al*. An observational study of initial HIV RNA decay following initiation of combination antiretroviral treatment during pregnancy. *AIDS Res Ther* 2020; **17**: 41.

76. British HIV Association. *BHIVA guidelines for the routine investigation and monitoring of adult HIV-1-positive individuals 2019*. Available at: https://www.bhiva.org/monitoring-guidelines (accessed June 2024).

77. Reeves I, Cromarty B, Deayton J *et al*. British HIV Association guidelines for the management of HIV-2 2021. *HIV Med* 2021; **22 Suppl 4**: 1–29.

78. Comparison of vertical human immunodeficiency virus type 2 and human immunodeficiency virus type 1 transmission in the French prospective cohort. The HIV Infection in Newborns French Collaborative Study Group. *Pediatr Infect Dis J* 1994; 13: 502-506.

79. Adjorlolo-Johnson G, De Cock KM, Ekpini E *et al*. Prospective comparison of mother-to-child transmission of HIV-1 and HIV-2 in Abidjan, Ivory Coast. *JAMA* 1994; **272**: 462–466.

80. O'Donovan D, Ariyoshi K, Milligan P *et al*. Maternal plasma viral RNA levels determine marked differences in mother-to-child transmission rates of HIV-1 and HIV-2 in The Gambia. MRC/Gambia Government/University College London Medical School working group on mother-child transmission of HIV. *AIDS* 2000; **14**: 441–448.

81. Brites C, Nóbrega I, Luz E *et al*. Raltegravir versus lopinavir/ritonavir for treatment of HIV-infected late-presenting pregnant women. *HIV Clin Trials* 2018; **19**: 94–100.

82. Rimawi BH, Johnson E, Rajakumar A *et al*. Pharmacokinetics and placental transfer of elvitegravir, dolutegravir, and other antiretrovirals during pregnancy. *Antimicrob Agents Chemother* 2017; **61**: e02213-16.

83. Ikumi NM, Anumba D, Matjila M. Pharmacokinetics and placental transfer of dolutegravir in pregnancy. *J Antimicrob Chemother* 2022; **77**: 283–289.

84. Dickinson L, Walimbwa S, Singh Y *et al*. Infant exposure to dolutegravir through placental and breast milk transfer: a population pharmacokinetic analysis of DolPHIN-1. *Clin Infect Dis* 2021; **73**: e1200-e7.

85. Musoke P, Guay LA, Bagenda D *et al*. A phase I/II study of the safety and pharmacokinetics of nevirapine in HIV-1-infected pregnant Ugandan women and their neonates (HIVNET 006). *AIDS* 1999; **13**: 479–486.

86. Gabagaya G, Rukundo G, Amone A *et al*. Prevalence of undetectable and suppressed viral load in HIV-infected pregnant women initiating Option B+ in Uganda: an observational study nested within a randomized controlled trial. *BMC Infect Dis* 2021; **21**: 907.

87. Benes LR, Yee LM, Levesque J, Miller ES. 596: Is food insecurity during pregnancy associated with risk factors for maternal-to-child transmission of HIV? *Am J Obstet Gynecol* 2020; **222**: S382–S383.

88. Cassimatis IR, Miller ES, Benes L *et al*. Housing instability is associated with failure to achieve virologic control among pregnant individuals with HIV. *Am J Obstet Gynecol MFM* 2021; **3**: 100406.

89. Cooper R, Collini P, Greig J. HIV control in post-partum mothers: still a turbulent time. *HIV Med* 2021; **22 Suppl 2**: 52.

90. Cabrera T, Ramos U, Nava C *et al*. Factors associated with virological failure in women with HIV. *J Int AIDS Soc* 2018; **21**: 24–25.

91. Adeniyi OV. Risk factors for peripartum virological failure in South African pregnant women on anti-retroviral therapy: East London Prospective Cohort Study. *HIV Med* 2019; **20**: 207. Available at: https://onlinelibrary.wiley.com/doi/10.1111/hiv.12814 (accessed August 2024).

92. Atanga PN, Ndetan HT, Fon PN *et al*. Using a composite adherence tool to assess ART response and risk factors of poor adherence in pregnant and breastfeeding HIV-positive Cameroonian women at 6 and 12 months after initiating option B. *BMC Pregnancy Childbirth* 2018; **18**: 418.

93. Burdorf RM, Zhou S, Amon C *et al*. Low-level resistance mutations correlate with HIV therapy failure in pregnant women. *Topics Antivir Med* 2022; **30 1 Suppl**: 195–196.

94. Wilhelmson S, Månsson F, Lindman JL *et al*. Prevalence of HIV-1 pretreatment drug resistance among treatment naïve pregnant women in Bissau, Guinea Bissau. *PLoS One* 2018; **13**: e0206406.

95. Lyatuu GW, Mwashemele SZ, Urrio R *et al*. Long-term virological outcomes in women who started option B+ care during pregnancy for prevention of mother-to-child transmission of HIV in Dar es Salaam, Tanzania: a cohort study. *Lancet HIV* 2021; **8**: e256–e265.

96. Osmundo GDS, Da Costa RA, Ruocco RMA, Francisco RPV. Pregnancy in women living with perinatally acquired HIV: perinatal outcomes and drug resistance profile. *Clinics* 2023; **78**: 100174.

97. Paton NI, Musaazi J, Kityo C *et al*. Efficacy and safety of dolutegravir or darunavir in combination with lamivudine plus either zidovudine or tenofovir for second-line treatment of HIV infection (NADIA): week 96 results from a prospective, multicentre, open-label, factorial, randomised, non-inferiority trial. *Lancet HIV* 2022; **9**: e381–e393.

98. Underwood M, Horton J, Nangle K *et al*. Integrase inhibitor resistance mechanisms and structural characteristics in antiretroviral therapy-experienced, integrase inhibitor-naive adults with HIV-1 infection treated with dolutegravir plus two nucleoside reverse transcriptase inhibitors in the DAWNING study. *Antimicrob Agents Chemother* 2022; **66**: e0164321.

99. Boucoiran I, Tulloch K, Pick N *et al*. A case series of third-trimester raltegravir initiation: impact on maternal HIV-1 viral load and obstetrical outcomes. *Can J Infect Dis Med Microbiol* 2015; **26**: 145–150.

100. Cecchini DM, Martinez MG, Morganti LM, Rodriguez CG. Antiretroviral therapy containing raltegravir to prevent mother-to-child transmission of HIV in infected pregnant women. *Infect Dis Rep* 2017; **9**: 7017.

101. Puthanakit T, Thepnarong N, Chaithongwongwatthana S *et al*. Intensification of antiretroviral treatment with raltegravir for pregnant women living with HIV at high risk of vertical transmission. *J Virus Era*d 2018; **4**: 61–65.

102. Castagna A, Maggiolo F, Penco G *et al*. Dolutegravir in antiretroviral-experienced patients with raltegravir- and/or elvitegravir-resistant HIV-1: 24-week results of the phase III VIKING-3 study. *J Infect Dis* 2014; **210**: 354–362.

103. Nelson-Piercy C, Dean C, Shehmar M et al.; Royal College of Ostetricians and Gynaecologists. The management of nausea and vomiting in pregnancy and hyperemesis gravidarum (Green-top Guideline No. 69). *BJOG* 2024; **131**: e1–e30.

9 HIV and hepatitis co-infection

9.1 HBV

9.1.1 Background and epidemiology

The combination of HIV, chronic HBV and pregnancy presents unique management considerations. Referral to the local designated specialist is advised to ensure that all aspects of care are addressed, including the effects of HIV/HBV on pregnancy, the effects of pregnancy on the course of co-infection, antiretroviral management for both HBV and HIV, and prevention of vertical transmission for both viruses. Pregnant women/people with advanced cirrhosis should be managed in a tertiary centre with specialist hepatology input.

9.1.2 Impact of HIV/HBV co-infection

The effect of HIV on HBV disease progression in non-pregnant people includes higher levels of HBV replication (HBV DNA levels and proportion hepatitis B e antigen [HBeAg] positive), higher mortality when compared to HIV or HBV mono-infection, a higher rate of chronicity (20–80% compared to 3–5% in individuals without HIV with risk increasing with lower CD4 cell counts at the time of HBV acquisition), lower alanine transaminase (ALT) levels, higher rate of hepatocellular cancer (HCC), lower rate of spontaneous loss of HBeAg or hepatitis B surface antigen (HBsAg) and seroconversion to anti-hepatitis B e (HBe) and anti-hepatitis B surface (HBs), faster progression to cirrhosis and a higher incidence of lamivudine resistance [1].

Although plausible because of higher levels of HBV DNA in women living with both HBV and HIV, there is no evidence of increased vertical transmission of HBV in co-infection compared with mono-infection. The impact of pregnancy on women with HBV is only small. There appears to be no worsening of liver disease in the majority of women, although there have been case reports of hepatic exacerbations/fulminant hepatic failure [2]. There can be wide variations during pregnancy in HBV viral and liver markers including ALT levels; a small minority of HBeAg-positive women might experience an anti-HBe seroconversion-related flare. HBV DNA levels usually remain stable or may rise by as much as 1-log unit.

Studies linking chronic HBV with intrahepatic cholestasis in pregnancy have had contradictory results, although a recent meta-analysis of data from four studies suggested an association (OR 1.68, 95% CI 1.43–1.97; I^2=0%) [3]. Therefore, women/people with HIV/HBV need careful assessment if there is any suspicion of intrahepatic cholestasis. Data from the HPTN046 randomised controlled study in sub-Saharan Africa demonstrated an increased risk of low birth weight among infants born to women with HIV/HBV with a high HBV viral load [4].

9.1.3 Investigation and monitoring

Recommendations

- On diagnosis of new HBV infection, we recommend the following (Grade 1C):
  - Confirmation of viraemia with quantitative HBV DNA, HBV ‘e’ antigen and ‘e’ antibody testing;
  - Hepatitis A virus (HAV) immunity, HCV and hepatitis D virus (HDV) testing;
  - LFTs, bilirubin, serum albumin, platelet count and clotting tests;
  - Assessment of hepatic inflammation/fibrosis.

- We recommend that LFTs should be repeated at 2 and 4 weeks after commencing ART to detect the presence of hepatotoxicity or immune reconstitution inflammatory syndrome (IRIS), and then monitored regularly throughout pregnancy and the postpartum period (Grade 1C).

Auditable outcome

- The proportion of women/people living with HIV who accept HBV screening in pregnancy.

Rationale

In a pregnant woman/person living with HIV and newly diagnosed with HBV (HBsAg positive on antenatal screening or diagnosed preconception), the following investigations are indicated.

HBV markers: HBsAg (confirmed by a second test), anti-hepatitis B core (HBc), anti-HBc IgM, HBeAg, anti-HBe and quantitative HBV DNA.

Other hepatitis viruses: anti-HAV IgG to assess immunity, and anti-HCV (and HCV RNA if positive) and anti-HDV (and HDV RNA if positive) to exclude HCV and/or HDV infections.

Liver function: ALT, aspartate transaminase (AST), albumin and international normalised ratio and the exclusion of additional causes of liver disease (e.g. haemochromatosis and autoimmune hepatitis).

Liver fibrosis assessment: liver biopsy is relatively contraindicated during pregnancy [5] and should only be performed if deemed essential and after consultation with a hepatologist. Ultrasound transient elastography and/or FibroScan® (Echosens) can be used if needed. FibroScan is no longer contraindicated in pregnancy since the manufacturer altered the guidance for use [5], however results should be interpreted with caution in pregnancy as a transient reversible increase in liver stiffness is expected because pregnancy leads to an increase in blood flow through the liver [6]. Non-invasive liver fibrosis scores such as AST-to-platelet ratio index (APRI) [7] or the Fibrosis-4 score [8] can be used as an alternative.

HCC screening: liver ultrasound should be performed ideally early in pregnancy if assessment is not available prior to pregnancy. Alpha fetoprotein (AFP) measurements cannot be used for HCC screening during pregnancy as they are invariably very high due to the transplacental passage of fetal AFP from early in the first trimester. HCC screening should resume at postnatal follow-up.

9.1.4 Acute HBV infection

Where acute HBV infection is suspected, testing for anti-HBc IgM is recommended. Acute HBV is uncommon during pregnancy and each case needs to be managed with specialist advice. Data suggest that lamivudine as part of ART does not completely protect against the development of acute HBV infection, although it is unlikely that this is also the case with tenofovir DX with or without lamivudine/emtricitabine [9]. Although there is a theoretical risk of high HBV DNA levels and the linked association with increased risk of vertical transmission combined with the potential for acute hepatitis and a threat to maternal/parental and fetal health, it is assumed that this would be mitigated by the woman/person already being on ART including tenofovir DX or tenofovir AF and either lamivudine or emtricitabine. Where the woman/person is not on ART, a tenofovir DX- or tenofovir AF-based regimen should be commenced immediately.

9.1.5 Antiviral treatment

Recommendations

- We recommend that tenofovir DX or tenofovir AF plus lamivudine or emtricitabine should form the backbone of an ART regimen in treatment-naïve patients with wild-type HIV/HBV and no contraindication to any of these drugs (Grade 1B).
- We recommend against using lamivudine or emtricitabine as the only active drug against HBV in ART because of the likelihood of emergent HBV resistance (Grade 1B).
- We recommend that ART active against both HBV and HIV should be continued postpartum in all women/people with HIV/HBV co-infection (Grade 1B).

Auditable outcome

- The proportion of pregnant women/people who receive active ART for HIV/HBV co-infection that includes tenofovir DX or tenofovir AF and lamivudine or emtricitabine.

Rationale

Given the evidence on safety at conception, pharmacokinetic profile and other safety outcomes (see Section 8), we recommend that women/people with HIV and chronic HBV who conceive on tenofovir DX or tenofovir AF combined with lamivudine or emtricitabine should continue this NRTI backbone with a suitable third agent through pregnancy and the postpartum period, to minimise the risk of HBV viral rebound. Similarly, women/people with HIV/HBV who are not yet on treatment should commence a recommended regimen with tenofovir DX or tenofovir AF combined with lamivudine or emtricitabine and continue this treatment through pregnancy and the postpartum period.

Tenofovir DX or tenofovir AF and lamivudine or emtricitabine should be included in the ART regimen even in cases in which HIV resistance to tenofovir might be predicted; these cases should be discussed in an HIV MDT.

Although lamivudine and emtricitabine are potent anti-HBV agents, HBV monotherapy with these agents is associated with a high likelihood of HBV resistance in individuals with HIV/HBV co-infection and is not recommended. It was shown that tenofovir DX is effective at suppressing HBV DNA in individuals with HBV mono-infection and those with HIV/HBV co-infection whether HBeAg positive or negative, and independent of the presence of HBV lamivudine resistance [10]. More recently, tenofovir AF has also been shown to have non-inferior efficacy and improved renal and bone toxicity compared to tenofovir DX in the management of HBV mono-infection [11,12]. Phenotypic HBV resistance has not been ascribed to tenofovir DX in people with both HIV and HBV with up to 5 years of follow-up and has only been demonstrated *in vitro* in treated individuals with suboptimal control [13] as represented by detectable HBV DNA levels. There are only a few case reports of tenofovir-related resistance in severely immunosuppressed people with variable drug levels. In combination with lamivudine or emtricitabine, tenofovir DX/AF is effective at suppressing HBV DNA and may induce HBeAg seroconversion. Combining lamivudine/emtricitabine with tenofovir DX/AF may also reduce the risk of breakthrough HBV viraemia [14], however the most important advantage is that currently emtricitabine is co-formulated with tenofovir DX/AF and therefore convenient for dosing.

It was found that in pregnant women with mono-infection, an HBV DNA level <200,000 IU/mL was achieved within 3–7 weeks of tenofovir DX treatment and the rate of transmission in women receiving tenofovir (30%) was significantly reduced compared to those not receiving any antiviral treatment (45%); however, when women have a very high baseline HBV viral load (i.e. >8-log units), treatment should be initiated much earlier than 28 weeks [15]. Tenofovir is preferred as an agent with a higher barrier to resistance even in women with documented resistance to lamivudine [16].

Emtricitabine is structurally similar to lamivudine but has a longer intracellular half-life and is more potent *in vitro* and *in vivo* as monotherapy when initiated in individuals with HIV/HBV [17]. It also selects for resistance for both HIV and HBV less rapidly and less often than lamivudine [17]. Although not currently approved for HBV treatment, emtricitabine induces a sharp reduction in HBV DNA levels in both mono-infection and co-infection. In individuals with both HIV and HBV initiated on ART, combining emtricitabine with tenofovir DX has been shown in a randomised controlled trial to be more effective than emtricitabine alone (median time-weighted average concentration decrease was −5.32 log IU/mL in the tenofovir DX/emtricitabine group versus −3.25 log IU/mL in the emtricitabine group; *P*=0.036) [18]. Further studies comparing tenofovir DX/lamivudine with lamivudine alone showed similar results [19].

The effects of entecavir in pregnancy have not been studied in humans, however there is some evidence of carcinogenesis in animal studies at supratherapeutic doses and there are minimal registry safety data, and therefore entecavir should not be used in pregnancy [20]. A combination of lamivudine and telbivudine has been used in pregnant women with HBV mono-infection and has been found to be safe [21]. If there is a contraindication to tenofovir DX/AF, specialist advice should be sought.

9.1.6 Complications of HIV/HBV co-infection

Cirrhosis

It is important where cirrhosis is found to be present that there is close liaison with a hepatologist because of a significantly increased rate of complications. Under the care of a hepatologist an oesophago-gastro-duodenoscopy (in the absence of a recent test) might be required to exclude varices and guide decisions around the mode of delivery. Additionally, acute liver failure can occur on reactivation of HBV disease if anti-HBV treatment is discontinued [22]. However, in the absence of decompensated disease and with ART including anti-HBV drugs and close monitoring, most women/people with cirrhosis do not experience obstetric complications as a result of HBV infection.

Inflammatory flares

Because of the risk of ART-related hepatotoxicity and a hepatitis flare from immune reconstitution, it is important to repeat LFTs at 2 and 4 weeks after initiation of ART and periodically thereafter. Through pregnancy, LFTs are routinely monitored at each antenatal clinic appointment as a marker for potential obstetric complications (e.g. HELLP, pre-eclampsia and acute fatty liver), particularly in the final trimester.

In those diagnosed late and not receiving HBV treatment incorporated into ART, LFT flares may be seen shortly after delivery, which in some cases relates to HBeAg seroconversion or fluctuations in HBV DNA levels. Inflammatory flares may be severe, particularly in women/people with cirrhosis, and can occur as a result of viral escape and HBV viraemia if drugs with anti-HBV activity are stopped. In a randomised controlled trial in women with HBV mono-infection comparing lamivudine with placebo for reducing vertical transmission of HBV, an immediate increase in HBV DNA levels was observed on discontinuation

of lamivudine postpartum [23]. Similarly, hepatitis flares among individuals with HIV/HBV have been reported on discontinuation of lamivudine, emtricitabine and tenofovir DX; in the Swiss HIV observational cohort, elevation of liver enzyme levels occurred in 29% of those who discontinued lamivudine and in 5% this was severe with three participants presenting with fulminant hepatitis [24] at a median time of 6 weeks after discontinuation.

Pregnancy induces a state of relative immune suppression. Postpartum flares of liver inflammation have been described for HBV, HCV and autoimmune hepatitis. Although rarely leading to fulminant hepatitis, careful monitoring of flares is needed in the postpartum period. HBeAg positivity is a common predictor of flares, most of which are asymptomatic and resolve within 12 months [25].

9.1.7 Obstetric management of HIV/HBV co-infection

Recommendation

- We suggest against routine caesarean section for the purpose of reducing vertical transmission of HBV (Grade 2A) when all suggested immunoprophylaxis is followed.

Rationale

No data exist to support any benefit from caesarean section in women/people with both HIV and HBV, and no robust randomised controlled trial has been conducted in pregnant women/people with HBV alone. A meta-analysis including 10 eligible studies confirmed that there may not be additional benefit beyond appropriate vaccination and hepatitis B immunoglobulin (HBIG) use [26]. The findings of another meta-analysis suggested that oral antiviral therapies in pregnancy, including lamivudine, telbivudine and tenofovir DX, reduce the rates of vertical HBV transmission [27].

The efficacy of oral nucleos(t)ide inhibitors in reducing the rate of vertical transmission in mono-infection, the efficacy of these agents in reducing HBV DNA in non-pregnant individuals with HBV and HIV, and the use of tenofovir with emtricitabine as standard practice in those with co-infection collectively provide further support against recommending caesarean section in pregnant women/people with HIV and HBV.

9.1.8 Management of neonates born to women/people with HIV/HBV co-infection

Recommendation

- We recommend that infants born to women/people with HIV/HBV co-infection should be managed with HBV vaccination with or without HBIG (Grade 1D).

Auditable outcome

- The proportion of infants born to women/people with HIV/HBV who receive infant HBV vaccination.

Rationale

Infants born to women/people with HIV/HBV co-infection should be given HBV vaccination with or without HBIG according to the recommendations in the Green Book [28].

The Green Book currently recommends that all infants born to mothers with HBV should receive a complete course of vaccination; the first dose of vaccine should be given as soon as possible, and ideally within 24 hours of birth.

Current guidance is that HBIG should be given to the neonate if the mother/birthing parent:

- Has an HBV DNA concentration >1x10^6 IU/mL at any point during the pregnancy;
- Is positive for both HBsAg and HBeAg;
- Is HBsAg positive and anti-HBe negative;
- Is HBsAg positive and anti-HBe status is unknown;
- Is HBsAg positive and the neonate weighs ≤1500 g [28].

Immunoprophylaxis with HBV vaccine with or without HBIG given to the neonate has been shown in separate meta-analyses of randomised controlled trials to significantly reduce vertical transmission from women with HBV alone. In the absence of neonatal immunisation with HBV vaccine with or without HBIG, the rate of vertical transmission from a pregnant woman with HBV alone is 70–90% if the woman is both HBsAg and HBeAg positive and 10–40% if HBsAg positive but HBeAg negative [29]. By co-administering HBV vaccine (effectiveness of vaccine *vs* placebo: relative risk [RR] 0.28, 95% CI 0.2–0.4) and HBIG (effectiveness of HBIG/vaccine *vs* vaccine alone: RR 0.54, 95% CI 0.41–0.73), transmission rates can be reduced to between 0% and 14% [30]. The most important determinant of prophylaxis failure has been shown to be maternal serum HBV DNA levels. Failure of the 'birth dose' of the vaccine and HBIG in up to 9% of neonates despite appropriate post-delivery immunoprophylaxis occurs mainly because of infection *in utero* [31].

A randomised controlled trial of tenofovir DX given to mothers with HBV alone (in addition to the birth dose of the vaccine and HBIG for the neonate) showed a significant reduction in vertical transmission in the tenofovir DX group compared to those who received usual care without antiviral therapy [15]. All mothers randomly assigned to the tenofovir DX group received therapy from week 32 onwards. Vertical transmission of infection was only seen from mothers with HBV DNA >200 IU/mL.

9.2 HCV

9.2.1 Background and epidemiology

Antenatal prevalence of chronic HCV ranges from less than 1% to about 2.5%, increasing to 3–50% in women living with HIV; the wide range reflects the variation in the proportion of people who inject drugs or who are from high HCV prevalence areas in the cohorts studied [32-35]. The overall rate of vertical transmission for HCV is approximately 5% (range 2–10%) if the woman has HCV mono-infection [36,37].

In untreated HIV/HCV, there is a 2-fold increase in perinatal HCV transmission compared to HCV alone [38,39]. In more recent European cohort studies in which the majority of women had HIV/HCV co-infection and were on ART, there was a lower rate of HCV vertical transmission (4.0–5.9%) [40,41]. Effective use of ART in mothers with co-infection has been shown to reduce the risk of HCV transmission (OR 0.26) [36,42].

Numerous studies have shown that the HCV viral load correlates with the risk of HCV vertical transmission, and it is likely that there is a linear relationship between HCV viral load and transmission as for HIV [43-45]. The risk of vertical HIV transmission is increased in HIV/HCV co-infection in the absence of ART [46,47].

9.2.2 Diagnosis and monitoring

Recommendations

- On diagnosis of new HCV infection in pregnant women/people living with HIV, we recommend confirmation of HCV viraemia with quantitative analysis of RNA and genotype, and assessment of hepatic inflammation/fibrosis and liver function and concomitant liver disease should be performed (Grade 1C).
- In pregnant women/people with HIV/HCV co-infection, we recommend that LFTs should be repeated at 2 and 4 weeks after commencing ART to detect the presence of hepatotoxicity or IRIS and then monitored regularly throughout pregnancy and the postpartum period (Grade 1C).
- All pregnant women/people with HIV and newly diagnosed HCV, or those with detectable HCV RNA and HIV, should be managed jointly with an experienced clinician, and those with advanced cirrhosis should be managed in a tertiary centre with a hepatologist (GPP).
- The following investigations are indicated (these should also be available for women/people diagnosed preconception) (GPP):
  - HCV markers: HCV antibody (confirmed by a second test), HCV RNA (viral load) and genotype;
  - Other hepatitis viruses: HAV IgG to assess immunity, HBsAg, anti-HBc and anti-HBs.

Rationale

See Section 9.1.3 for details about liver function testing, liver inflammation/fibrosis assessment and HCC screening, and Section 9.1.6 for discussion about inflammatory flares.

It is important where cirrhosis is found to be present that there is close liaison with a hepatologist because of a significantly increased rate of complications [48]. However, in the absence of decompensated disease, most women with cirrhosis do not have obstetric complications from their HCV infection.

It is recognised that a small number of individuals with both HIV and HCV are HCV antibody negative but HCV viraemic [49]. Where there is evidence of liver inflammation or fibrosis, profound immune deficiency or risk factors, an HCV viral load assay should be performed. There is no evidence that HCV can be transmitted vertically in the absence of HCV viraemia. Infants born to women/people who achieved sustained virological response with HCV treatment prior to the pregnancy, and remain aviraemic but HCV antibody positive, do not need any additional follow-up, unless there is evidence of re-infection in the birth parent.

Despite the rarity of acute HCV infection in pregnancy, HCV RNA should be measured where there is a sudden unexplained increase in transaminases and/or a history of exposure even if an HCV antibody test is negative. Where acute HCV infection is confirmed, HCV viral load should be monitored throughout pregnancy in case there is spontaneous clearance. Involvement of a clinician experienced in the management of hepatitis is important both for initial and postpartum care when treatment decisions are made.

9.2.3 Antiviral treatment

Recommendations

- We suggest that women/people of reproductive potential with both HIV and HCV wishing to become pregnant should be prioritised for direct-acting antiviral (DAA)-based HCV therapy prior to conception (Grade 2D).
- We recommend that all women/people with HIV/HCV co-infection with HCV viraemia in pregnancy should be referred for postpartum HCV treatment (Grade 1A).
- We recommend that ART should be continued postpartum in all women/people with HIV/HCV regardless of HCV viraemia, fibrosis stage or CD4 cell count (Grade 1A).

Auditable outcomes

- The proportion of women/people with HIV/HCV co-infection who are referred to an HCV management service.
- The proportion of women/people with HIV/HCV co-infection who receive postpartum HCV treatment.

Rationale

The current standard treatment for HCV is DAA-based interferon (IFN)-free therapy with or without ribavirin [50]. There is a lack of available data on the safety, pharmacokinetics and efficacy of HCV antiviral therapy during pregnancy, therefore HCV treatment is not recommended during pregnancy. If conception occurs during treatment for HCV with ribavirin or pegylated IFN, HCV treatment should be discontinued immediately.

Ribavirin is teratogenic and/or embryocidal in animals, and the risk of teratogenicity may persist for weeks after discontinuation. The results from the Ribavirin Pregnancy Registry do not clearly support teratogenicity of ribavirin in humans, although the small sample size meant the study lacked power [51]. Care must be taken to avoid pregnancy during therapy and for the 6 months after completion of therapy in both women/people of reproductive potential and in any partner of those who are taking ribavirin therapy. At least two reliable forms of effective contraception must be used.

There are only limited data on the possible teratogenicity of DAA-based IFN-free therapy without ribavirin. The currently licensed DAA therapies sofosbuvir, sofosbuvir/ledipasvir fixed-dose combination (FDC), daclatasvir, dasabuvir, grazoprevir/elbasvir FDC and sofosbuvir/velpatasvir FDC have not shown teratogenicity in small-animal studies, but have variable ability to cross the placenta and enter breastmilk [52-54]. Paritaprevir/ribavirin/ombitasvir FDC and daclatasvir have both shown a risk of malformations in small animals at supranormal dose exposures [55,56]. An open-label Phase 1 pharmacokinetic study involving 29 pregnant women demonstrated no clinically significant pharmacokinetic differences in ledipasvir/sofosbuvir in pregnant women compared to the non-pregnant

group. This study demonstrated that ledipasvir/sofosbuvir was tolerated and safe, albeit the sample size was small [57]. To date, there remains insufficient evidence to recommend the use of DAA therapies in pregnancy. If pregnancy has occurred during treatment with DAA-based therapy, individual case-by-case risk assessment should be followed, and the case should be discussed and managed in a multidisciplinary approach.

Therefore, the view of the writing group is that women/people living with HIV/HCV wishing to become pregnant should be prioritised for DAA-based anti-HCV therapy regardless of fibrosis stage and should delay pregnancy until after treatment is completed or 6 months following ribavirin-based treatment completion.

9.2.4 HBV vaccination

See Section 9.3 for recommendations on HAV vaccination.

Recommendation

- We recommend vaccination against HBV in non-immune women/people with HIV and HCV co-infection after the first trimester, unless already immune, as per the BHIVA immunisation guidelines [58] (Grade 1C).

Auditable outcomes

- The proportion of women/people living with HIV/HCV co-infection who are non-immune to HBV.
- The proportion of women/people living with HIV/HCV co-infection who accept HBV vaccination.
- The proportion of women/people living with HIV/HCV co-infection who are non-immune to HAV.
- The proportion of women/people living with HIV/HCV co-infection who accept HAV vaccination.

Rationale

Immunisation for HBV uses an inactivated vaccine. There are limited data available on the use of HBV vaccination in pregnancy, with no studies in pregnant women living with HIV, and no randomised trials have been conducted to determine the optimum dosing schedule for use in pregnancy. Nevertheless, according to national guidelines, HBV immunisation is not contraindicated in pregnancy, including in pregnant women/people with HIV/HCV co-infection [58].

In single-arm, open-label studies in persons without HIV, seroconversion rates for HBV are no different in the pregnant and non-pregnant woman and no fetal risks have been reported [59]. A retrospective cohort study of pregnancies in the US Vaccine Safety Datalink demonstrated no increased risk of adverse events among 1399 pregnant women who received HBV vaccination [60]. In a prospective clinical trial in pregnant women, an accelerated schedule at 0, 1 and 4 months was found to be effective, well tolerated and had the advantage of potential completion prior to delivery [61]. Individuals with higher CD4 cell counts and on ART generally show improved responses to vaccination. Regardless of CD4 cell count, anti-HBs level should be measured 6–8 weeks after completion of the vaccination schedule. In a systematic review and meta-analysis of five studies, an increased-dose HBV vaccination schedule improved anti-HBs response rates compared to standard-dose HBV vaccination (OR 1.96, 95% CI 1.47–2.61) with separate randomised trial data demonstrating improved serological response with four-dose regimens [62].

It is essential to vaccinate non-immune women/people with HIV/HCV co-infection against HBV, especially if they are not receiving a tenofovir-based regimen.

9.2.5 Mode of delivery

Recommendation

- We suggest vaginal delivery can be planned if the woman/person is on effective ART for HIV with an undetectable HIV viral load irrespective of HCV viral load in the absence of obstetric complications (Grade 2C).

Rationale

As HCV antiviral therapy is contraindicated in pregnancy due to possible teratogenicity, mode of delivery remains the only possible risk factor amenable to intervention. No randomised studies of caesarean section compared to vaginal delivery to prevent vertical transmission of HCV have been performed.

Among women with HCV alone, a meta-analysis failed to show a significant decrease in HCV vertical transmission following caesarean section compared with vaginal delivery (OR 1.10–1.19) [63]. In 2001, in the European Paediatric Hepatitis Network (EPHN) cohort (1474 women with HCV), a subgroup analysis of women with both HIV and HCV (*n*=503; 35.4%) demonstrated a reduced risk of vertical transmission of HCV with caesarean section (OR 0.43, 95% CI 0.23–0.80) [64]. However, in a later analysis in 2005, also from the EPHN, of 1479 women with HCV (HIV/HCV co-infection in 208; 15.0%), no such association was found (OR 0.76, 95% CI 0.23–2.53) [42]. In the 2005 analysis, the rate of vertical transmission of HCV was reduced (8.7% in 2005 *vs* 13.9% in 2001). Widespread use of ART in the 2005 cohort was associated with a significant HCV viral load reduction compared with HIV monotherapy or no HIV therapy (OR 0.26, 95% CI 0.07–1.01), possibly explaining the finding of reduced vertical transmission of HCV. In addition, in a small French cohort of women with both HIV and HCV (29% on ART), rates of vertical transmission did not differ significantly among infants born by vaginal delivery or caesarean section [65]. The authors of a systematic review concluded that no intervention, in terms of mode of delivery, obstetric intervention or avoidance of breastfeeding, reduces the risk of HCV transmission [66].

For pregnant women/people with HIV/HCV and cirrhosis, mode of delivery should be discussed in conjunction with a hepatologist.

9.2.6 Management of neonates born to women/birthing parents with HIV/HCV co-infection

Infants born to women/people with HIV/HCV co-infection should be screened for HCV according to national guidance [67] and vaccinated against HBV as per the national schedule [28] (see also Section 11.5 for guidance on management of the infant).

9.3 HAV vaccination

Recommendation

- We recommend HAV vaccination for all HAV non-immune women/people with HIV and HBV and/or HCV after the first trimester, unless already immune as per the BHIVA immunisation guidelines [58] (Grade 1A).

Rationale

An inactivated vaccine is used for HAV vaccination. Data for HAV vaccination in pregnancy are limited. Nevertheless, according to guidelines, HAV vaccination is not contraindicated in pregnancy, including in pregnant women with both HIV/HBV and HIV/HCV co-infection [58]. Individuals with higher CD4 cell counts and on ART generally show improved responses to HAV vaccination [68]. People living with HIV with CD4 cell counts <350 cells/mm^3 should receive three instead of the standard two doses of HAV vaccine [58].

9.4 References

1. Lacombe K, Bottero J, Lemoine M *et al*. HIV/hepatitis B virus co-infection: current challenges and new strategies. *J Antimicrob Chemother* 2010; **65**: 10–17.

2. Wong GL, Wen WH, Pan CQ. Hepatitis B-management of acute infection and active inflammation in pregnancy-a hepatologist's perspective. *Best Pract Res Clin Obstet Gynaecol* 2020; **68**: 54–65.

3. Jiang R, Wang T, Yao Y *et al*. Hepatitis B infection and intrahepatic cholestasis of pregnancy: a systematic review and meta-analysis. *Medicine (Baltimore)* 2020; **99**: e21416.

4. Bhattacharya D, Guo R, Tseng C-H *et al*. Maternal HBV viremia and association with adverse infant outcomes in women living with HIV and HBV. *Pediatr Infect Dis* 2021; **40**: e56–e61.

5. Echosens. *FibroScan® procedure for users*. Available at: https://www.echosens.com/fibroscanprocedure/ (accessed August 2024).

6. Stenberg Ribeiro M, Hagström H, Stål P, Ajne G. Transient liver elastography in normal pregnancy - a longitudinal cohort study. *Scand J Gastroenterol* 2019; **54**: 761–765.

7. Hepatitis C Online. *AST to Platelet Ratio Index (APRI) Calculator.* 2024. Available at: https://www.hepatitisc.uw.edu/page/clinical-calculators/apri (accessed August 2024).

8. Hepatitis C Online. *Fibrosis-4 (FIB-4) Calculator.* 2024. Available at: https://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4 (accessed August 2024).

9. Shilaih M, Marzel A, Scherrer AU *et al*. Dually active HIV/HBV antiretrovirals as protection against incident hepatitis B infections: potential for prophylaxis. *J Infect Dis* 2016; **214**: 599–606.

10. Schmutz G, Nelson M, Lutz T *et al*. Combination of tenofovir and lamivudine versus tenofovir after lamivudine failure for therapy of hepatitis B in HIV-coinfection. *AIDS* 2006; **20**: 1951–1954.

11. Chan HL, Fung S, Seto WK *et al*. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of HBeAg-positive chronic hepatitis B virus infection: a randomised, double-blind, phase 3, non-inferiority trial. *Lancet Gastroenterol Hepatol* 2016; **1**: 185–195.

12. Brunetto M, Lim YS, Gane E *et al*. A phase 3 study comparing tenofovir alafenamide to tenofovir disoproxil fumarate in patients with HBeAg-negative, chronic hepatitis B: efficacy and safety results at week 96. *J Hepatol* 2017; **66**: S25–S26.

13. Matthews G. The management of HIV and hepatitis B coinfection. *Curr Opin Infect Dis* 2007; **20**: 16–21.

14. Brook G, Main J, Nelson M *et al*. British HIV Association guidelines for the management of coinfection with HIV-1 and hepatitis B or C virus 2010. *HIV Med* 2010; **11**: 1–30.

15. Pan CQ, Duan Z, Dai E *et al*. Tenofovir to prevent hepatitis B transmission in mothers with high viral load. *N Engl J Med* 2016; **374**: 2324–2334.

16. Hu YH, Liu M, Yi W *et al*. Tenofovir rescue therapy in pregnant females with chronic hepatitis B. *World J Gastroenterol* 2015; **21**: 2504–2509.

17. Dore GJ, Cooper DA, Pozniak AL *et al*. Efficacy of tenofovir disoproxil fumarate in antiretroviral therapy-naive and -experienced patients coinfected with HIV-1 and hepatitis B virus. *J Infect Dis* 2004; **189**: 1185–1192.

18. Avihingsanon A, Lewin SR, Kerr S *et al*. Efficacy of tenofovir disoproxil fumarate/emtricitabine compared with emtricitabine alone in antiretroviral-naive HIV-HBV coinfection in Thailand. *Antivir Ther* 2010; **15**: 917–922.

19. Matthews GV, Avihingsanon A, Lewin SR *et al*. A randomized trial of combination hepatitis B therapy in HIV/HBV coinfected antiretroviral naive individuals in Thailand. *Hepatology* 2008; **48**: 1062–1069.

20. US Food and Drug Administration. *NDA 21-797 and NDA 21-798. Baraclude™*. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2005/021797,021798lbl.pdf (accessed June 2024).

21. Zhang H, Pan CQ, Pang Q *et al*. Telbivudine or lamivudine use in late pregnancy safely reduces perinatal transmission of hepatitis B virus in real-life practice. *Hepatology* 2014; **60**: 468–476.

22. Tiribelli C, Rigato I. Liver cirrhosis and pregnancy. *Ann Hepatol* 2006; **5**: 201.

23. Xu WM, Cui YT, Wang L *et al*. Lamivudine in late pregnancy to prevent perinatal transmission of hepatitis B virus infection: a multicentre, randomized, double-blind, placebo-controlled study. *J Viral Hepat* 2009; **16**: 94–103.

24. Bellini C, Keiser O, Chave JP *et al*. Liver enzyme elevation after lamivudine withdrawal in HIV-hepatitis B virus co-infected patients: the Swiss HIV Cohort Study. *HIV Med* 2009; **10**: 12–18.

25. Giles M, Visvanathan K, Lewin S *et al*. Clinical and virological predictors of hepatic flares in pregnant women with chronic hepatitis B. *Gut* 2015; **64**: 1810–1815.

26. Chang MS, Gavini S, Andrade PC, McNabb-Baltar J. Caesarean section to prevent transmission of hepatitis B: a meta-analysis. *Can J Gastroenterol Hepatol* 2014; **28**: 439–444.

27. Brown RS Jr, McMahon BJ, Lok AS *et al*. Antiviral therapy in chronic hepatitis B viral infection during pregnancy: a systematic review and meta-analysis. *Hepatology* 2016; **63**: 319–333.

28. The Green Book on Immunisation. *Chapter 18: Hepatitis B*. 2024. Available at: https://assets.publishing.service.gov.uk/media/66bb6f4749b9c0597fdb0eed/Hepatitis-B-green-book-chapter_18_20240813.pdf (accessed June 2024).

29. Umar M, Hamama-Tul-Bushra, Umar S, Khan HA. HBV perinatal transmission. *Int J Hepatol* 2013; **2013**: 875791.

30. Lee C, Gong Y, Brok J *et al*. Effect of hepatitis B immunisation in newborn infants of mothers positive for hepatitis B surface antigen: systematic review and meta-analysis. *BMJ* 2006; **332**: 328–336.

31. Wiseman E, Fraser MA, Holden S *et al*. Perinatal transmission of hepatitis B virus: an Australian experience. *Med J Aust* 2009; **190**: 489–492.

32. Barth RE, Huijgen Q, Taljaard J, Hoepelman AI. Hepatitis B/C and HIV in sub-Saharan Africa: an association between highly prevalent infectious diseases. A systematic review and meta-analysis. *Int J Infect Dis* 2010; **14**: e1024–1031.

33. Landes M, Newell ML, Barlow P *et al*. Hepatitis B or hepatitis C coinfection in HIV-infected pregnant women in Europe. *HIV Med* 2008; **9**: 526–534.

34. Thomas SL, Newell ML, Peckham CS *et al*. A review of hepatitis C virus (HCV) vertical transmission: risks of transmission to infants born to mothers with and without HCV viraemia or human immunodeficiency virus infection. *Int J Epidemiol* 1998; **27**: 108–117.

35. Thompson P, Mpody C, Sayre W *et al.*; CQI-PMTCT study team. Hepatitis C prevalence and quality of health services among HIV-positive mothers in the Democratic Republic of the Congo. *Sci Rep* 2022; **12**: 1384.

36. Benova L, Mohamoud YA, Calvert C, Abu-Raddad LJ. Vertical transmission of hepatitis C virus: systematic review and meta-analysis. *Clin Infect Dis* 2014; **59**: 765–773.

37. Conte D, Fraquelli M, Prati D *et al*. Prevalence and clinical course of chronic hepatitis C virus (HCV) infection and rate of HCV vertical transmission in a cohort of 15,250 pregnant women. *Hepatology* 2000; **31**: 751–755.

38. Mast EE, Hwang LY, Seto DS *et al*. Risk factors for perinatal transmission of hepatitis C virus (HCV) and the natural history of HCV infection acquired in infancy. *J Infect Dis* 2005; **192**: 1880–1889.

39. Gibb DM, Goodall RL, Dunn DT *et al*. Mother-to-child transmission of hepatitis C virus: evidence for preventable peripartum transmission. *Lancet* 2000; **356**: 904–907.

40. Benhammou V, Tubiana R, Matheron S *et al*. HBV or HCV coinfection in HIV-1-infected pregnant women in France: prevalence and pregnancy outcomes. *J Acquir Immune Defic Syndr* 2018; **77**: 439–450.

41. Snijdewind IJ, Smit C, Schutten M *et al*. Low mother-to-child-transmission rate of hepatitis C virus in cART treated HIV-1 infected mothers. *J Clin Virol* 2015; **68**: 11–15.

42. European Paediatric Hepatitis C Virus Network. A significant sex – but not elective cesarean section – effect on mother-to-child transmission of hepatitis C virus infection. *J Infect Dis* 2005; **192**: 1872–1879.

43. Garcia-Tejedor A, Maiques-Montesinos V, Diago-Almela VJ *et al*. Risk factors for vertical transmission of hepatitis C virus: a single center experience with 710 HCV-infected mothers. *Eur J Obstet Gynecol Reprod Biol* 2015; **194**: 173–177.

44. Ngo-Giang-Huong N, Jourdain G, Sirirungsi W *et al*. Human immunodeficiency virus-hepatitis C virus coinfection in pregnant women and perinatal transmission to infants in Thailand. *Int J Infect Dis* 2010; **14**: e602–607.

45. Zanetti AR, Tanzi E, Romano L *et al*. A prospective study on mother-to-infant transmission of hepatitis C virus. *Intervirology* 1998; **41**: 208–212.

46. Hershow RC, Riester KA, Lew J *et al*. Increased vertical transmission of human immunodeficiency virus from hepatitis C virus-coinfected mothers. Women and Infants Transmission Study. *J Infect Dis* 1997; **176**: 414–420.

47. England K, Thorne C, Newell ML. Vertically acquired paediatric coinfection with HIV and hepatitis C virus. *Lancet Infect Dis* 2006; **6**: 83–90.

48. Tiribelli C, Rigato I. Liver cirrhosis and pregnancy. *Ann Hepatol* 2006; **5**: 201.

49. George SL, Gebhardt J, Klinzman D *et al*. Hepatitis C virus viremia in HIV-infected individuals with negative HCV antibody tests. *J Acquir Immune Defic Syndr* 2002; **31**: 154–162.

50. European Association for the Study of the Liver. EASL recommendations on treatment of hepatitis C 2016. *J Hepatol* 2017; **66**: 153–194.

51. Sinclair SM, Jones JK, Miller RK et al. Final results from the ribavirin pregnancy registry, 2004-2020. *Birth Defects Res* 2022; **114**: 1376–1391.

52. eMC. *SmPC Sovaldi 400 mg film coated tablets (sofosbuvir).* Available at: www.medicines.org.uk/emc/product/5247 (accessed June 2023).

53. eMC. *SmPC Harvoni 90 mg/400 mg film-coated tablets (sofosbuvir/ledipasvir).* Available at: www.medicines.org.uk/emc/product/3461/smpc (accessed June 2023).

54. eMC. *SmPC Exviera 250 mg film-coated tablets (dasabuvir sodium monohydrate).* Available at: www.medicines.org.uk/emc/product/6529/smpc#gref (accessed June 2023).

55. eMC. *SmPC Zepatier 50 mg/100 mg film coated tablets (elbasvir/grazoprevir).* Available at: www.medicines.org.uk/emc/medicine/32584 (accessed June 2023).

56. eMC. *SmPC Epclusa 400 mg/100 mg film coated tablets (sofosbuvir/velpatasvir).* Available at: www.medicines.org.uk/emc/product/7294 (accessed June 2023).

57. Chappell CA, Scarsi KK, Kirby BJ *et al*. Ledipasvir plus sofosbuvir in pregnant women with hepatitis C virus infection: a phase 1 pharmacokinetic study. *Lancet Microbe* 2020; **1**: e200–e208.

58. Geretti AM, Brook G, Cameron C *et al*. British HIV Association guidelines on the use of vaccines in HIV-positive adults 2015. *HIV Med* 2016; **17**: s2–s81. Available at: https://www.bhiva.org/vaccination-guidelines (accessed June 2024).

59. Gupta I, Ratho RK. Immunogenicity and safety of two schedules of hepatitis B vaccination during pregnancy. *J Obstet Gynaecol Res* 2003; **29**: 84–86.

60. Groom HC, Irving SA, Koppolu P *et al*. Uptake and safety of hepatitis B vaccination during pregnancy: a Vaccine Safety Datalink study. *Vaccine* 2018; **36**: 6111–6116.

61. Sheffield JS, Hickman A, Tang J *et al*. Efficacy of an accelerated hepatitis B vaccination program during pregnancy. *Obstet Gynecol* 2011; **117**: 1130–1135.

62. Ni JD, Xiong YZ, Wang XJ, Xiu LC. Does increased hepatitis B vaccination dose lead to a better immune response in HIV-infected patients than standard dose vaccination: a meta-analysis? *Int J STD AIDS* 2013; **24**: 117–122.

63. Ghamar Chehreh ME, Tabatabaei SV, Khazanehdari S, Alavian SM. Effect of cesarean section on the risk of perinatal transmission of hepatitis C virus from HCV-RNA+/HIV- mothers: a meta-analysis. *Arch Gynecol Obstet* 2011; **283**: 255–260.

64. European Paediatric Hepatitis C Virus Network. Effects of mode of delivery and infant feeding on the risk of mother-to-child transmission of hepatitis C virus. European Paediatric Hepatitis C Virus Network. *BJOG* 2001; **108**: 371–377.

65. Marine-Barjoan E, Berrebi A, Giordanengo V *et al*. HCV/HIV co-infection, HCV viral load and mode of delivery: risk factors for mother-to-child transmission of hepatitis C virus? *AIDS* 2007; **21**: 1811–1815.

66. Cottrell EB, Chou R, Wasson N *et al*. Reducing risk for mother-to-infant transmission of hepatitis C virus: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2013; **158**: 109–113.

67. Public Health England. *UK Standards for Microbiology Investigations*. 2018. Available at: https://www.rcpath.org/static/9d226b34-3c49-4f5c-b0e4f9a2b3318d60/uk-smi-v-8i3-vertical-and-perinatal-transmission-of-hepatitis-c-december-2018-pdf.pdf (accessed August 2024).

68. Jabłonowska E, Kuydowicz J. Durability of response to vaccination against viral hepatitis A in HIV-infected patients: a 5-year observation. *Int J STD AIDS* 2014; **25**: 745–750.

10 Obstetric management

10.1 Antenatal management

Recommendation

- We recommend the combined screening test for fetal aneuploidies and non-invasive prenatal testing (NIPT) following a high-risk screening result, as this has the best sensitivity and specificity and will minimise the number of women/people who may need invasive testing (Grade 1A).

Rationale

The National Screening Committee [1] and the NICE antenatal guidelines [2] recommend that ultrasound screening for fetal anomaly should be offered to all pregnant women between 18^{+0} and 20^{+6} weeks' gestation. There is no evidence to support altering this for pregnant women/people living with HIV because there is no increase in fetal anomalies in HIV-exposed infants or infants who acquire HIV *in utero*.

The evidence from prospective reports of first-trimester ART exposure to the APR [3] does not support the need for increased surveillance with the most commonly prescribed therapies, although with newer medication the knowledge base is inevitably more limited (see Section 8.1.2).

NICE antenatal guidelines [2] also recommend that all women should be offered screening for Down's syndrome, Edwards' syndrome and Patau's syndrome. The screening test most commonly used is the combined test carried out between 11^{+0} and 13^{+6} weeks' gestation. This includes maternal age, nuchal translucency, crown–rump length and β-human chorionic gonadotrophin (βHCG) and pregnancy-associated plasma protein A (PAPP-A) levels. PAPP-A levels and nuchal translucency are unaltered by HIV infection or ART, but levels of βHCG are increased [4]. In the general population the combined test has a detection rate of 92.6% with a false-positive rate of 5.2% [5].

If the nuchal translucency measurement cannot be obtained or for women/people who present too late for the combined test, the most cost-effective serum screening test for Down's syndrome is the quadruple test which should be offered between 14^{+2} and 20^{+0} weeks' gestation [2]. However, significantly increased levels of βHCG and AFP and lower levels of unconjugated oestriol (three of the four elements of the quadruple test) have been observed in women living with HIV [6-9]. A reduction in AFP in individuals treated with PI-based ART has also been reported compared to no ART or a different ART regimen [9]. Down's syndrome is associated with increased βHCG levels, therefore HIV infection *per se* may increase the false-positive rate and thus increase the number of NIPT as well as invasive tests offered to pregnant women/people living with HIV compared with the general population [10].

NIPT of free fetal DNA in maternal serum is offered to women following a higher-risk screening result (between 1 in 2 and 1 in 150) [2]. NIPT has been shown to be highly effective at screening for fetal aneuploidy, with a lower false-positive rate and higher positive predictive value than standard screening [11].

10.2 Invasive prenatal testing

Recommendations

- We recommend that invasive prenatal diagnostic testing should not be performed until after the HIV status of the woman/person is known (Grade 1C).
- We recommend that if not virally suppressed, the invasive diagnostic test or procedure should be delayed until viral suppression is achieved; if an invasive procedure cannot be delayed, there should be a multidisciplinary discussion with the obstetric and HIV teams about the timing of the procedure and intensification of the ART regimen with the suggestions in Section 8.7.2 (Grade 1D).

Rationale

Data suggest that amniocentesis does not increase the risk of HIV vertical transmission among pregnant women virologically suppressed on ART [12-16]. There are minimal data on other forms of prenatal invasive testing. All clinicians performing a prenatal invasive test should know the HIV status of the woman/person; if the HIV status is unknown, the invasive test should be delayed until the HIV result is available. Amniocentesis should be deferred until the viral load is <50 copies/mL. The fetal medicine team should discuss management with an HIV physician in cases in which a woman/person has a detectable HIV viral load.

In the pre-ART era, the French Paediatric HIV Infection Study Group observed an increased risk of HIV vertical transmission from women, the majority of whom had not received any ART, who had 'antenatal procedures' that included amniocentesis, cerclage, laser therapy and amnioscopy (RR 1.9, 95% CI 1.3–2.7; *P*=0.003) [17].

Studies in the ART era support the safety of invasive testing in women/people on suppressive ART. A study of 9302 pregnancies in France (including 166 during which an amniocentesis was performed) showed an increased risk of vertical transmission of HIV among untreated women; there were no transmissions among those on combination ART [15]. In an Italian study, there were no cases of vertical transmission in 86 women on combination ART; 78 of these women underwent amniocentesis and eight underwent chorionic villus sampling [13]. The NSHPC (now ISOSS) reported on 2163 pregnancies in the UK and Ireland with no transmissions among the 27 pregnancies in which invasive procedures were performed (25 had amniocentesis, one chorionic villus sampling and one cordocentesis) [12]. Further studies have shown no evidence of HIV transmission among women on ART, including nine women on ART in France (2001–2006) [14] and 17 women on ART in Portugal (1996–2011) [16]. In the Portuguese study, transmission occurred from one of seven women either not diagnosed with HIV prior to amniocentesis or not treated prior to the procedure.

There have been no studies and few case reports in the effective ART era examining cordocentesis. For evidence relating to choice of antiretroviral agents associated with rapid viral load decay, see Section 8.

10.3 Multiple pregnancy

There have been no published studies comparing multiple versus singleton pregnancies in women/people living with HIV. Based on expert opinion, there is no evidence of increased risk of vertical transmission in multiple pregnancies.

Multiple pregnancies are more common in older pregnant women with HIV than in the general population without HIV [18]. The proportion of pregnant women living with HIV over 40 years of age has increased from 2% in the period 2000–2004 to 9% in 2010–2014 [18], therefore it is likely that further data on multiple pregnancies will emerge. Multiple pregnancies should be managed according to the obstetric need of the woman/person and as per the NICE multiple pregnancy guidelines [19].

10.4 External cephalic version (ECV)

Recommendation

- We suggest that ECV can be offered at term to women/people living with HIV on ART with a plasma viral load <50 copies/mL (Grade 2D).

Rationale

There is less obstetric risk to the infant and mother/birthing parent when the fetus is cephalic (head down) at the time of birth. ECV is the manipulation of the fetus, through the maternal/parental abdomen, from a breech presentation to a cephalic presentation. If the fetus is not cephalic by 36 weeks of pregnancy, ECV reduces the likelihood that the fetus will present as breech at the time of birth, and thus reduces the chance of needing a caesarean section. There is no published evidence to help decision-making regarding ECV in the pregnant woman/person living with HIV. For the general maternity population, ECV is recommended [20]. There is a low rate of complications, with an estimated 0.5% incidence of caesarean section within 24 hours of ECV [20].

There is no direct evidence to suggest that ECV increases the risk of vertical transmission of HIV. The incidence of fetomaternal haemorrhage after ECV has been estimated at 2.4%, which represents the new presence of fetal blood cells in the maternal circulation after the procedure [21]. It has been postulated that, due to the structure and function of the placenta, the risk of maternal blood entering the fetal circulation due to ECV is much lower [21]. It is also reassuring that no evidence of maternal–fetal transfusion was found in a randomised trial of fundal pressure to expel the neonate during caesarean section [22].

Therefore, it is the opinion of the writing group that ECV can be offered to women/people taking ART with a breech presentation who have a plasma viral load <50 copies/mL. ECV may be offered from 36 weeks of gestation to nulliparous women/people and from 37 weeks for those who are multiparous, in line with current guidance [20].

10.5 Fetal surveillance

Recommendations

- We recommend referring pregnant women/people living with HIV to a clinician with an interest in PTB prevention if additional risk factors for PTB are present (Grade 1C).
- We recommend that HIV infection (treated or untreated) should be considered a moderate risk factor in the risk assessment for fetal growth restriction (Grade 1C).

Auditable outcome

- Proportion of women/people living with HIV referred to a clinician with an interest in PTB prevention if additional risk factors for PTB are present.

Rationale

Preventing PTB and management of fetal growth restriction are two elements of the NHS England guidance 'Saving babies' lives', a care bundle for reducing perinatal mortality (SBLCB3) [23]. This guidance recommends that all women are assessed for risk of PTB at booking, and women at increased risk are referred to an obstetrician with an interest in PTB prevention. Data on the association between adverse perinatal outcomes, including PTB, and maternal HIV and ART are complex and are summarised in Appendix 3.

Pregnant women/people living with HIV (whether or not receiving ART) may be at higher risk of PTB compared with those without HIV; the writing group recommends referral to a clinician with an interest in PTB prevention if additional risk factors are present.

The evidence also suggests that pregnant women/people living with HIV (whether or not receiving ART) may be at increased risk of fetal growth restriction compared to those without HIV. Therefore we recommend that HIV infection should be considered a moderate risk factor for fetal growth restriction in the risk assessment that is recommended in NHS England's guidance SBLCB3 for all women by 14 weeks' gestation [23].

There are currently insufficient data on the associations between HIV and ART and gestational diabetes, hypertension and weight gain to recommend additional screening or interventions. See Appendix 3 for further details.

10.6 Management of term SROM

Recommendations

- We recommend that delivery within 24 hours should be the aim in the case of prelabour SROM at term (Grade 1C).
- For prelabour SROM at term and when the most recent HIV viral load is <50 copies/mL, we recommend immediate induction or augmentation of labour with a low threshold for treatment of intrapartum pyrexia (Grade 1C).
- For prelabour SROM at term and when the most recent viral load is 50–399 copies/mL, we recommend a caesarean section; however, the mode of delivery decision should take into account the actual viral load, trajectory of the viral load, length of time on treatment, adherence, obstetric factors and the views of the woman/person (Grade 1C).
- For SROM at term and when that most recent viral load is ≥400 copies/mL, we recommend an urgent (category 2) caesarean section (Grade 1C).
- For prelabour SROM at term and a viral load >50 copies/mL, we recommend that attempts should be made to optimise the ART regimen to reduce the risk of vertical transmission while facilitating delivery (see Section 8.7) (Grade 1C).

- We recommend that viral load should be assessed on admission with term prelabour SROM but immediate management decisions should be based on the most recent available viral load result (Grade 1C).

Auditable outcome

- Proportion of women/people living with HIV with prelabour SROM at term and delivery within 24 hours.

Rationale

In the pre-ART era, several studies [24-26] showed that prolonged duration of ruptured membranes, usually defined as membranes that ruptured more than 4 hours before delivery, resulted in a significantly increased risk of vertical transmission. A meta-analysis showed a 2% increase in relative risk of transmission per hour of membrane rupture before delivery (for each 1-hour increment: adjusted OR 1.02, 95% CI, 1.01–1.04) [27].

There have been few published studies on SROM from the effective ART era. In a study from Spain, duration of ruptured membranes >6 hours compared to <6 hours was only significantly associated with transmission in women receiving no treatment (26.6% *vs* 11.9%; *P*<0.01) [28].

The NSHPC (now ISOSS) reported data on 1464 women with an undetectable viral load and duration of SROM for births at term between 2007 and 2012. Among these 1464 women delivering with a viral load <50 copies/mL, the vertical transmission rate was 0.12% (1/809) in women with SROM duration <4 hours and 0.15% (1/655) in women with SROM duration between ≥4 hours and <24 hours (OR 1.14, 95% CI 0.07–18.27). There were no transmissions from the 55 women with viral load <50 copies/mL and duration of SROM >24 hours, but this represents very few cases [29].

Data from North America from 1996 to 2008 showed similar results. Among more than 700 women with HIV (89% received triple ART), the perinatal transmission rate was 1% and 1.9% in those with SROM duration of <4 hours and ≥4 hours respectively. Among those with a viral load of <1000 copies/mL, there were no cases of perinatal transmission. Only viral load >10,000 copies/mL was shown to be an independent risk factor [30]. Therefore, for women/people on ART with SROM at term with a viral load <50 copies/mL and no obstetric contraindications to vaginal delivery, caesarean section is not recommended for the prevention of vertical transmission.

As both acute and chronic chorioamnionitis have been associated with perinatal transmission [26,31-33], albeit from studies largely performed in the pre-effective ART era, it is recommended that labour should be expedited for all women/people with SROM at term. Hence women/people with SROM at term with a viral load <50 copies/mL should receive immediate induction with a low threshold for the treatment of intrapartum pyrexia. The NICE induction of labour guidelines [34] and the NICE intrapartum guidelines [35] should be followed with regard to mode of induction and use of antibiotics. When planning the birth, women/people should be advised to contact their maternity unit for in-person assessment as soon as SROM is suspected.

It is the opinion of the writing group that an immediate caesarean section should be recommended for women/people with a viral load of 50–399 copies/mL at term. If a caesarean section is not carried out, delivery should be expedited to occur within 24 hours, as above.

Until further data are available, an urgent (category 2) caesarean section is recommended where the viral load is >400 copies/mL regardless of treatment [36].

ART should be optimised in women/people who have a viral load >50 copies/mL near delivery (see Section 8.7).

10.7 Management of preterm prelabour rupture of membranes (PPROM)

Recommendations

- We recommend that where PPROM occurs, HIV viral load should be assessed on admission. Decisions should be made based on the most recent available viral load, taking into account the actual viral load, trajectory of the viral load, length of time on treatment, adherence, obstetric factors and the views of the woman/person (Grade 1C).
- We recommend that when PPROM occurs at ≥35 weeks' gestation (Grade 1D):
    - Timing and mode of birth should be discussed among the MDT with careful consideration of the ongoing clinical assessment and preferences of the woman/person;
    - In most women/people, the management of PPROM will be the same as that of term SROM, except that those at 35–37 weeks' gestation will require group B streptococcus prophylaxis in line with national guidelines [37];
    - Conservative management of PPROM can be considered until 37 weeks' gestation for women/people who have been on ART for longer than 10 weeks and where the two most recent maternal/parental HIV viral loads are <50 copies/mL at least 4 weeks apart, during pregnancy. This requires multidisciplinary discussions, regular clinical assessment and a robust management plan;
    - If conservative management is chosen, erythromycin should be given as per the RCOG Green-top Guideline on PPROM [38].
- We recommend that when PPROM occurs at <35 weeks' gestation (Grade 1D):
    - Where HIV viral load is >50 copies/mL, ART should be optimised as per management advice in Section 8.7;
    - There should be a multidisciplinary discussion about the timing and mode of delivery. For those at 34 weeks' gestation it may be beneficial to expedite delivery if the woman/person is a known group B streptococcus carrier. Where delivery is expedited at <35 weeks' gestation, group B streptococcus prophylaxis is required in line with national guidance;
    - Corticosteroids should be administered in accordance with national guidance;
    - Erythromycin should be given in accordance with national guidance on PPROM.

Rationale

There are no data to inform the optimum management of preterm labour in women/people living with HIV. Decisions regarding the optimum management of early preterm SROM require the assessment of a

number of factors including the exact gestation, the facilities available, maternal/parental viral load and the presence of other comorbidities such as infection and pre-eclampsia.

Erythromycin should be given as per the RCOG Green-top Guideline on PPROM [38]. Corticosteroids to improve fetal lung maturation should be given as per the RCOG Green-top Guideline on antenatal corticosteroids [39,40]. Dosing should take into account ART and possible drug–drug interactions requiring dose adjustment. Intravenous magnesium sulphate for neuroprotection should be administered in accordance with national guidelines [41].

Decisions regarding timing of delivery should be made in consultation with the full MDT including the neonatal unit and take into account the preferences of the woman/person.

If maternal/parental HIV viral load is >50 copies/mL, consideration should be given to the options available to optimise ART. An additional concern is that the early preterm infant may be unable to tolerate oral therapy and therefore loading the infant through the transplacental route with maternal/parental ART is recommended (see Section 8.7 for further information on ART in pregnancy).

There is no evidence to suggest that group B streptococcus is more prevalent in women/people living with HIV. Antibiotics as group B streptococcus prophylaxis should be administered in labour according to national guidelines [37].

10.8 Preterm labour

Recommendations

- We recommend for women/people in preterm labour that viral load should be assessed urgently on admission and ART optimised if the viral load is >50 copies/mL (see Section 8.7) (Grade 1C).
- We recommend that corticosteroids should be administered in accordance with national guidelines, taking ART into account (Grade 1A).
- We recommend that intravenous antibiotics for group B streptococcus prophylaxis should be administered in labour according to national guidelines (Grade 1C).
- We recommend that intravenous magnesium sulphate for neuroprotection should be administered in accordance with national guidelines (Grade 1A).
- We recommend that tocolysis may be used to allow administration of steroids or antiretrovirals or to arrange transfer to a unit with appropriate neonatal intensive care facilities (Grade 1C).

Rationale

Viral load should be assessed on admission. If the viral load is >50 copies/mL, ART should be optimised as discussed in Section 8. In addition, the early preterm infant may be unable to tolerate oral therapy and therefore pre-loading the infant through the transplacental route with maternal/parental ART is recommended as discussed in Section 8.

Mode of delivery should be determined by the viral load, obstetric factors and preferences of the woman/person, as discussed below.

Administration of corticosteroids, antibiotics for group B streptococcus prophylaxis, intravenous magnesium sulphate for neuroprotection and tocolysis, if indicated, should be administered according to local and national guidelines [37,39,41].

10.9 Mode of delivery

Recommendations

- We recommend that a decision regarding recommended mode of delivery should be agreed with the pregnant woman/person after review of the last measured plasma viral load, which is usually the plasma viral load measured at 36 weeks (Grade 1C).
- Following the agreement on mode of delivery, we recommend that a birth plan is clearly documented in the medical notes of the pregnant woman/person (see https://bhiva.org/clinical-guideline/pregnancy-guidelines/). This should be drafted before the third trimester and finalised by 36 weeks' gestation (Grade 1D).
- We recommend that planned vaginal delivery should be supported where HIV viral load is <50 copies/mL in the absence of obstetric contraindications (Grade 1C).
- We recommend that vaginal birth after caesarean section (VBAC) can be offered where HIV viral load is <50 copies/mL (Grade 1C).
- We recommend planned caesarean section where HIV viral load is 50–399 copies/mL, taking into account the actual viral load, the trajectory of the viral load, length of time on treatment, adherence, obstetric factors and the views of the woman/person (Grade 1C).
- We recommend caesarean section where HIV viral load is ≥400 copies/mL (Grade 1C).

Auditable outcomes

- Proportion of women/people living with HIV who undergo caesarean section because of a viral load of >50 copies/mL to prevent vertical transmission.
- Proportion of women/people living with HIV who have a documented birth plan by 36 weeks.

Rationale

Published cohort data from the UK and other European countries have shown vertical transmission rates of <0.5% in women with a plasma viral load <50 copies/mL taking ART, irrespective of mode of delivery [42-47]. These studies support the practice of recommending planned vaginal delivery for women/people on ART with a viral load <50 copies/mL.

The NSHPC (now ISOSS) investigated HIV vertical transmission rates in women delivering between 2000 and 2011 (*n*=2000); for all modes of delivery, risk of transmission was significantly higher when viral load was 50–399 copies/mL than when fully suppressed (<50 copies/mL) [47]. Excluding five *in utero* transmissions, the vertical rate among women with viral loads of 50–399 copies/mL was 0.26% (2 of 777) following elective caesarean section and 1.1% (2 of 188) following planned vaginal delivery (*P*=0.17).

In an analysis from the ANRS French Perinatal cohort of 8977 women delivering on ART during the period 2000–2010, no difference in unadjusted vertical transmission rates by mode of delivery was found among 3075 women delivering at term (>37 weeks) with a viral load <50 copies/mL (0.3% for

vaginal delivery, 0.3% for caesarean section and 0.3% for non-caesarean section; *P*=1.00). Among 707 women who delivered at term with a viral load of 50–399 copies/mL, there was also no significant difference in transmission by mode of delivery (1.0%, 1.0% and 2.5% respectively; *P*=0.24). The authors did not comment on the timing of transmission in the infants diagnosed with HIV [48].

By contrast, data from the European Collaborative Study of 5238 women delivering from 1985 to 2007 showed that prelabour caesarean section was associated with an 80% decreased risk of vertical transmission after adjusting for ART and prematurity among 960 women delivering with a viral load <400 copies/mL (adjusted OR 0.2, 95% CI 0.05–0.65). There were only two transmissions among 599 women delivering with a viral load <50 copies/mL (transmission rate 0.4%) [42].

A potential explanation for the different conclusions in these two studies regarding the effect of mode of delivery on vertical transmission when plasma viral load at delivery is <400 copies/mL is that there may be a significant difference in the viral load distribution <400 copies/mL between studies. This highlights the fact that it is not possible to infer that vertical transmission rates from studies using a viral load assay with a cut-off value <400 copies/mL can necessarily be applied to individuals with plasma viral loads of 50–399 copies/mL using current assays with lower limits of detection of 50 copies/mL or less.

Although neither of the most recent UK and French analyses showed a statistically significant difference in vertical transmission by mode of delivery for women with plasma viral loads between 50 and 399 copies/mL, in the UK/Ireland dataset the risk of vertical transmission for women delivering vaginally was about twice that of those delivering by caesarean section, and this increased to 4-fold when *in utero* transmissions are excluded. Therefore, we recommend that caesarean section should be considered in this group taking into account the actual viral load, the trajectory of the viral load, length of time on treatment, adherence issues, obstetric factors and the views of the woman/person.

Given the conflicting data regarding the effect of mode of delivery on vertical transmission when viral load is <400 copies/mL, together with the data from the UK study showing a 2.4-fold increased risk of transmission for every 1-$\log_{10}$ unit increase in viral load associated with vaginal delivery [45], the writing group continues to recommend caesarean section for all women/people with a viral load ≥400 copies/mL.

In the absence of randomised trial data in women/people with HIV who undergo VBAC, support for a benefit of vaginal birth, including VBAC, compared with caesarean section is limited to expert judgement. Therefore, where a vaginal birth has been recommended on the basis of ART and viral load, delivery management of the woman/birthing parent, including a decision regarding VBAC, should be as for individuals without HIV in line with national guidelines [49].

10.10 Timing of birth

Recommendations

- We recommend that where induction of labour or prelabour caesarean section is undertaken and plasma viral load is <50 copies/mL, the usual obstetric considerations should apply regarding timing of delivery (Grade 1C).
- We recommend that where caesarean section is undertaken at a viral load of >50 copies/mL to prevent vertical transmission, delivery should be considered from 38 weeks' gestation (Grade 1C).

Rationale

The timing of caesarean section is a balance between the risks of transient tachypnoea of the newborn and the likelihood of spontaneous onset of labour before the scheduled caesarean section [50]. Where the indication for caesarean section is prevention of vertical transmission, the timing reflects the importance of avoiding the onset of labour while taking into account the actual viral load, the trajectory of the viral load, length of time on treatment, adherence, obstetric factors and the views of the woman/person. Where caesarean section is undertaken only for obstetric indications, the optimal timing of prelabour caesarean section is after 39 weeks of gestation [49].

10.11 Intrapartum management

Recommendations

- We recommend that women/people are advised to give birth in a facility that has direct access to neonatal care (Grade 1D).
- We recommend that obstetric management in women/people who plan for a vaginal delivery should follow the same guidelines as for those without HIV, apart from duration of ruptured membranes (see Sections 10.6 and 10.7) (Grade 1D).
- We recommend that women/people with no additional risk factors can opt for midwifery-led intrapartum care (Grade 1D).
- There is minimal evidence on vertical HIV transmission risk and delayed cord clamping; however, we recommend that delayed cord clamping should be supported if the viral load is <50 copies/mL (Grade 1D).
- There is minimal evidence to support water birth; however, we recommend that women/people who choose a water birth should be supported to achieve this if the viral load is <50 copies/mL (Grade 1D).
- We recommend intravenous zidovudine infusion through labour and/or delivery, which should be discontinued following cord clamping, for (Grade 1C):
    - Women/people who are admitted for planned caesarean section, where HIV viral load is >1000 copies/mL; infusion should be commenced 4 hours prior to the planned caesarean section;
    - Women/people who present in labour or with SROM who are planning vaginal delivery, where HIV viral load is >1000 copies/mL;
    - Women/people who present in labour or with SROM who are planning caesarean section where HIV viral load is >1000 copies/mL; infusion should be commenced at presentation but should not delay the caesarean section;
    - Untreated women/people with an unknown viral load who present in labour or with SROM irrespective of mode of delivery.

- The use of intrapartum intravenous zidovudine infusion can be considered for women/people on ART with a plasma viral load of 50–1000 copies/mL, along with other interventions recommended in Section 8.7 (Grade 1C).

Auditable outcomes

- Proportion of women/people living with HIV who are supported to achieve delayed cord clamping.
- Proportion of women/people living with HIV who receive intravenous zidovudine in labour.

Rationale

Given that infants born to women/birthing parents with HIV will require both PNP as soon as possible after birth and within 4 hours (see Section 11) and a blood test, the writing group recommends that all women/people living with HIV give birth in a facility that has direct access to neonatal care (i.e. a co-located birth centre or obstetric unit).

Traditionally amniotomy, fetal scalp electrodes and blood sampling, instrumental delivery and episiotomy have been avoided in women/people with HIV because of theoretical transmission risks. Data from the pre-effective ART era have been reviewed, and show little or no risk for many of these procedures. Trial data since the advent of effective ART are not available.

The NSHPC (now ISOSS) reported data on operative vaginal deliveries between 2008 and 2016; of 3023 deliveries, 251 infants were delivered using forceps or vacuum; one infant was diagnosed with HIV, but the timing of infection is unclear and other risk factors were present [12]. This is consistent with previously reported transmission rates in this population, and the numbers are too small to draw further conclusions.

Several cohort studies which predate effective ART did not show increased risk of vertical transmission with various obstetric procedures such as instrumental delivery, artificial rupture of membranes, fetal scalp electrodes, and pH blood sampling [15,24,51]. In a retrospective study from Spain, predominantly in the pre-ART era, HIV transmission occurred in 26.3% of infants exposed to fetal scalp monitoring (electrodes or pH sampling or both) compared with 13.6% exposed to neither type of monitoring (RR 1.94, 95% CI 1.12–3.37) [52]. However, prolonged rupture of membranes was a significant contributor to the risk of transmission associated with this invasive monitoring.

In the absence of trial data for women/people with HIV who undergo an operative vaginal delivery, support for a benefit of any type of operative vaginal delivery compared to caesarean section for women/people or their infants is limited to expert judgement and extrapolation from other datasets. It is generally accepted that low cavity traction forceps are associated with lower rates of fetal trauma than vacuum-assisted deliveries and therefore may be favoured. In women/people with a viral load <50 copies/mL it is unlikely that the type of instrument used will affect transmission risk and thus the one the operator feels is most appropriate should be used as in the general population without HIV (and following national guidance [35]).

A Cochrane review published in 2018 examined obstetric outcomes following immersion in water during the first and second stages of labour (15 trials included). Outcomes related to HIV were not specifically reviewed. Overall, there was little or no difference in spontaneous vaginal birth, instrumental birth or caesarean delivery with water immersion in the first stage (moderate- to low-quality evidence), but immersion in the first stage may reduce the use of regional anaesthesia (moderate-quality evidence). For women immersed in the second stage of labour, there was little or no difference between groups for spontaneous vaginal birth. There was one reported death in the immersion group in one trial. The infant was born alive to a woman living with HIV who was treated 2 weeks prior to birth for vaginal infection.

The infant died at 2.5 hours after birth. After investigation the cause of death was determined to be intrauterine infection [53]. The writing group recommends that the lack of safety evidence should be discussed with women/birthing parents with HIV who are considering a water birth. Individuals who choose to give birth in water should be supported to do so where the viral load is <50 copies/mL.

Women/people with no additional risk factors can opt for midwifery-led intrapartum care. Women/birthing parents will need to continue with ART through labour and adequate provision needs to be made for examination and testing of, and dispensing of medication to, the newborn infant in a timely manner (see Section 11).

The use of intravenous zidovudine for women/birthing parents on ART with a viral load between 50 and 1000 copies/mL can be considered regardless of mode of delivery. However, optimising the current oral ART regimen as per guidance in Section 8.7 is a reasonable alternative. French data provided no evidence that intrapartum intravenous zidovudine further reduces the risk of vertical transmission in women on ART, unless maternal HIV viral load is >1000 copies/mL, if intensive neonatal therapy is given [54]. However, individual circumstances vary, and intravenous zidovudine may be considered as one of a number of maternal intrapartum antiretroviral options (see Section 8.7) for those with a viral load >50 copies/mL who present in labour or with SROM or who are admitted for caesarean section provided this does not delay other interventions.

10.12 References

1. Public Health England. *Fetal anomaly screening: programme handbook*. 2015. Available at: www.gov.uk/government/publications/fetal-anomaly-screening-programme-handbook (accessed June 2024).

2. National Institute for Health and Care Excellence. *Antenatal care. Nice guideline [NG201]*. 2021. Available at: https://www.nice.org.uk/guidance/ng201 (accessed June 2024).

3. Antiretroviral Pregnancy Registry Steering Committee. *The Antiretroviral Pregnancy Registry Interim Report. 1 January 1989 through 31 July 2022. (Issued: December 2022)*. Wilmington, NC, USA: Registry Coordinating Center; 2022. Available at: http://www.apregistry.com/forms/interim_report.pdf (accessed June 2024).

4. Savvidou MD, Samuel I, Syngelaki A *et al.* First-trimester markers of aneuploidy in women positive for HIV. *BJOG* 2011; **118**: 844–848.

5. Nicolaides KH, Spencer K, Avgidou K *et al.* Multicenter study of first-trimester screening for trisomy 21 in 75 821 pregnancies: results and estimation of the potential impact of individual risk-orientated two-stage first-trimester screening. *Ultrasound Obstet Gynecol* 2005; **25**: 221–226.

6. Gross S, Castillo W, Crane M *et al.* Maternal serum alpha-fetoprotein and human chorionic gonadotropin levels in women with human immunodeficiency virus. *Am J Obstet Gynecol* 2003; **188**: 1052–1056.

7. Spencer K. First and second trimester markers of fetal aneuploidy in pregnant women with HIV infection. *Fetal Diagn Ther* 2011; **29**: 135–138.

8. Yudin MH, Prosen TL, Landers DV. Multiple-marker screening in human immunodeficiency virus-positive pregnant women: screen positivity rates with the triple and quad screens. *Am J Obstet Gynecol* 2003; **189**: 973–976.

9. Einstein FH, Wright RL, Trentacoste S *et al.* The impact of protease inhibitors on maternal serum screening analyte levels in pregnant women who are HIV positive. *Am J Obstet Gynecol* 2004; **191**: 1004–1008.

10. Charlton TG, Franklin JM, Douglas M *et al.* The impact of HIV infection and antiretroviral therapy on the predicted risk of Down syndrome. *Prenat Diagn* 2014; **34**: 121–127.

11. Bianchi DW, Parker RL, Wentworth J *et al.* DNA sequencing versus standard prenatal aneuploidy screening. *N Engl J Med* 2014; **370**: 799-808.

12. Peters H, Francis K, Harding K *et al.* Operative vaginal delivery and invasive procedures in pregnancy among women living with HIV. *Eur J Obstet Gynecol Reprod Biol* 2017; **210**: 295–299.

13. Floridia M, Masuelli G, Meloni A *et al.* Amniocentesis and chorionic villus sampling in HIV-infected pregnant women: a multicentre case series. *BJOG* 2017; **124**: 1218–1223.

14. Ekoukou D, Khuong-Josses MA, Ghibaudo N *et al.* Amniocentesis in pregnant HIV-infected patients. Absence of mother-to-child viral transmission in a series of selected patients. *Eur J Obstet Gynecol Reprod Biol* 2008; **140**: 212–217.

15. Mandelbrot L, Jasseron C, Ekoukou D *et al.* Amniocentesis and mother-to-child human immunodeficiency virus transmission in the Agence Nationale de Recherches sur le SIDA et les Hepatites Virales French Perinatal Cohort. *Am J Obstet Gynecol* 2009; **200**: 160e1–9.

16. Simões M, Marques C, Gonçalves A *et al*. Amniocentesis in HIV pregnant women: 16 years of experience. *Infect Dis Obstet Gynecol*. 2013; **2013**: 914272.

17. Mandelbrot L, Mayaux MJ, Bongain A *et al.* Obstetric factors and mother-to-child transmission of human immunodeficiency virus type 1: the French perinatal cohorts. SEROGEST French Pediatric HIV Infection Study Group. *Am J Obstet Gynecol* 1996; **175**: 661–667.

18. Townsend CL, de Ruiter A, Peters H *et al.* Pregnancies in older women living with HIV in the UK and Ireland. *HIV Med* 2017; **18**: 507–512.

19. National Institute for Health and Care Excellence. *Twin and triplet pregnancy. Nice guideline [NG137]*. 2019. Available at: https://www.nice.org.uk/guidance/ng137 (accessed June 2024).

20. Royal College of Obstetricians and Gynaecologists. *External Cephalic Version and Reducing the Incidence of Term Breech Presentation*. Green-top Guideline No. 20a. 2017. Available at: https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/external-cephalic-version-and-reducing-the-incidence-of-term-breech-presentation-green-top-guideline-no-20a/ (accessed August 2024).

21. Holmes WR, Hofmeyr GJ. Management of breech presentation in areas with high prevalence of HIV infection. *Int J Gynaecol Obstet* 2004; **87**: 272–276.

22. Owens M, Bhullar A, Carlan SJ *et al.* Effect of fundal pressure on maternal to fetal microtransfusion at the time of cesarean delivery. *J Obstet Gynaecol Res* 2003; **29**: 152–156.

23. NHS England. *Saving babies lives version 3*. 2023. Available at: https://www.england.nhs.uk/long-read/saving-babies-lives-version-3/ (accessed June 2024).

24. Landesman SH, Kalish LA, Burns DN *et al.* Obstetrical factors and the transmission of human immunodeficiency virus type 1 from mother to child. The Women and Infants Transmission Study. *N Engl J Med* 1996; **334**: 1617–1623.

25. Minkoff H, Burns DN, Landesman S *et al.* The relationship of the duration of ruptured membranes to vertical transmission of human immunodeficiency virus. *Am J Obstet Gynecol* 1995; **173**: 585–589.

26. Van Dyke RB, Korber BT, Popek E *et al.* The Ariel Project: a prospective cohort study of maternal-child transmission of human immunodeficiency virus type 1 in the era of maternal antiretroviral therapy. *J Infect Dis* 1999; **179**: 319–328.

27. International Perinatal HIV Group. Duration of ruptured membranes and vertical transmission of HIV-1: a meta-analysis from 15 prospective cohort studies. *AIDS* 2001; **15**: 357–368.

28. Garcia-Tejedor A, Perales A, Maiques V. Duration of ruptured membranes and extended labor are risk factors for HIV transmission. *Int J Gynaecol Obstet* 2003; **82**: 17–23.

29. Peters H, Byrne L, De Ruiter A *et al.* Duration of ruptured membranes and mother-to-child HIV transmission: a prospective population-based surveillance study. *BJOG* 2016; **123**: 975–981.

30. Cotter AM, Brookfield KF, Duthely LM *et al.* Duration of membrane rupture and risk of perinatal transmission of HIV-1 in the era of combination antiretroviral therapy. *Am J Obstet Gynecol* 2012; **207**: 482.e1–5.

31. Chi BH, Mudenda V, Levy J *et al.* Acute and chronic chorioamnionitis and the risk of perinatal human immunodeficiency virus-1 transmission. *Am J Obstet Gynecol* 2006; **194**: 174–181.

32. Mofenson LM, Lambert JS, Stiehm ER *et al.* Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. Pediatric AIDS Clinical Trials Group Study 185 Team. *N Engl J Med* 1999; **341**: 385–393.

33. Wabwire-Mangen F, Gray RH, Mmiro FA *et al.* Placental membrane inflammation and risks of maternal-to-child transmission of HIV-1 in Uganda. *J Acquir Immune Defic Syndr* 1999; **22**: 379–385.

34. National Institute for Health and Care Excellence. *Inducing labour. NICE guideline [NG207]*. 2021. Available at: www.nice.org.uk/guidance/ng207 (accessed June 2024).

35. National Institute for Health and Care Excellence. *Intrapartum care for healthy women and babies. Clinical guideline [CG190]*. 2022. Available at: www.nice.org.uk/guidance/cg190 (accessed June 2024).

36. Brookfield K, Duthely L, Cotter A. Rupture of membranes greater than four hours is not a risk factor for perinatal HIV transmission in the era of combination antiretroviral therapy. Abstract 74. *Am J Obstet Gynecol* 2011; **204**: S42–S43.

37. Royal College of Obstetricians and Gynaecologists. Prevention of early-onset neonatal group B streptococcal disease. Green-top Guideline No. 36. *BJOG* 2017; **124**: e280–e305.

38. Thomson AJ; Royal College of Obstetricians and Gynaecologists. Care of women presenting with suspected preterm prelabour rupture of membranes from 24+0 weeks of gestation. *BJOG* 2019; **126**: e152–e166.

39. Stock SJE, Thomson A, Papworth S; Royal College of Obstetricians and Gynaecologists. Antenatal corticosteroids to reduce neonatal morbidity and mortality; Green-top Guideline No. 47. *BJOG* 2022; **129**: e35–e60.

40. McGoldrick E, Stewart F, Parker R, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev* 2021; **12**: CD004454.

41. National Institute for Health and Care Excellence. *Preterm labour and birth. NICE Guideline NG25*. 2022. Available at: https://www.nice.org.uk/guidance/ng25 (accessed June 2024).

42. Boer K, England K, Godfried MH, Thorne C. Mode of delivery in HIV-infected pregnant women and prevention of mother-to-child transmission: changing practices in Western Europe. *HIV Med* 2010; **11**: 368–378.

43. Boer K, Nellen JF, Patel D *et al.* The AmRo study: pregnancy outcome in HIV-1-infected women under effective highly active antiretroviral therapy and a policy of vaginal delivery. *BJOG* 2007; **114**: 148–155.

44. Mandelbrot L, Tubiana R, Le Chenadec J *et al.* No perinatal HIV-1 transmission from women with effective antiretroviral therapy starting before conception. *Clin Infect Dis* 2015; **61**: 1715–1725.

45. Townsend CL, Cortina-Borja M, Peckham CS *et al.* Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000-2006. *AIDS* 2008; **22**: 973–981.

46. Warszawski J, Tubiana R, Le Chenadec J *et al.* Mother-to-child HIV transmission despite antiretroviral therapy in the ANRS French Perinatal Cohort. *AIDS* 2008; **22**: 289–299.

47. Townsend CL, Byrne L, Cortina-Borja M *et al.* Earlier initiation of ART and further decline in mother-to-child HIV transmission rates, 2000-2011. *AIDS* 2014; **28**: 1049–1057.

48. Briand N, Jasseron C, Sibiude J *et al.* Cesarean section for HIV-infected women in the combination antiretroviral therapies era, 2000-2010. *Am J Obstet Gynecol* 2013; **209**: 335.e1–335.e12.

49. National Institute for Health and Care Excellence. *Caesarean birth. NICE guideline [NG192]*. 2021. Available at: www.nice.org.uk/guidance/ng192 (accessed June 2024).

50. Morrison JJ, Rennie JM, Milton PJ. Neonatal respiratory morbidity and mode of delivery at term: influence of timing of elective caesarean section. *Br J Obstet Gynaecol* 1995; **102**: 101–106.

51. Kind C, Rudin C, Siegrist CA *et al.* Prevention of vertical HIV transmission: additive protective effect of elective Cesarean section and zidovudine prophylaxis. Swiss Neonatal HIV Study Group. *AIDS* 1998; **12**: 205–210.

52. Maiques V, Garcia-Tejedor A, Perales A, Navarro C. Intrapartum fetal invasive procedures and perinatal transmission of HIV. *Eur J Obstet Gynecol Reprod Biol* 1999; **87**: 63–67.

53. Cluett ER, Burns E, Cuthbert A. Immersion in water during labour and birth. *Cochrane Database Syst Rev* 2018; **5**: Cd000111.

54. Briand N, Warszawski J, Mandelbrot *L et al*. Is intrapartum intravenous zidovudine for prevention of mother- to-child HIV-1 transmission still useful in the combination antiretroviral therapy era? *Clin Infect Dis* 2013; **57**: 903–914.

11 Neonatal management

11.1 Infant PNP

Recommendations

- In infants at low risk of acquiring HIV, we recommend 2 weeks of zidovudine monotherapy if *all* the following criteria are met in the mother/birthing parent (Grade 1C):
    - ART has been commenced at least 10 weeks prior to delivery;
    - There is evidence of good engagement with maternity, antenatal and HIV services;
    - At least one viral load measurement in the 6 weeks prior to delivery;
    - All viral load measurements in the 10 weeks prior to delivery are <50 copies/mL. Of note, individual risk assessment can be made for viral load between 50 and 200 copies/mL, especially if subsequent viral load is <50 copies/mL.
- In infants at high risk of acquiring HIV, we recommend use of combination PNP if the above criteria for low-risk infants are not met, especially if the mother/birthing parent is known or likely to have a viral load >50 copies/mL on the day of delivery, if there is uncertainty about recent adherence or if the viral load is unknown (Grade 1C).
- We recommend that standard combination PNP should consist of nevirapine for 2 weeks with zidovudine and lamivudine for 4 weeks (Grade 1D).
- We recommend that intravenous ART can be considered for neonates who cannot tolerate oral medication or are at significant risk of necrotising enterocolitis associated with prematurity (Grade 1D).
- We recommend that PNP should be commenced as soon as possible after birth, and at the latest within 4 hours (Grade 1D).
- We recommend that HIV RNA PCR results for both the woman/birthing parent and the infant should be available within 24 hours of samples taken at delivery being received by the laboratory (Grade 1D).
- If at high risk of acquiring HIV (i.e. combination PNP is indicated) and there is a documented history of genotypic resistance in the mother/birthing parent, we recommend that expert advice is sought. If advice is not immediately available, standard three-drug PNP (zidovudine, lamivudine and nevirapine) should be commenced until further advice is provided (Grade 1D).
- When an infant has been started on combination PNP because the criteria for low risk have not been fulfilled, and subsequently the viral load for the mother/birthing parent at delivery is <50 copies/mL, we recommend that simplifying infant PNP to zidovudine alone to complete 2 weeks in total is considered. This decision should be made in discussion with a paediatrician with expertise in prevention of vertical HIV transmission (Grade 1D).

Auditable outcomes

- The proportion of infants for whom PNP is commenced as soon as possible after birth, and at the latest within 4 hours.

- The proportion of day-of-delivery HIV RNA PCR results for both the woman/birthing parent and the infant available within 24 hours of receipt by the laboratory.
- The proportion of infants correctly risk stratified and receiving appropriate PNP according to guidance.

Rationale

Our overarching aims in this latest review of PNP guidance, based on updated evidence and review of the literature, aligned with the following basic principles:

- To ensure ongoing minimisation of risk of HIV transmission;
- To reduce unnecessary drug exposure for infants at minimal risk of acquiring HIV;
- To ensure full combination ART as early as possible for infants at highest risk of acquiring HIV.

Detailed and prospective audit and review of PNP use and outcomes will be completed following implementation of these guidelines to monitor the potential impact of these changes in relation to these principles.

11.1.1 General principles

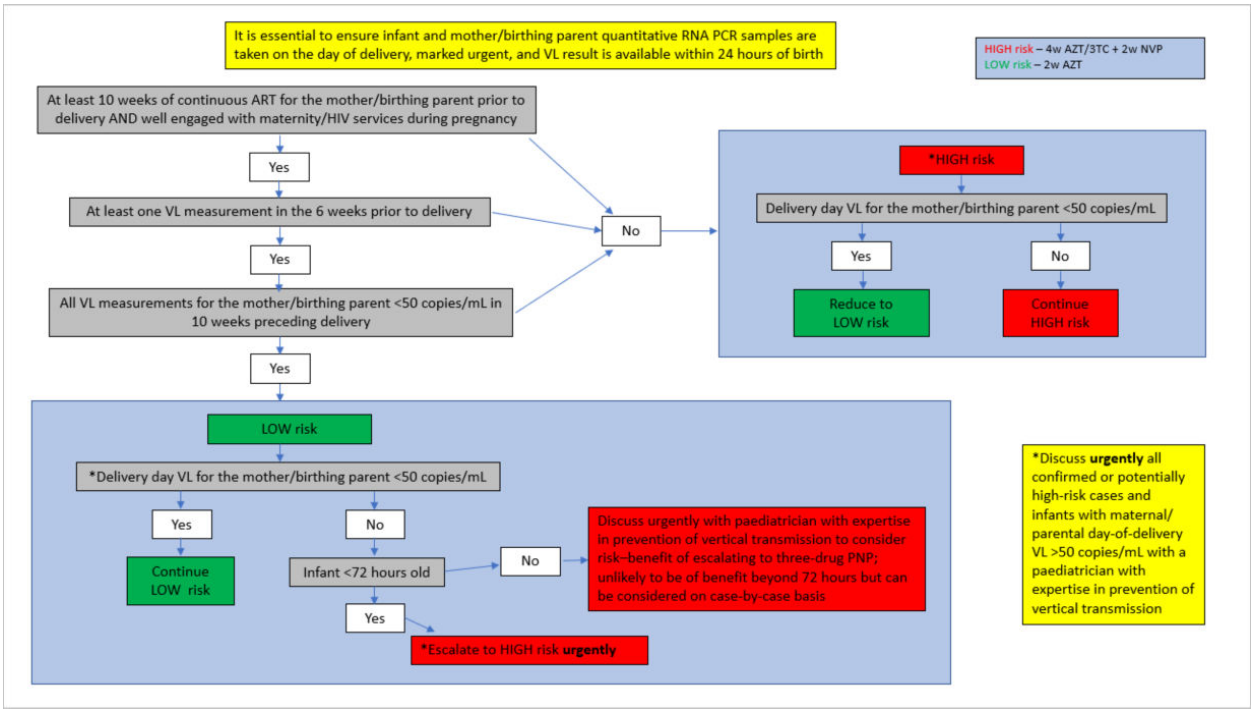
An updated algorithm for infant PNP is shown in Figure 11.1.

It is strongly recommended that the antenatal birth plan for PNP is documented prior to delivery and that measures are taken to ensure this is reviewed at every clinical contact during pregnancy, especially in the context of detectable viral load for the mother/birthing parent.

Standard medication for high-risk and low-risk PNP (see below) should be easily available in all clinical areas in which deliveries routinely take place, with robust local policies for prescribing and administering 24 hours a day. The administration of PNP should be considered urgent and should not be deferred if the infant is delivered out of normal working hours. Infant PNP should be commenced as soon as possible after birth, and at the latest within 4 hours.

It is essential to carry out RNA PCR tests for the mother/birthing parent and the infant on the day of delivery and that the results are available within 24 hours of birth to ensure that correct PNP is provided to the infant, so that appropriate advice relating to infant feeding is given and to allow urgent initiation of full treatment in cases of *in utero* infection. DNA PCR results (when applicable) should be available as soon as possible.

Figure 11.1 Updated algorithm for infant PNP



3TC, lamivudine; AZT, zidovudine; NVP, nevirapine; VL, viral load; w, week.

11.1.2 Low risk of vertical transmission

Cumulative observational data now clearly demonstrate that the risk of vertical transmission is reduced to almost zero if the mother/birthing parent starts ART prior to conception and the viral load remains undetectable throughout pregnancy, if the infant receives PNP and if there is no breast/chestfeeding.

Zidovudine monotherapy for the infant has been part of the strategy for prevention of vertical transmission of HIV since the publication of the results of the ACTG 076 trial in 1994. The relative contributions of the antenatal, peripartum and infant components in this study are difficult to quantify. In the ACTG 076 study, neonatal zidovudine 2 mg/kg every 6 hours was given for 6 weeks [1]. A further randomised placebo-controlled trial of zidovudine monotherapy in the pre-combination ART era, in non-breastfeeding women in Thailand, compared four strategies for the prevention of vertical transmission, including short (3 days) and long (6 weeks) PNP and short (from 35 weeks) and long (from 28 weeks) maternal treatment. Both PNP options were equally effective, when the mother started treatment at 28 weeks, suggesting that a short duration of PNP was sufficient to cover perinatal exposure after an adequate length of ART in pregnancy [2].

In the previous version of the BHIVA pregnancy guidelines, 2 weeks (very low risk) or 4 weeks (low risk) of oral zidovudine was recommended for all infants except in specific high-risk circumstances relating to detectable or unknown maternal viral load at the time of delivery [3]. Reducing the duration of PNP to 2 weeks was supported by data from Germany, where a strategy of using 2 weeks of neonatal zidovudine in the lowest-risk situations has been recommended for over 10 years with no signal that this

has resulted in increased vertical transmission. It was also associated with reduced haematological toxicity potentially attributed to postnatal zidovudine exposure [4].

Since the 2018 update to the BHIVA pregnancy guidelines, the vertical transmission rate in the UK continues to be extremely low, with transmission occurring only under exceptional circumstances [5].

French cohort data have provided further evidence of a very low risk of vertical transmission under specific circumstances. Zero vertical transmissions (95% CI 0–0.07) occurred among 5482 mothers on continuous ART from conception with undetectable HIV viral load near delivery. Infants received PNP (routine duration in France is 4 weeks) and were not breastfed. The absence of any transmission in this 'real world' setting is reassuring; the writing group is of the opinion that reducing from 4 weeks to shorter durations of PNP is very unlikely to increase the risk of vertical transmission under these low-risk circumstances. It should be noted that rare transmissions did occur when ART was commenced after conception, despite undetectable maternal viral load near the date of delivery, with increased rates of transmission with increasing gestational age at ART initiation and/or with premature delivery (vertical transmission rate 0.57% [26/4596], 95% CI 0.37–0.83) [6].

Adult PEP guidelines for exposure to HIV now recommend against PEP in the context of known sexual exposure to viral loads <200 copies/mL, based on strong evidence provided by large randomised trials investigating treatment as prevention of transmission [7]. In some countries, for example Switzerland, this evidence has now been extrapolated to the context of the prevention of vertical transmission of HIV, supporting the national guidelines recommending the option of no PNP to infants born to women on ART with an undetectable viral load on at least two consecutive occasions at least 4 weeks apart and including after 36 weeks' gestation, especially if on suppressive ART prior to conception and throughout pregnancy [8]. Preliminary observational data indicate that this approach has not been associated with increased risk of transmission, although absolute numbers are small [9].

It is the writing group's opinion that adult 'treatment as prevention of transmission' studies should not be fully extrapolated to the prevention of vertical transmission. The HIV transmission risk without intervention for peripartum exposure is much higher than for sexual or occupational exposure (10–20% *vs* 0.1–1.5%) [7,10]. The nature of exposure is also different. The fetus may be exposed at any time from conception to delivery; exposure at the time of delivery carries a particularly high risk. Transplacental trafficking of maternal cells (including CD4 cells) occurs and maternal lymphocytes can persist in the infant circulation after birth [11]. Although the relevance of this process in HIV transmission is not known, it has been suggested to have implications for vertical transmission of HBV and human T-cell lymphotropic virus type 1 (HTLV-1) [12]. Of note, this theoretical risk was part of the justification for 6 weeks of neonatal PEP in the original ACTG 076 study [1].

European cohort data indicate that the risk of transmission remains low if maternal ART is initiated more than 10 weeks prior to delivery [13]. French cohort data support the observation that ART initiation at earlier gestation correlates with reduced transmission risk [6].

For these reasons, we continue to recommend PNP for all infants born to women/birthing parents living with HIV. In the context of low transmission rates in the UK, we now recommend a 2-week course of zidovudine for all low-risk situations, as shown in Figure 11.1. In view of additional observational data supporting that 2 weeks of zidovudine is likely to be as effective as 4 weeks in the low-risk situation, and to simplify guidance, the option of 4 weeks of zidovudine has now been removed as a routine

recommendation. Extending the duration of zidovudine PNP to 4 weeks may still be considered on a case-by-case basis in discussion with a relevant expert or MDT.

In some countries, alternatives to zidovudine are recommended in the low-risk situation, partly in order to minimise the risk of toxicity from zidovudine [14]. In view of the potential risk of transmitted NNRTI resistance, as well as concern about potential exposure to nevirapine monotherapy prior to HIV diagnosis in infants who have acquired HIV despite efforts to prevent transmission, we continue to recommend zidovudine as the preferred agent for low-risk situations. Of note, development of NNRTI resistance could jeopardise future use of long-acting injectable ART.

In summary, we now recommend 2 weeks of infant zidovudine (see Appendix 4 for dosing) if *all* the following criteria are met in the mother/birthing parent:

- ART has been commenced at least 10 weeks prior to delivery;
- There is evidence of good engagement with maternity, antenatal and HIV services;
- Viral load has been measured at least once in the 6 weeks prior to delivery;
- All viral load measurements in the 10 weeks prior to delivery are <50 copies/mL. Of note, individual risk assessment can be made for viral load between 50 and 200 copies/mL especially if viral load is subsequently <50 copies/mL.

There is no need to extend the duration of PNP for breast/chestfed infants (see Section 12).

Unexpected detectable viral load at delivery

If the criteria for low risk of transmission are fulfilled and the infant commences 2 weeks of zidovudine PNP, but the day-of-delivery HIV viral load for the mother/birthing parent is subsequently found to be greater than 50 copies/mL, this should be urgently discussed with a paediatrician with expertise in the prevention of vertical transmission to consider escalating to three-drug PNP (see Section 11.1.3). The likelihood of this providing additional benefit reduces with increasing time since delivery and is very unlikely to be of benefit beyond 72 hours after birth, however it may still be considered on an individual basis.

If regional advice is not immediately available, cases can be discussed with extra-regional specialist teams (e.g. St Mary's Hospital, London; Great Ormond Street Hospital for Children, London; Birmingham Heartlands Hospital; St George's Hospital, London) and also referred to the national paediatric virtual clinic which can discuss urgent referrals in addition to their monthly routine meetings (caroline.foster5@nhs.net, a.bamford@nhs.net, hermione.lyall@nhs.net).

Pre-term birth

Cohort data have historically indicated that prematurity is a potential risk factor for vertical HIV transmission [15]. More recent observational data indicate that this may not be the case in the low-risk scenario [6]. In view of this, prematurity is no longer considered an additional strong risk factor for transmission and should not modify low-risk versus high-risk stratification. However, prematurity may still be taken into account on an individual case basis, especially if other potential risk factors have been identified.

11.1.3 High risk of vertical transmission

There are few trials of infant PNP comparing single-drug to two- or three-drug combination PNP for infants at high risk of vertical transmission. Randomised trials have shown benefit of combination PNP over monotherapy when a mother has not received ART prior to delivery [16,17], while two trials have shown no advantage of two-drug combination PNP compared with monotherapy when the pregnant woman has received short-course ART immediately prior to delivery [18,19]. A more recent adaptive, single-arm, multicentre, Phase 3 clinical trial with a Bayesian design in Thailand investigated the efficacy of 'ART intensification' for mother and infant in reducing rates of vertical transmission from women initiating ART ≤8 weeks before delivery. Women fulfilling the criteria for intensification received single-dose nevirapine at onset of labour in addition to initiation of standard-of-care three-drug ART in pregnancy. Infants received three-drug PNP (2 weeks of nevirapine plus 4 weeks of lamivudine and zidovudine) and were not breastfed. No transmissions occurred in 88 mother/infant pairs receiving intensification. The probability of superiority of intensification over standard of care (maternal ART and infant zidovudine) was 94.4% [20].

Observational surveillance data from the UK and Ireland (2001–2008) demonstrated that use of combination PNP in neonates has increased over time [21]. In total, 99% of 8205 infants received any PNP; for the 86% with data on type of PNP, 3% and 11% received dual and triple regimens respectively. The use of triple PNP increased significantly over this period, from 43% to 71% for infants born to untreated women, and from 13% to 32% where women were viraemic despite ART. HIV status was known for 89% of infants with information on PNP; 14.7% (5 of 34) of infants who received no PNP acquired HIV (all born vaginally to untreated women) compared to 1.0% (72 of 7286) of those who received any PNP. Among infants born vaginally to untreated women, those who received PNP were significantly less likely to acquire HIV than those who did not (8.5% [4/47] *vs* 45.5% [5/11]; *P*=0.002). However, in this cohort study, because of the overall low rate of transmission and selective use of triple PNP for infants at higher risk of HIV, it was not possible to explore the association between type of PNP and HIV transmission.

Data from the European Pregnancy and Paediatric Cohort Collaboration (1996–2010) demonstrated increasing use of combination PNP across Europe. In 5285 high-risk mother–infant pairs (27.7% no antenatal or intrapartum antiretroviral prophylaxis, 17.3% only intrapartum prophylaxis and 55.0% detectable viral load at delivery despite antenatal ART), 23.9% of infants received combination PNP. The study results did not indicate an advantage of combination PNP compared to single-drug PNP; however, the authors concluded that this observation may be due to confounding or combination PNP only being effective in a subgroup of high-risk infants [22].

More recent observational data from England have shown that the proportion of infants receiving three-drug PNP has now reduced, as the proportion of pregnant women/people on suppressive ART has increased. Of 1269 infants with information available on PNP, only 54 (4.3%) received three-drug PNP. Reported indications for three-drug PNP included maternal viral load blips during breastfeeding, high viral load at delivery, ART resistance, reduced adherence/engagement and later booking for or no antenatal care [23].

When the low-risk criteria described above have not been met, the infant is considered high risk and combination PNP with zidovudine plus lamivudine for 4 weeks and nevirapine for 2 weeks is

recommended (see Appendix 4 for dosing). The case should be urgently discussed with a paediatrician with expertise in prevention of vertical HIV transmission.

If regional advice is not immediately available, cases can also be referred urgently to extra-regional specialist centres (at St Mary's Hospital, London, Great Ormond Street Hospital for Children, London, Birmingham Heartlands Hospital, St George's Hospital, London) and the national paediatric virtual clinic (caroline.foster5@nhs.net, a.bamford@nhs.net, hermione.lyall@nhs.net).

When an infant has been started on combination PNP because of not fulfilling the criteria for low risk and subsequently the viral load in the mother/birthing parent at delivery is found to be <50 copies/mL, it is reasonable to consider simplifying the infant PNP to 2 weeks of zidovudine monotherapy as in Section 11.1.2. This decision should be made in discussion with a paediatrician with expertise in prevention of vertical HIV transmission.

11.1.4 Choice of triple-combination PNP for high-risk neonates

For dosing recommendations of all current PNP options, see Appendix 4.

Almost all neonates born in the UK to women/birthing parents known to have HIV will have been exposed to ART *in utero*, during delivery and in the first weeks of life. The range of combinations of ART to which neonates are being exposed *in utero* continues to increase. Neonatal drug metabolism is generally slower than that of older infants or children and is even less efficient in premature neonates. Due to a lack of neonatal pharmacokinetic and efficacy studies and suitable formulations, ART regimens for infants remain restricted to a small number of antiretroviral agents.

Neonatal pharmacokinetic studies have been performed for zidovudine [24], lamivudine [25,26], tenofovir DX [27], emtricitabine [28], abacavir [29], lopinavir [30-33] and raltegravir [34]. The pharmacokinetic profile of nevirapine in neonates has been described in detail [35-39]. Dosing simulation via physiologically based pharmacokinetic modelling for dolutegravir in neonates predicts that a dose of 5 mg every 48 hours for the first 3 weeks followed by daily dosing during the fourth week may be suitable for prophylaxis or treatment of HIV [40]**,** however pharmacokinetic studies of treatment of HIV are underway.

Nevirapine

In high-risk neonates, 4 weeks of zidovudine and lamivudine plus 2 weeks of nevirapine remains the recommended regimen for standard three-drug PNP. It is a well-tolerated combination regimen with the most clinical experience [20,21,22,41-44]. Owing to its long half-life, nevirapine should be stopped 2 weeks before co-prescribed antiretroviral drugs to reduce the risk of nevirapine monotherapy exposure and the potential development of NNRTI resistance should transmission have occurred.

A significant change in dosing recommendations from previous guidelines is that the treatment dose of nevirapine (6 mg/kg), rather than the prophylactic dose (2 mg/kg), is now recommended to reduce the potential for confusion between the two dosing regimens and to optimise very early treatment in case an infant has already acquired HIV *in utero* [45]. Starting the treatment dose of nevirapine at birth achieved therapeutic dosing levels within 1 week of life in 90% (314/349; 95% CI 88–94%) of infants in one study [45], but in two smaller studies therapeutic levels were only achieved in the second week [46,47]. This has been shown to be a well-tolerated regimen [44,45,47]. Of note, a lower nevirapine

dose (4 mg/kg) in the first week is advised for infants born at 34–37 weeks' gestation. No standard dosing recommendations are available for more premature infants [45].

Raltegravir

Raltegravir dosing for neonates changes with evolving hepatic metabolism and requires increasing doses after the first and fourth weeks of life [34]. As raltegravir may affect bilirubin metabolism, total and split bilirubin levels should be monitored during the first week of life, although the rate of discontinuation due to hyperbilirubinaemia is low [34]. Appropriate raltegravir dosing for premature neonates is not yet available, and they are more vulnerable to hyperbilirubinaemia. Therefore we recommend that raltegravir should only be prescribed to preterm neonates in exceptional circumstances, after seeking expert advice and with TDM [48].

Neonatal pharmacokinetic studies of the more robust INSTI dolutegravir are underway. In future, this may become the optimal INSTI for PNP.

Ritonavir-boosted lopinavir

Dosing for lopinavir/ritonavir is based on pharmacokinetic data in infants who have acquired HIV initiating therapy in the first 6 weeks of life [30-32] and the findings of a study that included infants treated from birth [33]. However, adrenal suppression has been documented in some neonates, particularly preterm neonates [49]. This is in addition to case reports of cardiac, renal and neurological toxicity, especially in, but not restricted to, premature infants, and including one death during PNP with lopinavir/ritonavir [50]. No effects have been observed with maternal lopinavir/ritonavir in the absence of neonatal dosing. It remains unclear whether these effects are related to lopinavir/ritonavir specifically or could be seen with other ritonavir-boosted PIs. Therefore we recommend that lopinavir/ritonavir should be avoided in routine infant PNP and should only be prescribed to preterm neonates in exceptional circumstances. The use of lopinavir/ritonavir should only be considered after seeking expert advice and where the mother/birthing parent has NNRTI or INSTI resistance. Close metabolic monitoring should be undertaken for the first 5 days of life.

Other agents

A neonatal dose for maraviroc has now been defined in a small pharmacokinetic study [51]; however, there are no efficacy data for this antiretroviral agent as PNP. The study did not take into account issues of tropism of potentially transmitted virus for the CCR5 co-receptor, which would impact potential efficacy. Therefore we recommend that maraviroc should be avoided in routine infant PNP until more data are available.

Proof-of-concept, pharmacokinetic and safety studies in neonates have now been undertaken for broadly neutralising monoclonal antibodies against HIV [52]. Subcutaneous injections are required, probably monthly. In future, these antibodies could be a particularly effective PNP for breast/chestfed infants, but efficacy data are awaited.

11.1.5 Intravenous ART in the neonate

For dosing of intravenous ART, see Appendix 4.

The only licensed ART available for intravenous use in sick and/or premature neonates who are unable to take oral medication is zidovudine [24,53]. Reduced oral and intravenous dosing schedules for premature infants are available.

The extremely premature neonate is at risk of necrotising enterocolitis if enteral feeding is commenced too soon or increased too rapidly. It is not known whether very early enteral administration of ART can exacerbate this risk. In a large French case–control study, being an infant born to a woman with HIV was associated with an increased risk of necrotising enterocolitis (OR 6.63, 95% CI 1.26–34.8; *P*=0.025), although the numbers were too small to ascertain the effect of maternal and/or infant ART [54]. Premature infants should be commenced on intravenous zidovudine until enteral feeding is established, when zidovudine may be given enterally. The premature dosing regimen should be used; in a scenario that fulfils low-risk criteria, zidovudine monotherapy can be used.

In a high-risk premature infant, combination PNP should be achieved with intravenous zidovudine together with transplacental loading of the neonate via oral dosing for the mother/birthing parent with antiretrovirals that efficiently cross the placenta and have long half-lives in the neonate. Options include single-dose nevirapine, double-dose tenofovir DX and dolutegravir (or raltegravir); see Section 8.7.2. With intravenous zidovudine in addition to transplacental ART, exposure to ART in the premature infant should be equivalent to combination PNP for at least the first 5–7 days of life.

The fusion inhibitor enfuvirtide is usually administered subcutaneously. It is a large molecule that does not cross the placenta. Although intravenous enfuvirtide has been given to a small number of infants born to women with multidrug-resistant HIV, no formal neonatal pharmacokinetic studies have been conducted to date. An unlicensed intravenous dosing regimen for infants at risk of multidrug-resistant HIV has been adapted from the paediatric subcutaneous treatment study [55] and an adult intravenous dosing study [56] (see Appendix 4 and seek expert advice).

11.1.6 Timing of neonatal PNP

Infant PNP should be started within 4 hours of delivery (see general principles in Section 11.1.1).

There are no clear data on how late infant PNP can be initiated and still be effective, but studies of infant PNP have started treatment early and animal data show a clear relationship between time of initiation and effectiveness, with no benefit demonstrated if commenced after >72 hours [57-59]. In an early cohort study of zidovudine monotherapy, PNP was only effective if started within 72 hours of birth [60]. Immediate administration of PNP is especially important where the woman/birthing parent has not received any ART before delivery.

11.1.7 Genotypic resistance in the mother/birthing parent

Proposed PNP for infants born to women/birthing parents with known ART resistance should be discussed in advance of delivery at a local or regional MDT, including a paediatrician with expertise in prevention of vertical HIV transmission. Cases can also be referred to the national paediatric virtual clinic (caroline.foster5@nhs.net, a.bamford@nhs.net, hermione.lyall@nhs.net). This is particularly important if ART is commenced or switched in pregnancy, if viral load in the mother/birthing parent is not suppressed or if difficulties are anticipated with regard to adherence and achieving viral

suppression. Proposed PNP regimens can be considered again and revised if viral load suppression is subsequently attained later in pregnancy.

If no antenatal plan for PNP is available at the time of delivery, the priority should be to start PNP within 4 hours with a standard regimen of nevirapine, zidovudine and lamivudine for high-risk scenarios, and zidovudine monotherapy if the low-risk criteria are met. PNP regimens can subsequently be modified after discussion with a paediatrician with expertise in prevention of vertical HIV transmission or by a local or national MDT.

Low-risk infants born to women/birthing parents with known genotypic resistance

For infants born to women/birthing parents on fully suppressive ART with a viral load <50 copies/mL and meeting all of the low-risk criteria, zidovudine monotherapy PNP remains a reasonable approach, even where the woman/birthing parent has a previous history of zidovudine exposure with resistance (thymidine-associated mutations). On ART, the risk of transmission from a woman/birthing parent with fully suppressed viral replication is extremely low (~0.1%) and the frequency of transmission of zidovudine-resistant virus is concomitantly very low. There are very limited data on the risk of transmission of zidovudine-resistant HIV in the context of fully suppressed viral load in the mother/birthing parent at the time of delivery. Where the resistance history is known in advance, expert advice should be sought to plan infant PNP in advance of delivery.

High-risk infants born to women/birthing parents with known genotypic resistance

There are no data available on the efficacy of modified combination PNP when NRTI and/or nevirapine resistance in the mother/birthing parent has been demonstrated. Expert advice should be sought, preferably early in pregnancy, and use of alternative drug combinations should be considered following careful risk assessment. As outlined in Section 11.1.4, dosing in term neonates is established for tenofovir DX, lamivudine, emtricitabine, abacavir, lopinavir/ritonavir and raltegravir and these are possible alternatives where there is resistance, but dosing for preterm infants is not well established for most of these agents. Options for the best regimen should be discussed by an expert MDT.

Where there is uncertainty regarding the choice of regimen or lack of availability of alternatives, priority should be given to starting the standard regimen (nevirapine, lamivudine and zidovudine) as soon as possible and modifying this later if needed after seeking urgent expert advice.

11.1.8 HIV-2

Recommendation

- We suggest that if a woman/person is known to have HIV-2 infection, the same advice should be followed as for HIV infant PNP but if high risk (combination PNP indicated), nevirapine will not be effective. Expert advice should be sought; if advice is not immediately available, zidovudine, lamivudine and raltegravir should be commenced until guidance is available (see Appendix 4) (Grade 2C).

Rationale

There are no data available to suggest that neonates born to women/birthing parents with HIV-2 who are at low risk of vertical transmission should be managed differently from neonates born to those with HIV-1. The same guidance should be followed as described above for infants exposed to HIV-1.

HIV-2 is intrinsically resistant to NNRTIs. There are no data to guide practice in the event of a high-risk delivery in the context of HIV-2 infection. The same guidance for the use of three-drug PNP should be followed as in Sections 11.1.3 and 11.1.4, replacing nevirapine with raltegravir. If raltegravir is not available, lopinavir/ritonavir could be used but with caution, as discussed above. Infants receiving raltegravir or lopinavir/ritonavir PNP should be monitored for toxicity in the first few days of life (see Appendix 4). Blood samples for infant testing should be sent to a UK laboratory that routinely provides HIV-2 testing.

11.1.9 PNP duration and PEP during breast/chestfeeding

Recommendations

- We recommend that infant PNP should not usually be given beyond 2 weeks for low-risk infants even if the infant is breast/chestfed (Grade 1C).
- We recommend that infants whose mothers/feeding parents become viraemic during breast/chestfeeding are considered HIV exposed and should be managed according to Chiva guidelines for PEP [61] (Grade 1D).

Rationale

Detailed guidance on monitoring of the mother/feeding parent and the infant during breast/chestfeeding is given in Section 12, including stopping or interrupting and in what circumstance breast/chestfeeding can be resumed. As supported breast/chestfeeding is only recommended in the context of low risk of HIV transmission, PNP beyond 2 weeks' duration is not recommended.

If a mother/feeding parent becomes viraemic while breast/chestfeeding, formula milk or alternative milk feeding should commence. The infant is considered postnatally exposed to HIV and should be managed according to Chiva guidelines for PEP in children [61]. Urgent clinical assessment of the infant is advised and HIV RNA PCR, and if aged over 4 weeks PEP should be started with dolutegravir, lamivudine and zidovudine for 4 weeks. If dispersible dolutegravir is not available, lopinavir/ritonavir or raltegravir can be used as alternatives as indicated in the Chiva PEP guidance [61]. PEP should be started as soon as possible with immediately available formulations and if necessary modified later after seeking expert advice. A risk assessment will need to take into account how long the infant might have been exposed to potentially infectious human milk, and when the most recent exposure occurred. A paediatrician with expertise in preventing and treating HIV in infants should be consulted, via the national MDT (caroline.foster5@nhs.net, a.bamford@nhs.net, hermione.lyall@nhs.net) if expertise is not available locally.

Further details on HIV and infant feeding, including information on monitoring during breast/chestfeeding, can be found in Section 12.

11.2 Immunisation

Recommendations

- We recommend that immunisations should be given as per the national schedule outlined in the Green Book [62] (Grade 1C).
- We recommend that rotavirus vaccine is not contraindicated (unless an HIV diagnosis has been confirmed and the infant is severely immunosuppressed) (Grade 1C).
- We recommend that infants at low risk of HIV transmission should receive BCG at the same time and for the same indication as for infants unexposed to HIV (including those who are breast/chestfed) (Grade 1D).
- For infants at high risk of HIV transmission, we recommend that BCG should be deferred until PCR testing is completed at 12 weeks of age and they are known to be negative (Grade 1D).

11.3 Diagnosing or excluding HIV

Recommendations

For infants at high risk:

- We recommend that molecular diagnostics for HIV infection should be performed on the following occasions (Grade 1C):
  - As soon as possible after birth, during the first 24 hours, prior to hospital discharge by HIV RNA and DNA PCR;
  - At 2 weeks by HIV RNA and DNA PCR (additional testing for high-risk infants only);
  - At 6 weeks by HIV RNA PCR (or DNA PCR instead);
  - At 12 weeks by HIV RNA PCR (or DNA PCR instead).
- We recommend HIV antibody testing to detect seroreversion at 24 months of age (Grade 1C).

For infants at low risk and not breast/chestfed:

- We recommend that molecular diagnostics for HIV infection should be performed on the following occasions (Grade 1C):
  - As soon as possible after birth, during the first 24 hours, prior to hospital discharge by HIV RNA PCR (or DNA PCR; only one test needed);
  - At 4–6 weeks (at least 2 weeks after cessation of PNP) by HIV RNA PCR (or DNA PCR; only one test needed);
  - At 10–12 weeks by HIV RNA PCR (or DNA PCR; only one test needed).
- We recommend HIV antibody testing to detect loss of placentally transferred antibody at 24 months of age (Grade 1C).

For infants at low risk and breast/chestfed:

- We recommend that molecular diagnostics for HIV infection should be performed on the following occasions:
  - As soon as possible after birth, during the first 24 hours, prior to hospital discharge by HIV RNA PCR (or DNA PCR) (Grade 1C);

- Monthly for the duration of breast/chestfeeding by HIV RNA PCR; following fully informed, shared decision-making, as long as viral load monitoring for the mother/feeding parent is taking place monthly, the interval between infant testing during breast/chestfeeding can be extended to a maximum of 2 months (Grade 1D);
- At 4 and 8 weeks after cessation of breast/chestfeeding by HIV RNA PCR (or DNA PCR) (Grade 1D).

- We recommend HIV antibody testing to detect seroreversion at 24 months of age, or at a minimum of 8 weeks after cessation of breast/chestfeeding if this is later (Grade 1C).

Rationale

HIV RNA PCR and HIV DNA PCR are both acceptable tests for diagnosing HIV in infancy. In a number of studies, including the large French perinatal cohort, equal or increased early sensitivity with amplification of viral RNA has been reported with no false-positive results [63,64].

Infants acquiring HIV intrapartum may have a very low peripheral blood HIV viral load, so HIV RNA/DNA may not be amplified at the time of birth from all infants who have acquired HIV. A positive HIV RNA/DNA result within 72 hours of birth is considered presumptive evidence of intrauterine transmission. Within the first few weeks of life the sensitivity of the viral diagnostic tests increases dramatically and detection by PCR is likely in 100% of non-breast/chestfed infants with HIV by 3 months of age [63].

Although HIV RNA and DNA assays have similar sensitivities, RNA assays commonly require 1 mL plasma and have faster turnaround times, whereas DNA assays can be performed on smaller samples but with longer turnaround times. If the sample requires dilution due to a low volume, which is often the case with paediatric samples, the lower limit of detection will be increased (with a corresponding decrease in assay sensitivity). In addition, where transmission may have occurred *in utero*, subsequent ART received by the mother/birthing parent including agents that cross the placenta may also lead to a false-negative RNA result in an infant who has acquired HIV infection. In this situation, the infant should be tested using DNA PCR. As HIV DNA PCR is not widely available, a faster result may be obtained with a local RNA test. However, if HIV RNA is detected, HIV DNA PCR is recommended as a confirmatory test.

As DNA PCR assays are usually in-house tests and considering the genomic diversity of HIV, there may be greater variability in performance than for current commercial HIV RNA tests. Where HIV DNA PCR is used for infant diagnosis, a sample from the mother/birthing parent should therefore always be obtained for HIV DNA amplification with, or prior to, the first infant sample to confirm that the primers used detect the virus of the mother/birthing parent. If the virus of the mother/birthing parent cannot be detected, a different primer set and/or test should be used.

The first test after birth should be conducted using infant blood, *not* cord blood, due to the risk of contamination of cord blood with the blood of the mother/birthing parent. Either RNA or DNA PCR may be used for low-risk infants, and it is recommended that both should be used for high-risk infants. This allows both sensitive detection of early infection by RNA PCR, and detection of intrauterine infection which has since been suppressed by transplacental ART by DNA PCR.

Evidence from the French perinatal cohort demonstrated that neonatal ART can delay the detection of both HIV RNA and DNA in the infant [64,65]. For this reason, subsequent routine HIV molecular tests are

performed at 2 weeks and 8 weeks after stopping PNP (i.e. usually at 4–6 weeks and 10–12 weeks of age depending on PNP duration). If all tests are negative and the infant has not been breast/chestfed, mothers/parents can be informed that the infant does not have HIV. For infants at high risk of infection, an additional early HIV test is recommended at 2–3 weeks of age. For breast/chestfed infants (see Section 12), HIV viral diagnostic tests should be undertaken monthly for the woman/feeding parent and infant while breast/chestfeeding, and then additionally for the infant at 4 and 8 weeks after cessation of breast/chestfeeding. Following fully informed shared decision-making, if viral load monitoring for the mother/feeding parent is taking place monthly, the interval between infant tests during breast/chestfeeding may be extended to a maximum of 2 months. The rationale for a maximum interval of 2 months for testing is the risk of rapid progression of HIV infection in the infant, with significant risk of morbidity and mortality should infection occur, even with an undetectable viral load in the mother/feeding parent during breast/chestfeeding.

For regular monitoring of the parent–infant pair during breast/chestfeeding, it is recommended that an RNA PCR is used as the turnaround time is faster, and urgent action is needed following a positive test.

Loss of transplacentally acquired HIV antibodies should be confirmed at 24 months of age [66]. Ideally an HIV antibody test should be used to confirm loss of antibodies rather than a combined HIV antibody–antigen test, and this will almost always be negative by 18 months of age in an infant without HIV. However, combined tests (fourth generation and above) are commonly used and may still give a positive HIV result until up to 2 years of age [67]. Laboratories providing testing for services following up infants at risk of vertical transmission of HIV are encouraged to provide access to HIV antibody testing. In addition, testing for loss of transplacentally aquired antibody remains important as, rarely, late postnatal infection may occur, even when all early HIV viral genome diagnostic tests were negative [68]. This may be due to breast/chestfeeding, premastication of infant food or intrafamilial or unknown exposure.

11.4 Management of infants diagnosed with HIV and prophylaxis for *Pneumocystis jirovecii* pneumonia

Recommendations

- We recommend that infants with a positive test for HIV should be referred urgently to a specialist centre for management of HIV according to Chiva guidelines/standards (https://www.chiva.org.uk/professionals/clinical-guidelines/) (Grade 1C).
- We recommend that infants should be started on trimethoprim-sulfamethoxazole (co-trimoxazole) prophylaxis from 4 weeks of age if HIV PCR testing is positive at any stage, or if the infant is confirmed to have HIV infection; this should be stopped if HIV infection is subsequently excluded (Grade 1C).
- We recommend that an HIV diagnosis in an infant should be reported to the obstetric unit in which the infant was born to allow investigation of any avoidable factors in transmission (Grade 1D).

Rationale

HIV services for children in the UK are organised in managed networks; details of regional centres for managing infants and children with HIV and contacts for local paediatricians can be found on the Chiva website (www.chiva.org.uk).

If any of the infant molecular HIV tests are found to be positive, an immediate repeat test on a new sample should be requested to confirm infection. When an infant is diagnosed with HIV, *P. jirovecii* prophylaxis should be started as soon as possible after the age of 4 weeks. An urgent referral should be made to the linked regional specialist HIV clinic for advice on initial clinical management and initiation of ART. HIV resistance testing for the mother/birthing parent and the infant should be undertaken to guide treatment. The transmission of HIV should be reported to the obstetric unit in which the infant was delivered to enable investigation of the circumstances of the transmission.

P. jirovecii pneumonia in infants with HIV is associated with high mortality and morbidity. However, as the risk of neonatal HIV infection has fallen to <1% where interventions for the prevention of vertical transmission are in place, the necessity for *P. jirovecii* prophylaxis has declined and in most European countries it is no longer prescribed routinely for infants at risk of vertical HIV transmission, even when an infant is born to a woman/birthing parent with a detectable viral load.

Neonates and infants with a first positive HIV molecular diagnostic test result should be started on trimethoprim-sulfamethoxazole prophylaxis immediately (for neonates this should only be once they reach 4 weeks of age) until HIV infection is confirmed or excluded (dosing information is available in the Penta guidelines [69]).

11.5 Management of infants born to mothers/birthing parents with hepatitis co-infection

Recommendations

- We recommend following national guidance for management of HBV in pregnant women/people and for prevention of transmission of HBV to the infant (see also Section 9.1) [70] (Grade 1D).
- We recommend following usual practice for investigation and management of HCV in pregnant women/people (Grade 1D).

Rationale

Immunoprophylaxis with HBV vaccine with or without HBIG given to the neonate has been shown to significantly reduce vertical transmission from women with HBV alone.

According to current guidance [70], HBIG should be given to the neonate if the mother/birthing parent:

- Is HBsAg positive and HBeAg positive;
- Is HBsAg positive, HBeAg negative and anti-HBe negative;
- Had acute HBV infection during pregnancy;
- Is HBsAg positive and known to have an HBV DNA level ≥1x10^6 IU/mL in any antenatal sample during this pregnancy (regardless of HBeAg and anti-HBe status);
- Is HBsAg positive and the infant weighs ≤1500 g.

In the absence of neonatal immunisation with HBV vaccine, with or without HBIG, the rate of vertical transmission from a pregnant woman with HBV alone who is both HBsAg and HBeAg positive is 70–90% and for a woman who is HBsAg positive but HBeAg negative the rate is 10–40% [71]. By co-administering vaccination (effectiveness of vaccine *vs* placebo: RR 0.28, 95% CI 0.2–0.4) and HBIG (effectiveness of HBIG/vaccine *vs* vaccine alone: RR 0.54, 95% CI 0.41–0.73), transmission rates can be reduced to between 0% and 14% [72]. The most important determinant of prophylaxis failure has been shown to be maternal serum HBV DNA levels [73].

Failure of birth-dose vaccine and HBIG in up to 9% of infants despite appropriate post-delivery immunoprophylaxis occurs mainly because of HBV infection *in utero* [74]. Receipt of ART by the mother/birthing parent together with prompt post-delivery neonatal immunoprophylaxis is the ideal approach for preventing vertical transmission of HBV.

No postnatal interventions are currently available for reducing the risk of transmission of HCV to infants born to women with HIV and HCV. Testing and follow-up of these infants should follow usual practice recommended for infants born to women with HCV mono-infection, with consideration of combining HIV and HCV follow-up assessments in the first 18 months to 2 years (see also Section 9.2). Curative therapy for HCV is now available from 3 years of age.

11.6 HIV-exposed HIV-negative children

Recommendation

- We recommend that in light of evidence of possible increased infectious morbidity in children who are HIV exposed and HIV negative, timely routine vaccination should be ensured and GPs, health visitors and secondary care physicians should be made aware of a possible increased risk in order to inform decisions when assessing risk in primary/secondary care (Grade 1D).

Rationale

With the increasingly successful rollout worldwide of interventions for the prevention of vertical transmission of HIV, the number of children who are HIV exposed and HIV negative is increasing in parallel. Growing evidence, mainly from observational studies in low- and middle-income countries, suggests that these children may be at increased risk of morbidity (mainly infection related) in early life (for reviews see [75,76]). Interpreting and drawing conclusions from these studies is challenging because of multiple potential confounding factors. *In utero* exposure to an altered maternal immune system and ART have both been proposed as potential factors contributing to an impairment in immunity among HIV-exposed HIV-negative neonates [76]. Much less information is available from high-income settings and findings are inconsistent [77-82].

In view of these concerns, although it remains to be demonstrated that children who are HIV exposed and HIV negative in the UK are at increased risk of morbidity, the writing group recommends that all healthcare professionals involved in the care of these children are made aware of this potential additional risk factor. The need for timely and complete routine immunisations should also be emphasised. Services providing prevention of vertical transmission follow-up care should provide

general information relating to this and should also be available to answer any questions on specific risk from individual families and any healthcare professionals involved in their ongoing care.

11.7 References

1. Connor EM, Sperling RS, Gelber R *et al.* Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med* 1994; **331**: 1173–1180.

2. Lallemant M, Jourdain G, Le Coeur S *et al.* A trial of shortened zidovudine regimens to prevent mother-to-child transmission of human immunodeficiency virus type 1. Perinatal HIV Prevention Trial (Thailand) Investigators. *N Engl J Med* 2000; **343**: 982–991.

3. Gilleece Y, Tariq S, Bamford A *et al*. British HIV Association guidelines for the management of HIV in pregnancy and postpartum 2018. *HIV Med* 2019; **20 Suppl 3**: s2–s85.

4. Nguyen TTT, Kobbe R, Schulze-Sturm U, *et al*. Reducing hematologic toxicity with short course postexposure prophylaxis with zidovudine for HIV-1 exposed infants with low transmission risk. *Pediatr infect Dis J* 2019; **38**: 727–730.

5. NHS England. ISOSS HIV report 2022. 2023. Available at: https://www.gov.uk/government/publications/infectious-diseases-in-pregnancy-screening-isoss-hiv-report-2022/isoss-hiv-report-2022 (accessed July 2024).

6. Sibiude J, Le Chenadec J, Mandelbrot L *et al*. Update of perinatal human immunodeficiency virus type 1 transmission in france: zero transmission for 5482 mothers on continuous antiretroviral therapy from conception and with undetectable viral load at delivery. *Clin Infect Dis* 2023; **76**: e590–e598.

7. Cresswell F, Asanati K, Bhagani S *et al.* UK guideline for the use of HIV post-exposure prophylaxis 2021. *HIV Med* 2022; **23**: 494–545.

8. Federal Office of Public Health. *Guidelines and recommendations on sexually transmitted infections*. Available at: https://www.bag.admin.ch/en/guidelines-and-recommendations-on-sexually-transmitted-infections (accessed September 2025).

9. Traytel A, Scherrer A, Aebi-Popp K *et al.* Discontinuation of neonatal postexposure prophylaxis in infants born to HIV-infected mothers with suppressed plasma viral load: safety and implementation of the new Swiss recommendations. *HIV Med* 2019; **20 Suppl 9**: 3–316.

10. Lehman DA, Farquhar C. Biological mechanisms of vertical human immunodeficiency virus (HIV-1) transmission. *Rev Med Virol* 2007; **17**: 381–403.

11. Kinder JM, Stelzer IA, Arck PC, Way SS. Immunological implications of pregnancy-induced microchimerism. *Nat Rev Immunol* 2017; **17**: 483-494.

12. Xu YY, Liu HH, Zhong YW *et al.* Peripheral blood mononuclear cell traffic plays a crucial role in mother-to-infant transmission of hepatitis B virus. *Int J Biol Sci* 2015; **11**: 266–273.

13. Townsend CL, Byrne L, Cortina-Borja M *et al.* Earlier initiation of ART and further decline in mother-to-child HIV transmission rates, 2000-2011. *AIDS* 2014; **28**: 1049–1057.

14. Dollfus C, Le Chenadec J, Mandelbrot L *et al*.; ANRS CO1/CO11 study group. Improved hematologic outcomes in HIV1-exposed infants receiving nevirapine compared with zidovudine for postnatal prophylaxis in a high resource setting. *Pediatr Infect Dis J* 2022; **41**: 420–423.

15. European Collaborative Study. Mother-to-child transmission of HIV infection in the era of highly active antiretroviral therapy. *Clin Infect Dis* 2005; **40**: 458–465.

16. Nielsen-Saines K, Watts DH, Veloso VG *et al.* Three postpartum antiretroviral regimens to prevent intrapartum HIV infection. *N Engl J Med* 2012; **366**: 2368–2379.

17. Taha TE, Kumwenda NI, Gibbons A *et al.* Short postexposure prophylaxis in newborn babies to reduce mother-to-child transmission of HIV-1: NVAZ randomised clinical trial. *Lancet* 2003; **362**: 1171–1177.

18. Moodley D, Moodley J, Coovadia H *et al.* A multicenter randomized controlled trial of nevirapine versus a combination of zidovudine and lamivudine to reduce intrapartum and early postpartum mother-to-child transmission of human immunodeficiency virus type 1. *J Infect Dis* 2003; **187**: 725–735.

19. Taha TE, Kumwenda NI, Hoover DR *et al.* Nevirapine and zidovudine at birth to reduce perinatal transmission of HIV in an African setting: a randomized controlled trial. *JAMA* 2004; **292**: 202–209.

20. Lallemant M, Amzal B, Sripan P *et al*.; PHPT-5 site investigators. Perinatal antiretroviral intensification to prevent intrapartum HIV transmission when antenatal antiretroviral therapy is initiated less than 8 weeks before delivery. *J Acquir Immune Defic Syndr* 2020; **84**: 313–322.

21. Haile-Selassie H, Townsend C, Tookey P. Use of neonatal post-exposure prophylaxis for prevention of mother-to-child HIV transmission in the UK and Ireland, 2001-2008. *HIV Med* 2011; **12**: 422–427.

22. Chiappini E, Galli L, Giaquinto C *et al.* Use of combination neonatal prophylaxis for the prevention of mother-to-child transmission of HIV infection in European high-risk infants. *AIDS* 2013; **27**: 991–1000.

23. Francis K, Toledo G, Georgiou S *et al*. *Current overview of paediatric follow-up of infants exposed to HIV in England*. Available at: https://www.ucl.ac.uk/integrated-screening-outcomes-surveillance/sites/integrated_screening_outcomes_surveillance/files/current_overview_of_paediatric_followup_final.pdf (accessed July 2024).

24. Boucher FD, Modlin JF, Weller S *et al.* Phase I evaluation of zidovudine administered to infants exposed at birth to the human immunodeficiency virus. *J Pediatr* 1993; **122**: 137–144.

25. Mirochnick M, Nielsen-Saines K, Pilotto JH *et al.* Nelfinavir and lamivudine pharmacokinetics during the first two weeks of life. *Pediatr Infect Dis J* 2011; **30**: 769–772.

26. Tremoulet AH, Capparelli EV, Patel P *et al.* Population pharmacokinetics of lamivudine in human immunodeficiency virus-exposed and -infected infants. *Antimicrob Agents Chemother* 2007; **51**: 4297–4302.

27. Hirt D, Ekouevi DK, Pruvost A *et al.* Plasma and intracellular tenofovir pharmacokinetics in the neonate (ANRS 12109 trial, step 2). *Antimicrob Agents Chemother* 2011; **55**: 2961–2967.

28. Hirt D, Urien S, Rey E *et al.* Population pharmacokinetics of emtricitabine in human immunodeficiency virus type 1-infected pregnant women and their neonates. *Antimicrob Agents Chemother* 2009; **53**: 1067–1073.

29. Bekker A, Capparelli EV, Violari A et al. Abacavir dosing in neonates from birth to 3 months of life: a population pharmacokinetic modelling and simulation study. *Lancet HIV* 2022; **9**: e24–e31.

30. Chadwick EG, Capparelli EV, Yogev R *et al.* Pharmacokinetics, safety and efficacy of lopinavir/ritonavir in infants less than 6 months of age: 24 week results. *AIDS* 2008; **22**: 249–255.

31. Chadwick EG, Yogev R, Alvero CG *et al.* Long-term outcomes for HIV-infected infants less than 6 months of age at initiation of lopinavir/ritonavir combination antiretroviral therapy. *AIDS* 2011; **25**: 643–649.

32. Chadwick EG, Pinto J, Yogev R *et al.* Early initiation of lopinavir/ritonavir in infants less than 6 weeks of age: pharmacokinetics and 24-week safety and efficacy. *Pediatr Infect Dis J* 2009; **28**: 215–219.

33. Urien S, Firtion G, Anderson ST *et al.* Lopinavir/ritonavir population pharmacokinetics in neonates and infants. *Br J Clin Pharmacol* 2011; **71**: 956–960.

34. Clarke DF, Acosta EP, Cababasay M *et al.* Raltegravir (RAL) in neonates: dosing, pharmacokinetics (PK), and safety in HIV-1-exposed neonates at risk of infection (IMPAACT P1110). *J Acquir Immune Defic Syndr* 2020; **84**: 70–77.

35. Mirochnick M, Siminski S, Fenton T *et al.* Nevirapine pharmacokinetics in pregnant women and in their infants after in utero exposure. *Pediatr Infect Dis J* 2001; **20**: 803–805.

36. Taylor GP, Lyall EG, Back D *et al.* Pharmacological implications of lengthened in-utero exposure to nevirapine. *Lancet* 2000; **355**: 2134–2135.

37. Benaboud S, Ekouevi DK, Urien S *et al.* Population pharmacokinetics of nevirapine in HIV-1-infected pregnant women and their neonates. *Antimicrob Agents Chemother* 2011; **55**: 331–337.

38. Mirochnick M, Dorenbaum A, Blanchard S *et al.* Predose infant nevirapine concentration with the two-dose intrapartum neonatal nevirapine regimen: association with timing of maternal intrapartum nevirapine dose. *J Acquir Immune Defic Syndr* 2003; **33**: 153–156.

39. Mirochnick M, Nielsen-Saines K, Pilotto JH *et al.* Nevirapine concentrations in newborns receiving an extended prophylactic regimen. *J Acquir Immune Defic Syndr* 2008; **47**: 334–337.

40. Bunglawala F, Rajoli RKR, Mirochnick M *et al*. Prediction of dolutegravir pharmacokinetics and dose optimization in neonates via physiologically based pharmacokinetic (PBPK) modelling. *J Antimicrob Chemother* 2020; **75**: 640–647.

41. Kakkar FW, Samson L, Vaudry W *et al.* Safety of combination antiretroviral prophylaxis in high-risk HIV-exposed newborns: a retrospective review of the Canadian experience. *J Int AIDS Soc* 2016; **19**: 20520.

42. Smith C, Forster JE, Levin MJ *et al.* Serious adverse events are uncommon with combination neonatal antiretroviral prophylaxis: a retrospective case review. *PLoS One* 2015; **10**: e0127062.

43. Bitnun A, Samson L, Chun TW *et al.* Early initiation of combination antiretroviral therapy in HIV-1-infected newborns can achieve sustained virologic suppression with low frequency of CD4+ T cells carrying HIV in peripheral blood. *Clin Infect Dis* 2014; **59**: 1012–1019.

44. Lau E, Brophy J, Samson L *et al.* Nevirapine pharmacokinetics and safety in neonates receiving combination antiretroviral therapy for prevention of vertical HIV transmission. *J Acquir Immune Defic Syndr* 2017; **74**: 493–498.

45. Ruel TD, Capparelli EV, Tierney C *et al*. Pharmacokinetics and safety of early nevirapine-based antiretroviral therapy for neonates at high risk for perinatal HIV infection: a phase 1/2 proof of concept study. *Lancet HIV* 2021; **8**: e149–e157.

46. Cressey TR, Punyawudho B, Le Coeur S *et al.* Assessment of nevirapine prophylactic and therapeutic dosing regimens for neonates. *J Acquir Immune Defic Syndr* 2017; **75**: 554–560.

47. Maswabi K, Ajibola G, Bennett K *et al*. Safety and efficacy of starting antiretroviral therapy in the first week of life. *Clin Infect Dis* 2021; **72**: 388–393.

48. Trahan MJ, Lamarre V, Metras ME, Kakkar F. Use of riple combination antiretroviral therapy with raltegravir as empiric HIV therapy in the high-risk HIV-exposed newborn. *Pediatr Infect Dis J* 2019; **38**: 410–412

49. Simon A, Warszawski J, Kariyawasam D *et al.* Association of prenatal and postnatal exposure to lopinavir-ritonavir and adrenal dysfunction among uninfected infants of HIV-infected mothers. *JAMA* 2011; **306**: 70–78.

50. US Food and Drug Administration. *FDA drug safety communication: serious health problems seen in premature babies given Kaletra (lopinavir/ritonavir) oral solution*. 2011. Available at: www.fda.gov/Drugs/DrugSafety/ucm246002.htm (accessed August 2024).

51. Rosebush JC, Best BM, Chadwick EG *et al*.; the IMPAACT 2007 Study Team. Pharmacokinetics and safety of maraviroc in neonates. *AIDS* 2021; **35**: 419–427.

52. McFarland EJ, Cunningham CK, Muresan P *et al*. Safety, tolerability, and pharmacokinetics of a long-acting broadly neutralizing human immunodeficiency virus type 1 (HIV-1) monoclonal antibody VRC01LS in HIV-1-exposed newborn infants. *J Iinfect Dis* 2021; **224**: 1916–1924.

53. Capparelli EV, Mirochnick M, Dankner WM *et al.* Pharmacokinetics and tolerance of zidovudine in preterm infants. *J Pediatr* 2003; **142**: 47–52.

54. Desfrere L, de Oliveira I, Goffinet F *et al.* Increased incidence of necrotizing enterocolitis in premature infants born to HIV-positive mothers. *AIDS* 2005; **19**: 1487–1493.

55. Wiznia A, Church J, Emmanuel P *et al.* Safety and efficacy of enfuvirtide for 48 weeks as part of an optimized antiretroviral regimen in pediatric human immunodeficiency virus 1-infected patients. *Pediatr Infect Dis J* 2007; **26**: 799–805.

56. Zhang X, Nieforth K, Lang JM *et al.* Pharmacokinetics of plasma enfuvirtide after subcutaneous administration to patients with human immunodeficiency virus: inverse Gaussian density absorption and 2-compartment disposition. *Clin Pharmacol Ther* 2002; **72**: 10–19.

57. Van Rompay KK, Otsyula MG, Marthas ML *et al.* Immediate zidovudine treatment protects simian immunodeficiency virus-infected newborn macaques against rapid onset of AIDS. *Antimicrob Agents Chemother* 1995; **39**: 125–131.

58. Tsai CC, Emau P, Follis KE *et al.* Effectiveness of postinoculation (R)-9-(2-phosphonylmethoxypropyl) adenine treatment for prevention of persistent simian immunodeficiency virus SIVmne infection depends critically on timing of initiation and duration of treatment. *J Virol* 1998; **72**: 4265–4273.

59. Bottiger D, Johansson NG, Samuelsson B *et al.* Prevention of simian immunodeficiency virus, SIVsm, or HIV-2 infection in cynomolgus monkeys by pre- and postexposure administration of BEA-005. *AIDS* 1997; **11**: 157–162.

60. Wade NA, Birkhead GS, Warren BL *et al*. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. *N Engl J Med* 1998; **339**: 1409–1414.

61. Foster C, Lees EA, Lyall EGH *et al*. Post-exposure prophylaxis (PEP) guidelines for infants, children and adolescents potentially exposed to blood-borne viruses. 2023 Available at: https://www.chiva.org.uk/wp-content/uploads/2023/11/CHIVA_PEP_2023-Final.pdf (accessed July 2024).

62. UK Health Security Agency. *UK immunisation schedule: the green book, chapter 11*. 2022. Available at: www.gov.uk/government/publications/immunisation-schedule-the-green-book-chapter-11 (accessed June 2024).

63. Burgard M, Blanche S, Jasseron C *et al.* Performance of HIV-1 DNA or HIV-1 RNA tests for early diagnosis of perinatal HIV-1 infection during anti-retroviral prophylaxis. *J Pediatr* 2012; **160**: 60–66.e61.

64. Burgard M, Blanche S, Mayaux MJ *et al.* Impact of neonatal prophylaxis on early diagnosis in newborns. *Conference on Retroviruses and Opportunistic Infections*. February 2003. San Francisco, CA, USA.

65. Millar JR, Mvo Z, Bengu N *et al*.; Ucwaningo Lwabantwana Consortium Group. Increasing diagnostic uncertainties in children with in utero HIV infection. *Pediatr Infect Dis J* 2019; **38**: e166–e168.

66. Hindocha A, Foster C, Randell P *et al.* Optimal timing for serological screening for HIV-exposed uninfected infants: the later the better? *Annual Conference of the British HIV Association (BHIVA)*. April 2019. Bournemouth, UK. Available at: https://www.bhiva.org/file/5ca469a56b895/AbstractBook2019.pdf (accessed August 2024).

67. Nastouli E, Atkins M, Seery P *et al.* False-positive HIV antibody results with ultrasensitive serological assays in uninfected infants born to mothers with HIV. *AIDS* 2007; **21**: 1222–1223.

68. Frange P, Burgard M, Lachassinne E *et al.* Late postnatal HIV infection in children born to HIV-1-infected mothers in a high-income country. *AIDS* 2010; **24**: 1771–1776.

69. Penta. *Treatment guidelines*. *Guidance on dosing and use of paediatric formulations*. 2024. Available at: https://penta-id.org/hiv/treatment-guidelines/ (accessed November 2024).

70. UK Health Security Agency. *Hepatitis B: the green book, chapter 18*. 2024. Available at: https://www.gov.uk/government/publications/hepatitis-b-the-green-book-chapter-18 (accessed July 2024).

71. Gentile I, Zappulo E, Buonomo AR, Borgia G. Prevention of mother-to-child transmission of hepatitis B virus and hepatitis C virus. *Expert Rev Anti Infect Ther* 2014; **12**: 775–782.

72. Lee C, Gong Y, Brok J *et al*. Effect of hepatitis B immunisation in newborn infants of mothers positive for hepatitis B surface antigen: systematic review and meta-analysis. *BMJ* 2006; **332**: 328–336.

73. Kumar M, Singh T, Sinha S. Chronic hepatitis B virus infection and pregnancy. *J Clin Exp Hepatol* 2012; **2**: 366–381.

74. Wiseman E, Fraser MA, Holden S *et al.* Perinatal transmission of hepatitis B virus: an Australian experience. *Med J Aust* 2009; **190**: 489–492.

75. Evans C, Jones CE, Prendergast AJ. HIV-exposed, uninfected infants: new global challenges in the era of paediatric HIV elimination. *Lancet Infect Dis* 2016; **16**: e92–e107.

76. Afran L, Garcia Knight M, Nduati E *et al.* HIV-exposed uninfected children: a growing population with a vulnerable immune system? *Clin Exp Immunol* 2014; **176**: 11–22.

77. Taron-Brocard C, Le Chenadec J, Faye A *et al.* Increased risk of serious bacterial infections due to maternal immunosuppression in HIV-exposed uninfected infants in a European country. *Clin Infect Dis* 2014; **59**: 1332–1345.

78. Epalza C, Goetghebuer T, Hainaut M *et al.* High incidence of invasive group B streptococcal infections in HIV-exposed uninfected infants. *Pediatrics* 2010; **126**: e631–638.

79. Adler C, Haelterman E, Barlow P *et al.* Severe infections in HIV-exposed uninfected infants born in a European country. *PLoS One* 2015; **10**: e0135375.

80. Macdonald EM, Ng R, Yudin MH *et al.* Postpartum maternal and neonatal hospitalizations among women with HIV: a population-based study. *AIDS Res Hum Retroviruses* 2015; **31**: 967–972.

81. Moseholm E, Helleberg M, Sandholdt H *et al*. Children exposed or unexposed to human immunodeficiency virus: Weight, height, and body mass index during the first 5 years of life-a Danish nationwide cohort. *Clin Infect Dis* 2020; **70**: 2168–2177.

82. Dauby N, Chamekh M, Melin P *et al*. Increased risk of group B streptococcus invasive infection in HIV-exposed but uninfected infants: a review of the evidence and possible mechanisms. *Front Immunol* 2016; **7**: 505.

12 HIV and infant feeding

12.1 Infant feeding decision-making

Recommendations

- We recommend a model of shared decision-making, facilitating open and supportive discussions about infant feeding, and tailoring advice to women/feeding parents (and their families where appropriate and with their consent) (Grade 1D).
- Where possible, we recommend that infant feeding should be discussed proactively by the HIV MDT by the end of the second trimester at the latest, and revisited in the third trimester, with the decision documented in the antenatal notes and birth plan (Grade 1D).
- We recommend that the HIV MDT shares HIV-specific sources of information and support, including peer support, with individuals making infant feeding decisions (Grade 1D).

Auditable outcomes

- Proportion of pregnant women/people living with HIV for whom a discussion about infant feeding by the end of the second trimester has been documented.
- Proportion of pregnant women/people living with HIV with a documented infant feeding decision in their birth plan.
- Proportion of pregnant women/people for whom provision of HIV-specific patient information resources (printed or online) has been documented.

Rationale

How to feed a baby is an important decision that is taken seriously by parents, irrespective of HIV status. In almost all cases, the decision is motivated by what parents feel is best for their baby. Abstaining from breast/chestfeeding completely remains the only way of removing *all* risk of postpartum transmission of HIV. However, there is a lack of data on the risk of HIV transmission through breast/chestfeeding in high-income settings when the mother/feeding parent has been on long-term suppressive ART. In addition, there have been no comparisons of long-term non-HIV-related mother/parent and child outcomes among those who breast/chestfeed and those who exclusively formula feed.

We recognise that decisions about infant feeding can be complex, requiring parents to balance the very low risk of HIV transmission through breast/chestfeeding (when the mother/feeding parent is adherent to ART and virologically suppressed) with the benefits of breast/chestfeeding to both the infant and mother/feeding parent. These decisions are usually based on the relative importance ascribed by the family to feeding preferences or the absolute avoidance of HIV transmission.

The decision-making process is further complicated by differences in HIV and infant feeding guidelines worldwide. It is important that the reasons underlying these differences are addressed directly with parents. The WHO advises that women with HIV breastfeed for 12–24 months, with ART or antiretroviral prophylaxis and adherence support [1]. However, WHO guidance is aimed at low- and middle-income countries where there is a high risk of infant morbidity and mortality from diarrhoea, pneumonia and other infections, and where formula feeding may not be safe or affordable for families. In high-income

settings such as the UK, where we assume access to safe and clean water and formula, these risks are much lower and therefore formula feeding can be recommended.

We recommend a model of shared decision-making, facilitating open and supportive discussions about infant feeding, tailoring advice to the individual family, and providing sufficient information for them to make an informed decision based on available data and their preferences [2,3]. It is important to ascertain the views of women/birthing parents on infant feeding prior to delivery, and to ensure that they have evidence-based information and support to make their decision. Data suggest that many women are unaware of current HIV and infant feeding data and guidelines and/or would like more information about feeding options [4-6]. Therefore we recommend that infant feeding is discussed proactively by the HIV MDT by the end of the second trimester at the latest, where possible, allowing women/birthing parents sufficient time to make an informed decision. This should be revisited in the third trimester, prior to delivery, and the feeding decision documented in the clinical notes and the birth plan.

Qualitative data from a study on infant feeding decision-making by parents living with HIV in the UK highlight the important role played by male partners of women living with HIV [7]. Therefore, we encourage the HIV MDT to include partners in conversations about infant feeding, when safe and appropriate [7], and to provide support to women/birthing parents to enable them to have such discussions themselves.

Infant feeding decision-making can be further supported by HIV-specific resources such as mentor mothers (via https://4mmm.org/) and the online platform 'Feeding a baby when living with HIV' (https://hexi.ox.ac.uk/Feeding-a-baby-while-living-with-HIV/overview). An information leaflet to support decision-making based on the findings from the NOURISH-UK HIV and infant feeding study, as well as two patient breast/chestfeeding information leaflets produced by the writing group, can be found on the BHIVA website (https://www.bhiva.org/pregnancy-guidelines).

12.2 HIV transmission via breastmilk/human milk

Recommendation

- We recommend that the HIV MDT should discuss with all pregnant women/people the evidence that U=U does not apply to breast/chestfeeding, and that the risk of transmission is greatly reduced by ART but is not zero (Grade 1B).

Rationale

There are very limited data on the risk of HIV transmission via breastmilk in high-income countries [8,9]. Between 2012 and 2021, 203 (2.4%) women living with HIV in the UK were reported to have been supported to breastfeed, with no reported cases of postnatal HIV transmission at the time of study publication [10]. Of note, 34 infants were still awaiting confirmatory testing and testing was not completed for five infants. The Swiss Mother and Child HIV Cohort Study has reported on a smaller number (*n*=25) of mother–child pairs where women had breastfed their infants (median duration 6.3 months); there had been no cases of postnatal transmission at the time of publication in 2023 [11].

In the IMPAACT PROMISE study, a randomised, open-label, clinical trial conducted at 14 sites in Africa and India, the effect of prolonged infant PNP on vertical transmission was compared with the effect of maternal ART throughout the breastfeeding period (*n*=2431) [12]. There was no significant difference in vertical transmission when the infant received PNP or the mother received ART. In the maternal ART arm, postnatal HIV transmission rate was 0.3% (95% CI 0.1–0.6) at 6 months, equating to 1/333, and 0.6% (95% CI 0.4–1.1) at 12 months, equating to 1/167 [12]. The more recent DolPHIN-2 trial, comparing dolutegravir and efavirenz initiated late in pregnancy and continued after delivery during breastfeeding (*n*=268), reported that one infant, in the efavirenz arm, acquired HIV postnatally [13].

The U=U statement applies only to sexual transmission; U=U does not apply to breast/chestfeeding. Two infants acquired HIV through breastfeeding in the PROMISE study [14]. The case of postnatal transmission in the DolPHIN-2 trial was detected at 72 weeks postpartum, in the context of optimal maternal virological suppression and no other known risk factors (e.g. mastitis, drug resistance or receiving breastmilk from another woman) [13]. All women enrolled in this study commenced ART after 28 weeks of pregnancy [13]. Potential explanations for HIV transmission to infants despite maternal/parental virological suppression include viraemia between monitoring tests in the mother/feeding parent, discordant plasma and breastmilk/human milk HIV viral load and cell-associated HIV viral reservoirs in milk [13]. There is a lack of data on the effects of long-term ART or newer antiretroviral agents on these reservoirs.

Factors associated with increased risk of HIV transmission through breast/chestfeeding include detectable HIV plasma and/or breastmilk/human milk viral load [14-16], shorter duration of ART prior to initiating breast/chestfeeding [17,18], reduced plasma and milk antiretroviral drug concentrations [19] and HIV drug resistance [16] or a low CD4 count in the mother/feeding parent [14] (Box 12.1).

Longer duration of breast/chestfeeding increases the risk of HIV transmission. The PROMISE study demonstrated a doubling of risk of transmission at 12 months of breastfeeding (compared to 6 months). A meta-analysis of studies on postnatal transmission of HIV through breastfeeding in low- and middle-income countries reported transmission rates of 1.08% (95% CI 0.32–1.85) at 6 months and 2.93% (95% CI 0.68–5.18) at 12 months when a woman was treated with ART [17]. Postnatal transmission rates at 18 months of breastfeeding ranged from 0.7% to 6.7%. However, women did not receive ART beyond 6 months postpartum and often breastfed for longer than 6 months in the included studies. In an analysis of data from four studies (all published before 2012) in Africa in which women were on ART prior to conception, it was estimated that postnatal HIV transmission probability was 0.16% per month of breastfeeding for women on ART [20].

Other factors that increase the risk of HIV transmission through breastfeeding, reported in older studies in which women were not on ART, include breast and nipple infection/inflammation, infant mouth or gut infection/inflammation and mixed feeding, in particular solid food given to infants less than 2 months of age (see Section 12.5) [21]. Of note, the majority of factors are established from studies of women not on ART and there are no data on risk factors for women/feeding parents who are virologically suppressed on ART in high-income countries [8,9,22]. In the absence of data, we have to assume that these factors may still increase the risk of transmission, albeit less so in the setting of virological suppression on ART.

Box 12.1 Factors associated with increased risk of HIV transmission through breast/chestfeeding (all data from studies in which women were not on ART during the breastfeeding period)

- Detectable HIV plasma or breastmilk/human milk viral load
- New HIV infection during breast/chestfeeding
- Shorter duration of ART prior to initiating breast/chestfeeding
- Reduced plasma or breastmilk/human milk drug concentration
- HIV drug resistance
- Lower maternal CD4 count
- Longer duration of breast/chestfeeding
- Breast/chest and nipple infection/inflammation
- Infant mouth or gut infection/inflammation
- Mixed feeding (giving both breastmilk/human milk *and* formula, other non-human milks, other liquids and/or solids) (see Section 12.7)

12.3 Formula (and other alternative) feeding and HIV in the UK

Recommendation

- Exclusive formula feeding removes all risk of postpartum HIV transmission to infants, therefore we recommend that women/birthing parents feed their babies with formula milk (or other alternatives outlined below) exclusively to ensure that the risk of HIV transmission to their infants postpartum is zero (Grade 1A).

Rationale

Exclusive formula feeding (or alternative feeding methods such as use of donor breastmilk/human milk where the donor has had an HIV negative test) is currently the only way to reduce the risk of postpartum transmission of HIV to zero. There have been cases of transmission of HIV through breastfeeding despite undetectable maternal HIV viral load [13,14]. Furthermore, adherence to ART can be compromised in the postpartum period as a result of the demands of caring for a newborn infant (see Section 13.2). Incomplete adherence and the resulting detectable HIV plasma or breastmilk/human milk viral load increases the risk of HIV transmission.

Other considerations are the lack of lactation studies for some antiretroviral agents, meaning that the pharmacokinetic properties of antiretrovirals in breastmilk/human milk, as well as the potential effects of exposure to ART in milk on infants who do not acquire HIV, are poorly understood [8].

Infant 'humanised' formula is usually derived from cow's milk and is available in powdered or ready-to-use liquid form. There is no clinically significant difference in nutrient content of infant milks available in the UK due to strict regulations governing the composition of infant formula. Further information on formula milk is available at https://infantmilkinfo.org/.

The writing group has previously been asked to include in these guidelines information on the option of donor breastmilk/human milk in place of formula feeding. In the UK, this is a highly limited resource

which requires specific funding and is prioritised for infants with the highest clinical needs (e.g. very preterm or very ill infants). Therefore, donor milk from regulated sources is unlikely to be available as an alternative to breast/chestfeeding for women/birthing parents with HIV without additional needs. In Scotland, the Scottish Donor Milk Bank may be able to support local breast/chestfeeding for women/birthing parents with HIV (email: tay.arvservice@nhs.scot).

It is unsafe to obtain donor breastmilk/human milk from sources that do not adhere to NICE recommendations, which ensure that donor milk is screened for viral and bacterial infections and is processed and stored safely [23]. A list of donor milk banks in the UK is available from the UK Association of Milk Banks (http://www.ukamb.org/). Breast/chestfeeding undertaken by someone who has tested negative for HIV (such as a partner) is also a potential alternative method of feeding that would remove the risk of postpartum HIV transmission.

As highlighted in Section 12.1, we advise a model of shared decision-making with women/birthing parents.

12.3.1 Supporting women/people living with HIV to formula feed

Recommendations

- We recommend that women/birthing parents who do not breast/chestfeed should receive support from the HIV MDT because of the possibility of financial, social and psychological repercussions (Grade 1C).
- We recommend that efforts should be made to provide free formula and equipment to minimise vertical transmission of HIV (Grade 1D).

Rationale

Not breast/chestfeeding can have emotional, financial and social impacts on women/birthing parents living with HIV [6,24-27]. We advise the HIV MDT to provide appropriate support during and after pregnancy (which may include peer, psychological, practical and financial support) [24,25,28].

Some parents will forgo their own nutritional needs in order to afford formula milk for their infant, thus compromising their own health [25]. Women/birthing parents with irregular immigration status and no recourse to public funds and/or on low incomes may experience significant financial barriers to accessing formula milk [25]. The provision of free formula milk, and the appropriate equipment to use it, alleviates the financial burden of this key HIV prevention tool [24]. This ensures that parents can make decisions about how to feed their infant without being influenced by cost. Free provision of formula milk also has the potential to improve longer-term retention in HIV care postpartum [29,30].

We acknowledge that provision of free formula milk to mothers/feeding parents living with HIV remains inconsistent across the UK. In Scotland, mothers/feeding parents living with HIV can access free infant formula milk and a starter pack (steriliser, bottles and a cleaning brush) through the HIV charity Waverley Care (https://www.waverleycare.org/find-a-service/free-infant-formula/). This scheme is funded by a group of NHS Boards in Scotland. We advise clinics and voluntary sector organisations in

other parts of the UK to map local services (e.g. the George House Trust in Manchester [https://ght.org.uk/] and the London-based food bank for people living with HIV [www.foodchain.org.uk]). Other examples of formula milk schemes can be found in the National AIDS Trust policy briefing on access to formula milk for women living with HIV [25]. Some families may also qualify for the Healthy Start scheme, which provides financial assistance to buy infant formula milk, and other essential food and vitamins (https://www.gov.uk/healthy-start).

12.4 Suppression of lactation

Recommendation

- We recommend that women/birthing parents who do not breast/chestfeed their infant, either by choice or because of a viral load ≥50 copies/mL, should be offered cabergoline to suppress lactation (Grade 1C).

Rationale

Cabergoline should be offered for suppression of lactation, after discussion in advance with all women/birthing parents, and the decision documented in the birth plan. It should be made clear that it will reduce the discomfort of lactation if not breast/chestfeeding, but that it will prevent them from breast/chestfeeding once taken.

A prospective study of 67 women living with HIV in Canada who received cabergoline postpartum reported 98.3% (95% CI 89.5–99.9) partial or complete efficacy (i.e. inhibition of lactation) at day 14; adverse events were relatively mild and transient [31].

Cabergoline should be administered during the first day postpartum. The recommended dose is 1 mg (two 0.5 mg tablets) given as a single dose. If lactation needs to be suppressed once already established, the recommended dose is 0.25 mg every 12 hours for 2 days (1 mg total dose) (see https://bnf.nice.org.uk/drugs/cabergoline/).

12.5 Breast/chestfeeding and HIV in the UK

Recommendations

- We recommend that women/birthing parents with a viral load <50 copies/mL on ART with good adherence, and who choose to breast/chestfeed, should be supported to do so by the HIV MDT (Grade 1D).
- We recommend that the HIV MDT should inform all women/birthing parents who want to breast/chestfeed about the ongoing low risk of transmission of HIV through breast/chestfeeding even when viral load is <50 copies/mL on ART, the importance of adherence to ART to minimise the risk of transmission and the requirement for extra clinical monitoring for both themselves and their infants (Grade 1B).

Rationale

Increasing numbers of women/birthing parents living with HIV in high-income countries want to breast/chestfeed, or have done so [32-35]. A UK questionnaire study conducted in women living with HIV during pregnancy and the postpartum period (*n*=94) reported that 38% of respondents would like to breastfeed, although only 27% believed it was safe to breastfeed if their HIV viral load was <40 copies/mL [5]. The number of women living with HIV in the UK opting to breastfeed has increased 4-fold, from <10 per year in 2012–2014 to 40–50 per year in 2019–2021. The most common reasons for wanting to breast/chestfeed are the health benefits of breastmilk/human milk and infant bonding [5,33,36]. Other reasons include pressure from family, cultural expectation, avoidance of signalling of HIV status and inability to afford formula [5,24,27,35,36].

Breast/chestfeeding has health benefits for both the mother/feeding parent and the infant [2]. Beneficial impacts for the mother/feeding parent include reduced risks of cardiometabolic disease, depression and some malignancies. For the infant, breast/chestfeeding can reduce the risks of many infectious diseases, sudden infant death syndrome, obesity, asthma and diabetes. The health benefits of breastmilk/human milk may be even more important for socioeconomically marginalised populations who experience pre-existing health inequities.

There are no data comparing long-term non-HIV-related clinical and developmental outcomes of exclusive formula feeding versus exclusive breast/chestfeeding in women/birthing parents living with HIV and their infants.

At the population level, the majority of infants and woman/birthing parents who are consistently virologically suppressed on ART can enjoy the benefits of breast/chestfeeding and still avoid postpartum HIV transmission. At the individual level, it is for each mother/feeding parent or family to decide whether the benefits of breast/chestfeeding outweigh the small risk of HIV transmission through breastmilk/human milk (or indeed other reasons not to breast/chestfeed). The role of the HIV MDT is to provide as much information as possible about what is known and what remains uncertain, to promote open discussion to allow parents to come to a decision and to provide care and testing as outlined below to maximise the safety of breast/chestfeeding.

When a woman/birthing parent is not virologically suppressed on ART, or there are other risk factors for transmission, it is the role of the HIV MDT to advocate for the infant by advising against breast/chestfeeding. We recommend that the HIV MDT has an open discussion with women/birthing parents early in pregnancy, stating clearly the lack of data on breast/chestfeeding in the context of HIV in high-income settings.

Women/birthing parents should be supported to make choices about infant feeding in a model of shared decision-making (see Section 12.1). If they choose to breast/chestfeed, and are fully aware of the low risk of HIV transmission, women/birthing parents and their infants will need to fulfil the criteria for low risk of transmission as in Section 11.1.2:

- Commenced ART at least 10 weeks prior to delivery;
- Evidence of good engagement of the mother/birthing parent with maternity/antenatal/HIV services;
- At least one HIV viral load measurement in the mother/birthing parent during the 6 weeks prior to delivery;

- All HIV viral load measurements in the mother/birthing parent during the 10 weeks prior to delivery are <50 copies/mL.

In addition, they should be prepared to attend for regular monthly clinic review (where possible, and not more than 2 months between review appointments) and blood HIV viral load tests for themselves and their infant during and for 2 months after stopping breast/chestfeeding.

Women/birthing parents who do not fulfil the above criteria should be advised against breast/chestfeeding.

Women/birthing parents who have been on ART with viral load <50 copies/mL for a short duration (less than 10 weeks), and especially if the infant is born prematurely, should be counselled that their risk of transmission may be higher because of a higher risk of transient viral expression in plasma and breastmilk/human milk, and because of the immaturity of the neonatal gut.

Women/birthing parents who breast/chestfeed with a known HIV viral load ≥50 copies/mL must be reviewed urgently by the HIV MDT. This is a safeguarding issue as it places the infant at significant risk of HIV infection and should be discussed with local child safeguarding leads. The safeguarding team can make a decision about onward social care referral. A supportive approach of working openly together is recommended, to maintain trust and reduce the risk of breast/chestfeeding in secret and disengagement from care [24,37].

12.5.1 Supporting women/people to breast/chestfeed in the UK

Recommendations

- We recommend lifelong ART for the woman/feeding parent (rather than extended infant PNP) to minimise HIV transmission through breastmilk/human milk and in line with the BHIVA adult HIV treatment guidelines [38] (Grade 1A).
- We recommend that *both* women/feeding parents *and* their infants are reviewed monthly for HIV RNA viral load testing (or HIV DNA for infants) during and for 2 months after stopping breast/chestfeeding (Grade 1D).
- Wherever possible, we recommend that blood monitoring for women/feeding parents and infants should be co-located and undertaken at the same appointment to minimise the risk of missed appointments (Grade 1D).
- We recommend exclusive breast/chestfeeding (i.e. not combining breastmilk/human milk with formula, or other milk or liquids, or with solids or both), especially in infants aged <6 months, except in certain circumstances outlined in Box 12.2 (Grade 1C).
- We recommend that breast/chestfeeding is discontinued before, or soon after, 6 months to minimise the cumulative risk of HIV transmission (Grade 1B).
- We recommend that the HIV MDT should provide clear and accessible written information about breast/chestfeeding to all pregnant women/people and mothers/feeding parents (Grade 1D).

Rationale

Given the personal health benefits of ART for the woman/person and the equivalent efficacy of ART and infant PNP in reducing the risk of vertical transmission of HIV through breast/chestfeeding, we recommend lifelong maternal/parental ART rather than infant PNP [39]. Data are not available on combined ART for the feeding parent *plus* infant PNP during breast/chestfeeding [40]. Healthcare providers requiring advice on use of medicines during the breast/chestfeeding period can contact the UK Drugs in Lactation Advisory Service (https://www.sps.nhs.uk/home/guidance/safety-in-breastfeeding/). There is no need to extend infant PNP beyond 2 weeks during supported breast/chestfeeding.

We continue to advise monthly HIV RNA monitoring for women/feeding parents and their infants during and for 2 months after stopping breast/chestfeeding, where possible (and no longer than 2 months between monitoring tests). Monthly testing of infants has been shown to be acceptable to women living with HIV [5]. Data suggest that in practice the intervals between tests postpartum are often greater than 4 weeks [32,41]. The postpartum period is a time when parental ART adherence may be challenging (see Section 13) and we believe that monthly testing allows for prompt action in the event of rebound HIV viral load (see Section 12.6).

There are no data on mixed feeding (the mixing of breastmilk/human milk and formula, solids or both) in the context of suppressive ART in resource-rich settings. Therefore we continue to recommend exclusive breast/chestfeeding (see Section 12.7 for specific circumstances in which mixed feeding can be considered). Increased duration of breast/chestfeeding increases the risk of vertical transmission (see Section 12.2). We recommend that breast/chestfeeding is discontinued before 6 months to minimise the risk of vertical transmission, and to minimise the duration of mixed feeding with solids when the infant is weaned. When weaning to solids, standard UK guidance should be followed, with complementary foods introduced after 6 months of age, even if still breast/chestfeeding. Abrupt weaning from breastmilk/human milk to formula and/or solids can be avoided, as long as the HIV viral load of the woman/feeding parent remains fully suppressed on ART (see Section 12.7).

The HIV MDT should give women/feeding parents clear information about breast/chestfeeding, including how to manage common complications, and provide easy access to clinical advice and peer support. Information for women/feeding parents considering breast/chestfeeding should be provided in written form and can be adapted locally from patient information leaflets developed by the writing group (available at: https://www.bhiva.org/pregnancy-guidelines). Women/birthing parents who choose to breast/chestfeed, and who have a consistently undetectable HIV viral load, may be advised to express their milk and freeze it, in case they need to interrupt breast/chestfeeding as a result of breast/chest infection or experiencing gastrointestinal symptoms.

Women/feeding parents should be advised to discontinue breast/chestfeeding immediately, and seek advice from the HIV MDT in the following circumstances:

- Bilateral nipple or breast/chest tissue infection or inflammation (e.g. mastitis or candida);
- Reduced ART adherence;
- Maternal/parental gastrointestinal symptoms;
- Infant gastrointestinal symptoms;
- Infant oral lesions.

For specific guidance on management in these situations, refer to Section 12.7.

If invasive procedures are considered for the infant (e.g. frenotomy), women/feeding parents should be advised to seek urgent advice about infant feeding from the antenatal HIV MDT (most importantly a paediatrician).

Women/birthing parents should be encouraged to inform partners, families and healthcare providers (including midwives, health visitors and GPs) and anyone else involved in their care (such as lactation consultants) about their HIV status. This will help them access appropriate support and advice.

There is currently a lack of specialist lactation support for women/feeding parents living with HIV [26]. Lactation support can facilitate safer and easier breast/chestfeeding journeys for women/feeding parents living with HIV. One example of good practice is at Bradford Teaching Hospitals NHS Trust, where an infant feeding specialist midwife is part of the HIV MDT. The specialist midwife is aware of BHIVA guidelines on HIV and infant feeding and her role includes supporting women/parents living with HIV who are breast/chestfeeding. A similar role could be considered in other units.

12.6 Management of detectable HIV viral load during breast/chestfeeding

Recommendation

- In the event of a detectable HIV maternal/parental viral load ≥50 copies/mL while breast/chestfeeding, we recommend that (Grade 1D):
  - Breast/chestfeeding should be discontinued immediately;
  - Women/feeding parents should attend clinic as soon as possible for a repeat HIV RNA testing for both themselves and their infant;
  - The infant should start PEP, as per Chiva guidelines [42];
  - Further management should be based on the result of the urgent repeat viral load sample.

Rationale

There are limited data to inform the management of a detectable viral load in breast/chestfeeding women/parents [43], therefore these recommendations are based on expert opinion; see Section 12.2 for a summary of evidence on HIV transmission through breast/chestfeeding.

In the event of a detectable HIV viral load ≥50 copies/mL during breast/chestfeeding, women/feeding parents should be advised:

- To discontinue breast/chestfeeding and switch to exclusive formula/alternative feeding;
- To attend clinic as soon as possible for repeat HIV RNA testing for both the woman/parent and the infant; the HIV MDT should inform the laboratory that a rapid turnaround of the HIV test is required, and HIV resistance testing should be requested on the rebound sample as this is relevant for infant treatment if transmission has occurred;
- That the infant should be assessed for PEP, as per Chiva guidelines [42]; PEP will usually comprise dolutegravir, lamivudine and zidovudine;
- That adherence and intercurrent illness should be assessed.

If the repeat maternal/parental HIV viral load result is <50 copies/mL:

- Breast/chestfeeding can be restarted if desired and if the MDT considers the ongoing risk to be low;
- Infant PEP can be stopped.

If the repeat maternal/parental HIV viral load is 50–199 copies/mL:

- An individual risk assessment should be undertaken including history of adherence and the actual viral load result and trajectory with the second sample;
- The case should be discussed with a specialist in paediatric infectious diseases with experience in HIV. We would advise total cessation of breast/chestfeeding and continuance of infant PEP in most cases unless thought to be very low risk.

If the repeat maternal/parental HIV viral load is ≥200 copies/mL:

- Breast/chestfeeding should NOT be restarted;
- Infant PEP should be continued for the full 4-week duration;
- The case should be discussed with a specialist in paediatric infectious diseases with experience of HIV management. Follow-up testing of the infant may include DNA as well as RNA testing if the infant is on PEP;
- Cabergoline should be offered to the mother/feeding parent to suppress lactation (note that for established lactation cabergoline dosing is over 2 days; see Section 12.4);
- The HIV MDT should advise the mother/feeding parent about expressing milk to relieve discomfort and monitoring for blocked ducts or mastitis.

12.7 Mixed feeding and HIV

Recommendations

- We recommend that infants receiving breastmilk/human milk from a woman/parent living with HIV should not be given solids before 6 months of age due to the potential increased risk of HIV transmission (Grade 1D).
- For infants aged <6 months, we recommend that breastmilk/human milk and formula milk should only be used concurrently in certain situations outlined in Box 12.2, based on the hydration and nutritional needs of the infant (Grade 1D).
- We recommend that breast/chestfeeding should be stopped in the event of infant gastroenteritis (with discussion with paediatricians if concerns about infant fluid intake), and not resumed thereafter (Grade 1D).

Rationale

Mixed feeding (also known as combination feeding) is when infants are given *both* breastmilk/human milk and formula, other non-human milks, other liquids and/or solids. In a combined analysis of studies of breastfeeding women in Africa who were not on ART, duration of breastfeeding and rates of HIV transmission were investigated in exclusively breastfed babies, versus those also fed other water-based drinks and those given solid food [21]. HIV acquisition rates did not differ between infants exclusively

breastfed or those who also received water-based drinks or formula milk (although infants who received formula milk were breastfed for a shorter duration). However, for women who breastfed and introduced solids before the infant was 6 months old, the risk of HIV transmission to the infant significantly increased (from 9 to 40 per 100 person-years). It remains unclear whether the association between increased HIV transmission and mixed feeding is causal [44]. It was previously thought that increased transmission resulted from breaches in the infant intestinal mucosa, however data to support this are lacking. We also lack data about risk of HIV transmission and mixed feeding in the context of virological suppression on ART.

In the context of HIV, infants should never be given solids *together* with breastmilk/human milk before 6 months of age due to the significantly increased HIV transmission risk. Combined breast/chestfeeding and formula feeding, even in the context of virological suppression on ART, may potentially increase the risk of HIV transmission. This risk is unquantifiable based on current evidence. However, there may be times when supplementation with formula milk is necessary to ensure an infant receives adequate nutrition and hydration. Breastmilk/human milk and formula milk should only be used concurrently in certain situations (see Box 12.2). This guidance does not apply to the mixing of breastmilk/human milk with any milk other than recommended infant formula.

Box 12.2 Situations in which supplementing breast/chestfeeding with formula feeding may be necessary

Situation	Guidance
Establishing breast/chestfeeding	The most important benefits of breast/chestfeeding for an infant are in the first weeks of life. Therefore, extra support for people who choose to breast/chestfeed exclusively is recommended. If an infant requires the occasional formula feed to support establishment of breast/chestfeeding, this is considered acceptable
Switching from breastmilk/human milk to formula milk	The breast/chestfeeding period should be as short as possible, and ideally less than 6 months. If by 6 months the infant is established exclusively on formula (or other alternatives; see Section 12.3), then solids can be introduced without risk of HIV transmission. It is advisable to change from breastmilk/human milk to formula as quickly as possible. Bottles of expressed milk may be introduced early on so the infant is used to sucking from a bottle as well as the nipple. This also gives co-parents (and other people providing support) the opportunity to feed and bond with the infant
Bilateral mastitis (and other breast/chest tissue conditions)	Women/feeding parents should express and discard their milk and use formula exclusively until symptoms resolve. It is reasonable to consider re-establishing breast/chestfeeding after mastitis has fully resolved, on a case-by-case basis in consultation with the HIV MDT. Whether there is any increased risk of HIV transmission when experiencing mastitis in high-income settings in the context of fully suppressive maternal/parental ART is not known. We do not know whether the risk of HIV transmission is reduced if the woman/feeding parent continues to feed from the unaffected side but it is

	unlikely to present a significant risk. In the case of unilateral nipple or breast/chest tissue conditions, the woman/feeding parent can continue to feed from the unaffected breast/side of chest
Maternal/parental gastroenteritis	The recommendations are the same as for bilateral mastitis
Infant gastroenteritis	Breast/chestfeeding should be stopped and not resumed thereafter. Infant gastroenteritis may lead to loss of gut lining integrity, which may take some time to fully recover, increasing the risk of HIV transmission. It is difficult to establish clinically when the infant gut lining has fully recovered

12.8 References

1. World Health Organization. 2016. *Guideline: updates on HIV and infant feeding*. Available at: https://www.who.int/publications/i/item/9789241549707 (accessed July 2024).

2. Gross MS, Taylor HA, Tomori C, Coleman JS. Breastfeeding with HIV: an evidence-based case for new policy. *J Law Med Ethics* 2019; **47**: 152–160.

3. Ramos MI, Sánchez BS, Orellana DM *et al*.; Madrid Cohort of HIV-infected Mother-infant pairs. Safety and experience with combined antiretroviral prophylaxis in newborn at high-risk of perinatal HIV infection, in a cohort of mother living with HIV-infant pairs. *Pediatr Infect Dis J* 2021; **40**: 1096–1100.

4. Phillips JC, Etowa J, Hannan J *et al*. Infant feeding guideline awareness among mothers living with HIV in North America and Nigeria. *Int Breastfeed J* 2020 **15**: 27.

5. Nyatsanza F, Gubbin J, Gubbib T *et al*. *Over a third of childbearing women with HIV would like to breastfeed: A UK survey of women living with HIV. Int J STD AIDS* 2021; **32**: 856–860.

6. Kasadha B, Hinton L, Tariq S *et al*. How women living with HIV in the UK manage infant-feeding decisions and vertical transmission risk - a qualitative study. *BMC Public Health* 2024; **24**: 2130.

7. Kasadha B, Tariq S, Freeman-Romilly N *et al*. "We decided together": a qualitative study about women with HIV navigating infant-feeding decisions with the father of their children. *BMC Pregnancy Childbirth* 2024; **24**: 41.

8. Waitt C, Low N, Van de Perre P *et al*. Does U=U for breastfeeding mothers and infants? Breastfeeding by mothers on effective treatment for HIV infection in high-income settings. *Lancet HIV* 2018; **5**: e531–e536.

9. Moseholm E, Weis N. Women living with HIV in high-income settings and breastfeeding. *J Intern Med* 2020; **287**: 19–31.

10. Francis K, Sconza R, Thorne C, Peters H. Monitoring clinical practice of BHIVA-supported breastfeeding guidelines for women living with HIV in the UK. BHIVA conference, 2023. Oral abstract O12. Available at: https://onlinelibrary.wiley.com/doi/full/10.1111/hiv.13476 (accessed August 2024).

11. Crisinel PA, Kusejko K, Kahlert CR *et al*. Successful implementation of new Swiss recommendations on breastfeeding of infants born to women living with HIV. *Eur J Obstet Gynecol Reprod Biol* 2023; **283**: 86–89.

12. Flynn PM, Taha TE, Cababasay M *et al*. Prevention of HIV-1 Transmission through breastfeeding: efficacy and safety of maternal antiretroviral therapy versus infant nevirapine prophylaxis for duration of breastfeeding in HIV-1-infected women with high CD4 cell count (IMPAACT PROMISE): a randomized, open-label, clinical trial. *J Acquir Immune Defic Syndr* 2018; **77**: 383–392.

13. Malaba TR, Nakatudde I, Kintu K *et al*. 72 weeks post-partum follow-up of dolutegravir versus efavirenz initiated in late pregnancy (DolPHIN-2): an open-label, randomised controlled study. *Lancet HIV* 2022; **9**: e534–e543.

14. Flynn PM, Taha TE, Cababasay M *et al*. Association of maternal viral load and CD4 count with perinatal HIV-1 transmission risk during breastfeeding in the PROMISE postpartum component. *J Acquir Immune Defic Syndr* 2021; **88**: 206–213.

15. Davis NL, Miller WC, Hudgens MG *et al*. Maternal and breastmilk viral load: impacts of adherence on peripartum HIV infections averted-The Breastfeeding, Antiretrovirals, and Nutrition study. *J Acquir Immune Defic Syndr* 2016; **73**: 572–580.

16. Boyce CL, Sils T, Ko D *et al*. Maternal human immunodeficiency virus (HIV) drug resistance is associated with vertical transmission and is prevalent in infected infants. *Clin Infect Dis* 2022; **74**: 2001–2009.

17. Bispo S, Chikhungu L, Rollins N *et al*. Postnatal HIV transmission in breastfed infants of HIV-infected women on ART: a systematic review and meta-analysis. *J Int AIDS Soc* 2017; **20**: 21251.

18. Ndarukwa V, Zunza M. Combination antiretroviral treatment use in prevention of mother-to-child transmission programmes: 6-week HIV prevalence and relationship to time of antiretroviral treatment initiation and mixed feeding. *S Afr J Infect Dis* 2019; **34**: 117.

19. Davis NL, Corbett A, Kaullen J *et al*. Antiretroviral Drug Concentrations in Breastmilk, Maternal HIV viral load, and HIV Transmission to the infant: results from the BAN study. *J Acquir Immune Defic Syndr* 2019; **80**: 467–473.

20. Rollins N, Mahy M, Becquet R *et al.* Estimates of peripartum and postnatal mother-to-child transmission probabilities of HIV for use in Spectrum and other population-based models. *Sex Transm Infect* 2012. **88 Suppl 2**: i44-51.

21. Becquet R, Bland R, Leroy V *et al*. Duration, pattern of breastfeeding and postnatal transmission of HIV: pooled analysis of individual data from West and South African cohorts. *PLoS One* 2009; **4**: e7397.

22. Prendergast AJ, Goga AE, Waitt C et al. Transmission of CMV, HTLV-1, and HIV through breastmilk. *Lancet Child Adolesc Health* 2019; **3**: 264–273.

23. National Institute for Health and Care Excellence. *Donor milk banks: service operation. Clinical guideline [CG93]*. 2010. Available at: https://www.nice.org.uk/guidance/cg93 (accessed July 2024).

24. Tariq S, Elford J, Tookey P *et al*. "It pains me because as a woman you have to breastfeed your baby": decision-making about infant feeding among African women living with HIV in the UK. *Sex Transm Infect* 2016; **92**: 331–336.

25. National AIDS Trust. *Policy briefing: access to formula milk for mothers living with HIV in the UK*. 2017. Available at: https://www.nat.org.uk/publication/policy-briefing-access-formula-milk-mothers-living-hiv-uk (accessed June 2024)

26. Rai T, Kasadha B, Tariq S *et al*. Infant feeding as a transgressive practice in the context of HIV in the UK: a qualitative interview study. *Women's Studies International Forum* 2023; 101, p. 102834. Pergamon.

27. Griswold MK, Pagano-Therrien J. Women living with HIV in high income countries and the deeper meaning of breastfeeding avoidance: a metasynthesis. *J Hum Lact* 2020; **36**: 44–52.

28. Karpf B, Smith G, Spinks R. Affording formula: HIV-positive women's experiences of the financial strain of infant formula feeding in the UK. Abstract O27. *HIV Med* 2017; **18 Suppl S1**: 3–13.

29. Williams E, Barnes L, Rowsell C *et al*. The impact of financial support for replacement infant feeding on postpartum attendance and outcomes for women with HIV. *HIV Med* 2014; **15 Suppl 3**: 17–159. Abstract P139.

30. Hegazi A, Ramskill N, Norbrook M *et al*. Genital tract infections in HIV-infected pregnant women in South West London. *Int J STD AIDS* 2020; **31**: 587–592.

31. Boucoiran I, Roy M, Poliquin V *et al*. Evaluation of cabergoline for lactation inhibition in women living with HIV. *Int J STD AIDS* 2021; **32**: 654–661.

32. Haberl L, Audebert F, Feiterna-Sperling C *et al*. Not recommended, but done: breastfeeding with HIV in Germany. *AIDS Patient Care STDS* 2021; **35**: 33–38.

33. Crisinel PA, Kusejko K, Kahlert C *et al*. Successfull implementation of new HIV vertical transmission guidelines in Switzerland. HIV Med 2021; **22 Suppl 3:** Abstract BPD2/3.

34. Weiss F, von Both U, Rack-Hoch A *et al*. HIV-positive and breastfeeding in high-income settings: 5-year experience from a perinatal center in Germany. *J Acquir Immune Defic Syndr* 2022; **91**: 364–367.

35. Tuthill EL, Tomori C, Van Natta M, Coleman JS. "In the United States, we say, 'No breastfeeding,' but that is no longer realistic": provider perspectives towards infant feeding among women living with HIV in the United States. *J Int AIDS Soc* 2019; **22**: e25224.

36. Fitzgerald N, Williams C, Issa R *et al*. Breastfeeding with HIV: a retrospective case review. *HIV Med* 2019; **20 Suppl 5**: 16–75; Abstract p38.

37. Johnson G, Levison J, Malek J. Should providers discuss breastfeeding with women living with HIV in high-income countries? An ethical analysis. *Clin Infect Dis* 2016; **63**: 1368–1372.

38. Waters L, Winston A, Reeves I *et al*. BHIVA guidelines on antiretroviral treatment for adults living with HIV-1 2022. *HIV Med* 2022; **23 Suppl 5**: 3-115.

39. Taha T, Flynn P, Cababasay MP *et al.* Maternal triple antiretrovirals (mART) and infant nevirapine (iNVP) prophylaxis for the prevention of mother-to-child transmission (MTCT) of HIV during breastfeeding (BF). *International AIDS Conference*. 2016: Durban, South Africa. Available at: https://www.impaactnetwork.org/sites/default/files/2020-12/1077BP_Taha_AIDS2016.pdf (accessed August 2024).

40. Van de Perre P, Kankasa C, Nagot N *et al*. Pre-exposure prophylaxis for infants exposed to HIV through breast feeding. *BMJ* 2017; **356**: j1053.

41. Russell J, Mabonga E, Buckberry K, Perez K. Breastfeeding and women with HIV living in the UK: BHIVA guidelines and real world experience. HIV Med 2020; **21 Suppl 4**: Abstract O3.

42. Foster C, Lees EA, Lyall EGH *et al*. Post-exposure prophylaxis (PEP) guidelines for infants, children and adolescents potentially exposed to blood-borne viruses. 2023 Availble at: https://www.chiva.org.uk/wp-content/uploads/2023/11/CHIVA_PEP_2023-Final.pdf (accessed July 2024).

43. Lees EA, Tickner N, Lyall H *et al*. Infant postnatal prophylaxis following maternal viraemia during breastfeeding. *AIDS* 2023; **37**: 1185–1186.

44. Filteau S. The elusive mechanistic link between exclusive breast-feeding and lower risk of postnatal mother-to-child HIV transmission. *Clin Infect Dis* 2010; **51**: 474–475. Available at: https://academic.oup.com/cid/article/51/4/474/479836 (accessed July 2024).

13 Supporting women/birthing parents during the postpartum period

13.1 ART

Recommendation

- We recommend that all women/birthing parents should be advised to continue lifelong ART postpartum (Grade 1A).

Rationale

It is recommended that all women/birthing parents remain on ART postpartum, although ultimately this is the individual's choice.

During the postpartum period women/birthing parents should be managed according to BHIVA adult antiretroviral treatment guidelines [1]. The postpartum period provides an opportunity to simplify regimens, for example by switching to newer regimens or to a once-daily dosing or co-formulated tablet.

13.2 Postpartum adherence to ART and retention in care

Recommendations

- We recommend that women/birthing parents should be assessed for risk factors for reduced ART adherence and engagement in HIV care postpartum (see Table 13.1) by the MDT during antenatal care, and those found to be at risk should be supported by care coordination, case management, peer support and the use of technologies as available (Grade 1C).
- We recommend that, prior to discharge after delivery, all women/birthing parents should receive an appointment to see a named member of the HIV MDT within 4–6 weeks and receive an adequate ART supply until this appointment (Grade 1D).
- We recommend that the postpartum review should include an assessment of mental health, adherence to ART, infant feeding, medical and social issues and birth experience, and contraception options should be discussed (Grade 1C).

Auditable outcomes

- Proportion of women/birthing parents who have been assessed antenatally for risk factors for low adherence and poor engagement in HIV care postpartum.
- Proportion of women/birthing parents reviewed by 6 weeks postpartum.

Rationale

Adherence to ART can be challenging postpartum due to the considerable physical and emotional demands of caring for a baby [2], and there is evidence that adherence to ART declines postpartum [3].

Postpartum retention in HIV care is essential for women/birthing parents, their families and the wider population in terms of U=U. Women/birthing parents can experience difficulties engaging in HIV care postpartum as a result of the physical and emotional demands of having a baby. Data from the UK

and Switzerland both demonstrated that 12% of women are not retained in HIV care at 1 year postpartum [4,5].

A more recent analysis from the UK Collaborative HIV Cohort study comparing pregnant and non-pregnant women living with HIV, found that women were more likely to be retained in HIV care during pregnancy or the postpartum period than prior to their pregnancy and when compared to women living with HIV who had not been pregnant. The authors suggested that their findings indicate that the antenatal period provides a key opportunity to empower women to engage in HIV care in the immediate postpartum period [6].

In a retrospective notes review of women living with HIV giving birth in the UK, 17% had a detectable viral load in the postpartum period, with 44% missing at least one HIV clinic follow-up appointment. Of those with a detectable HIV viral load, 56% experienced psychological or social challenges, including financial, relationship, housing and asylum concerns [7]. Another study in Kenya measuring tenofovir DX levels in pregnancy and the postpartum period found that levels of the drug declined during this period; 47.8% of women had adequate tenofovir DX levels in the early postnatal period (0–3 months), 37.0% at 6 months and 31.6% between 9 and 12 months postpartum [8].

Identifying women/birthing parents who are at risk of reduced postpartum adherence and engagement in HIV care allows the MDT to provide proactive and appropriate support. The key risk factors are summarised in Table 13.1.

Table 13.1 Risk factors for reduced ART adherence and engagement in HIV care postpartum

Risk factors	Reduced postpartum adherence (references)	Reduced postpartum engagement in HIV care (references)
Age <40 years	[29,30]	[31]
Unintended pregnancy	[32]	
New diagnosis of HIV during pregnancy		[33]
Perinatally acquired HIV		[34]
Difficulties engaging in antenatal care (e.g. late antenatal booking, <12 weeks of ART in pregnancy or missed ART in previous 4 weeks)	[35]	[36]
Detectable HIV viral load preconception, during antenatal care or at delivery	[30]	[11]
Missed postpartum follow-up appointment		[11]
Difficulties telling partner or others about HIV status	[37]	
Concerns about or experiences of HIV-related stigma	[9]	[12]
Poor mental health (e.g. depression or drug/alcohol use)	[30,37]	[12,26]
Intimate partner violence		[12]
Adverse social circumstances (e.g. food and housing insecurity, immigration issues or financial difficulties)	[7,38]	[7,26]

Some of these risk factors will be identifiable during pregnancy, which provides an opportunity to promptly implement interventions to improve adherence and retention in care postpartum. Support from peers and partners are key interventions for optimising postpartum adherence to ART [2,9]. We recommend that all women/birthing parents are assessed for these risk factors during the antenatal period and those found to be at risk of reduced adherence and disengagement from care postpartum should be referred for peer support during pregnancy.

13.2.1 Postpartum review appointment

The postpartum follow-up review should be within 4–6 weeks post-delivery; the infant's postnatal 6-week blood test appointment provides a good opportunity to engage with women/birthing parents postpartum.

NICE has published guidance highlighting areas to be assessed during postnatal visits for the general population [10]. These areas include:

- What to expect in the postnatal period and how to seek help;
- Physical and mental wellbeing;
- The importance of pelvic floor exercises, how to do them and when to seek help;
- Fatigue;
- Nutrition and diet;
- Physical activity;
- Smoking, alcohol consumption and recreational drug use;
- Sexual intercourse and contraception;
- Safeguarding concerns, including intimate partner violence.

For those living with HIV, this is also an opportunity to review:

- Adherence to ART;
- Optimising ART;
- Linkage to HIV care;
- Completion of infant PEP;
- Infant feeding and follow-up;
- Completion of partner notification.

The MDT should create a safe and supportive space in which women/birthing parents can discuss their concerns.

Missing this first postpartum appointment is associated with longer-term disengagement from HIV care [11]. If women/birthing parents miss the first postpartum appointment, every effort should be made by the HIV MDT to contact them and address any barriers to re-establish care including ensuring care is coordinated across services [12].

13.2.2 Care coordination

Care coordination is defined as the organisation of patient care activities to facilitate delivery of services. In the case of women/people living with HIV during pregnancy it may include the allocation of a member of the MDT as a case manager, working closely with pregnant women/people and their family/partner,

coordinating services, facilitating appointments, communication, referrals and documentation as dictated by their needs.

The findings of a US review study investigating different interventions to improve postnatal retention in care for women living with HIV suggest that care coordination, perinatal case management, peer support and the use of technologies (such as text messages) should be implemented to improve postpartum retention and clinical outcomes [12].

13.2.3 Birth experience

In addition, NICE guidelines recommend assessment of the birth experience, with advice and support offered to women/birthing parents who have had a traumatic birth or miscarriage and wish to talk about their experience [10].

A discussion about the birth experience can also provide important feedback to the HIV antenatal MDT on issues related to care pathways.

13.3 Assessing mental health needs postpartum

Recommendations

- We recommend that women/birthing parents should have their mental health needs assessed during the postpartum period as well as during pregnancy (Grade 1D).
- We recommend that women/birthing parents assessed as having mental health problems should be referred to their GPs and/or appropriate mental health services and offered support from community and/or voluntary groups (Grade 1D).

Auditable outcomes

- Proportion of women/birthing parents with a documented mental health assessment at 4–6 weeks postpartum.

Rationale

The screening and management of mental health problems in pregnancy in the context of HIV is outlined in Section 6. It is important to assess postnatal mental health; the 2023 MBRRACE report shows that, along with cardiovascular disorders, thrombosis and thromboembolism, psychiatric disorders represent 38% of maternal deaths in the UK [13].

A meta-analysis of 23 studies from different African countries and regions of the USA reported a mean prevalence of postnatal depression of 21% (95% CI 14–27%), compared to 16% (95% CI 10–22%) in women without HIV, showing that those with HIV had higher odds of postnatal depression (OR 1.58, 95% CI 1.08–2.32) than those without HIV [14]. In the postnatal period, women living with HIV were also more likely to access mental health services (adjusted OR 1.26, 95% CI 1.03–1.55) and to require an emergency psychiatric visit or hospitalisation postpartum [15].

Factors associated with postpartum mental health problems in women living with HIV include not being in a relationship, social isolation, financial difficulties, experiences of racism, not having shared their HIV status, prenatal depression and intimate partner violence [16-20]. This highlights the importance of prenatal assessment for these risk factors, and of ensuring that appropriate support is available for women/birthing parents at the earliest opportunity. NICE guidance [21] on antenatal and postnatal mental health recognises that women who have a mental health problem may be unwilling to discuss their problem because of fear of stigma or fear that their baby might be taken into care. NICE recommends screening for depression and anxiety at the booking visit and during the early postnatal period, as part of a general discussion about mental health and wellbeing.

If there are any concerns about postnatal mental health, women/birthing parents should be referred to either their GP or to perinatal mental health or psychiatric liaison teams. For women/birthing parents using drugs or alcohol, continued support should be offered as per local guidelines and pathways. In addition, support from community and voluntary organisations should be offered.

For further information about assessment tools, see Section 6.

13.4 Contraception

Recommendation

- We recommend that contraceptive needs should be discussed with all women/birthing parents, and ART should be optimised to accommodate the contraception choices of women/birthing parents as long as it remains fully active against the viral genotype (Grade 1A).

Rationale

During pregnancy there should be a discussion of and plan for contraception postnatally with a view to initiating contraception as soon as possible in the postpartum period. The Faculty of Sexual and Reproductive Health suggests that maternity services should be able to provide a full range of contraceptive methods and recommends that a woman's chosen method of contraception should be initiated immediately post-delivery if she is medically eligible and not later than 21 days after childbirth. Women should be advised that intrauterine contraception and the progesterone-only implant can be inserted immediately after birth, irrespective of breast/chestfeeding status [22].

Women/birthing parents should be advised that it is possible to conceive before the first postnatal menses even if breast/chestfeeding and therefore to use condoms, if necessary, until their long-term contraception can be started.

It is important to try to accommodate both the contraceptive and the ART preferences of individuals. Multiple antiretroviral agents, including all NRTIs, raltegravir, dolutegravir, bictegravir, cabotegravir, rilpivirine and doravirine, do not interact with systemic oestrogens and/or progestogens. ART may be changed to optimise contraception choice as long as the ART prescribed is fully active against the viral genotype. A full guide to drug–drug interactions between ART and hormonal contraceptives is available from the University of Liverpool's HIV drug interaction checker [23]. Dedicated postnatal contraception services for people living with HIV may improve uptake of contraception and consequently reduce

unintended pregnancies; an evaluation of one such service in the UK demonstrated a 50% increase in the uptake of long-acting reversible contraception [24].

13.5 Cervical cytology

Recommendation

- We recommend that cytology should be scheduled 3 months post-delivery as per the NHS guidance [25] for cervical screening (Grade 1C).

Rationale

Cervical screening is not routinely recommended in pregnancy but can be resumed 3 months postpartum, in line with NHS guidance for cervical screening [25]; this should be offered on an annual basis as per BHIVA guidance.

13.6 Support services and interventions

Recommendation

- We recommend that women/birthing parents should have their support needs assessed postpartum and be referred to appropriate services in the trust, the community and/or voluntary groups without delay (Grade 1D).

Rationale

The support required by women/birthing parents and the support available at each HIV service will vary considerably and therefore should be individualised. Assistance required may include access to food and formula milk (see Section 12), peer mentoring, housing support and legal and advocacy services.

The HIV MDT should work with local peer-led and voluntary organisations to provide tailored support to individuals postpartum. Referrals to partner organisations should be offered at first presentation in pregnancy and be continued in the postnatal period. It has been shown that peer support is highly acceptable to women living with HIV during and after pregnancy, and can improve treatment literacy and postpartum engagement in HIV care [26]. Peer support is an essential part of the HIV MDT and can be accessed throughout the UK via https://4mmm.org/.

Ensuring the sexual and reproductive wellbeing of women/people should also include providing an opportunity for women/people to discuss sexual pleasure; there is evidence that including conversations around sexual desire and sexual pleasure in sexual health programmes improves knowledge and attitudes around sex and increases condom use [27]. For more information see https://thepleasureproject.org/.

13.7 Pregnancy loss

Women/birthing parents who experience pregnancy loss may require additional support through services such as the Miscarriage Association (www.miscarriageassociation.org.uk/), Sands

(www.sands.org.uk/) or Tommy's (https://www.tommys.org/). Women/birthing parents who experience second trimester loss or stillbirth should still be invited for a postpartum review to assess their birth experience, mental health and ongoing support needs; this review should be led by the obstetric team responsible for their care.

13.8 Testing of partners and older children

Recommendation

- We recommend testing of partners and older children at risk of HIV for individuals newly diagnosed with HIV in pregnancy, if not previously tested (Grade 1D).

Rationale

Postpartum follow-up may be an opportune time to revisit testing of partners and/or older children at risk of HIV. Women/people newly diagnosed with HIV in pregnancy should be counselled and supported regarding testing of their partner and informed that as well as significantly reducing the risk of vertical transmission of HIV, being on ART will also prevent sexual transmission. They should be advised to use condoms with any untested or HIV-negative partner until they have been on ART for 6 months or longer, with an undetectable viral load and maintaining adherence to treatment. The risk of intimate partner violence associated with telling partners about their HIV status should be considered and support discussed.

Testing of older children at risk of HIV may be a source of stress and anxiety for families. This should be reviewed and completed during the postnatal period, but ideally a discussion should start with the support of the MDT at the beginning of pregnancy [28].

13.9 References

1. Waters L, Winston A, Reeves I *et al*. BHIVA guidelines on antiretroviral treatment for adults living with HIV-1 2022. *HIV Med* 2022; **23 Suppl 5**: 3–115.

2. Momplaisir FM, Fortune K, Nkwihoreze H *et al*. Outcome expectancies toward adherence to antiretroviral therapy for pregnant and postpartum women with HIV. *Womens Health (Lond)* 2021; **17**: 17455065211061094.

3. Patel M, Tedaldi E, Armon C *et al*. HIV RNA suppression during and after pregnancy among women in the HIV Outpatient Study, 1996 to 2015. *J Int Assoc Provid AIDS Care* 2018; **17**: 2325957417752259.

4. Tariq S, Elford J, Chau C *et al*. Loss to follow-up after pregnancy among sub-Saharan Africa-born women living with human immunodeficiency virus in England, Wales and Northern Ireland. *Sex Transm Dis* 2016; **43**: 283–289.

5. Aebi-Popp K, Kouyos R, Bertisch B *et al*. Postnatal retention in HIV care: insight from the Swiss HIV Cohort Study over a 15-year observational period. *HIV Med* 2016; **17**: 280–288.

6. Okhai H, Tariq S, Burns F *et al*. Association of pregnancy with engagement in HIV care among women with HIV in the UK: a cohort study. *Lancet HIV* 2021; **8**: e747–e754.

7. Cooper, R, Collini, P, Greig, J. HIV control in post partum mothers: still a turbulent time. *HIV Med* 2021; Abstract P088. Available at: https://onlinelibrary.wiley.com/doi/10.1111/hiv.13131 (accessed August 2024).

8. Abuogi LL, Castillo-Mancilla J, Hampanda K *et al*. Tenofovir diphosphate in dried blood spots in pregnant and postpartum women with HIV in Kenya: a novel approach to measuring peripartum adherence. *J Acquir Immune Defic Syndr* 2022; **89**: 310–317.

9. Gill MM, Umutoni A, Hoffman HJ *et al*. Understanding antiretroviral treatment adherence among HIV-positive women at four postpartum time intervals: qualitative results from the Kabeho Study in Rwanda. *AIDS Patient Care STDS* 2017; **31**: 153–166.

10. National Institute for Health and Care Excellence. *Postnatal care. NICE guideline [NG194]*. 2021. Available at: https://www.nice.org.uk/guidance/ng194/chapter/Recommendations#postnatal-care-of-the-woman (accessed August 2024).

11. Adhikari EH, Yule CS, Roberts SW *et al*. Factors associated with postpartum loss to follow-up and detectable viremia after delivery among pregnant women living with HIV. *AIDS Patient Care STDS* 2019; **33**: 14–20.

12. Momplaisir FM, Storm DS, Nkwihoreze H *et al*. Improving postpartum retention in care for women living with HIV in the United States. *AIDS* 2018; **32**: 133–142.

13. MBRRACE-UK. Saving lives, improving mothers' care. 2023. Available at: https://www.npeu.ox.ac.uk/assets/downloads/mbrrace-uk/reports/maternal-report-2023/MBRRACE-UK_Maternal_Compiled_Report_2023.pdf (accessed August 2024).

14. Zhu QY, Huang DS, Lv J-D *et al*. Prevalence of perinatal depression among HIV-positive women: a systematic review and meta-analysis. *BMC Psychiatry* 2019; **19**: 330.

15. Sparrow-Downes VM, Loutfy M, Antoniou T, Vigod SN. Postpartum mental health service utilization in women with human immunodeficiency virus (HIV): a population-based study. *AIDS Care* 2019; **31**: 1332–1339.

16. Moseholm E, Aho I, Mellgren Å *et al*. Psychosocial health in pregnancy and postpartum among women living with - and without HIV and non-pregnant women living with HIV living in Nordic countries – results from a longitudinal survey study. *BMC Pregnancy Childbirth* 2022; **22**: 20.

17. Bhushan NL, Stockton MA, Harrington BJ *et al*. Probable perinatal depression and social support among women enrolled in Malawi's Option B+ program: a longitudinal analysis. *J Affect Disord* 2022; **306**: 200–207.

18. Khan S, Ion A, Alyass A *et al*. Loneliness and perceived social support in pregnancy and early postpartum of mothers living with HIV in Ontario, Canada. *AIDS Care* 2019; **31**: 318–225.

19. Larsen AM, Osborn L, Ronen K *et al*. Trajectories of depression symptoms from pregnancy through 24 months postpartum among Kenyan women living with HIV. *J Acquir Immune Defic Syndr* 2022; **90**: 473.

20. Mbatha NL, Mokwena KE, Madiba S. Clinical and obstetric risk factors for postnatal depression in HIV positive women: a cross sectional study in health facilities in rural KwaZulu-Natal. *Int J Environ Res Public Health* 2020; **17**: 8425.

21. National Institute for Health and Care Excellence. *Antenatal and postnatal mental health: clinical management and service guidance. Clinical guideline [CG192]*. 2020. Available at:

https://www.nice.org.uk/guidance/cg192/chapter/Recommendations#recognising-mental-health-problems-in-pregnancy-and-the-postnatal-period-and-referral-2 (accessed August 2024).

22. The Faculty of Sexual and Reproductive Healthcare. *FSRH clinical guideline: contraception after pregnancy (January 2017, amended October 2020).* 2020. Available at: https://www.fsrh.org/standards-and-guidance/documents/contraception-after-pregnancy-guideline-january-2017/ (accessed August 2024).

23. University of Liverpool. *HIV Drug Interactions*. Available at: https://www.hiv-druginteractions.org/ (accessed August 2024).

24. Mabonga E. Does the introduction of a dedicated postnatal contraception clinic improve reproductive choices for HIV positive women? BHIVA conference 2017. Available at: https://www.bhiva.org/file/oKcXEjquyiUQt/EmilyMabonga.pdf (accessed August 2024).

25. NHS England. *Cervical screening: programme and colposcopy management*. 2023. Available at: https://www.gov.uk/government/publications/cervical-screening-programme-and-colposcopy-management (accessed August 2024).

26. Akinde Y, Groves AK, Nkwihoreze H *et al*. Assessing the acceptability of a peer mentor mother intervention to improve retention in care of postpartum women living with HIV. *Health Equity* 2019; **3**: 336–342.

27. Zaneva M, Philpott A, Singh A *et al*. What is the added value of incorporating pleasure in sexual health interventions? A systematic review and meta-analysis. *PLoS One* 2022; **17**: e0261034.

28. British HIV Association, Children's HIV Association and British Association for HIV and Sexual Health. *Don't forget the children*. 2009. Available at: https://www.chiva.org.uk/wp-content/uploads/2022/02/dont-forget.pdf (accessed August 2024).

29. Patel K, Karalius B, Powis K *et al*. Trends in post-partum viral load among women living with perinatal HIV infection in the USA: a prospective cohort study. *Lancet HIV* 2020; **7**: e184–e192.

30. Cruz Zonenschein AC, João Filho EC, Cruz MLS *et al*. Treatment dropout after pregnancy: a study of women living with HIV in Rio de Janeiro. *AIDS Care* 2020; **32**: 1283–1289.

31. Knettel BA, Cichowitz C, Ngocho JS *et al*. Retention in HIV care during pregnancy and the postpartum period in the Option B+ era: a systematic review and meta-analysis of studies in Africa. *J Acquir Immune Defic Syndr* 2018; **77**: 427–438.

32. Brittain K, Phillips TK, Zerbe A *et al*. Long-term effects of unintended pregnancy on antiretroviral therapy outcomes among South African women living with HIV. *AIDS* 2019; **33**: 885–893.

33. Cichowitz C, Mazuguni F, Minja L *et al*. Vulnerable at each step in the PMTCT care cascade: high loss to follow up during pregnancy and the postpartum period in Tanzania. *AIDS Behav* 2019; **23**: 1824–1832.

34. Meade CM, Hussen SA, Momplaisir F *et al*. Long term engagement in HIV care among postpartum women with perinatal HIV infection in the United States. *AIDS Care* 2018; **30**: 488–492.

35. Hoffman RM, Warshaw MG, Amico KR *et al*. Predictors of viremia in postpartum women on antiretroviral therapy. *J Acquir Immune Defic Syndr* 2020; **83**: 72–80.

36. Swain CA, Smith LC, Nash D *et al*. Postpartum human immunodeficiency virus care among women diagnosed during pregnancy. *Obstet Gynecol* 2016; **128**: 44–51.

37. Adeniyi OV, Ajayi AI. Level and determinants of postpartum adherence to antiretroviral therapy in the Eastern Cape, South Africa. *PLoS One* 2020; **15**: e0229592.

38. Wang M, Miller JD, Collins SM *et al*. Social support mitigates negative impact of food insecurity on antiretroviral adherence among postpartum women in Western Kenya. *AIDS Behav* 2020; **24**: 2885–2894.

14 Acknowledgments

The writing group thanks Dr Karoline Aebi-Popp, University Hospital Bern, Switzerland, Dr Caroline Foster, Imperial College Healthcare NHS Trust, London, and Dr Sharon Walmsley, University Health Network, Canada, for their reviews and helpful comments. The writing group also thanks Jo Sinclair, University Hospitals Sussex NHS Foundation Trust, for taking part in the planning meetings and literature review and Neil Tickner, Imperial College Healthcare NHS Trust, and Caroline Dalton, Great Ormond Street Hospital for Children NHS Foundation Trust, for reviewing the dosing table (Appendix 4).

15 List of abbreviations

AFP	Alpha fetoprotein
ALT	Alanine transaminase
APR	Antiretroviral Pregnancy Registry
APRI	AST-to-platelet ratio index
ART	Antiretroviral therapy
AST	Aspartate transaminase
AUC	Area under the curve
AUCtau	Area under the curve over 24 hours
BASHH	British Association for Sexual Health and HIV
βHCG	β-human chorionic gonadotrophin
BHIVA	British HIV Association
BV	Bacterial vaginosis
Chiva	Children's HIV Association
CI	Confidence interval
DAA	Direct-acting antiviral
EC_{90}	90% effective concentration
EC_{95}	95% effective concentration
ECV	External cephalic version
EPHN	European Paediatric Hepatitis Network
FDC	Fixed-dose combination
GAD-2	Two-item Generalised Anxiety Disorder scale
GMC	General Medical Council
GP	General practitioner
GPP	Good practice point
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HAV	Hepatitis A virus
HBe	Hepatitis B e
HBeAg	Hepatitis B e antigen

HBc	Hepatitis B core
HBIG	Hepatitis B immunoglobulin
HBs	Hepatitis B surface
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCC	Hepatocellular cancer
HCV	Hepatitis C virus
HDV	Hepatitis D virus
HELLP	Haemolysis, elevated liver enzymes, low platelet count
HIV	Human immunodeficiency virus
HSV	Herpes simplex virus
HTLV-1	Human T-cell lymphotropic virus type 1
IC_{90}	90% inhibitory concentration
ID	Infectious diseases
IFN	Interferon
INSTI	Integrase inhibitor
IPV	Intimate partner violence
IQR	Interquartile range
IRIS	Immune reconstitution inflammatory syndrome
ISOSS	Integrated Screening Outcomes Surveillance Service
LFT	Liver function test
MDT	Multidisciplinary team
MMR	Measles, mumps and rubella
NICE	National Institute for Health and Care Excellence
NIPT	Non-invasive prenatal testing
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NSHPC	National Study of HIV in Pregnancy and Childhood
NTD	Neural tube defect

OR	Odds ratio
PAPP-A	Pregnancy-associated plasma protein A
PCR	Polymerase chain reaction
PEP	Postexposure prophylaxis
PI	Protease inhibitor
PNP	Postnatal prophylaxis
PPROM	Preterm prelabour rupture of membranes
PrEP	Pre-exposure prophylaxis
PTB	Preterm birth
RCOG	Royal College of Obstetricians and Gynaecologists
RR	Relative risk
RSV	Respiratory syncytial virus
SBLCB3	‘Saving babies’ lives’, a care bundle for reducing perinatal mortality
SROM	Spontaneous rupture of membranes
STI	Sexually transmitted infection
TDM	Therapeutic drug monitoring
Tenofovir AF	Tenofovir alafenamide
Tenofovir DX	Tenofovir disoproxil
UK-CAB	UK Community Advisory Board
U=U	Undetectable=untransmittable
VBAC	Vaginal birth after caesarean section
WHO	World Health Organization

16 List of appendices

The appendices can be found on the BHIVA website (https://bhiva.org/clinical-guideline/pregnancy-guidelines/):

Appendix 1 Summary of the modified GRADE system

Appendix 2 Literature search strategies

Appendix 3 Evidence summaries

Appendix 4 Drug dosing for postnatal prophylaxis in infants