**UK National Screening Committee**

**Screening for Fetomaternal alloimmune thrombocytopenia (FMAIT)**

**8th February 2017**

**Aim**

1. To ask the UK National Screening Committee (UK NSC) to make a recommendation, based on the evidence presented in this document, whether screening for fetomaternal alloimmune thrombocytopenia (FMAIT) meets the UK NSC criteria to support the introduction of a population screening programme.

This document provides background on the item addressing screening for FMAIT.

**Current recommendation**

1. The previous, 2012 review, of antenatal screening for FMAIT concluded that population screening should not be introduced in the UK. The 2012 review found:

* no test that could reliably predict which cases of FMAIT would be more severe. Therefore it would not be able to identify a group likely to benefit from medical intervention
* that the lack of a reliable test may result in over-diagnosis and unnecessary intervention
* no convincing evidence that an intervention (intravenous immunoglobulin (IVIG) or Caesarean section) improves the outcomes of pregnancies that are identified through antenatal screening
* that no randomised controlled trials of screening for FMAIT had been conducted

**Review**

1. The current review was undertaken by Solutions for Public Health in accordance with the triennial review process <http://legacy.screening.nhs.uk/musculardystrophy>. Expert input was provided by Professor Mike Murphy.
2. The review considered 3 criteria: (1, the condition, 9, the intervention, and 11, the screening programme). The review sought to evaluate the published evidence relating to key questions identified as areas of uncertainty in the previous review.
3. The conclusion of this review is that a population screening programme for FMAIT should not be introduced in the UK. The key reasons are:
4. the test; a reliable predictor of severe cases of FMAIT has not been identified. Therefore there is no reliable method of identifying cases that are more likely to benefit from medical intervention in a first pregnancy. **Criterion 1 not met.**
5. There were some additional studies published since 2011. They examined giving intravenous immunoglobulin (IVIG) to the mother to prevent haemorrhaging and /or the delivery of the baby by caesarean section. However the evidence was not robust enough to support a management strategy for women considered to be high risk and prevent adverse outcomes in their first pregnancy.

In addition the studies identified since 2011 involved the medical management of women who had been identified as at high risk of their babies developing FMAIT because of a previous affected pregnancy. These findings could not be assumed to apply to a first high risk pregnancy identified through a screening programme. **Criterion 9 not met.**

1. No additional high grade evidence which indicates the most effective screening strategy to identify first pregnancies at high risk of adverse outcomes from the development of FMAIT was identified since the last UK NSC review.  **Criterion 11 not met.**

**Consultation**

1. A three month consultation was hosted on the UK NSC website. Direct emails were sent to the following 13 stakeholder organisations; BLISS, British Paediatric Allergy, Immunology and Infection Group, The British Society for Haematology, British Association of Perinatal Medicine, Faculty of Public Health, Maternal Neonatal Unit, Bradford Teaching Hospitals NHS Foundation Trust, NAIT Babies, NHS Blood and Transplant, Royal College of General Practitioners, Royal College of Midwives, Royal College of Obstetricians and Gynaecologists, Royal College of Paediatric and Child Health and the UK Newborn Screening Laboratories Network (**Annex A**)
2. Responses were received from the following four stakeholders:

* Royal College of Obstetricians and Gynaecologists and British Maternal and Fetal Medicine Society (joint response)
* International Collaboration for Transfusion Medicine Guidelines
* Royal College of Paediatrics and Child Health
* Naitbabies

All comments are in **Annex B,** below.

1. The responses indicated broad agreement with the review’s recommendations, however one stakeholder disagreed with the review’s conclusion that there is insufficient evidence relating to maternal HPA-1a antibody levels as a predictor of severity from FMAIT. An unpublished systematic review manuscript was provided in support of this criticism. However, the conclusion of the manuscript was that a suitable antibody level threshold had not been identified and that more research is needed in this area. This systematic review will be considered for inclusion in the next review if published.

Another point of discussion raised by the stakeholder was the need to test sisters of women, whose pregnancies have been affected by FMAIT. Cascade testing strategies are outside the remit of the UK NSC.

Some consultees raised issues relating to the conduct of the review, interpretation of individual papers and overall analysis. These were addressed by the reviewer and alterations made to the evidence review where appropriate. See **Annex B**

**Recommendation**

1. The committee is asked to approve the following recommendation:

*A whole population screening programme for FMAIT is not recommended because there is no reliable screening test for use within a population screening programme and the lack of evidence that screening improves outcomes in comparison with current practice.*

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| --- | --- | --- |
| **Criteria** | | **Met /**  **Not met** |
| **The Condition** | | |
| 1 | The condition should be an important health problem as judged by its frequency and/or severity. The epidemiology, incidence, prevalence and natural history of the condition should be understood, including development from latent to declared disease and/or there should be robust evidence about the | Not met  🗶 |
| **The Intervention** | | |
| 9 | There should be an effective intervention for patients identified through screening, with evidence that intervention at a pre-symptomatic phase leads to better outcomes for the screened individual compared with usual care. Evidence relating to wider benefits of screening, for example those relating to family members, should be taken into account where available. However, where there is no prospect of benefit for the individual screened then the screening programme shouldn’t be further considered. | Not met  🗶 |
| **The Screening Programme** | |  |
| 11 | There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity. Where screening is aimed solely at providing information to allow the person being screened to make an “informed choice” (such as Down’s syndrome or cystic fibrosis carrier screening), there must be evidence from high quality trials that the test accurately measures risk. The information that is provided about the test and its outcome must be of value and readily understood by the individual being screened. | Not met  🗶 |

**Annex A**

**List of organisations contacted:**

1. BLISS
2. British Paediatric Allergy, Immunology and Infection Group
3. The British Society for Haematology
4. British Association of Perinatal Medicine
5. Faculty of Public Health
6. Maternal Neonatal Unit, Bradford Teaching Hospitals NHS Foundation Trust
7. NAIT Babies
8. NHS Blood and Transplant
9. Royal College of General Practitioners
10. Royal College of Midwives
11. Royal College of Obstetricians and Gynaecologists
12. Royal College of Paediatric and Child Health
13. UK Newborn Screening Laboratories Network

**Annex B**

**UK National Screening Committee**

**Screening for fetomaternal alloimmune thrombocytopenia**

**Consultation comments and responses: January 2017**

**Note that the four consultation comments are listed in the table below, grouped by the section of the draft review document to which they refer.**

| **No.** | **Stakeholder Name,**  **Consented for names to be published:**  **Yes**  **NO** | **Section and / or page number** | **Text or issue to which comments relate** | **Comment** |
| --- | --- | --- | --- | --- |
| 1. | Dr. Jane M Hawdon, Consultant Neonatologist  on behalf of :Royal College of Paediatrics and Child Health  Yes | Whole document | Whole document | Our commenter advised that they agree with the evidence review |
| 2. | Members of the ICTMG FNAIT guideline panel. Heather Hume;   |  | | --- | | Andreas Greinacher  Yes | | |  | | --- | | Whole document | | Whole document | Unfortunately I have not been able to review this document & will not be able to do so in the day few days. However I do agree with their recommendation not to proceed with screening of all pregnant women for FNAIT  on the whole the UK National screening committee's recommendation is based on a careful review of the literature. Some of the areas of uncertainty have been addressed already by other members of the FNAIT guideline group in the comments in my opinion these comments do not change the overall conclusion made by the UK committee. I found no really important additional information or lacking in the report. As it is requested and typical for such reports the interpretation of data is rather conservative which may leave room for discussions but does not require a change of the current document (at least in my opinion). |
| 2.1 | Members of the ICTMG FNAIT guideline panel.  Cecile Kaplan  Yes |  | I don't favor absence of screening for HPA-1a immunisation | Up to now the testing is at low cost of and there is still even low risk to have severe FMAIT (sometimes with ICH) detected when it's too late. What's about the sisters of the women with FMAIT? |
| 2.2 | Members of the ICTMG FNAIT guideline panel. Jens Kjeldsen-Kragh  Yes | Page 6, question 2, 2nd bullet point | HLA typing as potential predictor | For more than 20 years it has been known that more than 90 % of HPA-1a-immunized women are HLA DRB3\*01:01 positive, whereas this HLA-type is only found in approximately 30 % of unselected pregnant women. The risk of HPA-1a-immunization in HLA DRB3\*01:01 positive women is around 20 times higher than in women not carrying this HLA type. Furthermore, the levels of anti-HPA-1a in HLA DRB3\*01:01 negative women who do become HPA-1a-immunized are significantly lower than the antibody levels in HLA DRB3\*01:01 positive women who develop HPA-1a antibodies. In addition, HPA-1a-immunized women who are HLA DRB3\*01:01 negative give birth to children with significantly higher platelet count than children born of HPA-1a-immunized women who are HLA-DRB3\*01:01 positive; in fact, severe thrombocytopenia is very rarely seen in new-borns of HPA-1a-immunized women who are HLA-DRB3\*01:01 negative.  The reason why HPA-1a negative, HLA DRB3\*01:01 positive women become HPA-1a-immunized is related to the ability for the peptide carrying the HPA-1a epitope to be presented efficiently for antigen-specific T cells. Two independent groups (Ahlen et al. Blood 2009;113:3838-44 and Rayment et al. J Immunol 2009;183:677-86) have shown that the antigenic peptide is efficiently presented to T cells by antigen presenting cells carrying he HLA molecule encoded by the HLA DRB3\*01:01 allele. These T cells will become activated and provide help to antigen-specific B-cells which in turn will develop into anti-HPA-1a-producing plasma cells.  Hence, I disagree with the statement: “The relationship between potential predictors such as blood typing, HLA genotyping and FMAIT is still not fully understood although correlations between these factors and severe FMAIT have been reported. The evidence is not clear that these predictors could be clinically useful in identifying women at high risk of having a fetus/newborn with severe FMAIT in their first pregnancy.” The association between HLA DRB3\*01:01 and FMAIT is very well understood and HLA DRB3\*01:01 typing of women, who turns out to be HPA-1a negative, could be a useful tool to reduce the size of the population of pregnant women who needs to be followed up. |
| 2.3 | Members of the ICTMG FNAIT guideline panel.  Mette Kjær  Yes | Introduction/page 8 “year of age.” | The 2012 UK NSC review included an earlier systematic review of studies of women screened antenatally with severe NAIT3 (Kamphus et al 2011) and reported a rate of 0.04% (40 per 100,000). Knight et al (2011)4 estimated the incidence of clinically-detected FMAIT in the UK as 12.4 (95% CI 10.7 – 14.3) per 100,000 births, equivalent to approximately 85 babies per year. Of those 85 babies 8 will die or be severely disabled by 1 | It should be added that the study from Kamphus et al (Pediatrics, 2014:133:715-7201), reported an ICH rate of 0.01% (10 per 100 000), equivalent to approximately 54 babies that will die in UK or be severely disabled by 1 year of age. The estimated incidence of clinically-detected FMAIT by Knight et al (2011)4 is probably and underestimation, and fits well with the study by Tiller H et al. (BJOG 2009:116:594-598) who found that only 15% of severe FMAIT cases are identified without a screening program (hence 8 of 54 ICH cases) |
| 2.4 | Members of the ICTMG FNAIT guideline panel. Mette Kjær  Yes | Introduction: Basis for current recommendation/page 9 “There is not yet consistent evidence that the level of maternal anti-HPA-1a antibodies can reliably predict which cases of FMAIT will be more severe, and therefore more likely to benefit from medical intervention” |  | Results from a literature review (by the ICTMG guideline group) demonstrate that the HPA-1a antibody level correlates with fetal/neonatal platelet count. |
| 2.5 | Members of the ICTMG FNAIT guideline panel. Mette Kjær  Yes | Introduction: Basis for current recommendation/page 9“ | If the estimates derived from screening studies are applied to a UK birth cohort of 700,000 births one would expect to find approximately 1400 cases of FMAIT each year, of which 420 would have severe thrombocytopenia” | This is not correct. The number 1400 is the estimated number of immunized women, not FMAIT. |
| 2.6 | Members of the ICTMG FNAIT guideline panel. Mette Kjær  Yes | Introduction: Basis for current recommendation/page 9 | “However the number of babies with clinically-detected FMAIT appears to be only about 85 per year.” | It should be added that this could be an underestimation since only 15% of the severe cases are identified without screening (Tiller et al. BJOG 2009:116:594-598). |
| 2.7 | Members of the ICTMG FNAIT guideline panel. Mette Kjær  Yes | Introduction: Basis for current recommendation/page 9 screening” | “There is not yet any convincing evidence that medical intervention improves the outcomes of pregnancies that are identified through antenatal | It should be mention that in the study by Mendani et al (BJOG 2012;119:1612–1616) they concluded that screening would be effective to improve the outcome in subsequent pregnancies |
| 2.8 | Members of the ICTMG FNAIT guideline panel. Jens Kjeldsen-Kragh  Yes | Page 13, last sentence after Table 2 | Sample size. | I cannot see how the statement “…sample sizes are small and the study underpowered to detect statistical differences” is relevant when the paper actually reports a statistically significant difference. The question about sample size is only relevant if the data analysis concludes there is no statistically significant difference between groups. |
| 2.9 | Members of the ICTMG FNAIT guideline panel. Jens Kjeldsen-Kragh  Yes | Page 14, Discussion, 2nd paragraph | Risk of bias. | In my opinion the comment “...as soon as a pregnancy is identified as high risk a range of possible interventions will be used to reduce the likelihood of an adverse outcome” is not relevant in relation to the review by Kamphuis et al. (Pediatrics 2014;133:715-721). The authors excluded studies “…when the method of screening was a method other than measuring platelet count in cord blood”. Hence, antenatal intervention would not have been possible before delivery, unless FMAIT was expected due to a previous sibling with FMAIT. |
| 2.10 | Members of the ICTMG FNAIT guideline panel. Jens Kjeldsen-Kragh  Yes | Page 14, Discussion, last paragraph | “It remains unclear as to what extent these differences between the numbers predicted from unselected population studies and the numbers that are clinically diagnosed represents over-diagnosis through routine testing, or under-diagnosis by paediatricians in the absence of screening. Therefore it is uncertain how the evidence would apply to a potential NHS screening programme.” | An obvious explanation of the difference in rates of ICH between the antenatal review (3-4 per 100,000 births) and the postnatal review (10 per 100,000 births) is antenatal intervention. In the studies included in the antenatal review, HPA-1a-immunized women received a number of different treatments such as IVIG, intrauterine transfusions and preterm delivery by Caesarean section, and it is likely that these treatments may have prevented some cases of ICH. In the studies included in the postnatal review, such intervention was not possible. To talk about over-diagnosis in these studies does not make sense because the damage, i.e. ICH, had already occurred - it is difficult to understand now ICH could have been over-diagnosed in these studies. There may be a number of reasons why the number of clinically detected FMAIT-associated ICH cases is as low as 1.5 per 100,000 births, but it is well known from other rare medical conditions that under-diagnosis is a general problem Therefore, in my opinion the data from the discussed reviews allow for a much more tangible conclusion: There are good reasons to assume that the estimate of 10 cases of ICH per 100,000 births (Kamphuis et al. Pediatrics 2014;133:715-721), currently is the most accurate reflection of the natural history of FMAIT |
| 2.11 | Members of the ICTMG FNAIT guideline panel. Mette Kjær  Yes | Discussion/Applicability/page 14 | “It remains unclear as to what extent these differences between the numbers predicted from unselected population studies and the numbers that are clinically diagnosed represents over-diagnosis through routine testing, or under-diagnosis by paediatricians in the absence of screening. Therefore it is uncertain how the evidence would apply to a potential NHS screening programme. | The study by Tiller H et al. BJOG 2009:116:594-598 found an underdiagnoses of severe FMAIT cases; only 15% of severe FMAIT cases are identified without a screening program. Hence, Kamphus et al 2014 would be the most reliable source for the natural history. |
| 2.12 | Members of the ICTMG FNAIT guideline panel.  Jens Kjeldsen-Kragh  Yes | Page 15, Description of the evidence. | Maternal anti-HPA alloantibody level | The International Collaboration for Transfusion Medicine Guidelines (ICTMG) has conducted a systematic review to examine which evidence exists on the association between maternal HPA-1a antibody level and fetal/neonatal platelet count. This review has been submitted to the American Journal of Obstetrics & Gynecology and is attached to the ICTMG’s comments to the draft of the new British guidelines on screening for FMAIT. Based on the results of this systematic review, we conclude there was a significant association between maternal antibody level and fetal/neonatal platelet count in studies using MAIPA for quantification of anti-HPA-1a and where samples for platelet count and maternal antibody quantification were collected simultaneously |
| 2.13 | Members of the ICTMG FNAIT guideline panel.; Mette Kjær  Yes | Discussion/Applicability/page 15” | “…However, the number of babies with clinically-detected FMAIT appears to be lower, at about 85 per year4 | Kamphus et al 2014 would be a more reliable source than Knight et al 2011. Hence, the comments should be removed. |
| 2.14 | Members of the ICTMG FNAIT guideline panel.  Jens Kjeldsen-Kragh  Yes | Page 17, 1st paragraph, | HPA antigen typing | A more appropriate heading would be “HLA typing |
| 2.15 | Members of the ICTMG FNAIT guideline panel.  Jens Kjeldsen-Kragh  Yes | Page 17, line 5 | Typo | Author’s name is “Kjeldsen-Kragh” |
| 2.16 | Members of the ICTMG FNAIT guideline panel.  Mette Kjær  Yes | Page 18 | The paragraph just above “Criterion 9” states: “There is as yet no robust evidence for other potential predictors of severe FMAIT such as AOB typing and HLA genotyping.” | As mentioned above, the systematic review conducted by the ICTMG has shown that there is a significant association between maternal HPA-1a antibody levels and fetal/neonatal platelet count. Moreover, as pointed out in my comment regarding HLA typing, there is substantial evidence that HLA DRB3\*01:01 is a significant risk factor for HPA-1a-immunization, production of high levels of anti-HPA-1a and giving birth to a child with severe thrombocytopenia. Yet, as an additional tool for identifying risk pregnancies I would recommend non-invasive fetal HPA-1a-typing (Scheffer et al.BJOG 2011; DOI: 10.1111/j.1471-0528.2011.03039.x). Approximately 15 % of HPA-1a negative women will carry a HPA-1a negative fetus and for these pregnancies, there will, of cause, not be any risk of FMAIT |
| 2.17 | Members of the ICTMG FNAIT guideline panel.  Mette Kjær  Yes | Discussion/Summery criterion 9/page 18 available.” | “There should be an effective intervention for patients identified through screening, with evidence that intervention at a pre-symptomatic phase leads to better outcomes for the screened individual compared with usual care. Evidence relating to wider benefits of screening, for example those relating to family members, should be taken into account where | Mendani et al. (BJOG 2012;119:1612–1616) found that missing FMAIT diagnosis in first pregnancy could have severe consequences for subsequent pregnancies. They concluded that screening all pregnant women for HPA-type would be effective to improve this. |
| 2.18 | Members of the ICTMG FNAIT guideline panel.  Mette Kjær  Yes | Description of evidence/page 19 | “One study reviews the development of prophylaxis against FMAIT in a screening context and 3 studies involve the use of medical management…” | This makes 4 studies in total. None of the studies in appendix 9-11 review the development of prophylaxis. |
| 2.19 | Members of the ICTMG FNAIT guideline panel. Mette Kjær | Discussion/Summery IVIG treated pregnancies and Caesarean section/page 20 | “Therapy failure was more likely to happen in women with ≤2 pregnancies than those with >2 pregnancies indicating that multigravida is a risk factor for therapy failure.” | The data from the paper by Bertrand et al (2014) do not allow this conclusion. On the contrary, the paper shows that the risk of therapy failure is 22 % (5/23) in women with 2 pregnancies as opposed to 44 % (16/36) in women with > 2 pregnancies. |
| 2.20 | Members of the ICTMG FNAIT guideline panel. Jens Kjeldsen-Kragh  Yes | Page 21 | Discussion. Quantity and quality of the evidence | It is stated that there is no evidence “…to indicate the most effective screening strategy to identify first pregnancies at high risk of adverse outcomes from the development of FMAIT.” I do not agree with this conclusion. By applying the screening algorithm below, the population at risk of FMAIT will amount to only 0.015 % of all primigravida. The proportion of pregnancies at risk can be further reduced by applying anti-HPA-1a quantification. A cut-off of 3 IU/mL has been used in Norway for more than 10 years to identify women at risk of clinically significant FMAIT. For primigravida a screening algorithm could look like the following: HPA-1a typing will identify around 2.1 % HPA-1a negative women. It should also be mentioned here that high throughput HPA-1a genotyping can now be performed for a price of around ₤ 2 per test. HLA DRB3\*01:01 typing will reduce the population to 0.6 % as around 30 % of the women will carry this HLA type. Non-invasive fetal HPA-1a typing will finally be applied to identify women carrying an HPA-1a positive fetus (85 %). By applying this series of tests the final population of women at risk of HPA-1a-immunization can be limited to 0.5 % (2.1 % × 30 % × 85 %). By screening these women for anti-HPA-1a this population can be further reduced to 0.015 % as only 3 % becomes HPA-1a immunized (0.5 % × 3 %). |
| 2.21 | Members of the ICTMG FNAIT guideline panel.  Cecile Kaplan  Yes | Appendix 3 |  | Appendix 3 shows that the number of pregnancies is important to consider especially miscarriages. This should be underlined. |
| 2.22 | Members of the ICTMG FNAIT guideline panel.  Cecile Kaplan  Yes | Appendix 4 |  | Other authors have shown the absence of correlation between the ABO groups and FMAIT |
| 2.23 | Members of the ICTMG FNAIT guideline panel.  Cecile Kaplan  Yes | Appendix 5 |  | It's important to go back to the publication as the authors have specified that the testings were done with the same methodology , all the details concerning the statistical studies have been reported. Therefore the remarks concerning the absence of rigor are somehow bizarre |
| 2.24 | Members of the ICTMG FNAIT guideline panel.  Cecile Kaplan  Yes | Appendix 6 |  | Again multigravida is important to be considered. Other genetic factors should be considered in the future studies as shown there. |
| 2.25 | Members of the ICTMG FNAIT guideline panel.  Cecile Kaplan  Yes | Appendix 8 |  | It has been shown that the level of anti HPA-1a maternal alloantibodies before delivery and after delivery is quite different and so is the correlation with the neonatal platelet count. Therefore to have a parameter predictive of the fetal status it is better to consider the maternal titration before delivery. Timing of sampling is very important. |
| 2.26 | Members of the ICTMG FNAIT guideline panel.  Cecile Kaplan  Yes | Appendix 11 |  | for success or failure of therapy the parity should be taken into account. It has been published that therapy failure is more frequent with multigravidae. |
| 2.27 | Members of the ICTMG FNAIT guideline panel.  Cecile Kaplan  Yes | To have RCT with IVIG antenatal therapy. (With or without CS) may be difficult: |  | Who may propose placebo with the risk of severe thrombocytopenia? We and others have shown that parity may play a role in the response to therapy.  Undetectable antibodies by MAIPA or similar technologies and clinical significance is under studies  Therefore to have a true response for the best therapy may take a very long time considering also the frequency of subsequent pregnancies. |
| 3 | Thea Palmer - Naitbabies UK charity  Yes | Page 8, para 2 The 2012 UK NSC included an earlier…… |  | As a charity run by and supporting families with FMAIT, we are contacted by many parents that have not been clinically diagnosed until after one or more pregnancies (including those with ICH or fetal death), by which time the following fetus or neonate may be even more severely affected.  Signs at birth are not always evident and some petechiae may be dismissed as birth trauma and not investigated further. It is our opinion that FMAIT may often go undiagnosed or misdiagnosed by obstetricians, paediatricians and other clinicians for various reasons and this may have severe consequences for future pregnancies |
| 3.1 | Thea Palmer - Naitbabies UK charity  Yes | Page 11 Table 1, criterion Evidence relating to wider benefits………. |  | We recommend that all sisters should be tested. Many sisters of whom we support have been shown to have the same platelet typing. Monitoring for antibodies in HPA1a negative mothers who have not shown antibodies has been very effective and has meant that IVIG treatment has not always been necessary in a first pregnancy although it may be required in subsequent pregnancies to avoid future risk of a more severe outcome. |
| 3.2 | Thea Palmer - Naitbabies UK charity  Yes | Page 20 Para 3 Therapy failure was more likely to happen in women with …….. |  | Since we began Naitbabies in 2011 IVIG treated pregnancies (in our support group of 800+ parents) have had a very high success rate of avoiding ICH which is our most feared complication. This includes mothers with documented severe previous history of ICH. Monitoring of first pregnancies (sisters) who have not yet developed antibodies has also been successful. Some mothers who have no history of ICH or fetal death have successfully delivered vaginally. |
| 3.3 | Thea Palmer - Naitbabies UK charity  Yes | Appendix 3 Relevant key question 1) Page 27 |  | Many FMAIT mothers who have contacted us have also suffered multiple miscarriages. |
| 4 | Mr Timothy G Overton BSc MD MRCGP FRCOG  Consultant in Fetal Medicine and Obstetrics, Clinical Director for Women’s Services, St Michael's Hospital, Bristol BS2 8EG  RCOG and the BMFMS  Yes |  |  | Dear Evidence Team  Please see below comments on behalf of the RCOG and the BMFMS on the FMAIT Document which we thought was a good and comprehensive document. We apologise that our comments are a little late in arriving but this has been due to annual leave over the summer period and the tight turn around in the request for comments.  1. We feel that at present, screening for HPA1a antibodies is unlikely to be adopted by NHSE/NSC because the prevalence of significant disease is too rare and the technology, to our knowledge, too expensive to screen.  2. The balance of using IVIG (and the dose of this drug) versus platelet transfusion remains controversial especially in the most severe cases. Research from Norway, Holland and Sweden will help but on-going research is to be supported.  3. There needs to be an overlap with documents such as these with other recent similar documents, most notably one spearheaded by the Fetal Medicine Clinical Reference Group (chaired by Prof Steve Robson which became the Complex Obstetric Clinical Reference Group and has recently changed name again) led by Christoph Lees from Imperial.  4. It would also be worth involving the Perinatal Blood Transfusion Group who will also have relevant comments on this topic. |