UK National Screening Committee

A pilot of the triage approach to assess whether existing population screening programmes should be continued

Screening Topic

Antenatal screening for HIV

V. Final consultation

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1. Executive Summary

Triage reviews are high level reviews which scan the literature to identify 'red flags' suggesting that further exploration of programme cessation may be necessary. These reviews have a surveillance function and are not intended as a comprehensive review of the programme.

This triage review identified no studies that discussed the cessation of an antenatal HIV screening programme and no papers clearly identifying harms from screening.

The search did identify two studies that reported concerns about the acceptability of an aspect of HIV screening in pregnancy. Both were qualitative cohort studies; the first was a survey of drug users in America and the second was a survey of Australian obstetricians. The first study found that a sub-group of drug users would not access antenatal care that included mandatory HIV screening tests. The second found that health professional's perception of false positives may be a barrier in the implementation and delivery of a universal screening programme. The authors of both studies concluded that, despite these findings, the surveyed population were supportive of screening.

A number of studies noted an increased risk of adverse perinatal outcomes in HIV positive women, notably preterm birth. It is unclear whether the underlying risk is untreated disease, anti-retroviral therapy or indeed if there even is a significant risk at all. National and international surveillance of treatment outcomes is ongoing to monitor, and act upon, any risk. However, to date, studies have not found a significant association that would suggest that programme cessation should be considered.

Screening in pregnancy for HIV infection has significantly contributed to reducing the mother to child transmission rate over the last 20 years in the UK and internationally. It is the conclusion of this triage report that there is no evidence suggesting that programme cessation should be explored further.

2. Background

Introduction to the condition

Human immunodeficiency virus (HIV), is a viral infection that is estimated to affect over 100,000 people in the United Kingdom (PHE 2015). There are two subtypes of HIV; HIV-1 and HIV-2. HIV-1 is the most common subtype, HIV-2 is rarely found outside of the African sub-continent. HIV is transmitted through contact with infected blood and/or bodily fluids. Sexual intercourse, intravenous drug use and mother to child transmission are common routes of exposure to the virus.

Mother to child transmission describes exposure to the virus through intrauterine infection (typically, shortly before delivery), during vaginal delivery and/or through breastfeeding. Exposure to the virus is most likely during vaginal delivery. In the absence of any intervention, mother to child transmission rates range from 15% to 45% depending on the type of exposure, maternal viral load and other factors.

Untreated HIV will cause a progressive failure of the immune system through the infection and destruction of specific cells vital for an immunological response, notably the CD4 (T-helper) cells. The reduced efficacy of the immune system means the individual is more susceptible to opportunistic infection and some cancers. AIDS (acquired immunodeficiency syndrome) is the final stage of HIV infection and is defined when the CD4 count has been reduced to be point where the body can no longer overcome "opportunistic infections".

The development of combination antiretroviral therapy (cART) in recent years has meant that HIV can be managed effectively as a chronic condition and many HIV positive adults' life expectancy will be similar to an uninfected individual.

3. National guidance

Since 1999, pregnant women in the UK have been offered HIV screening as part of routine antenatal care. In 2010, the UK National Screening Committee last reviewed the evidence for screening and

reaffirmed the recommendation to screen. The screening test is offered via a blood test, usually in the first 12 weeks of pregnancy. In addition to HIV/AIDS, the blood sample is also screened for hepatitis B and syphilis if the woman chooses. The NHS Infectious Diseases in Pregnancy Screening (IDPS) Programme has oversight of the screening programme in England and the standards to which the service providers should adhere.

Once diagnosed, the management of HIV is outlined in the British HIV Association clinical guideline for HIV in pregnancy (BHIVA 2014)

4. Methodology

Triage review

The UKNSC has committed to assess the viability of all national screening programmes every three years. Triage reviews will be the starting point for each of these assessments.

The purpose of a triage review is to search for evidence that indicates that a screening programme may cause harm in the screened population. The definition of harm in these reviews can be a clinical risk, a social complication or a reason to consider disinvestment. Evidence associated with the modification of the existing screening programme, for example diagnostic studies regarding improvements to screening test accuracy, is outside the scope of these triage reports.

Depending on the direction and volume of the evidence identified, the triage review may recommend that further investigation through a more rigorous evidence review is warranted or that no further investigation is required until the next three-year cycle. If no studies are identified then this report will recommend continuation of the programme without any further review until the next cycle. As such, triage reviews have a surveillance function.

Each triage review will undergo a three month public consultation on the UKNSC website. The screening committee will then make the final recommendation on the next stage of the review based on the findings of the triage review and the stakeholder consultation comments.

Search strategy and Inclusion criteria

The triage review will be based on a literature search over the last 10 years or since the publication date of the last formal UK NSC review, whichever is most recent. As noted above, studies will only be included that report on outcomes that highlight a reason for the cessation of the existing national screening programme. The search and inclusion criteria will therefore only consider studies that are relevant to one or more of the criteria below:

- The study reports outcomes that address screening programme cessation (including publications about the ending of screening programmes in countries similar to the UK)
- The study reports on the harms of screening for HIV
- The study reports on the balance of harms and benefits of screening for HIV in pregnancy

Triage reviews prioritise higher quality studies; systematic reviews, randomised controlled trials and large prospective cohort studies. Lower quality of evidence (i.e. case-series, narrative reviews etc.) are considered if they report a significant finding and there is no higher quality evidence to refute or support the outcome(s).

The process for study inclusion was undertaken in two stages. The first stage was undertaken by a UKNSC information scientist and aimed to remove studies that are clearly not relevant to the review (for example, animal studies, studies in a foreign language and duplicates). The second stage was undertaken by a single reviewer and considered the remaining studies and applied the above criteria; all studies excluded at this stage were noted in the excluded studies table in the appendix.

5. Evidence summary

Description of the evidence

The literature search identified 31 studies and three conference abstracts that matched the specifications outlined in the methodology. Two studies met the inclusion criteria, also outlined above. The full search strategy is outlined in appendix 1 and the rationale for the exclusion of each of the studies included after the first stage of the review can be found in appendix 2. Full details of the two included studies can be found in appendix 3.

One study surveyed obstetricians in Australia about their HIV antenatal screening practice. A multivariate analysis found that obstetricians who offer HIV antenatal screening were more likely to agree that false-positive results can make universal testing difficult than those who do not offer screening (Adjusted odds ratio, 0.17; 95% CI, 0.1–0.3) (Giles et al., 2007). The authors conclude that the perception of false positives is likely to have arisen due to the low prevalence of HIV/AIDs in Australia, not the diagnostic accuracy of the test. A universal screening programme was not implemented at the time of publication; therefore, the applicability of this finding to the UK is unclear.

A US study surveyed 661 female drug users and held focus groups about attitudes towards mandatory antenatal and newborn HIV screening (Fielder et al., 2005). The study noted, primarily through qualitative interview transcripts, that a perception of discrimination in the health system was a barrier in accessing screening. It also found that intravenous drug users were more likely to avoid antenatal care if mandatory HIV screening is included (16.2% vs. 6.1%, $p < 0.01$). The authors do note, however, that over 91% of respondents supported antenatal HIV screening. It is unclear whether the findings of this study are applicable to the UK, where screening is optional. Furthermore, the study did not quantify the clinical harms associated with avoiding antenatal care; perinatal outcomes and mother to child transmission rates were not reported.

Maternal antiretroviral treatment and adverse perinatal outcomes

In addition to the two studies summarised above, the search also identified three studies that reported an association between adverse perinatal outcomes and anti-retroviral therapy. In the UK, and internationally, antiretroviral therapy is recommended for all HIV positive pregnant women. The most recent BHIVA guideline considered the potential adverse outcomes in their recommendations about when to commence cART in pregnancy. An antenatal screening programme will enter women who screen positive into the diagnostic pathway with a view to developing a treatment strategy. Therefore, although a positive screening outcome is not the only indication to treat, the risks associated with antiretroviral therapy are relevant to this triage review.

The findings of the three studies are summarised below. The findings from an international and a domestic surveillance programme and a recent meta-analysis are also presented below to add further context.

Surveillance and meta-analysis findings

The National Study of HIV in Pregnancy and Childhood (NSHPC) published a retrospective surveillance study on the treatment effect of lopinavir/ritonavir between 2003 and 2012 (Tookey et al., 2016). This antiretroviral regimen is commonly used in the UK. The study included data from 4118 women and 4864 pregnancies and found that the use of lopinavir/ritonavir anti-retroviral regimens has significantly contributed to the reduction of the mother to child transmission rate in the UK. This was 1.1% in the period 2003–2007 and 0.5% in the period 2008–2012. Further, the authors note that maternal and neonatal outcomes in these women have demonstrated that this regimen is safe to use in pregnant women. The study reported that the median gestational age at delivery was 38 weeks (IQR, 38–39 weeks); 12.8 % of the deliveries (585/4556) were pre-term (<37 weeks) and the median birth weight was 3030 g (IQR, 2710–3360 g). The authors note that the pre-term birth rate is lower than that observed in other European observational studies but that the stillbirth rate (9.2 per 1000 infants) was higher than the background rate in the United Kingdom (5.8 per 1000 infants in 2003 and 4.7 per 1000 infants in 2013).

A recent meta-analysis of fifty-two cohort studies found that HIV was significantly associated with both low birth weight (pooled odds ratio (OR):1.73, 95 % confidence interval (CI): 1.64, 1.82, $P < 0.001$) and preterm birth (pooled OR: 1.56, 95 % CI: 1.49, 1.63, $P < 0.001$). However, no significant

association was found between preterm birth and anti-retroviral treatment during pregnancy (Xiao et al., 2015)

The International Antiretroviral Pregnancy Registry is designed to identify major teratogenic effects involving any of the Registry drugs. It collects data annually from approximately 1300 US women who are exposed to anti-retroviral drugs. Its findings to date have found “no apparent increases in frequency of specific defects with first trimester exposures and no pattern to suggest a common cause” (APR 2016).

Studies identified in the search

The United States Preventive Services Task Force (USPTF) published a literature review to update their 2005 recommendation to screen for HIV in pregnancy (Chou et al., 2012). The format was a narrative review based on three clinical questions and a number of sub-questions. The three questions considered the balance of benefits and harms for 1) screening vs. no screening, 2) the accuracy of the screening test(s) and 3) the effect of antiretroviral therapy for mother and neonate.

No high quality studies were identified for the first question and the few that were included for the second question considered the diagnostic accuracy of screening tests, not the harms associated, and are therefore outside of the scope of this triage review. The third question did identify a number of studies, published since 2005, that reported the association between perinatal antiretroviral therapy and the following:

- Pre-term birth (1 randomised control trial and 10 cohort studies)
- Mitochondrial dysfunction (3 laboratory studies)
- Congenital abnormalities (3 cohort studies)
- Neurodevelopmental harms (2 cohort studies)
- Maternal harms (2 cohort studies)

The review concluded that the identified studies showed antiretroviral therapy was associated with an increased risk of preterm birth but there was no clear association with low birthweight, congenital abnormalities or impaired neurodevelopment. No studies included in this review reported the outcomes from antiretroviral treatment that was indicated after an antenatal screening result. Therefore, no studies that were included in this part of the USPSTF review, met the search criteria for this triage review.

While the findings in the USPSTF review identified an association between cART and preterm birth, two cohort studies identified in the search found that untreated HIV was associated with more adverse perinatal outcomes, including preterm birth. Both were cohort studies, the first was undertaken in Nigerian women (N=249) and the second was in HIV positive Swiss women between 2003 and 2008 (Joseph et al., 2011; Aebi-Popp et al., 2010).

Conclusion

No studies were identified that discussed the cessation of an antenatal HIV screening programme.

The search did identify two studies that reported on potential acceptability issues associated with antenatal HIV screening. One qualitative cohort study found that practitioners in Australian states where screening is optional may not routinely screen women because of a perception that the false positive rate is high. A second qualitative cohort study reported on the acceptability amongst a high risk population outside the UK.

The significance of these papers in relation to harms of screening is unclear. Furthermore, the two quantitative cohort studies were based on the opinion of a limited sample size that is arguably not representative of the same cohort in the United Kingdom. Further, the authors of each of the studies supported the provision of a universal antenatal screening programme and noted the benefits of screening. It is therefore reasonable to conclude that these findings relate more to potential barriers to implementation rather than reasons not to implement or to withdraw screening

There is some debate about whether HIV positive women are at increased risk of adverse perinatal outcomes and to what extent antiretroviral treatment may be a factor. UK surveillance data suggests that treatment has had a significant benefit in the reduction of mother to child transmission over the last 20 years. However, the same data found that treated women had a higher stillbirth rate than the population baseline. NSHPC and other surveillance systems will continue to monitor and publish results of treatment outcomes in the UK context.

It is the conclusion of this report that there is no evidence suggesting that programme cessation should be explored further.

6. References

Aebi-Popp et al., 2010

Aebi-Popp K, Lapaire O, Glass TR, Vilen L, Rudin C, Elzi L, et al. Pregnancy and delivery outcomes of HIV infected women in Switzerland 2003-2008. Journal of Perinatal Medicine. 2010;38(4):353-8

ARP 2016

Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry International Interim Report for 1 January 1989 through 31 January 2016. Wilmington, NC: Registry Coordinating Center; 2016. Available from URL: www.APRegistry.com.

BHIVA 2014

British HIV Association 2014, British HIV Association guidelines for the management of HIV infection in pregnant women 2012 (2014 interim review), British HIV Association, London. Available at: http://www.bhiva.org/documents/Guidelines/Pregnancy/2012/BHIVA-Pregnancy-guidelines-update-2014.pdf

Chou et al., 2012

Chou R, Cantor AG, Zakher B, Bougatsos C. Screening for HIV in pregnant women: systematic review to update the 2005 U.S. Preventive Services Task Force recommendation. Annals of Internal Medicine. 2012;157(10):719-28

Ekong et al., 2013

Ekong N, Parker H, Wilson J. Do women receiving a HIV diagnosis antenatally have worse pregnancy outcomes? International Journal of STD and AIDS. 2013;24:27

Giles et al., 2007

Giles ML, Garland SM, Lewin SR, Hellard ME. What are the barriers to offering HIV testing in an antenatal setting? A national study of obstetricians. AIDS. 2007;21(12):1601-6

Joseph et al., 2011

Joseph O, Biodun O, Michael E. Pregnancy outcome among HIV positive women receiving antenatal HAART versus untreated maternal HIV infection. JCPSP, Journal of the College of Physicians & Surgeons - Pakistan. 2011;21(6):356-9

PHE 2015

Public Health England 2015. *HIV in the UK – Situation Report 2015 Incidence, prevalence and prevention*. Public Health England, London, available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/477702/HIV_in_the_UK_2015_report.pdf

PHE 2015a

Public Health England 2015, *Antenatal screening for infectious diseases in England: summary report for 2014,* Public Health England, London, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/482642/hpr4315_ntntlscrng.pdf

PHE 2016

Public Health England 2016. *NHS Infectious Diseases in Pregnancy Screening Programme Laboratory Handbook 2016 to 2017*, Public Health England, London available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/539828/NHS_Infectious_Diseases_in_Pregnancy_Screening_Programme_Laboratory_Handbook_2016_2017_with_gateway_number.pdf

PHE 2016a

Public Health England 2016. *NHS Infectious Diseases in Pregnancy Screening Programme Standards 2016 to 2017*. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/512083/IDPS_Programme_Standards_2016_2017_final.pdf

Tookey et al., 2016

Tookey PA, Thorne T, Van Wyk J, Norton M. Maternal and foetal outcomes among 4118 women with HIV infection treated with lopinavir/ritonavir during pregnancy: analysis of population-based surveillance data from the national study of HIV in pregnancy and childhood in the United Kingdom and Ireland. BMC Infectious Diseases (2016) 16:65 DOI 10.1186/s12879-016-1400-y

Townsend et al., 2014

Townsend CL, Byrne L, Cortina-Borja M, Thorne C, de Ruiter A, Lyall H, Taylor GP, Peckham CS, Tookey PA. Earlier initiation of ART and further decline in mother-to-child HIV transmission rates, 2000-2011. AIDS. 2014 Apr 24;28(7):1049-57. doi: 10.1097

Xiao et al., 2015

Xiao P, Zhou Y, Chen Y, Yang M, Song X, Shi Y, Jiang Q, Association between maternal HIV infection and low birth weight and prematurity: a meta-analysis of cohort studiesBMC Pregnancy and Childbirth (2015) 15:246 DOI 10.1186/s12884-015-0684-z

Appendix 1 – Search strategy

SCOPE OF THE SEARCH:

- Addressing screening programme cessation
- Reporting harms from screening
- Reporting balance of harms and benefits from screening

SOURCES SEARCHED: Medline, PubMed, Embase, and the Cochrane Library.

DATES OF SEARCH: January 2005 – March 2016

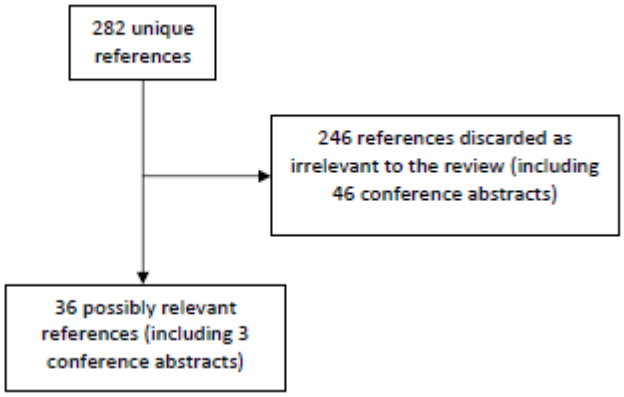
SEARCH STRATEGY:

1. exp HIV/ (86481)
2. HIV.tw. (250796)
3. human immunodeficiency virus.tw. (74294)
4. 1 or 2 or 3 (274019)
5. Prenatal Diagnosis/ (32698)
6. ((antenatal or prenatal or pregnan$) adj2 screen$3).tw. 6023
7. Mass Screening/ae [Adverse Effects] (574)
8. 5 or 6 or 7 (37040)
9. (ceas$ or cessation or stop or stopped or continu$ or discontinu$).tw. (991840)
10. (appropriate$ or inappropriate$ or unnecessary or question$).tw. (1150812)
11. (harm$ or adverse).tw. (447442)
12. (benefit$ and (risk$ or harm$)).tw. (120870)
13. ((side or adverse) adj effect$).tw. (298052)
14. (overdiagnos?s or over diagnos?s).tw. (2610)
15. Program Evaluation/ (50196)
16. Patient Safety/ (8818)
17. Patient harm/ (58)
18. exp Health Services Misuse/ (8212)
19. Risk Assessment/ (195363)
20. 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 (2785884)
21. 4 and 8 and 20 (277)
22. limit 21 to yr="2005 -Current" (126)

Similar searches were also carried out in Embase and the Cochrane Library.
A search for “Epub ahead of print” articles in PubMed was also undertaken.

Medline	126
PubMed	0
Embase	183
Cochrane Library	79
Total	388

Inclusions and exclusions:



After automatic and manual de-duplication, 282 unique references were sifted for relevance to the review.

Appendix 2 – Excluded studies table

Reference	Reason for exclusion
Lawi JDT, Mirambo MM, Magoma M, Mushi MF, Jaka HM, Gumodoka B, et al. Sero-conversion rate of Syphilis and HIV among pregnant women attending antenatal clinic in Tanzania: A need for re-screening at delivery. BMC Pregnancy and Childbirth. 2015;15 (1) (no pagination)(3)	Study undertaken in Tanzania. Not generalizable to a UK screening population. Study did not report harm outcomes associated with an antenatal HIV screening programme.
Charlton TG, Franklin JM, Douglas M, Short CE, Mills I, Smith R, et al. The impact of HIV infection and antiretroviral therapy on the predicted risk of Down syndrome. Prenatal Diagnosis. 2014;34(2):121-	Pre-existing maternal infection had a significant effect on the biochemical assays used in the prenatal trisomy screening test. Screening for HIV in pregnancy would have no effect on this outcome
Reitter A, Stucker AU, Buxmann H, Herrmann E, Haberl AE, Schlosser R, et al. Prenatal ultrasound screening for fetal anomalies and outcomes in high-risk pregnancies due to maternal HIV infection: a retrospective study. Infectious Diseases in Obstetrics and Gynecology. 2013;2013:208482	Study did not report harm outcomes associated with an antenatal HIV screening programme
Moyer VA. Screening for HIV: U.S. Preventive Services Task Force recommendation statement. Annals of Internal Medicine. 2013;159(1):51-60	Narrative review. Did not include any new primary evidence.
Liang K, Meyers K, Zeng W, Gui X. Predictors of elective pregnancy termination among women diagnosed with HIV during pregnancy in two regions of China, 2004-2010. BJOG: An International Journal of Obstetrics and Gynaecology. 2013;120(10):1207-14	Study undertaken in China. Not generalizable to a UK screening population.
Westling K, Pettersson K, Kaldma A, Naver L. Rapid decline in HIV viral load when introducing raltegravircontaining antiretroviral treatment late in pregnancy. AIDS Patient Care & Stds. 2012;26(12):714-7	Study did not report harm outcomes associated with an antenatal HIV screening programme.
Lindegren Mary L, Kennedy Caitlin E, Bain-Brickley D, Azman H, Creanga Andreea A, Butler Lisa M, et al. Integration of HIV/AIDS services with maternal, neonatal and child health, nutrition, and family planning services. Cochrane Database of Systematic Reviews [Internet]. 2012; (9)	No studies (20 included) included in the systematic review considered an antenatal HIV screening protocol that was analogous to the model used in the UK. Systematic review did not report any significant adverse effects arising from included interventions similar to screening.
Keogh SC, Urassa M, Roura M, Kumogola Y, Kalongoji S, Kimaro D, et al. The impact of antenatal HIV diagnosis on postpartum childbearing desires in northern Tanzania: a mixed methods study. Reproductive Health Matters. 2012;20(39 Suppl):39-49	Study undertaken in Northern Tanzania. Not generalizable to a UK screening population. Primary outcomes were attitudes towards childbearing following HIV diagnosis and contraceptive services. Harms of screening not reported.
Kinuthia J, Kiarie JN, Farquhar C, Richardson BA, Nduati R, Mbori-Ngacha D, et al. Uptake of prevention of mother to child transmission interventions in Kenya: health systems are more influential than stigma. Journal of the International AIDS Society. 2011;14:61	Study undertaken in Kenya. Not generalizable to a UK screening population. No outcomes related to harms of a screening programme. Author concludes that effective delivery ART and testing is

	beneficial despite stigma related to diagnosis.
Joseph O, Biodun O, Michael E. Pregnancy outcome among HIV positive women receiving antenatal HAART versus untreated maternal HIV infection. JCPSP, Journal of the College of Physicians & Surgeons - Pakistan. 2011;21(6):356-9	No outcomes related to screening, only pregnancy outcomes with untreated vs. treated HIV infection.
Fernandes RCDSC, Ribas GF, Pires ESD, Gomes AM, Medina-Acosta E. Persistent operational challenges lead to non-reduction in maternal-infant transmission of HIV. Jornal de Pediatria. 2010;86(6):503-8	Study reported risk factors that impeded effective maternal-infant HIV transmission rate reduction in brazil. Low screening coverage was highlighted to have a negative effect. Study did not report harm outcomes associated with an antenatal HIV screening programme
Aebi-Popp K, Lapaire O, Glass TR, Vilen L, Rudin C, Elzi L, et al. Pregnancy and delivery outcomes of HIV infected women in Switzerland 2003-2008. Journal of Perinatal Medicine. 2010;38(4):353-8	Study did not report harm outcomes associated with an antenatal HIV screening programme Study did note association between HIV positive women and high risk pregnancies.
Giles M. HIV and pregnancy: screening and management update. Current Opinion in Obstetrics & Gynecology. 2009;21(2):131-5	Narrative review that does not report any new findings related to the benefits or harms of screening
Desgrees-du-Lou A, Brou H, Traore AT, Djohan G, Becquet R, Leroy V. From prenatal HIV testing of the mother to prevention of sexual HIV transmission within the couple. Social Science and Medicine. 2009;69(6):892-9	Study undertaken in Ivory Coast. Not generalizable to a UK screening population. Study did not report harm outcomes associated with an antenatal HIV screening programme
Briand N, Pornprasert S, Ngo-Giang-Huong N, Galactéros F, Pissard S, Tatu T, et al. Perinatal zidovudine prophylaxis in HIV type-1-infected pregnant women with thalassaemia carriage in Thailand. Antiviral therapy [Internet]. 2009; 14(1):[117-22 pp.]	Study did note association between HIV positive women and high risk pregnancies. Study population was limited to HIV positive with thalassemia
Kumar A, Kilaru KR, Kumari G, Forde S, Waterman I. Follow-up of HIV-infected women diagnosed by antenatal screening in Barbados from 1996-2004. AIDS Patient Care & STDs. 2008;22(9):715-21	Study undertaken in Barbados. Not generalizable to a UK screening population. Retrospective cohort study only considered adherence to support services following antennal diagnosis.
Ersoy N, Akpinar A. Attitudes about prenatal HIV testing in Turkey. Nursing Ethics. 2008;15(2):222-33	Study undertaken in Turkey which, at the time, did not have a national HIV screening policy. Study did not report harm outcomes associated with an antenatal HIV screening programme
Kuhn L, Sinkala M, Kankasa C, Semrau K, Kasonde P, Scott N, et al. High uptake of exclusive breastfeeding and reduced early	Study did not report harm outcomes associated with an

post-natal HIV transmission. PLoS ONE [Internet]. 2007; 2(12):[e1363 p.].	antenatal HIV screening programme
Kominami M, Kawata K, Ali M, Meena H, Ushijima H. Factors determining prenatal HIV testing for prevention of mother to child transmission in Dar Es Salaam, Tanzania. Pediatrics International. 2007;49(2):286-92	Study undertaken in Tanzania. Unlikely to be applicable to a UK context Study primary outcome was test acceptance. Study did not consider adverse events related to prenatal screening.
Deblonde J, Claeys P, Temmerman M. Antenatal HIV screening in Europe: a review of policies. European Journal of Public Health. 2007;17(5):414-8	Study did not report harm outcomes associated with an antenatal HIV screening programme.
American College of Obstetrics & Gynecology. ACOG Committee Opinion No. 389, December 2007. Human immunodeficiency virus. Obstetrics & Gynecology. 2007;110(6):1473-8	Study did not report harm outcomes associated with an antenatal HIV screening programme.
Sherr L, Fox Z, Lipton M, Whyte P, Jones P, Harrison U, et al. Sustaining HIV testing in pregnancy- evaluation of routine offer of HIV testing in three London hospitals over 2 years. AIDS Care. 2006;18(3):183-8	Study did not report harm outcomes associated with an antenatal HIV screening programme.
Rogers A, Meundi A, Amma A, Rao A, Shetty P, Antony J, et al. HIV-related knowledge, attitudes, perceived benefits, and risks of HIV testing among pregnant women in rural Southern India. AIDS Patient Care & STDs. 2006;20(11):803-11	Study undertaken in India. Not generalizable to a UK screening population. Study did not report harm outcomes associated with an antenatal HIV screening programme
Naver L, Lindgren S, Belfrage E, Gyllensten K, Lidman K, Gisslen M, et al. Children born to HIV-1-infected women in Sweden in 1982-2003: trends in epidemiology and vertical transmission. Journal of Acquired Immune Deficiency Syndromes: JAIDS. 2006;42(4):484-9	Study undertaken in India. Not generalizable to a UK screening population. Study did not report harm outcomes associated with an antenatal HIV screening programme
Lyons F, Mulcahy F, Coulter-Smith S, Butler K. National guidelines for the management of HIV-1 in pregnancy. Irish Medical Journal. 2006;99(5)	Study did not report harm outcomes associated with an antenatal HIV screening programme
Daniel OJ, Oladapo OT. Acceptability of prenatal HIV screening at the primary care level in Nigeria. Journal of Obstetrics & Gynaecology. 2006;26(3):191-4	Study did not report harm outcomes associated with an antenatal HIV screening programme
Buchholz B, Beichert M, Marcus U, Grubert T, Gingelmaier A, Haberl A, et al. German-Austrian recommendations for HIV-therapy in pregnancy and in HIV-exposed newborn - Update 2005. European Journal of Medical Research. 2006;11(9):359-76	Study did not report harm outcomes associated with an antenatal HIV screening programme
Embree J. The impact of HIV/AIDS on children in developing countries. Paediatrics & Child Health. 2005;10(5):261-3	Study did not report harm outcomes associated with an antenatal HIV screening programme
Chou R, Smits AK, Huffman LH, Korthuis PT. Screening for human immunodeficiency virus in pregnant women: evidence synthesis2005; (1):[90 p.]	Study superseded by update review in 2012.
Chou R, Smits AK, Huffman LH, Fu R, Korthuis PT, US Preventive Services Task force. Prenatal screening for HIV: A review of the evidence for the U.S. Preventive Services Task Force. Annals of Internal Medicine. 2005;143(1):38-54	Study superseded by update review in 2012.
Ekong N, Parker H, Wilson J. Do women receiving a HIV diagnosis antenatally have worse pregnancy outcomes?	Conference abstract. Study did not report harm outcomes associated with an antenatal HIV screening programme

International Journal of STD and AIDS. 2013;24:27	
Waugh RML, Elamin MEMO, Peart LC, Vale JA, Thompson JP, Eddleston M, et al. Analysis of enquiries about antiretroviral therapy (ART) involving neonates, as reported to the UK National Poisons Information Service (NPIS). Clinical Toxicology. 2015;53 (4):285	Conference abstract. Study did not report harm outcomes associated with an antenatal HIV screening programme
James CP, David AL, Whitten SM, Roedling S. Cervical length measurement and pre-term birth risk in HIVpositive women on HAART. HIV Medicine. 2015;16:28	Conference abstract. Study did not report harm outcomes associated with an antenatal HIV screening programme

Appendix 3 – Included studies summary table

Publication details	Study details	Population	Intervention/test and comparator	Main findings	Comments
Screening cessation					
No studies identified					
Harms of screening					
Fielder et al., 2015 Fielder O, Altice FL. Attitudes toward and beliefs about prenatal HIV testing policies and mandatory HIV testing of newborns among drug users. AIDS & Public Policy Journal. 2005;20(3-4):74-91	Quantitative Cohort Study Interview and focus group with HIV positive drug users in USA	• 610 structured interviews conducted from 1997 to 2001 • 5 focus groups of five subjects in September 2003	Attitudes towards antenatal HIV screening	• Injectors were significantly more likely to avoid prenatal care if HIV testing was included (16.2 percent versus 6.1 percent, p < 0.01). • 31.8 percent respondents believed that "certain types of people" received better treatment than others	The authors concluded that the respondents were supportive of screening. It is unclear what the “harms” identified are, or if they are quantifiable. Note, the data reporting period and reference indicate that the this was a republication of an earlier study.
Giles et al., 2007 Giles ML, Garland SM, Lewin SR, Hellard ME. What are the barriers to offering HIV testing in an antenatal setting? A national study of obstetricians. AIDS. 2007;21(12):1601-6	Quantitative Cohort Study Questionnaire mailed to all obstetricians in Australia	817 Australian Obstetricians responded	Investigation into Australian antenatal screening practice.	90% of respondents disagreed with only testing women with risk factors compared with only 34% of those who undertook a selective screening approach (adjusted odds ratio, 87.7; 95% confidence interval, 40-192; P = 0.001) A multivariate analysis found that a significant barrier to universal screening was the perceived frequency of false positives (OR, 0.17; 95% CI, 0.1–0.3	The study outlines that perception about false positive results may negatively affect screening practice. There was no national screening programme when the study was undertaken.
Balance of benefits and harms					
No studies identified					
Adverse perinatal outcomes					
Chou et al., 2012 Chou R, Cantor AG, Zakher B, Bougatsos	Rapid systematic review to update USPSTF 2005 meta-analysis		Consider the benefits and harms of 1) screening vs. no	No studies directly evaluated effects of prenatal HIV screening on risk for mother-to-child transmission or maternal or infant clinical	The studies identified noted that antiretroviral therapy during pregnancy to be associated with increased risk for preterm delivery (<37 weeks' gestation);

C. Screening for HIV in pregnant women: systematic review to update the 2005 U.S. Preventive Services Task Force recommendation. Annals of Internal Medicine. 2012;157(10):719-28			screening 2) the accuracy of the screening test(s) 3) the effect of antiretroviral therapy for mother and neonate	outcomes. The following outcomes were reported in studies published since 2005 (number and type of study in brackets): • Pre-term birth (1 randomised control trial and 10 cohort studies) • Mitochondrial dysfunction (3 laboratory studies) • Congenital abnormalities (3 cohort studies) • Neurodevelopmental harms (2 cohort studies) • Maternal harms (2 cohort studies)	there were no clear associations with low birthweight, congenital abnormalities, or infant neurodevelopment. No studies included in the review would met the inclusion criteria for this triage review as they were not undertaken in a screened population.
Joseph et al., 2011 Joseph O, Biodun O, Michael E. Pregnancy outcome among HIV positive women receiving antenatal HAART versus untreated maternal HIV infection. JCPSP, Journal of the College of Physicians & Surgeons - Pakistan. 2011;21(6):356-9	Retrospective cohort study	249 HIV positive women delivering in University of Benin Teaching Hospital from Jan 2008 to June 2009	Women who received no antenatal antiretroviral therapy were compared with women who had HAART early in pregnancy	Perinatal outcomes significantly higher among women with untreated-HIV infection in pregnancy: • Intrauterine growth restriction (IUGR) (20.5% vs. 6.3%, p = 0.003) • Pre-term birth (25.0% vs. 9.8%, p = 0.005) • Caesarean delivery (45.5% vs. 29.8%, p = 0.04) Untreated maternal HIV-infection was associated with higher frequency of birth weight less than 2500g, 5-minutes Apgar score less than 7 and admission into neonatal unit ($p < 0.05$).	The study does not discuss the harms of a screening programme. This is included for information only. It is unclear whether the findings would be generalizable to a UK population.
Aebi-Popp et al., 2010 Aebi-Popp K, Lapaire O, Glass TR, Vilen L, Rudin C, Elzi L, et al. Pregnancy and delivery outcomes of HIV infected women in Switzerland 2003-2008. Journal of Perinatal Medicine. 2010;38(4):353-8	Prospective cohort study	266 Swiss HIV positive women delivering between Jan 2003 to Oct 2008 67 (25.2%) diagnosed during pregnancy	N/A	Advanced maternal age was reported to have adjusted odds ratio: 1.06, 95% confidence interval 1.01-1.12, P=0.02) associated with adverse perinatal outcomes.	The study does not discuss the harms of a screening programme. This is included for information only. The only statistically significant risk factor in HIV positive women was advanced maternal age. Preterm delivery was noted in 72 (27%) patients. It is unclear if this is significantly higher than in an unaffected population or if there is an associated with cART.