7. Dickerson MC, Johnston J, Delea TE *et al.* The causal role for genital ulcer disease as a risk factor for transmission of human immunodeficiency virus. An application of the Bradford Hill criteria. *Sex Transm Dis* 1996; **23**: 429–440.

8. Wald A, Link K. Risk of human immunodeficiency virus infection in herpes simplex virus type 2-seropositive persons: a meta-analysis. *J Infect Dis* 2002; **185**: 45–52.

9. Ghys PD, Fransen K, Diallo MO *et al.* The associations between cervicovaginal HIV shedding, sexually transmitted diseases and immunosuppression in female sex workers in Abidjan, Cote d'Ivoire. *AIDS* 1997; **11**: F85–93.

10. Lawn SD, Subbarao S, Wright TC, Jr. *et al.* Correlation between human immunodeficiency virus type 1 RNA levels in the female genital tract and immune activation associated with ulceration of the cervix. *J Infect Dis* 2000; **181**: 1950–1956.

11. Hashemi FB, Ghassemi M, Faro S *et al.* Induction of human immunodeficiency virus type 1 expression by anaerobes associated with bacterial vaginosis. *J Infect Dis* 2000; **181**: 1574–1580.

12. Hashemi FB, Ghassemi M, Roebuck KA, Spear GT. Activation of human immunodeficiency virus type 1 expression by *Gardnerella vaginali*s. *J Infect Dis* 1999; **179**: 924–930.

13. Gitau RW, Graham SM, Masese LN *et al.* Effect of acquisition and treatment of cervical infections on HIV-1 shedding in women on antiretroviral therapy. *AIDS* 2010; **24**: 2733–2737.

14. McClelland RS, Wang CC, Mandaliya K *et al.* Treatment of cervicitis is associated with decreased cervical shedding of HIV-1. *AIDS* 2001; **15**: 105–110.

15. Chuachoowong R, Shaffer N, Siriwasin W *et al.* Short-course antenatal zidovudine reduces both cervicovaginal human immunodeficiency virus type 1 RNA levels and risk of perinatal transmission. Bangkok Collaborative Perinatal HIV Transmission Study Group. *J Infect Dis* 2000; **181**: 99–106.

16. Hart CE, Lennox JL, Pratt-Palmore M *et al.* Correlation of human immunodeficiency virus type 1 RNA levels in blood and the female genital tract. *J Infect Dis* 1999; **179**: 871–882.

17. Fiore JR, Suligoi B, Saracino A *et al.* Correlates of HIV-1 shedding in cervicovaginal secretions and effects of antiretroviral therapies. *AIDS* 2003; **17**: 2169–2176.

18. Kovacs A, Wasserman SS, Burns D *et al.* Determinants of HIV-1 shedding in the genital tract of women. *Lancet* 2001; **358**: 1593–1601.

19. De Pasquale MP, Leigh Brown AJ, Uvin SC *et al.* Differences in HIV-1 pol sequences from female genital tract and blood during antiretroviral therapy. *J Acquir Immune Defic Syndr* 2003; **34**: 37–44.

20. 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.

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. 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.

23. 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.

24. 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.

25. Aebi-Popp K, Bailey H, Malyuta R *et al.* 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.

26. 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.

27. 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.

28. British Association for Sexual Health and HIV, Royal College of Obstetrics and Gyneacology. *Management of genital herpes in pregnancy*. 2014. Available at: www.bashhguidelines.org/media/1060/management-genital-herpes.pdf (accessed October 2018).

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

30. 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.

31. 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.

32. Newell ML, Dunn DT, Peckham CS *et al.* Vertical transmission of HIV-1: maternal immune status and obstetric factors. The European Collaborative Study. *AIDS* 1996; **10**: 1675–1681.

33. 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.

34. Taha TE, Brown ER, Hoffman IF *et al.* A phase III clinical trial of antibiotics to reduce chorioamnionitis-related perinatal HIV-1 transmission. *AIDS* 2006; **20**: 1313–1321.

35. Hillier SL, Nugent RP, Eschenbach DA *et al.* Association between bacterial vaginosis and preterm delivery of a low-birth-weight infant. The Vaginal Infections and Prematurity Study Group. *N Engl J Med* 1995; **333**: 1737–1742.

36. Taha TE, Gray RH. Genital tract infections and perinatal transmission of HIV. *Ann N Y Acad Sci* 2000; **918**: 84–98.

37. Brocklehurst P, Gordon A, Heatley E, Milan SJ. Antibiotics for treating bacterial vaginosis in pregnancy. *Cochrane Database Syst Rev* 2013; CD000262.

38. Varma R, Gupta JK, James DK, Kilby MD. Do screening-preventative interventions in asymptomatic pregnancies reduce the risk of preterm delivery--a critical appraisal of the literature. *Eur J Obstet Gynecol Reprod Biol* 2006; **127**: 145–159.

39. Farquhar C, Mbori-Ngacha D, Overbaugh J *et al.* Illness during pregnancy and bacterial vaginosis are associated with in-utero HIV-1 transmission. *AIDS* 2010; **24**: 153–155.

40. Fakoya A, Lamba H, Mackie N *et al.* British HIV Association, British Association of Sexual Health and HIV and Faculty of Sexual and Reproductive Health guidelines for the management of the sexual and reproductive health of people living with HIV infection 2008. *HIV Med* 2008; **9**: 681–720.

41. Public Health England. *NHS Cervical Screening Programme. Colposcopy and programme management. NHSCSP Publication number 20*. 2016. Available at: www.gov.uk/government/uploads/system/uploads/attachment_data/file/515817/NHSCSP_colposcopy_management.pdf (accessed October 2018).

42. British HIV Association, British Association for Sexual Health and HIV, Faculty of Sexual and Reproductive Healthcare. *BHIVA/BASHH/FSRH guidelines for the sexual and reproductive health of people living with HIV*. 2017. Available at: www.bhiva.org/srh-guidelines-consultation (accessed November 2018).

43. British HIV Association. *BHIVA guidelines for the routine investigation and monitoring of adult HIV-1-positive individuals*. 2016. Available at: www.bhiva.org/monitoring-guidelines (accessed October 2018).

6. Current issues in the use of ART in pregnancy and pregnancy outcomes

6.1 Conceiving on cART

6.1.1	It is recommended that women conceiving on an effective cART regimen should continue this treatment.	1B
	Exceptions are: Non-standard regimens, for example PI monotherapy; Regimens that have been demonstrated to show lower pharmacokinetics in pregnancy such as darunavir/cobicistat and elvitegravir/cobicistat, or where there is an absence of pharmacokinetic data such as raltegravir 1200 mg once daily (od) (should be administered 400 mg twice daily [bd]). These should be modified to include (depending on tolerability, resistance and prior antiretroviral history) one or more agents that cross the placenta. A woman planning a pregnancy and/or conceiving on dolutegravir should see her physician as soon as possible to discuss current evidence on neural tube defects (see section 6.5).	2D
6.1.2	Women taking dolutegravir who are trying to conceive or in the first trimester of pregnancy (<12 weeks' gestation) should be recommended to take folic acid 5 mg od (see section 6.5).	1B
	Women on regimens that do not contain dolutegravir should take the standard recommended dose of folic acid 400 μg once daily, unless they meet the criteria for a higher dose of folic acid (see NICE guidance on maternal and child nutrition: https://www.nice.org.uk/guidance/ph11). It is recommended that all women start folic acid supplementation before pregnancy and continue to 12 weeks' gestation (the end of the first trimester).	

Despite the lack of a licence for the use of ART in pregnancy, with the exception of zidovudine in the third trimester, there is global consensus that women who conceive on effective cART should continue cART throughout pregnancy and then lifelong. Pregnant women are a unique group within the HIV population as treatment is relevant not only for their own health but also for that of the unborn child and risk of congenital abnormality must be considered when assessing cART in pregnancy. Therefore it may not always be appropriate to use standard adult treatment guidelines as recommended regimens in pregnancy usually consist of triple therapy with less evidence for safety and efficacy of newer antiretrovirals and evolving combinations such as dual therapy and integrase inhibitors.

As pregnancy is a temporary state, concerns about long-term toxicity of cART for a woman may not be relevant during pregnancy. After delivery cART may be switched to a regimen preferable for long-term use in terms of both toxicity and tolerability. Our recommendations are shown in Table 6.1.

Table 6.1. Recommended and alternative agents in pregnancy

	Recommended	Alternative
Nucleoside reverse transcriptase inhibitor (NRTI) backbone	Abacavir/lamivudine Tenofovir DF/emtricitabine	Tenofovir alafenamide/ emtricitabine (after the first trimester) Zidovudine/lamivudine

Third agent	Efavirenz Atazanavir/r	Rilpivirine Darunavir/r Raltegravir 400 mg bd Dolutegravir (after 6 weeks' gestation)

The writing group recommends that choice of therapy should always be discussed in full with every woman and be individualised for the patient, taking into account a woman's concerns and preferences [1], in accordance with the standard treatment guidelines. Nucleoside backbone combinations recommended by BHIVA for HIV in pregnancy include tenofovir DF/emtricitabine and abacavir/lamivudine. Pregnant women may also want to consider zidovudine/lamivudine [1]. Considerations for the backbone include side-effect profile, frequency of dosing, interactions with the third agent, adverse outcome profiles and prior cART experience including a resistance profile where available. The writing group recommends that women are advised against the combination of tenofovir DF/emtricitabine and lopinavir/r (especially high-dose lopinavir/r), which demonstrated an increased risk of neonatal death and prematurity in the randomised controlled PROMISE trial [2].

Although zidovudine remains the only antiretroviral agent with a licence for use in pregnancy, non-pregnant adults are now rarely prescribed zidovudine as part of cART due to concerns about toxicity. Despite its proven efficacy in preventing vertical transmission of HIV, particularly in the pre-cART era [3], there are no data to support routinely switching to zidovudine, or adding zidovudine to a combination of antiretrovirals that is suppressing HIV viral load to <50 HIV RNA copies/mL in plasma. Analyses of data combined from two observational studies, the European Collaborative Study and the UK and Ireland NSHPC, have shown no difference in pregnancy outcomes between zidovudine-based and zidovudine-sparing cART [4].

Where the risk of treatment failure due to reduced or intermittent drug exposure with hyperemesis gravidarum exceeds the risk of treatment interruption, the writing group recommends that treatment is interrupted for the minimum time required to overcome the issue. If receiving non-nucleoside reverse transcriptase inhibitor (NNRTI)- or raltegravir-based cART, an additional resistance test may be performed. However, there are no data that specifically address this issue in pregnancy.

6.2 Woman is not already on cART: when to start

6.2.1	All pregnant women, including elite controllers, should start ART during pregnancy and be advised to continue lifelong treatment.	1A

Current BHIVA treatment guidelines recommend treatment of all people living with HIV, regardless of CD4 cell count or clinical status [5]. Studies have shown that immediate initiation of cART improves clinical outcomes for patients, regardless of initial CD4 cell count, and reduces transmission of HIV among serodiscordant partners if the partner with HIV has an undetectable HIV viral load on cART [6-8]. All pregnant women living with HIV should be counselled about the importance of continuation of cART postpartum.

6.2.1 Elite controllers

As advice to commence lifelong cART when HIV is diagnosed applies to elite controllers (people with HIV who maintain an undetectable viral load and high CD4 counts without having to take ART), we no longer provide specific recommendations on treatment for elite controllers.

6.2.2 All women not on cART should commence cART

6.2.2	All women not on cART should commence cART • As soon as they are able to do so in the second trimester where the baseline viral load ≤30,000 HIV RNA copies/mL; • At the start of the second trimester, or as soon as possible thereafter, in women with a	1C