UK National Screening Committee

Screening for maternal Group B Streptococcus carriage to prevent early-onset GBS disease

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 antenatal screening for maternal Group B Streptococcus (GBS) carriage, to prevent early-onset GBS disease meets the UK NSC criteria to support the introduction of a population screening programme.

   This document provides background on screening for antenatal culture-based screening for maternal GBS carriage to prevent early-onset GBS disease.

Current recommendation

The 2012 review on antenatal culture-based screening for maternal GBS carriage, to prevent early-onset GBS disease, concluded that population screening did not meet the UK NSC criteria and should not be introduced. This was because there was insufficient evidence to demonstrate that the benefits of screening would outweigh the harms. Screening women at 35 to 37 weeks would lead to large numbers of low risk women being given antibiotics which they would not need. The 2012 review highlighted key areas of uncertainly including;

a. the natural history of the transmission of GBS from the intestine and genital tract to the baby was poorly understood.
b. the benefit of screening was unclear as the UK had comparable rates of EOGBS compared to countries which do screen
c. screening at 35 to 37 weeks will not impact on the significant burden of EOGBS disease. For example EOGBS in premature births accounts for the majority of deaths whilst late-onset GBS accounted for the majority of GBS meningitis. Reductions of GBS disease in these other groups had not been observed.

d. The test is unable to distinguish between which babies would be affected by EOGBS and which babies would not. This would lead to over-detection of and over-treatment, with antibiotics for a very large number of women at very low risk.

2. **Current review**

3. The current review was undertaken by Warwick Medical School, in accordance with the triennial review process. https://legacyscreening.phe.org.uk/groupbstreptococcus.

4. The aim of this update review was to establish whether there have been any significant developments in the evidence since the last UK NSC review. For this purpose 22 key questions were examined investigating the following areas: the incidence, epidemiology, and natural history of GBS; test accuracy; treatment; and the clinical and cost-effectiveness for a GBS screening programme.

5. Two different methods were used for this review; 20 questions were analysed using rapid review methods while 2 underwent a systematic review approach.

   UK NSC evidence summaries are usually developed using rapid review methodologies. The UK Government Social Research Service[1] suggests that rapid evidence assessments provide a proportionate approach that fulfils the requirement of providing an evaluation of the 'volume and direction' of the evidence that the UK NSC evidence summaries.

   However, the UK NSC evidence review process also states that in particular circumstances a systematic review can be used to ensure a comprehensive review of the evidence; for example, when the review question is new and the subject have not been previously reviewed in the literature. Full systematic review methodology was applied to the questions examining;

   i) if there are maternal characteristics or characteristics in the bacterium that are predictive of GBS transmission (mother to baby) or GBS transition (from GBS colonised baby to early-onset GBS disease)

   ii) if the use of intrapartum antibiotic prophylaxis (IAP) treatment for any preventative reason had an adverse effect on the women or her baby.

[1] http://www.civilservice.gov.uk/networks/gsr/resources-and-guidance/rapid-evidence-assessment/how-to-do-a-rea

The reason for using systematic review methods for two questions was that these are new questions that have not been previously reviewed in the literature.

6. The conclusion of this review is to reaffirm the UK NSC recommendation not to screen for maternal GBS carriage in the general population. The reasons for this conclusion are:

    a. The natural history, particularly, the development from maternal GBS carriage to EOGBS disease remains poorly understood. More research is required on why some mothers transmit GBS, and why some colonised neonates develop EOGBS disease.

    b. The review also confirms the conclusions from the previous report that selective culture at 35 to 37 weeks gestation is not an accurate predictor of colonisation status in labour, or EOGBS disease in the neonate. Therefore, this could lead to a substantial proportion of women receiving unnecessary IAP.

    c. Better quality evidence is needed to address the effectiveness and adverse events from IAP. Evidence found that the effectiveness of IAP may be less effective in women who receive IAP for suboptimal durations or those who's IAP is appropriate for women with a penicillin allergy. However, the evidence is from studies that have a high risk of bias. Studies reported on potential harms included asthma, colonisation or infection with ampicillin resistant organisms, maternal thrush, atopic dermatitis, microbiota changes, neonatal infections, necrotising enterocolitis, respiratory problems, or Clostridium difficile bowel problems. However, this evidence was inconsistent and/or at high risk of bias. Of these, microbiota changes, maternal thrush, neonatal respiratory distress, and length of hospital stay were most applicable as there were some studies that explicitly included IAP for GBS prevention. However, this evidence comes from studies at high or unclear risk of bias, and the clinical significant of these reports (for example the effect that microbiota changes might have in the baby physiological development) has not been fully explored. .

    d. Better quality evidence is needed to assess the clinical effectiveness and the impact of the introduction of a universal screening programme for GBS in pregnancy.

    e. Evidence is also needed to understand the burden of GBS associated with stillbirth.

f. No new evidence on the cost effectiveness of antenatal culture screening for maternal GBS carriage was found.

7. The 22 questions examined related to 5 of the UK NSC criteria (the condition, epidemiology and natural history, the treatment and the screening programme) and **none of the 5 criteria were judged to be met**.

Consultation

8. A three month consultation was hosted on the UK NSC website; https://legacyscreening.phe.org.uk/groupbstreptococcus

   Direct emails were sent to 28 stakeholders organisations. **Annex A**

9. Sixty five responses to the public consultation were received — 57 individual members of the public, one individual health professional, and one from each of the following 7 stakeholder organisations:

   - Association for Improvements in the Maternity Services
   - The Birth Trauma Association
   - British Maternal and Fetal Medicine Society
   - Group B Strep Support
   - NCT
   - Royal College of Obstetricians & Gynaecologists
   - Royal College of Paediatrics and Child Health

   All comments can be found in **Annex C** below. In instances where the same sets of comments have been sent by different individuals, they have not been duplicated in the comments below.

   Amongst the individual responses all were in favour of screening. The Committee is asked to consider these and to note the personal experiences of EOGBS which is shared through many responses. The Committee is also asked to acknowledge an e-petition, with over

250,000 signatories that was presented to the Secretary of State for Health, the CMO and the Chief Executive of PHE on 23 January.

Given the number of national organisations contacted, the response rate was quite low. Three of the seven responses clearly favoured screening amongst the small set of responses. Some stakeholders commented on technical issues relating to the conduct of the review, interpretation of individual papers and overall analysis but did not clearly agree nor disagree with the conclusion of the review.

The following themes were reflected across all stakeholders' comments.

a. There were concerns about the methodology used by the review and biases in the interpretation of the evidence; including the fact that not all 20 UK NSC criteria points were examined and that more evidence were examined in this review than in other UK NSC reviews.

   Response: the UK NSC review process was followed in this review. The evidence review process used by the UK NSC reviews is published on the GOV.UK webpage[2] and is available to the public.

   UK NSC evidence summaries are developed using rapid review methodologies. They provide an evaluation of the 'volume and direction' of the literature on a single question or set of questions on a given screening topic. They consider whether there have been any significant developments in the evidence base relating to key issues identified from the previous review. Their function is to make a judgement on whether the current recommendation should be retained or whether further work is required. In some cases the review process will identify issues which will be addressed through the development of other evidence products and processes. In this case a series of Department of Health (DH) sponsored research prioritisation workshops have been held and the outputs of this are currently being considered. A report from the workshops is attached to this coversheet (**Annex B**). This should be treated as confidential. The scope of the review was defined by the evidence team and agreed with the reviewers. The UK NSC process for update reviews picks up key

[2] https://www.gov.uk/government/publications/uk-nsc-evidence-review-process/uk-nsc-evidence-review-process.

questions from previous reviews as a first step. It does not require examination of all 20 UK NSC criteria. It was also agreed that, because two of the clinical questions examined by this review were for the first time addressed by this Committee and no systematic reviews existed, a systematic review methodology would be used for these questions. External expertise was sought through the four UK Health Departments, Health Technology Assessment Programme[3], Health Protection Scotland and PHE infections networks.

b. Some stakeholders also questioned the qualifications and expertise of the reviews and expert advises.

   Response: the reviewers and expert advisers involved in this project are all named in the review and their subject area expertise will be added by the reviewers.

c. Several stakeholders raised the issue of the current lack of information available to pregnant women and their families about GBS colonisation. Stakeholders also made the point that GBS screening will provide pregnant women with knowledge about their colonisation status, thereby giving them the information they might need to support decision making and choices about the management of labour.

   Response: currently in the UK the information given to women and their families in the antenatal period reflects the recommendations produced by NICE and RCOG in their clinical guidelines. If antenatal culture-based screening for maternal GBS carriage were to be implemented in the UK then the screening programme would be responsible for the delivery of the appropriate information about the condition and interpretation of the screening results. In relation to the value of post-test information, the review estimates that the test has a positive predictive value of 0.2%. In the absence of a diagnostic, or risk refinement strategy, this suggests that a large number of women would undergo unnecessary treatment with GBS IAP.

d. Some stakeholders suggested that there is evidence of the cost effectiveness of a screening programme (stakeholders suggested some references for inclusion in the review), and suggested that the introduction of an antenatal screening programme for maternal GBS carriage would reduce the economic burden of EOGBS on the NHS.

[3] http://www.nets.nihr.ac.uk/projects/hta/138204

Response: this review aimed to establish if any new publications on the cost effectiveness of antenatal culture screening for maternal GBS carriage were available since the previous review. It did not aim to perform a cost-effectiveness evaluation. The search for new evidence was performed because the previous review reported that they found no new cost-effectiveness estimates relevant to the UK.

Two HTA studies were highlighted by the stakeholders. The outcomes of these evaluations have been described elsewhere, for example in previous UK NSC reviews and in the NICE Antibiotics for Early Onset Infections guideline. The cost effectiveness of screening was not certain in either evaluation.

e. Amongst the responses favouring screening the stakeholders considered screening an attractive option compared to the current UK risk-based strategy for a number of reasons. These included:

- the risk based approach does not address EOGBS in the majority of the population
- there is a perceived inconsistency between recommendations to treat incidentally detected GBS carriage with IAP but not to actively seek it through screening at 35 to 37 weeks gestation
- logistically, a screening programme is easier to be implemented consistently

Response: It is correct to say that some women who potentially will transmit the infection to their baby will not be identified by the current risk based strategy. However, the culture based screening methodologies appear to have a low positive predictive value resulting in the introduction of GBS IAP into an overwhelmingly low risk population and the potential for a large number of women to be treated unnecessarily. The review suggests that the consequences of such overtreatment are still poorly understood. While incidentally detected GBS carriage is a prompt for IAP in current guidance this is in a far smaller proportion of the pregnant population.

In terms of the logistics of screening, guidelines from countries where screening is undertaken, for example the USA, a UK NSC modelling exercise highlight that

screening would do little to alter practice in the higher risk groups. A well-managed risk based management pathway would still be necessary if a screening programme was added to the UK prevention strategy.

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 C**

Recommendation

10. The Committee is asked to approve the following recommendation:

A whole population screening programme for maternal GBS carriage to prevent early-onset GBS disease is not recommended.

Based on the 20 UK NSC criteria set to recommend a population screening programme, evidence was appraised against the following two criteria:

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 association between the risk or disease marker and serious or treatable disease	Not met ✗
The Test		
4	There should be a simple, safe, precise and validated screening test	Not met ✗
The treatment		

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	Not met ✘
14	The opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (value for money). Assessment against this criterion should have regard to evidence from cost benefit and/or cost effectiveness analyses and have regard to the effective use of available resource.	Not met ✘

Annex A

List of organisations contacted:

Action on pre-eclampsia

Antibiotic Research UK

Ante-natal Results and Choices

Association for Improvements in the Maternity Services

Association of Radical Midwives

BirthChoice UK

British Association of Perinatal Medicine

British Infection Association

British Maternal & Fetal Medicine Society

British Society for Antimicrobial Chemotherapy

Microbiology Society

MBRRACE-UK

New Day Foundation for Families

Group B Strep Support

Independent Midwives Association

Maternity Action

Meningitis Now

National Childbirth Trust

Royal College of General Practitioners

Royal College of Midwives

Royal College of Nursing

Royal College of Obstetricians and Gynaecologists

Royal Society for Public Health

SANDS

Tommy's

Twins and Multiple Births Association

United Kingdom Sepsis Group

The Public Health Agency, Northern Ireland

UK National Screening Committee

Annex B

GBS Research Prioritisation

An expert group was convened to discuss and agree high priority, tractable research questions to reduce the harm caused by Group B Streptococcus. The following research questions were agreed by the group.

Background

Group B Streptococcus (GBS) is a bacterium carried in the vagina, and gastrointestinal or urinary tract in around 25% of pregnant women which does not usually cause harm. If it is passed to the baby during birth, in a small proportion of infants (1-2%) it can cause septicaemia, pneumonia, meningitis and death. Long-term disability occurs most frequently (up to 50%) in the survivors of GBS meningitis. Group B Streptococcus (GBS) is the leading cause of serious infection in newborn babies, causing 421 cases of invasive early-onset disease in England (BPSU data unpublished; collected April 2014-April 2015). The incidence of early onset GBS disease in the newborn in England is currently 0.59 per 1000 live births (ibid). This rate is higher than that reported in the previous enhanced surveillance study (0.50 per 1000 live births in England in 2000 - 2001) despite the introduction of a national prevention strategy in 2003.

Administering intravenous antibiotics in labour is very effective at reducing early-onset GBS disease; however, it remains unclear which women should be offered antibiotics. In the UK, current RCOG recommendations are to offer intrapartum antibiotic prophylaxis to women identified as having one or more risk factors for GBS (previous baby with invasive GBS infection, GBS bacteriuria in the current pregnancy, vaginal swab positive for GBS in the current pregnancy) or pyrexia above 38^0C in labour or chorioamnionitis, but recent surveillance data have shown that of a cohort of 429 UK and Irish cases with early-onset GBS disease, only 35% had one or more of these risk factors. This compares with 65% in the 2000 – 2001 study. Thus a risk factor based approach provides only limited protection against invasive disease in the infant.

In some countries, all women, not already identified as at risk, are offered a test for GBS at 35-37 weeks' gestation ('universal screening') with subsequent intrapartum antibiotic prophylaxis for those who test positive for GBS carriage (around 25%).

Both approaches entail giving intrapartum antibiotic prophylaxis to a substantial proportion of pregnant women, the great majority of whom will not have an affected baby. Current tests identify GBS colonisation rather than invasive disease and the risk factors are not sensitive or specific for early-onset GBS disease. The possible advantages (reduction of neonatal deaths and morbidity) have to be weighed against the potential disadvantages for the mother (anaphylaxis, antimicrobial resistance, medicalisation of labour) and baby (short- and long-term effects on the gut microbiome, lengthier stay in hospital, antimicrobial resistance). A modelling study was undertaken to look at the potential impact of introducing universal screening, in addition to risk-based screening, on the number of cases of GBS detected and mortality and morbidity from EOGBS. However, the modelling did not aim to provide a definitive assessment of whether universal screening was more clinically- and cost-effective than risk-based screening alone, see **Annex A** for a short summary.

The current context has led to uncertainty for women and healthcare professionals. There is now concern that certain procedures (e.g. universal screening, use of home testing kits), will slip into

practice without proper evaluation of the benefits and harms compared with current care (risk-based prevention strategy) in the UK. An assessment of how this affects the existing inequities in screening or prevention is needed.

Section 1: Screening approaches for GBS

Research question 1a: What is the clinical and cost-effectiveness of universal test-based screening (and treatment) for Group B Streptococcus using currently available microbiological tests, compared to current care?

P: Pregnant women in the UK
I: Universal antenatal test-based screening (and treatment) for Group B Streptococcus (in addition to current usual care)
C: Care as usual: current risk-based management and treatment approach (treatment based on identification of risk factors as advised by RCOG Green Top Guideline)
O: Primary outcome: Neonatal mortality (all-cause) and neonatal morbidity (applicants to define and justify)
Other outcomes:

- Maternal anaphylaxis and other adverse events, maternal acceptability and satisfaction, other relevant maternal secondary outcomes
- Reason for admission to neonatal unit, and other relevant perinatal secondary outcomes
- Cost-effectiveness evaluation[1]

The trial work-up should include consideration of subsequent long-term follow up using routine data to capture outcomes relevant to a) early-onset Group B Streptococcus infection and b) consequences of intrapartum antibiotic prophylaxis *(but this would entail additional costs)*.

Design: Cluster RCT with an internal pilot with robust milestones to enable adequate progression to be confirmed.
Microbiological tests: It is likely that this will entail swabs (to be detailed) at around 36 weeks' gestation (applicants to define and justify timing and tests).
Treatment: Women who are identified to be carriers of Group B Streptococcus (by universal screening) and those whose babies are at increased risk for early onset Group B Streptococcus infection (by risk factor identification) should be offered intrapartum antibiotic prophylaxis.
Analysis: The main outcomes will be analysed by an intention-to-treat approach.
Evaluation of implementation: A per-protocol analysis to assess fidelity of intervention implementation should be undertaken.
Options: Qualitative evaluation of barriers and facilitators to uptake by women and healthcare professionals (HCP) and fidelity to the screening programmes by HCP could be included.

Research that answers questions around the clinical and cost-effectiveness of each option for the UK setting will enable decision makers to make evidence-based decisions to improve UK prevention strategies so that they reduce the burden of early-onset GBS disease.

Notes:

(i) We are aware that QALYs not usable for neonatal short-term outcomes but applicants should consider how cost-effectiveness can best be assessed.

A. Ease of study

It is most likely that this would be conducted as a cluster randomised controlled trial in the UK, and consideration should be given to institutional level consent (as has been undertaken in other cluster RCTs in maternity services) with routine data acquisition supplemented by confirmation of case ascertainment where indicated.

B. Likelihood of influencing clinical care – levers for change

This would be intended to be a definitive trial that would provide evidence which quantifies the benefits and harms of universal screening, likely to be by using an enriched culture-based test, at 35-37 weeks to enable an evidence-based decision by the National Screening Committee. The latest review of whether to screen for Group B Streptococcus undertaken by independent researchers at Warwick University for the UK National Screening Committee identified uncertainties in the balance of benefits and harms of introducing universal antenatal culture screening in addition to risk-based prevention, which would not be resolved without an RCT. The working group that led to this research priority being identified included representation from Group B Strep Support (PPI - Plumb), the National Childbirth Trust (PPI - Duff), the chair and members of the RCOG guideline development group on Group B Strep (Hughes, Brocklehurst, Heath, Steer), the chair of the intrapartum Clinical Studies Group at the RCOG (Bick), the chair of the Neonatal Clinical Studies Group at the NIHR (Turner), the RCPCH (Modi) and other key stakeholders.

C. Timeliness

This research is needed now to address a topical and clinically relevant research question. Recruitment should be planned to enable sufficient numbers of women to be included (which will require adequate number of clusters) but occur within a timely manner; consideration should be given to recruitment occurring within 2 years.

D. Uncertainties and risks to completion

The current context is that uncertainties about the current risk factor approach amongst women and clinicians make implementation of current guidelines poor (as described in RCOG audit reports) and may promote practice that does not have a strong evidence base (e.g. use of home testing kits) and for which the benefits and disadvantages are unclear. There are risks, therefore, with no action.

However, the trial will necessitate a high level of engagement and uptake from maternity services across the UK. Consideration will need to be given to the fidelity of the intervention, and care as usual, in maternity units allocated to universal screening. It is not anticipated that Group B Streptococcus vaccine will be widely available and recommended within the time-frame of the trial; even if it does become available, use of other vaccines in pregnancy mean that take-up is not likely to be 100% and screening/treatment) strategies may still be needed

A sample size estimate may be necessary to ensure this trial is achievable in the UK within a reasonable time frame with the outcomes of neonatal mortality and (severe) neonatal morbidity. A trial with only process outcomes with extrapolation to mortality and morbidity would not answer the research question. The latest UK National Screening Committee review and modelling exercises both projected that very few (0.1% to 0.2%) women who tested positive for GBS colonisation status in the third trimester and who remained untreated would go on to have a child with early onset group B streptococcus. This suggests that the sample size would need to be large.

Related areas: Short-, medium- and long-term outcomes of invasive GBS and its prophylactic treatment (IAP)

Research question 1b: What are the medium and long-term clinical sequelae and costs of infants with early-onset and late-onset GBS disease, stratified by clinical presentation? How can existing datasets and/or routine data be used to collect this information?

Research question 1c: Does intrapartum antibiotic prophylaxis have an impact on the infant's microbiome and if so what is the clinical significance of this change?

Current work in progress:

HTA commissioned call 16/150 - Long term impact of pre-incision antibiotics on babies born by caesarean section

Research Question 1d: What factors affect the adoption or uptake of a) a risk-based approach and b) intrapartum antibiotic prophylaxis after risk-based screening?

P: Pregnant women with risk factors for GBS and their healthcare professionals.
E: Risk-based screening and offer of intrapartum antibiotic prophylaxis.
O: Reasons for risk-based screening not being completed and women not having intrapartum antibiotic prophylaxis. This may include issues such as attitudes of the healthcare professionals, time of arrival at hospital, informed choice, home births, and communication issues.

Design: Qualitative research with midwives, obstetricians and pregnant women with risk factors for Group B Streptococcus to understand why some women with risk factors do not have intrapartum antibiotic prophylaxis. Understanding of whether or not receiving intrapartum antibiotic prophylaxis is associated with modifiable service attributes (such as insufficient information from midwife) or unmodifiable factors (such as woman's informed choice)

A. Ease of study
This could be achieved in the relatively short time scales, as it would be a qualitative study on women from the current service.

B. Likelihood of influencing clinical care – levers for change
This could influence the current risk based programme by identifying if there are ways in which the service could be improved. Furthermore it could influence any future trial of test-based screening for Group B Streptococcus by identifying modifiable and unmodifiable barriers to intrapartum antibiotic prophylaxis use.

C. Timeliness - timescale must be clear and have good justification
The study would take around 2 years to complete, and could commence as soon as funded.

D. Uncertainties and risks to completion
Such a study would be relatively low risk.

Section 2: Bacterial load/virulence – colonisation to invasive disease

It is recognised that one major barrier to screening and treatment for GBS disease is that current tests detect colonisation rather than invasive disease. A better understanding of the factors that determine bacterial virulence and host susceptibility is needed in order to enable development of a microbiological test that targets the women (and babies) that require antibiotic prophylaxis and treatment and avoids giving unnecessary antibiotics to the women and babies who would have otherwise remain well. This research should entail underpinning biological studies first, before addressing technological issues (e.g. development of cheaper PCR tests that incorporate antibiotic sensitivities) and subsequent clinical evaluation of any new microbiological test.

Research question 2a: What factors in the mother, infant and bacterium influence the development of invasive GBS disease and how do these relate to the identification of maternal (or neonatal) colonisation?

P: Pregnant women and their infants at birth in the UK:
E: Bacterial load, virulence factors, GBS-specific IgG in mother, cord and infant blood
C: None
O: Vertical transmission of GBS from mother to infant, development of disease in the infant, mortality and morbidity outcomes.
Design: study utilising existing biobanks of samples (related to bacteria and mother/ baby), with matched clinical data and / or a case-control study (rather than cohort study). Consideration should be given to whether additional sample collection could be nested in existing/future studies.

A. Ease of study

Uses existing data.

B. Likelihood of influencing clinical care – levers for change

Development of tests beyond simple detection of Group B Streptococcus colonisation, to reliably predict which women will transmit it to their child, and which infants will go on to develop disease could be used to replace the current risk-based strategies, and could be evaluated as a test in a future screening programme. This was highlighted as a research priority in the UK National Screening Committee's latest review of screening for Group B Streptococcus. Developing our understanding of the role of immunological factors and Group B Streptococcal strains on birth outcomes and combining this information with the population structure of Group B Streptococcus in carriage and disease will strengthen our knowledge of potential vaccine coverage. A study that captures total Group B Streptococcus antigen diversity and distribution in the UK and links with serological data will enable us to identify those targets that give good serological response, are low in sequence diversity and well distributed in the target pathogen population that would therefore form the optimal vaccine target.

C. Timeliness - timescale must be clear and have good justification

This research is needed now to address a topical and clinically relevant research question. More targeted assessment of women who require intervention will greatly enhance our ability to reduce the burden of Group B Streptococcus disease.

D. Uncertainties and risks to completion

Uncertainties can be reduced if this study is nested in a prospective cohort study of maternal colonisation.

Microbiological test sensitivity and specificity

Research question 2b: Can a microbiological test for Group B Streptococcus be developed for clinical practice that has sufficient accuracy, and convenience (for women and the health service), and could be implemented into current NHS service? Can the test be adapted to detect GBS isolates at high risk of causing invasive disease rather than colonisation alone (e.g. through detection of serotype/sequence type, bacterial load and/ or virulence)?

Current work in progress:

NIHR HTA 13/82/04: Accuracy of a rapid intrapartum test for maternal group B streptococcal colonisation and its potential to reduce antibiotic usage in mothers with risk factors (GBS2) (started May '16)

Questions to consider:

- Does the initial work on characterising GBS invasive disease need to be undertaken prior to further development of a new microbiological test?
- What is the appropriate reference standard against which to measure a new test? How should the reference standard reflect invasive disease rather than carriage alone?
- If timing between testing and labour determines accuracy, how should this inform test development and timing?
- How can implementation of screening test protocols (in clinical and laboratory settings) be improved to maximise screening performance?
- Could incorporation of antibiotic resistance genes into a PCR primer set enable development of a rapid test with additional information on antibiotic susceptibility?

Section 3: Group B Streptococcus vaccines

A vaccine for Group B Streptococcus has been in development since the 1990s. Phase II trials of a trivalent polysaccharide-protein conjugate vaccine have been completed in pregnant women in Southern Africa (Heyderman et al. 2016; Lancet Infect Dis 16; 546-55) and monovalent trials have been undertaken in the USA. Both GSK and Pfizer are now developing pentavalent formulations which have an estimated coverage of 96% for both early and late-onset Group B Streptococcus disease in the UK, as well as the potential to reduce GBS-associated preterm birth, stillbirth and maternal disease. An international working group funded by the Bill and Melinda Gates Foundation is working towards vaccine launch before 2020. The possible routes to licensure by determining an immunocorrelate of protection against GBS disease, as was the case for meningococcal B vaccine are being explored; discussions about this are ongoing with regulators in Europe and the USA. Once licensed and available, it is likely that uptake will not be 100%, and therefore research into optimal prevention strategies are still needed, in addition to acceptability of maternal vaccination and the effect on the EPI schedule. The UK is an excellent site for phase II trials of a new Group B Streptococcus vaccine as universal screening and IAP is not the standard of care.

Current work in progress includes:

- Standardisation of assays (Standardizing GBS capsular antibody concentration and functional assays to expedite GBS vaccine licensure (development). BMGF Grant number OPP1153630)
- Development of vaccines by GSK and Pfizer with likely readiness for phase III trial by 2019 (Heath PT. Status of vaccine research and development of vaccines for GBS. Vaccine. 2016 Jun 3;34(26):2876-9. doi: 10.1016/j.vaccine.2015.12.072; http://www.businesswire.com/news/home/20161019005443/en/Pfizer-Awarded-Grant-Evaluate-Vaccine-Protect-Newborns)

Development and testing of a vaccine for Group B Streptococcus

Research question 3a: What are the serological correlates of protective immunity against invasive GBS infection in UK women and infants?

Research question 3b: What is the safety, immunogenicity and effect on colonisation, in pregnant UK women and their infants, of a pentavalent GBS conjugate vaccine given from 28 weeks of pregnancy, and what is the tolerability, acceptability and safety profile of the vaccine in the UK population?

Serological correlates study:

The design would entail a case-control study, preferably nested within a prospective, longitudinal cohort of mothers and their infants <90 days of age. Women delivering will be prospectively enrolled. Maternal and cord blood will be collected at delivery. The enrolled cohort will be followed to identify cases (of invasive GBS disease) and controls (infants born to mothers colonized with GBS at delivery that do not develop GBS disease). The GBS anti-capsular antibody concentrations in maternal and newborn sera, obtained prospectively at delivery, will be compared between cases and controls to establish antibody levels that correlate with reduced risk of disease (and potentially with reduced risk of colonisation).

GBS vaccine study:

P: Pregnant women in UK
I: Single vaccination with GBS vaccine at 16-26 weeks given together with or separately to Boostrix and flu vaccines, plus care as usual
C: Women not receiving GBS vaccine (but receiving recommended Tdap and flu vaccinations)
O: Maternal, cord and infant (to 3 months of age) antibody concentrations, placental transfer ratio, adverse events, pregnancy outcomes, colonisation and isolate characterisation.

Other outcomes: maternal acceptability and satisfaction, cost evaluation, effect on infant primary vaccination schedule, effect of giving GBS vaccination together with Tdap (Boostrix) and flu vaccination.
NB: any woman found to be GBS colonised would be treated as per best practice with intrapartum antibiotics.

A. Ease of study

Discussions are now needed with the vaccine manufacturers to ensure availability and supply of vaccines for the vaccine study. The vaccine study would be conducted as an open label phase 2b trial. Similar vaccine studies have been undertaken successfully in the UK. Attitudinal work indicates that UK women would view participation in a GBS vaccine trial favourably (BMJ Open. 2016 Apr 20; 6(4):e010790). Further discussions also need to be undertaken with other relevant stakeholders related to licensure (e.g. regulatory bodies, JCVI, PHE).

B. Likelihood of influencing clinical care – levers for change

Completion of these studies would represent a major step towards introduction of a GBS vaccine in the UK by demonstrating its safety, acceptability and the ability of the vaccine to generate protective levels of immunity in UK women and infants.

C. Timeliness - timescale must be clear and have good justification

This research is needed now in order to facilitate planning and preparations for vaccine implementation in the UK and to ensure that the UK is able to be one of the early implementers of this vaccine. Recruitment should be planned to enable sufficient numbers of women to be included but occur within a timely manner. Pfizer have indicated that they may be prepared to discuss a UK phase 2b trial after March 2017.

D. Uncertainties and risks to completion

Barriers to vaccine trials include the following:

- Sufficiently high GBS incidence in birth cohort especially taking intrapartum antibiotic prophylaxis into consideration. In a setting where Group B Streptococcus early onset disease occurs in approximately 1/1000 live births, 80,000 women would be needed for a phase III trial. In the UK, where disease occurs in approximately 0.4/1000 live births, approximately 200,000 women would be needed. Issues remain about what the control group would be as in the UK risk-based screening and IAP will make analysis of effect difficult.
- Availability of vaccine and standardised assays need to be assured. Studies will require collaboration with vaccine manufacturers.
- Routes to licensure of a Group B Streptococcus vaccine need further exploration. Men B vaccine was licensed based on immunogenicity with a post-licencing phase IV trial.
- There remains limited knowledge of safety data of pentavalent formulations in Europe/ USA.
- A global phase III trial is planned but this is unlikely to occur before 2019 as a route for licensure through serocorrelates of protection from disease is being actively explored.

Although the clinical rationale for a Group B Streptococcus vaccine has been established by the working group, the deliverability of a trial of a type that would lead to licensure (i.e. phase II or phase III, with the outcome to be defined), and the appropriate funding route for this, needs further exploration.

Supplementary Research Questions on acceptability of vaccines to parents and Healthcare Professionals)

3c. What are the attitudes and knowledge of a) parents-to-be and b) healthcare professionals on antenatal vaccination for Group B Streptococcus and how can we learn from recent implementation of other vaccines into pregnancy (e.g. pertussis) to inform this? This should be

informed by appropriate theoretical and methodological implementation frameworks, i.e. the Theoretical Domains Framework and Behaviour Change Wheel.

3d. How do these attitudes and knowledge vary across groups of different ethnicity and socio-economic status and how would we work with these groups to maximise engagement, including attendance and take-up?

3e. What is the role of midwives, family physicians and obstetricians in ensuring good take-up?

Annex B(a): UK National Screening Committee end of project report: Early onset streptococcal (EOGBS) disease: a report of a modelling exercise prepared for the expert group

The UK National Screening Committee (UK NSC) brought together an expert group to develop an early onset group B streptococcal (EOGBS) disease model. The aim of the model was to explore the preventive potential of universal screening when added to the risk-based management strategy currently recommended in the UK.

A hypothetical disease model was constructed to mirror a UK maternity cohort's progress through the current EOGBS risk-based prevention strategy, over a one year period. The outcomes were compared to those in a second modelled scenario which added a 36 week selective media maternal GBS screening programme to the risk-based prevention strategy.

The risks and benefits of each prevention strategy were evaluated by comparing total EOGBS infections, EOGBS related mortality and morbidity, numbers needed to treat to prevent one EOGBS case and maternal anaphylaxis. Numbers needed to treat to prevent a death due to EOGBS were calculated for the screened population only.

The screening strategy within the model was based on that recommended by the Centre for Disease Control and management of the risk groups was based on UK guidance.

Results

Screening is estimated to prevent 52-57 additional cases of EOGBS when added to current practice. The model suggests that a **combined screening and risk factor based strategy would result in three to four deaths prevented and four severe disabilities prevented** in addition to those prevented by the risk based approach with no screening.

Table 7: Modelled comparison of risk-based and screening scenarios with sensitivity analyses of key parameters

	EOGBS infections	EOGBS related mortality	EOGBS related severe morbidity	Number of women given antibiotics
Risk-based strategy alone	351	37	24	30,666 (438 treated to prevent one additional case compared with no preventive strategy)
Screening and risk-based strategy combined	294 - 299	34	20 - 21	126,926
Effects of adding screening	52 – 57 additional cases prevented	3 additional deaths prevented	4‡ additional severe disabilities prevented	96,260 additional women receiving antibiotics † (1,675-1,854 additional women treated to prevent one additional EOGBS case compared with risk-based strategy alone, and 24,065-32,087 women to prevent one death)‡
Sensitivity analyses: range of effects of adding screening using different assumptions				

Sensitivity analysis: screening uptake (base case 90%)				
75%	43-48	2-3	3	80,217
95%	55-61	3	4	101,608
Sensitivity analysis: IAP uptake among GBS screen positive women (base case 80%)				
70%	46-51	3	3-4	84,228
90%	61-67	3-4	4-5	108,551
Sensitivity analysis: carriage status transition rates (base case 1: + to – 25%, - to + 7.1%; base case 2: + to – 17%, - to + 4.8%)				
Worst case transition rates*	40	2	3	96,260
Best case transition rates**	61	3	4	96,260
Sensitivity analysis: antibiotic effectiveness (base case: optimal 83%, suboptimal 42%)				
Optimal: 70% Sub-optimal: 35%	44-48	2-3	3	96,260
Optimal: 95% Suboptimal: 47.5%	59-66	3-4	4-5	96,260

† This does not include women who develop an infection in labour who would have received antibiotic treatment for this indication

‡ Rounding means that numbers do not exactly equivalent to e.g. 96,260 divided by 57 or 52

* GBS positive to GBS negative = 42.5%, GBS negative to GBS positive = 12%

** GBS positive to GBS negative = 11.7%, GBS negative to GBS positive = 3.3%

The modelled screening programme would increase the number of women receiving narrow spectrum antibiotic prophylaxis against EOGBS by 96,260. In this group 1,655 - 1,851 would be given IAP to prevent one additional case of EOGBS. If the incidence of EOGBS in colonised women was higher the number treated to prevent a case may be expected to be lower. However high NNTs are consistent with those reported elsewhere in the literature.[4]

Parameter limitations

The modelling exercise identified limitations in the evidence relating to a broad range of inputs required for an assessment of screening. Perhaps the most significant was that many of the parameters relating to the modelled screening programme were derived from non UK based sources.

Annex B(b): List of attendees and consultees

Attendees	
Professor Chris Whitty (part of WS1)	Department of Health - Chief Scientific Adviser
Professor Lucy Chappell (Chair)	NIHR Professor of Obstetrics, King's College London
Dr Mark Turner (Deputy Chair)	University of Liverpool (Neonatal Paediatrician)
Dr Baharak Afshar	Imperial College London
Professor Debra Bick	Chair of RCOG Intrapartum Clinical Studies Group; midwife

[4] Angstetra D et al, *Aust N Z J Obstet Gynaecol,* 2007 Oct;47(5):378-82

	representative
Professor Peter Brocklehurst (WS2)	RCOG GBS guideline group member, University of Birmingham
Dr Paul Cosford (WS1)	Director for Health Protection and Medical Director, Public Health England
Dr Kirsty Le-Doare	Imperial College London & Consultant of Paediatric Infection & Immunity, Guy's & St Thomas's NHS Trust
Dr Fiona Denison	University of Edinburgh NHS Trust
Ms Elizabeth Duff	National Childbirth Trust (NCT)
Professor Paul Heath	St George's Medical School
Dr Rhona Hughes	RCOG GBS guideline group lead; Consultant obstetrician – University of Edinburgh
Dr Theresa Lamagni	National Infection Service, Public Health England
Dr Shamez Ladhani (WS1)	Paediatric Infectious Disease Consultant, Public Health England
Dr Anne Mackie	National Screening Committee, Public Health England
Professor Neena Modi (WS2)	Imperial College London & President of RCPCH
Dr Heather Payne	Welsh Government
Mrs Jane Plumb	Group B Strep Support (GBSS)
Professor Philip Steer	Imperial College London & Medical Advisory Panel GBSS
Professor Catherine Peckham	University College London
Ms Farah Seedat	Warwick Medical School – NSC independent review of GBS
Dr Sian Taylor-Phillips	Warwick Medical School – NSC independent review of GBS
Dr Caroline Trotter	University of Cambridge & Public Health England
Prof Tom Walley (WS2)	University of Liverpool
Ms Sarah Manson	Scottish Government
Dr Esther Robinson	National Infection Service, Public Health England
Dr Natalie Owen (Secretariat)	Science Research and Evidence, DH
Ms Josephine Taylor (Secretariat)	Screening Lead, DH
Ms Cheryl Cavanagh (Observer)	Vaccinations Lead, DH
Ms Cristina Visintin (Observer)	National Screening Committee, Public Health England
Additional consultees for report	
Professor Jane Sandall	King's College London
Mr John Marshall	National Screening Committee, Public Health England
Dr Mary Ramsey	NVEC, JCVI & Public Health England
Mr Andrew Earnshaw	JCVI, Public Health England
Professor Androulla Efstratiou	Imperial College London & Public Health England

UK National Screening Committee

Annex C

Consultation comments

Note that sixty-five consultation submissions were received, with a total of 179 comments. The comments are listed in the table below, grouped by the section of the draft review document to which they refer.

Comment number	Stakeholder Name, Consented for names to be published: YES NO ?	Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*

1.	Association for Improvements in the Maternity Services YES	All		Our committee unanimously supported the recommendation that pregnant women should not be screened for Group B streptococcus.
2.	British Maternal and Fetal Medicine Society (David Howe) YES			The BMFMS supports the conclusions of this review
3.	Ahmad Hoque YES	General		'As complications are rare & EOGBS is manageable, I think it's unnecessary for screening GBS in pregnant women & administration of I/V antibiotics. Only high risk mother can be considered for screening.'
4.	NCT YES			We welcome this timely review of the evidence around GBS and an update to the screening recommendations.
5.	**xxxx xxxx** YES		Cost of not testing: how much is it to the NHS?	Treatment for my daughter was 2 weeks in special care and 4 weeks in the children's hospital in a private room. She had 2 lumbar punctures and 2 lots of intravenous antibiotics. This was a terrifying ordeal. I went into labour at 32 weeks + 4 days, expecting twins. Both born by caesarean. I was never offered testing, as far as I am aware was never tested, had never heard of GBS nor was I told what the infection was, until I asked. It is ridiculous and as far as I know this is the SINGLE BIGGEST KILLER OF NEWBORNS IN THE UK.
6.	**xxxx xxxx** YES		The evidence is from other countries results	Other countries are proving that testing is a success. The death rates and disability rates from GBS are reducing. I'm no rocket scientist but this is clear from general searches on the internet.
7.	**xxxx xxxx** YES		Give people the choice?	I find it unbelievable that we do not routinely discuss GBS with couples expecting a baby to give them the choice. My daughter was born in **xxxx xxxx**. Almost 13 years later we're still discussing the same issue in the UK. Is that approximately 520 babies dead, 520 couples and their families/children affected. Thousands of people campaigning for change and yet you are 'still' waiting for evidence. Who is funding the research to prove your point? I don't see any proven evidence ever being presented with these reports. Is there really proof of how may babies die from GBS? Do they die from meningitis, lung problems, etc, never listed as GBS? I doubt the figures are as good as any of us would believe.
8.	**xxxx xxxx** YES		The current system doesn't work	If you look at the guidelines in 2003 they weren't followed for me. How do you propose to ensure that all hospital trusts/NHS follow the guidelines you set? It seems that they get to choose. How can this change?

9.	**xxxx xxxx** YES		Current NHS test not effective enough	From the information available it would appear that the current NHS test offered for GBS is ineffective and unreliable. What do you propose to do about this?
10.	South Warwickshire NHS Trust - David D'Souza Consultant & Gynaecologist SWFT YES			1) The RCOG guideline (i.e.NOT protocol) does read : **Current evidence does not support screening for GBS or the administration of IAP (Intra Partum Antibiotics) to women in whom GBS carriage was detected in a previous pregnancy.** This is level D evidence (the lowest level) and following this statement they say - "If GBS was detected in a previous pregnancy, the likelihood of carriage in a subsequent pregnancy is around 38%." - **Are we happy therefore telling patients not to have IAP's because they've only got a 40 % chance of GBS carriage if they had it previously** !
11.	South Warwickshire NHS Trust - David D'Souza Consultant & Gynaecologist SWFT YES			2) At the end of the RCOG guideline they have a table which gives these figures below : Risk of EOGBS disease if IAP NOT given — Risk of EGOBS disease if IAP given Positive GBS **previous** pregnancy ? 1:1105 1:5525 Risk of death if IAP NOT given — Risk of death if IAP given Positive GBS **previous** pregnancy ? 1:10424 1:52122 These may indeed seem like small figures but **would you be happy to be told there is a 5 x increased risk of mortality and morbidity if you don't receive antibiotics in this pregnancy ?**
12.	South Warwickshire NHS Trust - David D'Souza Consultant & Gynaecologist SWFT YES			3) The RCOG does advise that we can treat with IAP's if it is picked up during this pregnancy but we don't do this as routine screening, as they do in the USA. The British Society of GBS doesn't agree with this part of the recommendations and are in the process of getting a petition to change this recommendation. If we did offer GBS screening obviously this would significantly increase the workload of taking vaginal swabs (although maybe we could look at LVS in this high risk group).
13.	South Warwickshire NHS Trust -			4) Over the years I have certainly seen a few cases of infant mortality from GBS and indeed we discussed one recently in our local clinical incident meeting. A miscarriage occurred at 23 weeks, and GBS chorioamnionitis was found on the histology/microbiology. Granted nothing could probably

	David D'Souza Consultant & Gynaecologist SWFT YES			have been done in this case, but she did have GBS in her first pregnancy and in this pregnancy would not have been offered IAP if we had been following NICE and it may have resulted in a similar outcome further on in the pregnancy. Will she be offered IAP in her subsequent pregnancies, as this was a miscarriage rather than EBOGS death ? The NICE guidelines are indeed guidelines and we have to justify reasons if we are following them fully, partially or not at all. I would also be interested in the paediatrician opinion on this matter. We do, again **ONLY OFFER** IAP's, and if the patients are fully informed and decline this option, fine, but otherwise I feel we should continue as we are, until universal screening is available.

14.	**xxxx xxxx** ?			I oppose the recommendation because the report is flawed and biased. It ignores the evidence from countries that have had a long-term screening programme and it seeks more evidence than has been required for other screening decisions
15.	**xxxx xxxx** YES	P1.	Current policy is that antenatal GBS screening in pregnancy is not recommended by the National Screening Committee. The last review of this policy took place in 2008/2009 and concluded that this policy should not be changed.2	I was offered no screening, it was not even something I was aware of and yet it resulted in emergency surgery and both my life and that of my daughter was only saved as a result of the surgery. I was ill thereafter for the first three months of her life and for that I blame the hospital and midwives for their total and callous dismissal. The problems I had were totally dismissed with utter scorn and my daughter was born covered in gunk, not breathing after an emergency caesarean. She was in the intensive care unit for nine days. Fortunately for me she suffered no long term effects, if she had, I would have sued the hospital for it as they ignored me at every and all opportunity. The cost of her having been in the unit must be extortionate, so why is it is easier to simply refuse to do a simple test? If she had suffered, or is proven at any point in the future to have suffered as a result of the infection, I would sue. All for the sake of an easily available test. To conclude that despite rising rates of infection, you should do nothing because you don't want to include a test that could prevent lengthy costly hospital stays is madness. A test that is done in other countries. More early-onset group B Strep infections would be prevented than using the current risk-based prevention strategy, clearly demonstrated by other developed countries. There would be less inappropriate use of antibiotics, as women identified as not carrying group B Strep will not be offered them (unless other risk factors are present). The UK's screening policy will be consistent with current movement towards helping pregnant women make informed choices about their care, and with the Government ambition to reduce significantly neonatal and maternal deaths.
16.	Caroline Constable YES		Numbers of babies affected by GBS.	Huge question mark over the numbers quoted on the report as based on a report dated 2012 and not as many babies as estimated by the GBSS charity.
17.	Caroline Constable YES		Current Risk Strategy.	The current risk strategy used hasn't changed since 2003 and the rate and number of babies infected by GBS has **increased.**

18.	Caroline Constable YES		Evidence from countries who use a national screening policy.	The percentage of babies infected by GBS since national screening was introduced in various other countries has been ignored. A huge decrease of at least **80%** in some countries. Why are we ignoring these facts and not following suit?
19.	Caroline Constable YES		Giving woman the choice to pay for the ECM test privately.	It's a disgrace as to the lack of information that pregnant woman are given in relation to GBS. There is still a huge lack of understanding within the medical profession and woman are often told inaccurate information (if any at all) as experienced by myself. All pregnant woman should be given the same information and have the choice to pay for the ECM test privately until such time that this is part of the antenatal care.
20.	Caroline Constable YES		Costs.	Studies and research have shown that national screening using the ECM method between 35-37 weeks and giving antibiotics in labour to those showing a positive culture can save the NHS millions (Due to the costs incurred by babies in SCBU, specialist treatment for disabilities, counselling for bereaved parents etc).
21.	**xxxx xxxx** NO	General **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**		The analyses seem to focus on mortality – is it worth considering morbidity as well? *(I see morbidity discussed on page 40).* I note that 50% of those with late onset sepsis have permanent neurological disability, though it might be worth looking at the data on the EOGBS group.
22.	**xxxx xxxx** NO	General **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**		Do we know whether screening and treatment alters the pattern of late onset GBS in any way, either increasing due to some delaying effect or change in the pathogenicity of the organisms, or reduced owing to the treatment?

		xxxx xxxx		
23.	xxxx xxxx NO	General xxxx xxxx xxxx xxxx xxxx xxxx xxxx xxxx xxxx xxxx	Bias Graphs	We are not sure the bias graphs add anything above the description of high and low bias of papers.
24.	xxxx xxxx NO	General xxxx xxxx xxxx xxxx xxxx xxxx xxxx xxxx xxxx xxxx	PPROM >18hours	It is mentioned several times that if RCOG and NICE risk factor screening included PPROM >18h then the number of high risk women not having IAP would decrease from 60% to 50%. Can this not be more emphasised as a recommendation that PPROM >18h should be included in the risk strategy.
25.	Susan Gregory YES	Whole report	Issue of giving antibiotics to large numbers of women, with the implied link to antibiotic resistance and unnamed, unknown potential consequences	The antibiotic recommended in labour against GBS infection is penicillin for a short period of time only. The issue of antibiotic resistance developing has not been linked to penicillin over such a short period so this argument has no validity and no relevance
26.	David Gregory YES	Whole report	Issue of giving antibiotics to large	Based on what was said on This Morning TV show today 24th Jan, the antibiotic recommended is penicillin for a short period of time only. The issue of antibiotic resistance developing has not been linked to penicillin over such a short period so this argument has no validity and no relevance

			numbers of women, with the implied link to antibiotic resistance and unnamed, unknown potential consequences	

27.	Susan Gregory YES	Whole report	Need for more research and controlled testing	Many developed countries have introduced screening with a huge reduction in GBS infected babies and attendant cost savings. Suggestions that the different ethnicities within a population make the results unusable for consideration for a UK strategy, when babies are getting sick every day and dying every week, is callous and unacceptable. It suggests a shocking intention to avoid doing the blindingly obvious life-saving screening for no good reason. The introduction of risk-based screening has been proved to have failed, with an increase in incidence of GBS since its introduction.
28.	David Gregory YES		Need for more research and controlled testing	There are other developed countries where screening for GBS infection is done and steps are taken to prevent infection in new born babies. Why can we not learn from them. Are they that different from us?
29.	Susan Gregory YES	General		Shame on you and your reviewers for refusing to see and take account of research results and population studies from other countries that demonstrate a national screening programme can reduce the incidence of GBS infection in newborn babies by up to 85% and save our ailing NHS significant amounts of money for no defensible reason. Those babies' deaths and disabilities are on your hands and consciences. Shame on you
30.	David Gregory YES	General		Putting aside the poor argument about antibiotics the financially it makes sense. A baby developing an infection costs a lot more to look after than the cost of screening. A baby that develops long term health issues will cost considerably more than the test. What if a member of the review board had a child that was infected?
31.	**xxxx xxxx** NO		General comments	I strongly disagree with the NSC's assessment of the evidence in relation to GBS, and with their recommendation against offering routine screening for Group B Streptococcus (GBS) in pregnancy. The evidence suggests that a risk-based approach to GBS is not effective. As stated on p48 of the report, 'more than half of UK and Irish mothers with EOGBS babies did not have any RCOG or NICE risk factors and therefore no indication for IAP'. EOGBS incidence is rising each year (p49). We urgently need an alternative approach, and routine screening for GBS in late pregnancy would

				provide this. I find it absolutely astonishing that although we have a safe, acceptable, validated and cost-effective test for GBS – the ECM test - we are choosing not to use it. We are effectively asking pregnant women and the professionals who care for them to guess their GBS status. If they guess wrong (which the evidence shows that they frequently do), the mother either receives antibiotics inappropriately if she was not in fact carrying GBS or, if she is a carrier, she will not receive the treatment she needs to prevent EOGBS infection in their baby – and the consequences of this can be absolutely devastating. I believe that screening will prevent more EOGBS infections than using the current risk based strategy – this has been clearly demonstrated in other countries, including the USA. Furthermore, offering screening is consistent with current emphasis on informed choice in antenatal and postnatal care, and goals to significantly reduce neonatal and maternal deaths.

32.	Royal College of Paediatrics and Child Health YES	Pg 1	Is long list of authors?	Our commenter felt that the following needs to be clarified: 'How many are clinicians treating babies affected by GBS?'
33.	Emmalene Bushnell YES	UK NSC criterion 9 (pages 16-17)	The treatment 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	A universal screening programme for GBS in pregnancy would result in less inappropriate use of IAP in labour. Women identified as not carrying GBS would not be offered IAP in labour unless risk factors present.

			individual screened then the screening programme shouldn't be further considered.	

34.	Immo H Huneke YES	Plain English Summary	Assumption that those testing positive for Group B Streptococcus would always be given antibiotics during labour.	I'm very sympathetic to mothers and babies who have been and will in future be affected by this bacterial infection. However, reading the NHS guidance notes reveals that between 20 and 25% of all women in the UK are carriers of a Group B streptococcus and that in the vast majority of cases this causes no harm to mother or baby. The possibility of preventing a few hundred infections per year by routinely administering antibiotics to those 20%-25% of expectant mothers has to be weighed against the danger of breeding antibiotic-resistant bacteria, which will in the long term cause far greater damage. That said, IF the ECM test is much more reliable than the existing non-specific test and IF it is easily affordable, it should be offered to all expectant mothers. Whether to administer antibiotics or take other measures if an infection is detected is another question.
35.	**xxxx xxxx** NO	Plain English Summary - page 10 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**	Plain English Summary	The paragraph 'EOGBS is a serious condition and the review found that about one in every 1,750 babies born in the UK and the Republic of Ireland develops EOGBS. About one in 19 babies with EOGBS will die from the infection'….to move before the paragraph above it...i.e. before 'Routine screening….
36.	**xxxx xxxx** NO	Plain English Summary - page 10 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**	Suggest re-phrase the following: We do not know whether there are any short or long-term harms to the mother or baby from giving antibiotics to the mother during labour, and so do not know how many of the 150,800 treated women and babies might be harmed.	Reads better if rephrased as: It is not known if there are any short or long-term harms to the mother or baby from giving antibiotics to the mother during labour, therefore it is not known if any of the 150,800 treated women and babies might be harmed by the treatment itself.

37.	Royal College of Paediatrics and Child Health YES	PG 10	"We do not know whether there are any short or long-term harms to the mother or baby from giving antibiotics to the mother during labour,"	The commenter pointed out that: -We know penicillin is safe. -We know the short and long term harms of EOGBS
38.	Fiona Paddon YES	Page 10	We do not know whether there are any short or long-term harms to the mother or baby from giving antibiotics to the mother during labour	The approach of UKNSC suggests that it is somehow an acceptable consequence for 333 babies out of 150,800 to contract EOGBS every year in the UK so that the remainder avoid receiving antibiotics, and yet this statement acknowledges that they do not know if that receipt would even cause any harm. This is compared with the 333 babies who would clearly suffer some harm (by contracting EOGBS) of which on average 50 will die and 25 will suffer permanent disabilities. How can an unknown level of harm be the basis of not taking steps to combat a very real known level of the most serious harm anyone can face?
39.	Fiona Paddon YES	Page 10	From the available research we do not know whether giving antibiotics in labour to women with a positive GBS screening test reduces the number of babies dying from EOGBS.	I find this statement very hard to accept. The experience of other countries (e.g. the USA) shows that screening reduces the number of babies dying from EOGBS. The UKNSC report appears to suggest that evidence and results from other countries is somehow not applicable to the UK, but how does this medically make sense? Pregnant women and their babies are physically the same the world over. Furthermore, from a common sense and logic point of view, how can more reliably identifying which women carry GBS, and whose babies are therefore at greater risk of contracting EOGBS, and then giving them the preventative antibiotics not reduce the number of those babies dying from EOGBS? I would even go so far as to say that this is an argument to implement GBS screening – to allow the research that UKNSC wants to see to be carried out.
40.	Lindsay Birkett YES	Page 10	From the available research we do not know whether giving	It is not difficult to make comparisons with the many other countries that have seen a dramatic fall in incidences of EOGBS in babies since the introduction of GBS screening-based strategies. Our population cannot be so different from theirs that it would mean that we would not experience the

			antibiotics in labour to women with a positive screening test reduces the number of babies dying from EOGBS.	same reduction in the number of babies dying from EOGBS. In fact there was a recent UK pilot at London North West Healthcare NHS Trust, which saw an 80% drop in the number of babies developing GBS infection after it introduced screening using the ECM method over an 18-month period. A reduction in the number of babies developing EOGBS would reduce the number of babies dying from it.

41.	Lindsay Birkett YES	Page 10	We do not know whether there are any short or long-term harms to the mother or baby from giving antibiotics to the mother during labour.	Research has shown that intravenous antibiotics given in labour to women whose babies are at higher risk of developing GBS infection, is highly effective at reducing the risk without any known long-term side-effects on the baby, and no apparent tendency to increase antibiotic resistance. In fact, GBS has remained sensitive to penicillin for over 60 years. If there was a real risk of harm to mother or baby, the current RCOG information on preventing GBS infection in newborns would not advocate offering intravenous antibiotics to all pregnant women with risk factors.
42.	Neil Guy Sarah Guy YES	Page 10 and page 84 – final para		It is recognised that there is insufficient evidence, however the recommendation to take no action is lazy and dangerous. It is unacceptable that mothers are denied the choice to be fully informed about GBS, how it might affect them and the baby they are responsible for, whether to be tested or to receive treatment.
43.	Neil Guy Sarah Guy YES	As above	Refers to using inaccurate testing methods	ECM testing should be used which, as the authors of this report will know, does not provide false results like the testing method they are proposing.
44.	Fiona Paddon YES	Page 10	It [carrying GBS] does not usually cause symptoms or harm.	This being the case, why does UKNSC appear to be content to continue to use a method of detecting and managing the risks of GBS based on factors that arise from symptoms in the mother?
45.	Fiona Paddon YES	Page 10	One in every 1,750 babies born in the UK and Republic of Ireland develops EOGBS	Why does the UKNSC use figures that include statistics from a country that is outside the UK? What is the impact of including Ireland in this statistic? What is the approach in Ireland to GBS screening? At other points in the report UKNSC appear to find studies from other countries to be non-representative in terms of whether screening would be effective in the UK. Is this contradictory with including another country in the statistics used here?
46.	Fiona Paddon YES	Page 10	The proposed screening programme	Which kind of test is being considered within this report? Is it the GBS-specific enriched culture medium test or the standard direct plating tests widely available in the NHS? It is clear that the

			would offer all 718,000 women pregnant at 37 weeks in the UK each year, a test for GBS colonisation in the third trimester of pregnancy	former should be used and therefore use of it should be the basis of this report.

47.	**xxxx xxxx** YES	Page 10	Unfortunately, even with the best care, a small number die and some who recover have after effects like deafness or brain damage.	I wasn't given any information on GBS during my pregnancy and, as a result, I didn't know my baby was at risk or that her death could have been prevented until it was too late. This can hardly be described as "the best care". Sadly, my experience is the norm rather than an exception in the prevention (or lack) of EOGBS in this country.
48.	**xxxx xxxx** YES	Page 10	Currently not all women with risk factors are having the antibiotic treatment during labour, which may be in part due to the woman's personal preference (as the drip can limit birth options).	I was automatically offered antibiotic treatment with my second child, as my first baby had died of EOGBS. The drip was quick and easy to administer and I was able to have a completely normal delivery. It is wrong to suggest that the drip can limit birth options and the report provides no evidence to support its claim that women with risk factors are choosing not to have IAP due to personal preference. The reason is more likely to be because health professionals find the risk factor approach confusing; each hospital is allowed to follow its own policy and the lack of antenatal information on GBS means that pregnant women are not in a position to make an informed choice.
49.	**xxxx xxxx** NO	page 10	"Only 333 of these 150,800 women would have babies that develop EOGBS, because the test is inaccurate for predicting EOGBS infection in the baby."	The test would determine which babies are at higher risk of GBS infection as their mother was carrying GBS, it's not designed to diagnose infection. The test is an effective way to prevent the life threatening infection happens to new born babies. Not every baby who is born to a mother who tests positive for GBS will become ill. Although GBS is rare in pregnant women, the outcome can be severe. The test is a routine part of prenatal care in the America. I would like to see it in this country as well.
50.	Lindsay Birkett YES	Page 10	Only 333 of these 150,800	The current risk-factor based approach is not an accurate test for predicting EOGBS in the baby

			women would have babies that develop EOGBS, because the test is inaccurate for predicting EOGBS in the baby. The rest would receive unnecessary treatment.	either. At least a screening-based approach would identify women known to be carrying GBS instead of making an assumption based on risk factors, which could be caused by something else entirely. The report states that 59-65% of EOGBS cases did not have any clinical risk factors for GBS based on current UK prevention guidelines, so not only is the current approach not an accurate method for predicting EOGBS in the baby but it is also leaving almost half of EOGBS babies unprotected.

51.	Fiona Paddon YES	Page 10	Only 333 of these 150,800 women would have babies that develop EOGBS, because the test is inaccurate for predicting EOGBS in the baby. The rest would receive unnecessary treatment.	As a reason for not recommending screening, this statement is illogical and overlooks some key points about the current system for managing GBS risk and of a morally acceptable approach to addressing the risks of GBS, which can ultimately be the most serious risks a mother and baby can face. 1. The current risk-based approach is also wholly unreliable in predicting which babies will develop EOGBS and yet all mothers within the risk categories are (or should be) offered antibiotics. Maintaining the risk-based approach does not combat the problem the UKNSC deems "unnecessary treatment", it merely spreads it amongst a less reliably populated section of pregnant women. 2. Whilst the test may be inaccurate in predicting which babies will develop EOGBS, if the ECM test is used, it is highly reliable in showing which women are carriers of GBS. This information will therefore help to identify which babies are AT RISK of contracting EOGBS. UKNSC's approach appears to be that less information in trying to accurately identify babies at risk of EOGBS is preferable to having more and better such information. This is a completely illogical stance to take, assuming that the objective of any approach to screening should be to reduce the instance of EOGBS wherever possible (*see below re purpose of a screening programme*). 3. I take huge issue with the description "unnecessary treatment". For me, the purpose of treatment is twofold: 1) to prevent harm and 2) where harm has already occurred, to reduce its impact. In the case of antibiotics given to a mother identified as being a carrier of GBS, the first purpose of treatment noted is every bit as relevant (if not more so) than the second. Considering that there is currently no way to know which babies will contract EOGBS from their mother, every single use of antibiotics that is used to prevent EOGBS is completely necessary. 4. The approach of UKNSC appears to be that we should not test unless the results are wholly reliable and we should not treat unless we can be certain that a baby will contract EOGBS. This is a counsel of perfection that is currently unachievable and morally unacceptable as an approach to address the potentially dire consequences of EOGBS. Furthermore, it does not appear to be an acceptable approach to medical testing and treatment in other areas, where sub-optimal testing is carried out whilst improvements are looked for. By way of recent example, the currently used biopsy test for prostate cancer only successfully identifies aggressive cancers in 48% of cases. It is hoped that MRI scans will prove to be a much better test, finding 93% of the same cancers. Biopsies have many side-effects (unlike the ECM test for GBS) and can lead to men receiving treatment "unnecessarily". And yet this imperfect way of testing has been carried out throughout the NHS, presumably and quite rightly being deemed much more

				preferable than doing nothing and just waiting for men to exhibit symptoms. Why then is it acceptable to deny pregnant women and their babies the best possible test for EOGBS available at the current level of medical knowledge, on the basis that it is not accurate enough?

52.	Fiona Paddon YES	Page 10	The purpose of a screening programme should be to prevent EOGBS disease in the baby and particularly its worst effects.	I disagree with this stated purpose of a screening programme and wonder whether this has led the UKNSC to overstep its reach and conclude that screening is not recommended because it cannot deliver something that is currently medically impossible (complete reliability of test results and targeted treatment - *see my 2. above*). In my view, the purpose of a screening programme should be to identify those most at risk from EOGBS, who can then be offered treatment to combat that risk. By doing this, the rates of EOGBS occurrence would fall, in the same way as has been experienced in the other countries that do screen.
53.	Fiona Paddon YES	Page 11	There was some evidence that the introduction of antenatal GBS screening for all pregnant women may lower the number of babies with EOGBS, but the review found that these studies have limitations, which means their findings may not be true	Is it acceptable to draw the conclusion that findings "may not be true" just because studies have limitations? The UKNSC seems to suggest that the studies are wholly without merit and should be ignored, rather than accepting what they found within the limitations and giving some weight to that evidence accordingly.
54.	**xxxx xxxx** YES	Page 10	It is not possible to know whether the introduction of a screening programme in the UK would do more harm than good.	The report provides no evidence to support its suggestion that the introduction of a screening programme would be harmful let alone outweigh the potential benefits. As the mother of a baby who died of EOGBS because I wasn't given the information or opportunity to do anything to prevent it, I find it inexcusable that the system continues to fail babies and their families due to an inability to change something that clearly isn't working. I agree that more research needs to be done to identify which babies will develop EOGBS disease

				but we cannot wait for that to happen. My daughter died 12 years ago and in that time the incidence of EOGBS has increased. The drain on the health service looking after those babies is huge, not to mention the devastating impact it has on the families affected. Please stop quoting wishy washy excuses for not introducing a GBS screening policy when the evidence in its favour is overwhelming, if you would only look at it. It's time for the NSC to step up and do the right thing.

55.	Fiona Paddon YES	Page 11	Because of these findings it is not possible to know whether the introduction of a screening programme in the UK would do more good than harm.	If it is not possible to know this, how can the UKNSC arrive at an opinion on not making a recommendation about screening for GBS? If this is truly their position, their report should state that they are unable to offer an opinion or arrive at a conclusion – not recommending screening amounts to a decision that screening will do more harm than good. This demonstrates the bias of the UKNSC towards not screening, in the absence of knowing where the balance lies.
56.	Fiona Paddon YES		We need more research to identify which pregnant women will go on to have a baby which develops EOGBS disease.	As stated above, my view is that this goes beyond the remit of the UKNSC and this review, which it is stated "will help to inform decisions about whether the benefits of introducing GBS screening would outweigh the harms". The review therefore needs to evaluate screening on the basis of current knowledge, evidence and information. It also needs to address the risk of 333 babies per year (and rising) of contracting EOGBS (50 of whom will die) whilst the UKNSC seeks more research to establish medical certainties that are not realistic or indeed applied in other areas of healthcare.
57.	NCT YES	Plain English summary- p.11	"We need more research to identify…'	We would add the word 'particularly' after 'We need more research to identify…' as research is needed in various domains related to GBS not just transmission though this is of course highly important. Other areas of key importance are the impacts of IAP, an RCT in to risk based versus universal screening and why there is such variation in implementation of the risk-based strategy.
58.	NCT YES	Executive summary 11-23	General	This is a lengthy executive summary; given that this is the part of the report that many stakeholders will mainly engage with, we recommend creating a shorter version.
59.	Royal College of Paediatrics and Child Health YES	Pg 11	We need more research to identify which pregnant women will go on to have a baby which develops	Our commenter asked a question regarding what "more research" means? Is it a rct, a cluster rct? They advised that it needs to be stated exactly what sort of research would be sufficient to change the minds of the NSC.

			EOGBS disease.	
60.	**xxxx xxxx** NO	Plain English Summary - page 11 **xxxx xxxx xxxx xxxx xxxx xxxx xxxx xxxx xxxx xxxx xxxx xxxx**	There was some evidence that the introduction of antenatal GBS screening for all pregnant women may lower the number of babies with EOGBS, but the review found that these studies have limitations, which means that their findings may not be true.	Suggest rewording the end of this statement, replacing “true” for “valid” or “reflect the actual number of babies who develop EOGBS”.
61.	NCT YES	Executive summary: Introduction (p.12); Introduction (p.22)	First paragraph	Percentages are used without clarity over what the denominators are. It is suggested that likelihoods (1 in xx) are used with specified denominators e.g. on line four: ‘1% will suffer from invasive GBS’. It is unclear whether this refers to 1% of all babies or of babies whose mothers carry GBS.
62.	NCT YES	Executive summary: Introduction (p.12)	General	Is it worth mentioning late onset GBS and why it is not being looked at in this review?
63.	Fiona Paddon YES	Page 14	The percentage of babies with	There appears to be no acknowledgement of the obvious fact this demonstrates, that the risk-based approach to GBS currently in place is completely unsatisfactory as a means by which to identify

			EOGBS born at term to mothers without any RCOG or NICE risk factors was 63 – 67%.	which babies are at risk of EOGBS. And yet the UKNSC appears to be content that this approach remains in place.
64.	Fiona Paddon YES	Page 14	Up to 33% of women with positive GBS-culture during their third trimester were GBS-negative at term and would have been unnecessarily treated with antibiotics in a universal screening programme.	The negative phrasing of this point demonstrates the bias of the UKNSC towards not screening. The factual basis of this statement could equally be expressed as 67% of women were successfully identified as being GBS-positive during their third trimester and at term. As stated above, the fact that there are limitations and known unreliabilities to a testing regime does not mean that it should not be implemented and that no testing is to be preferred.
65.	Fiona Paddon YES	Page 15	Up to 12% of women changed from GBS-negative to positive and would miss out on IAP in an universal screening programme	The negative phrasing of this point demonstrates the bias of the UKNSC towards not screening. The factual basis of this statement could equally be expressed as 88% of women were appropriately identified as being GBS-positive and treated with IAP due to universal screening. As stated above, the fact that there are limitations and known unreliabilities to a testing regime does not mean that it should not be implemented and that no testing is to be preferred.
66.	Lindsay Birkett YES	Page 16	Screening at 35-37 weeks is not a good predictor of GBS carriage	Research has shown that the result of a sensitive test for GBS is unlikely to change over a period of 5 weeks and doesn't come and go from one day to the next, as appears to be suggested in the report.

			in labour, GBS transmission to neonates, or EOGBS disease	The recommended ECM test is recognised as the gold standard sensitive test and is a significantly more accurate method of identifying pregnant women who are GBS carriers than the RCOG risk factor approach. The current approach does not predict GBS transmission to neonates or EOGBS disease either.
67.	Fiona Paddon YES	Page 19	Cost Effectiveness	The response to this question is wholly inadequate. There appears to be no consideration that the cost of caring for babies who have contracted EOGBS in NICU units and, even more so, the care of those who go on to live with permanent severe disabilities is huge compared to the cost to the NHS of offering screening. The comments that there are costs which are hard to incorporate into a cost-effective model are not acceptable. If a cost effectiveness criterion is required then this must be carried out fairly and effectively, and if it is not deemed possible to be so carried out, then the criterion should be removed, rather than decided in the negative.
68.	NCT YES	Executive summary	General	Although a definition is provided for risk of bias in the main body of the report, it is felt that this would be worth including at least as a reference to in the Executive summary as it is mentioned many times.
69.	Emmalene Bushnell YES	UK NSC criterion 11 (pages 17-18)	The screening programme – clinical effectiveness There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity. .	Despite a risk based approach being adopted in the UK since 2003 both the rate and number of preventable cases of early onset GBS have increased. GBS remains the most common cause of infection in new-borns and a leading cause of meningitis in babies under three months. Evidence demonstrating the effectiveness of screening programmes in reducing mortality or morbidity is available from the USA and other developed countries where screening programmes have been implemented.

70.	NCT YES	Executive summary: The treatment (p.17)	Second bullet point : 'this trial has limited applicability as it used a different drug'	It is unclear which drug this is referring to being different from- if penicillin this might need to be spelt out, including the fact that penicillin is the most frequently used drug in IAP for GBS.
71.	Emmalene Bushnell YES	UK NSC criterion 14 (pages 19-21)	The screening programme - cost effectiveness The opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (value for money). Assessment against this criterion should have regard to evidence from	Screening of women for GBS in pregnancy at 35-37 weeks and the use of IAP in labour would minimise the risk of GBS infection in neonates. The cost of screening is not disproportionate when one considers the number of babies and families affected by GBS infection. On average one baby each week dies from GBS infection and one baby each fortnight survives with long term difficulties. The financial cost to the NHS in providing care to very sick babies with GBS infection and any long term injuries they suffer, (which would be preventable with GBS screening) has to be a consideration when assessing the cost effectiveness of screening.

			cost benefit and/or cost effectiveness analyses and have regard to the effective use of available resource."	
72.	NCT YES	Executive summary: Conclusions and implications for policy (p.19) AND 6. Conclusions and implications for policy and practice (p.87)	"GBS is an important health problem"	We welcome this statement, but also suggest that there is some recognition of the human impact of GBS and its devastating consequences for some families. Although this is not a criteria for the NSC, we feel it is important to acknowledge the sad reality of GBS for some families.
73.	Birth Trauma Association YES			We have read in detail both the Strep B Group submission and the External Review. We are at a loss to understand the Review's conclusions. The following statement was particularly puzzling: "There was some evidence that the introduction of antenatal GBS screening for all pregnant women may lower the number of babies with GBS, but the review found that these studies have limitations, which means that their findings may not be true." This is not a reason to reject screening, it is a reason to do a more robust study. We fully support the arguments of Group B Step Support – there is potential to prevent illness in hundreds of babies each year, the cost of which could be a lifetime of support. The decision makes little sense in terms of effective use of NHS resources or the prevention of morbidity and disability.

74.	**xxxx xxxx** NO	Pp13-16 also later in the paper	Frequent references are made to Gambian study whilst explicitly stating that this is not necessarily significantly comparable to cases of EOGBS in the UK. (Criterion 1 summary on page 15) e.g. Approximately 58% of GBS-colonised women transmitted GBS to their neonates during labour when not treated with IAP. There are concerns of how applicable this figure is to the UK as this study was conducted in Gambia. Overall, EOGBS is an important health condition,	It is clearly apparent that at the very least that this paper should have been prepared more objectively and using a much wider basis of research. Regular references are made to the Gambian study and what does stand out from those would present a strong case for providing the test as standard in the UK and introducing treatment with IAP as a result of positive test with the expectation that the UK's better-equipped and available to all at point system could be expected to report a significant reduction in neonatal death from sepsis and more generally given that it does not appear to be the first consideration of many hospitals where another possibility also presents. Little reference is made to the US studies mentioned later in the paper and no clear effort is made to really compare and analyse the different studies on which this paper was based. I completely agree with this point – and would say that this forms the clear basis from which to proceed and work positively to remedy what is an acknowledged issue with potential life-threatening results, rather than concurring that there is a concern then striving to establish why no action should be taken. If the UK wants a world-class health service then it must continue to provide one and stay proactive in doing so (I don't believe that the answer is to privatise the NHS and create a painful caricature of the hugely disparate two-tier healthcare provision in the US). It is appalling that healthcare often chooses to remain blinkered to change and development in understanding of medical conditions and diagnoses, despite so many studies being carried out worldwide. In the UK this seems to be a consciously opted default to save time and money where possible and with the assumption that if there is a problem someone else can handle it - community midwives say the hospital, GPs say the midwife or the hospital, the hospital says the GP. Added to that, records are not shared partly to save administration time, partly for fear of unfavourable scrutiny. In personal experience I found that the older community midwives I saw during my pregnancies worked on a firm basis that all pregnancies are routine and complications are impossible to the point of being denied reference by the community midwife for an elective c-section when my second pregnancy was a week overdue because she did not believe in it (the hospital agreed a concern and provided for it).

			however, the natural history and the development from GBS carriage to EOGBS disease remain poorly understood. Therefore this criterion is not met. Research is required to fill this evidence gap on why mothers transmit GBS and why neonates develop EOGBS disease.	

75.	**xxxx xxxx** NO	P14 and p16	There were 10 deaths in babies with EOGBS born after 35 weeks' gestation; 60-70% (6/10 to 7/10) of them did not have any maternal risk factors based on RCOG and NICE risk factors. Approximately 1% (31/3,215) of all stillbirths in the UK were attributed mainly or partly to GBS. Up to 33% of women with positive GBS-culture during their third trimester were GBS-negative at term and would be unnecessarily treated with antibiotics in a universal screening programme.	Given the lack of community midwife provision during women's pregnancies (e.g. I went without a number of midwife appointments during my 2007/8 pregnancy and 2011 pregnancy due to lack of available mid-wife due to sickness, lack of cover, retirement and re-organisation of city midwife cover, and cover already over-stretched so unable to take more patients on) it is not surprising that many higher-risk pregnancies are not being identified and appropriate medical care being established in good time to significantly reduce labour and neo-natal risks. An additional simple test being a tabled part of all pregnancies or even just where one related risk factor presented during the pregnancy that must be offered to expectant mothers could reduce the infant mortality figures significantly. Introducing the test after another related risk-factor has presented in a pregnancy would be a solution and yet whilst page 16 refers to very positive results from IAP in an observational study, again the paragraph end-line seeks to discredit it as not enough evidence.

76.	**xxxx xxxx**	P14	The concern with the BPSU and stillbirth data is that they are from approximately a one-year period, and it is unclear how these incidence, mortality, and risk factor figures fluctuate between years and how different this year may be compared to the others.	Another example of the lack of properly drawn together clarity in the report. Isolated figures are thrown into the summary without real discussion yet frequent statements that data quoted does not necessarily represent a broad enough research basis.
77.	Rachel Plunkett YES	Pg 17 Plain English Summary	Clinical Screening Program- Criteria Not Met	Throughout the document, Criteria Not Met is worded. Not because that there is evidence proving that a screening program would be inefficient but because you have found things wrong with the rials that have occurred. What about the recent trial in NHS North West London who found an 80% reduction in infants poorly with GBS disease in 18 months. http://www.lnwh.nhs.uk/about-us/news-and-media/pressreleases/pilot-shows-that-screening-mothers-for-group-bstrep-gbs-saves-babies/
78.	NCT YES	Executive summary: Conclusions and implications for policy (p.19)	Second bullet point	It is suggested that brackets are removed from around ‘of which seven die’
79.	NCT	Executive summary:	‘In those term	Although this is factually correct, we would welcome an acknowledgement that nonetheless these three babies still do die and this is a result of a failure to fully implement the risk based strategy. We

	YES	Conclusions and implications for policy (p.19)	babies who die, three have maternal risk factors so delivery could be managed by current risk based strategies'	suggest changing the word 'could' to 'should'.
80.	NCT YES	Executive summary: Conclusions and implications for policy (p.19)	3rd bullet point	3rd bullet point cites 150,806 and then 150,800 for the same figure.
81.	NCT YES	Executive summary: Conclusions and implications for policy (p.19)	"of these only 0.2% would have a baby with EOGBS without IAP."	The wording of this phrase is slightly confusing. We suggest changing to 'would have a baby with EOGBS without IAP in the risk based strategy'
82.	**xxxx xxxx** NO	Overall report and pp18-19.		I am disappointed that the result of this routine review is the NSC recommendation that a systematic population screening programme is not recommended given that this is a known high-risk for infant mortality. Overall, I would like to comment that the paper lacks any real clarity or steering and the answer seems to be pre-presumed. The content is full of statistics but lacks any real clarity or analysis that runs through the document. A clear effort is made to state that there is a real lack of coherent evidence and possible bias makes almost all of the content inadmissible for real consideration. Given that this is a high-profile known risk that is routinely ignored until there is an emergency it seems ludicrous to eschew the simple introduction of a basic swab test to allow the possibility of identifying and addressing individual risks from GBS as standard. Not doing this does not make the risk go away, it just passes the financial buck a little further along the line with time to become more

				dangerous and cost more money. It is ludicrous that something so simple that is standard practice in so many other countries is denied in the UK's cloak-and-dagger approach to medical care. I have included personal details of my own experience in my feedback because I know that my own experiences are far from unique and should any of the paper's authors not have any close experience of neo-natal sepsis I would urge them to take something from it as example of one of the better outcomes from sepsis events in the current system and note something of how poor the standard of UK midwifery care has been in the last few years, not as a damnation of the NHS whose hospital staff are working over and above all conceivable hours and limits as far as they can and then some to provide the best care they can, but as a little towards the indication that the government seriously needs to listen to frontline medical staff and give them the facility to help shape a healthcare provision that works for all and is accessible to all. Very simply, it costs thousands for the care of a baby in the SCBU for around one to two weeks. 48 hours plus with IV drips, possibly oxygen and a heart monitor is expensive, plus the staffing of nurses to check child's stability and doctors monitoring the child. Twice daily or more heel-prick tests and course of penicillin or safe alternative all over a 1-2 week period is also expensive. That is basic sepsis care for a newborn child, other complications obviously cost still more. The length of care time and expense is much greater that the cost of a simple test and I believe is still greater than that of necessary medical provision including IAP where needed. As a parent who nearly lost a child to sepsis after a catalogue of minor errors made in the name of 'probably nothing anyway', time-saving and money-saving I feel extremely lucky that that my child survived and is now healthy, only apparently retaining minor hearing issues from his traumatic delivery and first few days. I did not want to take badly needed money out of a very stretched and vital health service, potentially putting others at risk, by making a legal case against the hospital or the county midwifery service despite heavy pressure from unscrupulous legal agencies whilst my child was in the SCBU, and so have had no insight of the hospital's records of the issues or any real explanation of why things were handled as they were. What I do know is that the cost of my child's emergency care was easily several thousand pounds which would have covered many screening tests. I refused penicillin for my child in favour of the more expensive alternative because of penicillin allergy in myself, my husband, and other family members across some generations and in fear that a possible reaction to penicillin might be initially missed given the breathing difficulties my son was already having. On an emotional level I would not wish any other parent to go through what we went through or worse, and yet I meet others who have had very similar experiences, and realise just how lucky I am that my child is still alive and well.

				Now that I know more about GBS and have taken the time to take more academic study of it from publicly available medical papers I realise that in my case there were a number of red-flag issues during the pregnancy that were noted but considered to be minor or nothing out of the ordinary, including a severe kidney infection following a heavy cold that was not fully treated, unusual balances of white cells in blood tests and significant oedema from month 4 onwards. These symptoms are consistently flagged in web articles and online medical papers focusing on GBS, although there also remains the possibility that the sepsis was contracted during the caesarean itself from another party – I do not have access to hospital records to know what precisely happened – the notes the hospital made in my child's red book for the entire period just said 'sepsis'. Once my child was delivered by emergency caesarean and resuscitated after 23 hours of trying to induce him 10 days overdue because his heart rate was unstable I was led to believe that this was routine for c-sections, including the high fever symptoms I suffered in the immediate aftermath (described as usual for post-caesarean) and my child's sepsis. Looking back it was not going to have been straight-forward even had there been a test available but such a test would have ensured that the appropriate plans could have been made to avoid what for myself and my husband was nearly the loss of our first child and for the trust was likely to have been a less-than-glowing labour and neo-natal report to file for future audit. Having read through the NSC Report the main message I am getting from it is a note that the studies so far have not perhaps been wide enough or particularly geographically relevant to the UK and there is a consistent thread of attempting to argue that whilst there are positives in favour of IAP it is clearly not felt to be a high priority matter to introduce it as a standard test in NHS maternity care. In short, the report is apparently taking a stance of arguing against it rather than being an objective analysis.

83.	NCT YES	Executive summary: Research needs (p.20) AND 6.Conclusions and implications for policy (p.87)	First bullet point: "The risk based prevention strategy could be explored with the aim of identifying more EOGBS cases"	We agree with the sentiment of this statement but are unclear as to what exactly it is referring to in terms of possible research questions. In the discussion section it goes in to slightly more detail saying 'Risk factors might have to be refined to identify more mothers at risk of having a baby with EOGBS' which we feel would be an adequate elucidation.
84.	NCT YES	Executive summary: research needs (p.20)	"To measure these would require an RCT but …."	We would welcome a more explicit statement of whether an RCT is recommended and if not the reasons why not.
85.	NCT YES	Introduction: Prevention approaches (p.22)	"In the UK, women who present risk factors…are offered IAP.''	Although the guidance states that this should happen, in reality we know that many women with risk factors are not offered IAP. We suggest changing the wording to reflect this e.g. 'women who present risk factors should be offered IAP according to guidance"
86.	NCT YES	Introduction: Prevention approaches (p.22)	"A criticism of this approach is that approximately 30% of cases without risk factors are excluded from prevention"	This sentence is unclear. It needs to specify that 30% of cases of EOGBS will occur without any of the identified risk factors and so will not be picked up through the risk-based approach.
87.	**xxxx xxxx** NO	pp27 et seq	Methods	In general, this report seems to seek much more evidence than has been required for other antenatal screening decisions for less common conditions, which have recently been approved – for example on cost-effectiveness. The expertise of the researchers formulating and refining the research questions, defining the inclusion criteria for papers, and of those assessing the publications selected for systematic review has not been stated. Who are the 'experts in the field' (p27) that have been consulted regarding the

				search strategy for the systematic reviews? Such information is given as standard in any high-quality systematic review, and without it, it is hard to be confident in the conclusions stated. Why were studies outside the UK/non-English language not included in the review? Not including data from countries which regularly screen for GBS (and have seen decreased incidence, and none of the predicted adverse outcomes) gives an unbalanced assessment of the evidence, and gives the impression that this review has a forgone conclusion. The lack of due assessment of methodological quality of studies in the rapid review means that it is hard, for many questions, to make an assessment of the likely degree of bias. Where such assessment is made in the systematic review, the degree of bias is frequently high yet conclusions are presented all the same. Why were a number of key criteria for screening programmes not analysed at all? GBS would meet these.

88.	**xxxx xxxx** NO	UK NSC Criterion 1 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**		Considerable gaps in knowledge about the epidemiology and natural history of GBS carriage/EOGBS have been highlighted in this review. Large scale studies in the UK are needed to address this area. Methodologically robust studies may be feasible from linkage between existing clinical and administrative data that are collected routinely and available nationally.
89.	**xxxx xxxx** NO	UK NSC Criterion 1 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**		The authors conclude that the natural history and the development of EOGBS is poorly understood. However the authors present data from 18 studies including two published reports from Public Health England and preliminary data from MMBRACE. I don't think the conclusion from the authors is correct in light of this. There is a wealth of epidemiological data on a worldwide basis describing the natural history and epidemiology of this condition. The aim of screening in pregnancy should be to reduce the morbidity associated with this condition as it remains a major cause of morbidity and mortality in neonates. Information about which serotypes contribute most to the disease and identifying women who are more susceptible may be interesting but the lack of data to explain why some women are affected more than others shouldn't influence this consultation. We do not fully understand why some women are predisposed to gestational diabetes in pregnancy but we still advocate screening for it.
90.	**xxxx xxxx** NO	UK NSC Criterion 1 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**	GBS and stillbirth	Should this be stillbirth or perinatal mortality? With regards to GBS and stillbirth, it is usually an incidental finding due to vaginal passage of the dead fetus and the length of labour as this is the time of colonisation of the fetus.

91.	**xxxx xxxx** NO	UK NSC Criterion 4 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**		There is a clear validated test available. Just because the reported studies have failed to employ the correct swabs or failed to use the correct culture medium or have reported on a non-UK population, doesn't mean that the test is at fault. Screening at term when women present in labour would reduce the number of false positives inappropriately treated and the number of false negatives missed at 37 weeks *(see the point below from another member of the Committee).*
92.	**xxxx xxxx** NO	UK NSC Criterion 4 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**		You have not discussed rapid point of care testing
93.	**xxxx xxxx** NO	UK NSC Criterion 9 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**		The finding from this review reflect the results from the latest RCOG audit, which identified inconsistencies within and between UK obstetric units in reports of whether IAP is offered to women with clinical indication(s) for IAP *(Audit of Current Practice in Preventing Early-onset Neonatal Group B Streptococcal Disease in the UK. First report. RCOG, 2015)*. This review has highlighted the need for research to understand why the current risk-based prevention policy is not fully adhered to.
94.	**xxxx xxxx**	UK NSC Criterion 9		The authors have presented data that support a reduction in EOGBS disease, by 89% in the observational study and by 83% in the systematic review. The conclusion that it is of no benefit is

	NO	**xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**		therefore not justified. A further observational study showed a significant result. It cannot simply be dismissed when it forms part of the scientific evidence available. Co-amoxiclav and erythromycin aren't used for this indication The observational studies compare side effects such as thrush and increased length of stay with antibiotic use. Neither of these outcomes compare with the fetal morbidity and mortality associated with failure to provide antibiotic cover to reduce the risk of EOGBS. There is very little substantive evidence that these antibiotics cause harm and must be assessed in terms of a risk/benefit ratio

95.	**xxxx xxxx** NO	UK NSC Criterion 11 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**		A high quality RCT is urgently needed.
96.	**xxxx xxxx** NO	Page 14 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**	Up to 28% of women with positive GBS-culture during their third trimester were GBS-negative at term and would be unnecessarily treated with antibiotics in a universal screening programme.	It does not mean GBS “is not there” it means that the swab and culture failed to detect it because even by perineal swabbing and chocolate agar culture in research settings growth and sensitivities is at best 80%. Thus that does not mean they are “unnecessarily treated” it means that this is a group that has a higher risk as they have documented GBS. Again this raises the issue of rapid point of care testing.
97.	**xxxx xxxx** NO	Exec Summary Page 19 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**		I think the executive summary is important as most people will only read this section. I wonder if the second bullet point of the conclusions might be more complete with: Of the seven who might die, 5-10% will be missed because of false negative screening at 35-37 weeks, about 10% due to the estimated inadequacy of antibiotic prophylaxis, and an unknown proportion due the fact that giving antibiotics less than 4 hours before delivery is less effective.
98.	**xxxx xxxx**	Exec Summary Page 19		It would be worth mentioning the anaphylaxis question here I think, perhaps with something like below (though facts would need to be checked). I do think this is an important point if you are

	NO	**xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**		concluding against universal screening. The incidence of severe anaphylaxis with antibiotics is approximately 1:10,000, with fatal anaphylaxis estimated at 1:100,000. In addition, there is a suggestion that antibiotic treatment in late pregnancy has been associated with cerebral palsy.

99.	**xxxx xxxx** NO	Exec Summary Page 19 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**		Might it be worth adding something concise like this below the third bullet point: The potential 3-4 lives saved by introducing universal screening over selective screening in this theoretical group has to be weighed again the estimated 15 cases of severe maternal anaphylaxis and 1-2 maternal deaths from the antibiotic treatment. Furthermore, the evidence to support a benefit of universal screening over selective screening is conflicting in the three relevant studies where this has previously been introduced.
100.	**xxxx xxxx** NO	Exec Summary Page 20 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**	Exec Summary	Should highlight the limitations of the data ie EOGBS and Stillbirth incidence of GBS are only the minimum data as the cultures for GBS are poor. This is detailed in page 48.
101.	**xxxx xxxx** NO	Page 22 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**	As culture tests take 24 to 48 hours to process, culture screening cannot be offered at the point of prophylactic treatment in labour, as results would not be available	There is a point of care test *(please see comments above)*

			in time to treat.	

102.	**xxxx xxxx** NO	Page 33 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**	Fig 1	Needs formatting *(see comment above "We are not sure the bias graphs add anything above the description of high and low bias of papers").*
103.	**xxxx xxxx** NO	Pp35-40, p40 onwards		Many statistics presented although it is hard to follow a coherent path to understand the particular way in which this paper has applied them beyond frequent reference to possibility that many sources may be inadmissible from serious consideration due to potential bias in reporting.
104.	**xxxx xxxx** NO	Page 36 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**	1st paragraph	Needs formatting
105.	**xxxx xxxx** NO	Page 37 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**	It is important to note that not all of these infants with maternal risk factors would be treated with IAP under the UK risk-based prevention approach, as mothers in pre-term labour and no other risk factors are not	In the text preterm and pre-term is used. The correct is preterm with no hyphen.

			treated, and treatment for PROM in term deliveries is not included in the UK guidelines.13,15	

106.	NCT YES	Section 4.2 (p.47)	Figure 3	This diagram, whilst very useful, would be more useful if the title was more explanatory, e.g. as described on page 49: 'Natural history of GBS on a hypothetical cohort of 780,000 pregnant women'
107.	NCT YES	Section 4.3 (p.56)	Third paragraph (beginning 'Routine UK data…')	Although the evidence does suggest that fewer than 1% (0.2%) of mothers identified by universal screening would go on to have babies with EOGBS, there is not an acknowledgement that this would still then capture more women whose babies will develop EOGBS than with the current risk-based approach. It is also heavily implied, but not explicitly stated that 0.2% is too low a number to warrant such a programme; explicit statement and reasoning for this would be welcome.
108.	NCT YES	Section 4.4 (p.61)	Question 18 and 19: Analysis of the evidence	We welcome the analysis of evidence around the effectiveness of IAP particularly the duration of administration, and hope that this is fed in to practice.
109.	**xxxx xxxx** NO	Page 64-73 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**	Maternal and neonatal adverse effects of antibiotics given during pregnancy and labour	The evidence presented really didn't convince me that IAP is associated with maternal or neonatal harm. Anaphylaxis is mentioned in this document – but no apparent case series or even case reports to justify this claim.
110.	**xxxx xxxx** NO	Page 69 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**	Cerebral Palsy	I do not think this is an appropriate comparison to use as justification. ORACLE was using antibiotics (a different class) to prevent preterm labour not IAP at term to prevent GBS. To ascribe the 2 as similar is not correct.
111.	NCT YES	Section 4.4 p.74	Summary	We are struck by the variation in the evidence around the effectiveness of IAP in preventing EOGBS as well as its adverse effects and hope that this too is fed in to practice and research.
112.	Neil Guy Sarah Guy	Page 82	Cost benefit	A life is valued at £1million – testing is entirely cost effective. GBS is increasing and more babies are expectedly to simply suffer horrendously in silence.

	YES			

113.	Neil Guy Sarah Guy YES	Page 79/ 82		There is a clear gap in evidencing the effectiveness of universal screening and this should be explored further so that an evidence based decision can be made. It is not good enough to say the evidence doesn't exist one way or the other and therefore no action will be taken.
114.	Neil Guy Sarah Guy YES	Page 83		This evidence indicates that there is clearly a problem with both an insufficient number of mothers who display risk factors being treated (44%) and mothers not displaying any risk factors not being advised of or offered screening.
115.	Neil Guy Sarah Guy YES	Page 84- para 3		The report repeatedly comments on this issue being poorly understood. The recommendation should therefore stand that 'research is critically required'. The report goes to some length to highlight where there are gaps in knowledge and evidence- this should be taken forward accordingly.
116.	Neil Guy Sarah Guy YES	Page 85- para 1		The threat of treatment potentially putting mothers and babies at risk is repeatedly stated with regard to this issue – however this is little evidence to support this and further, more realistic, research should be undertaken to support any such claim.
117.	**xxxx xxxx** NO	P82	22. What is the cost effectiveness of GBS screening in the UK? These questions relate to UK NSC criterion 14: "The opportunity cost of the screening programme (including testing, diagnosis and	I do not have insight into cost of different medical care options, but as I stated early on in my reply, I would suggest that introducing a simple swab test, perhaps two if relevant where other related risk-factors have presented, plus better monitoring of pregnancies and IAP planned for and provided where it is likely to be needed (not necessarily in all positive GBS results from the swab?) is surely unlikely to outweigh the cost of the neo-natal care that is required by an infant with sepsis, and presumably the amount of reporting the hospital must undertake to account for these incidents especially where the child does not survive. As the paper says, the 'major cost driver' identified was prematurity which can include other risk factors needing specific care. Again, if the pregnancy care model was upgraded slightly and enforced better, I believe that a number of pregnancy and neo-natal risks that are currently blithely not picked up on or dismissed until there is an emergency could be better planned for resulting in better healthcare plans and cost-forecasting and management.

			treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (value for money). Assessment against this criterion should have regard to evidence from cost benefit and/or cost effectiveness analyses and have regard to the effective use of available resource." Description of the evidence Our electronic searches did not identify any new studies on the cost-effectiveness of GBS screening in the UK related to criterion 14 since 2012. Analysis of the evidence The previous review24 concluded, "*The*	

			update search identified no new cost-effectiveness estimates relevant to a UK setting published since the previous update report. One cost study has estimated that EOGBS is associated with an additional health and social care cost of about £3,000 in the first two years of an infant's life in England. These costs have not yet been incorporated into a cost-effectiveness model. A major cost driver identified in this study was prematurity, and the authors suggested that the needs of premature infants with GBS should be specifically addressed." The update search identified no new cost-	

			effectiveness estimates of universal GBS screening relevant to a UK setting published since 2012. Summary	

118.	RCPCH	PG 83	"These are the EOGBS deaths that universal screening would try to prevent	Our commenter advised that there is a presumption that the current risk-based strategy is applied correctly and consistently to all eligible women. In their opinion it is not (as e.g. midwives are busy, people forget, swabs go missing, wrong medium is used, results go missing or are not looked at). They advised that universal screening applied as a care bundle would sort this problem (e.g. it is hard to "miss" serology screening in pregnancy).
119.	**xxxx xxxx** NO	Page 85 **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx** **xxxx xxxx**	The best quality evidence from a single RCT found that mothers treated with IAP for preterm labour (erythromycin or co-amoxiclav), were more likely to have children suffering from cerebral palsy compared mothers not treated with erythromycin or co-amoxiclav	This is not IAP as these women were not in labour as soon as labour started the antibiotics were stopped – this is rather prevention of preterm labour so we do not think it is right to include this statement as justification against IAP. You are not comparing like-with-like here.
120.	**xxxx xxxx** NO	General	General	The RCOG GBS Green-top Guideline is currently being reviewed and updated with publication expected in February 2018.
121.	Group B Strep Support (GBSS) YES	General comments		The present state of affairs with GBS prevention in the UK is neither safe nor an effective use of NHS resources. The UK NSC review is at best an exhortation to do nothing, apart to wait for yet more research that may or may not be funded.

				Few would deny that where GBS carriage is detected during pregnancy antibiotics should be offered in labour. The question is how best to find the right people to give those antibiotics to. The current situation with the NHS haphazardly testing some pregnant woman with a test that is right only half the time is unacceptable. The UK NSC has a responsibility to sort this out once and for all. The Committee should have the courage to be honest with the public: either they do not consider neonatal GBS infection to be serious problem and therefore recommend we abandon altogether this patchwork of prevention, or, as we fervently wish, recommend that universal antenatal screening for GBS carriage using the ECM test be introduced, as in so many other developed countries. The Royal College of Obstetricians and Gynaecologists' recent audit report[i] confirmed that more than half of maternity units offered testing to at least some pregnant women, often on maternal request, though rarely using the ECM test recommended by Public Health England's UK Standard B58[ii]. This is a postcode lottery, with many pregnant women unaware of group B Strep so unable to request testing. Prevention is better than cure – and cheaper. The UK's rate of EOGBS infection continues to rise, with the RCOG's Greentop Guidelines, introduced in 2003 and updated in 2012, failing to stem that tide. The UK needs to catch up with other developed countries and offer pregnant women testing for group B Strep at 35-37 weeks of pregnancy (or 3-5 weeks before anticipated delivery e.g. with twins). With a clear and consistent policy, together with offering good patient information and ECM testing, the UK rate will fall. Screening would enable appropriate antibiotics in labour be more accurately targeted to women carrying group B Strep, so prevent more EOGBS infections, and minimise antibiotic use in women not carrying GBS. Over 80% of early-onset group B Strep infection could be prevented[iii] if the recommended intravenous antibiotics were offered in labour to all GBS carriers identified by testing late in pregnancy, plus to the mothers of babies in the recognised higher risk situations. As other countries have reported, screening prevents more early-onset group B Strep infections than a risk-based

				prevention strategy[iv] [v]. Screening allows appropriate antibiotics to be targeted at the women most likely to be carrying GBS at delivery, whose babies are therefore at greatest risk. Risk factors are poor predictors of who is likely to be carrying GBS at delivery[vi] and result in many women not carrying GBS being given antibiotics during labour despite their babies not being at risk of EOGBS infection. Knowing who is carrying GBS, screening not only improves prevention of early onset GBS disease (the recent BPSU study showed that more 64% of mothers of babies with EOGBS had no known risk factors at or before delivery[vii]) but also ensures that fewer women not carrying group B Strep are given unnecessary antibiotics. The ECM test is simple, safe and painless and samples can be self-taken. The cost is relatively small – estimated £11 to the NHS – in comparison to the huge cost of potentially avoidable infection, disability and even death in newborn babies. With the Government's ambition to reduce neonatal deaths, brain injury around term birth, stillbirths and maternal deaths by 50% by 2020, now is the ideal time to introduce screening for GBS in pregnancy. The Montgomery Ruling[viii] by the Supreme Court made it clear that expectant mothers need to be in a position to make informed choices about their care. Women want to be told about group B Strep and offered GBS screening during pregnancy – a survey conducted in 2015[ix] found that fewer than half of new and expectant mothers had heard of GBS, although over 90% considered that all women should be told about it during pregnancy and that all women should be offered testing for GBS during pregnancy. Implementation of the recommendations set out in Better Births will increase the number of women who give birth in midwifery-led settings. In denying women GBS-screening, some women may be falsely reassured as being low risk, when they are at risk of giving birth to a baby who may develop

				early-onset GBS infection. Current guidelines result in women who are not screened being managed as if they are GBS-negative, yet if incidentally tested and found to be positive, they are offered IAP. Women who are screened and found to be negative are not the same as those who are not screened at all. The issue of potential harms that may be caused by antibiotics in labour is of equal concern for either a risk-based or a screening-based strategy. A UK study[vi] reported that similar percentages of women would be offered antibiotics in labour whether identified by screening late in pregnancy or using risk factors. The difference would be that with screening, a far higher proportion of those offered antibiotics would be carrying group B Strep than under the risk-based strategy.

122.	GBSS YES	Evidence of the on-going benefit of screening in continued reduced rates of early-onset group B Strep infection in other countries		The requirement for new evidence demonstrating the benefit of screening, while ignoring evidence of sustained benefit, is unacceptable. Countries that do screen and have data from before and after the introduction of screening report their incidence has dropped by up to 86%[x] [xi] [xii] [xiii] and it remains low[xiv]. This is further evidence of continued benefit. In addition, in the UK, Northwick Park Hospital undertook a highly successful and well-received pilot of GBS screening in 2014/5. The pilot found that screening resulted in an 80% reduction in cases of early-onset group B Strep infection. In addition to reducing the number of GBS infections at the Trust, the pilot also proved to be cost effective, providing estimated savings of £250,000 per annum, by reducing the numbers of sick babies who needed care. Data were supplied to the UK NSC for this review, but do not seem to have been included. In countries where screening was implemented many years ago, it would be surprising if anyone would be prepared to commission new research to establish its effectiveness. This is understandable; the epidemiological data show beyond any reasonable doubt that screening works. The UK NSC review fails to explain why the introduction of screening in the UK would not produce a similar fall in the rate of EOGBS infection to that seen in other countries when screening was introduced. Nor does it explain why the introduction of a risk-based strategy in the UK has been associated with a *rise* in the rate and incidence of early onset GBS disease, rather than a fall.
123.	GBSS YES	Studies on the accuracy of the 'gold standard' ECM test should keep to those where the correct		The review questions the accuracy of the 'gold standard' enriched culture medium (ECM) test, but majors on studies where the testing programme has been implemented poorly, with recommended procedures not followed.

		procedures were followed.		A positive ECM test result is 87% predictive of whether a woman will still be carrying GBS (and a negative ECM test result is 96% predictive of her still not carrying GBS) when done within 5 weeks of delivery[xv] and when procedures are correctly followed. Countries that have implemented screening have seen their incidence of EOGBS infections fall dramatically, whilst in the UK, where a risk-based strategy is used, the incidence has increased. Screening using the ECM test is highly effective at identifying women carrying group B Strep so that antibiotics can be offered to them in labour to reduce the risk of their baby developing EOGBS infection. Even in those studies (cited in the UK NSC report) , where an ECM testing programme was not well followed, the results were still more accurate at predicting GBS carriage than either the result of a standard NHS test or using the risk factors approach.

124.	GBSS YES	Methodology		This report has not been prepared to an adequate standard and therefore is an inadequate document on which to base conclusions. Current best practice for systematic reviews and meta-analyses is for a PRISMA 2009 checklist to be completed and many professional journals would refuse publication of a report without such a checklist being completed. Although some elements of the report conform to PRISMA requirements, this is not the case for many of the questions. Moreover, much of the report was done by 'rapid review' in which there was only a second reviewer in 20% of cases. How was the review carried out? There is either little or no information on who undertook the study, their qualifications, or their expertise in relation to GBS. How do we know if they have the ability to make judgements about the quality of the evidence? Who did the first-pass appraisal and abstract reviews? What were their qualifications? Here again, the same question: who were the two 'independent assessors', and what were their qualifications to judge the quality of the papers and gauge any potential bias therein? Indeed, how were the research papers selected? Who constructed the 'Overview'? What were their qualifications for doing this? Such information is a standard requirement for formal papers reporting the results of any systematic review. Who were the 'experts in the field' who reviewed and sanctioned the final list of included studies, papers and reviews (p13)? Why were articles limited to those in the English language? Antenatal GBS screening is undertaken in over 20 developed countries; but for many of those countries English is not the main language.

				Why were the unpublished data from the Northwick Park pilot of GBS screening excluded from the report when similarly unpublished data from MBRRACE and the BPSU were included? Why was formal quality assessment undertaken for some but not all questions? Why did the authors not assess studies looking at different detection methods (e.g. different oxides, swab transport media, or culture broths or agar, or using rapid-testing technology)? Why do some of the statements give a misleading impression in relation to the references quoted? For example, on page 41 the report says "Five studies presenting data on the variation between antenatal and intrapartum GBS carriage status were identified in the search (Appendix 19).[41,42,44,45,48] Four were prospective cohort studies[41,42,44,45] and one was a retrospective cohort study.[48] All five studies reported that GBS carriage status varied in pregnancy; between 10.9% (5/46)41 and 32.7% (48/147)42 of women with positive GBS culture during the third trimester had a negative GBS culture at term". We assessed the five papers referenced to check their relevance and reliability. Reference 41 (Kunze et al 2015[xvi]) reported that in their study, only 22.7% (144/633) underwent a fully guideline-compatible PS (prepartum screening) – 33.6% had only a vaginal swab. A selective broth medium for enrichment of GBS was used in just 29.2 % of cases (185/633). In 83.7 % (784/937) of the women who received intrapartum GBS screening, screening was performed within 7 days of delivery, i.e. not actually intrapartum. Reference 42 (Kwatra et al[xvii]) referred only to testing during pregnancy, over many weeks

				(20-25, 26-30, 31-35, 37+) and no samples for culture were taken intrapartum. Reference 44 (MacKay et al[xviii]) reported on only 61 subjects known to be positive on antenatal screening and who had swabs taken on admission in labour, and the authors reported that "the numbers in our study are relatively small and our observation should be confirmed by a larger trial". Reference 45 (Scasso et al[xix]) also included only 60 subjects. Reference 48 (Szymusik et al[xx]) described the methodology used very poorly; in particular, they referred only to 'culture based screening' at 35-37 weeks and a "culture-based swab collected for GBS colonization at the time of admission", with no information given about where the swabs were taken from (e.g. low vaginal or low vaginal/anorectal) or the culture procedure. Without such information the study is impossible to interpret. In summary, two of the references did not contain information relevant to the GBS carriage rate in labour, two were of very small numbers, and in one there was inadequate information about methodology. Taken together, they do not justify the drawing of any firm conclusions about the efficiency of screening to predict intrapartum carriage. Much more relevant is the study of Yancey et al (The accuracy of late antenatal screening cultures in predicting genital group B streptococcal colonization at delivery. Obstet Gynecol 1996; 88(5):811-815) who studied 826 women and who found a sensitivity of late antenatal screening for the prediction of GBS carriage during labour of 87% and a specificity of 96%. This paper is, however, not mentioned in the review, despite being one of the best-conducted studies ever performed on this topic.

125.	GBSS YES	*UK NSC Criterion 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 association between the risk or disease marker and serious or treatable disease.*	Report finding - Not Met	GBSS view: Met Early-onset GBS (EOGBS) infection is recognised as an important health problem, with good data on its frequency and severity. The epidemiology, incidence, prevalence and natural history of the condition are understood. In respect of meeting the requirement for understanding the *"development from latent to declared disease and/or there should be robust evidence about the association between the risk or disease marker and serious or treatable disease."* evidence shows that the mother carrying GBS around the time of birth is a prerequisite for a baby developing EOGBS infection. The UK NSC report points out that the ECM test, designed to detect GBS carriage, does not specifically predict which women will have babies who develop group B Strep infection. It does however fulfil the requirement of a screening test – it does detect which women are at raised risk of their baby developing EOGBS infection, which is precisely what the risk-based approach also aims to do (albeit much less reliably and without any evidence of efficacy, unlike the screening approach). There is already ample evidence that meets this criterion. Additional research would be helpful in aiding better understanding and to improve prediction, but we already have enough information from epidemiological studies to be confident that the screening approach works. GBSS has a significant number of families who support the charity as a result of their experiences of EOGBS, which have left their children with significant neurodisability. This is an important area of concern but takes up just ½ a page of the main report and two tables in the appendix. There is published research on outcomes of meningitis: 1. Libster et al[xxi] reported long-term outcomes for children surviving GBS meningitis revealing that 56% are functioning normally. The remainder sustained mild-to-moderate (25%) or

				severe (19%) neurodevelopmental impairment. 2. Okike et al[xxii]I reported that group B Streptococcus (GBS) caused 150/302 [50%]; incidence, 0.16/1000 live births; 95% CI, .13–18. Overall case fatality was 8% (25/329) and was higher for pneumococcal meningitis (5/26 [19%]) than GBS meningitis (7/135 [5%]; P = .04). Conclusions. The incidence of bacterial meningitis in young infants remains unchanged since the 1980s and is associated with significant case fatality. Prevention strategies and guidelines to improve the early management of cases should be prioritized. 3. Poor neurodevelopmental outcome has been demonstrated in ELBW infants, when infection is non-cerebral, and this has been linked to the effect of pro-inflammatory cytokines in the developing brain[xxiii]. 4. Infection, including EOGBS infection, has also been shown to be the underlying cause of neurological dysfunction in some term babies who present at birth with features of hypoxic-ischaemic encephalopathy, and such babies are at significant risk of neurodisability[xxiv]

126.	GBSS YES	UK NSC Criterion *2. All the cost-effective primary prevention interventions should have been implemented as far as practicable.*	Report finding - Not specifically mentioned.	GBSS view: Met (but why has the UK NSC report failed to address this criterion?) The UK introduced a risk-based prevention strategy in 2003, which was updated in 2012. The implementation of this strategy has been the subject of two RCOG audits. This strategy has failed; the rate of babies with EOGBS infection reported by BPSU *(excluding GBS stillbirths)* in the UK and Republic of Ireland increased from 0.48 to 0.54 per 1,000 live births between 2000/1[xxv] and 2014/5[Error! Bookmark not defined.], despite the introduction of the risk-based strategy in 2003 and its update in 2012. The latest study reported 4.7% of the babies sick with GBS infection died, though failed to mention how many survivors suffer long-term disabilities. Other research has reported that overall 7% of survivors suffering long-term disability, with up to 50% of survivors of group B Strep meningitis being disabled. The risk-based strategy has been tried, tested and has failed. As the latest BPSU report states, "New strategies for preventing GBS in this age group are urgently needed." Preventing early-onset GBS infection in babies will save money compared with treating the effects. Within the last ten years, four reports have been commissioned through the Government's Health Technology Assessment Programme[vi] [xxvi] [xxviixxviii] to establish how to combat preventable GBS infection in newborn babies. All have found screening to be more cost effective than risk-based prevention and recommended that steps to introduce screening should be explored. This research has been ignored and no explanation is given as to why. In NHS risk management, a "Fresh Eyes" approach is used to reduce risk of harm to patients. This encourages an unbiased and unblinkered view of any given situation. We suggest that the NSC may consider such an approach to evaluating the data in relation to GBS infection and the benefits of a screening programme.
127.	GBSS YES	UK NSC Criterion	Report finding -	GBSS view: Not applicable

		3. If the carriers of a mutation are identified as a result of screening the natural history of people with this status should be understood, including the psychological implications	Not specifically mentioned.	

128.	GBSS YES	UK NSC Criterion *4. There should be a simple, safe, precise and validated screening test*	Report finding - Not Met	GBSS view: Met The criterion asks for a simple, safe, precise and validated screening test (not a diagnostic test). Offering pregnant women reliable testing for GBS carriage is international best practice; rates of early onset GBS disease have fallen significantly in countries that offer routine antenatal testing to pregnant women. The international 'gold standard' test for GBS carriage – the ECM test – is a simple, safe and widely recognised as the 'gold standard'. It is a non-invasive test, with samples taken from the low-vagina and ano-rectum, usually at 35-37 weeks of pregnancy, which are then cultured in enhanced media in the laboratory. The USA introduced a screening strategy in 2002, and the rate of EOGBS infection almost halved between 2002[xxix] and 2014[xxx], falling from 0.40 to 0.24/1000 live births (down from 0.7 in 1997[xxxi]). When the ECM test was properly performed no more than 5 weeks before delivery, a negative result was 96% predictive of not carrying GBS at delivery and a positive result was 87% predictive of carrying GBS at delivery (Yancey et al 1996[xv]). The ECM test is validated – it is described by PHE's UK SMI B58. Since the ECM method is the only test method for detecting GBS carriage considered by the report, the authors should only have used studies that followed the guidelines for ECM testing, including swab sites, transport media, culture methods and timing. The authors included papers reporting on tests that either did not follow the ECM guidelines properly or where it was unclear (and frankly doubtful) that they did. Therefore, the reported PPV and NPV will be the absolute minimum values. This test has been used for decades in other developed countries, and is described in PHE's UK

				Standard B58 (effectively therefore the UK 'gold standard' for detecting GBS carriage). However, even including the studies with poor adherence to the recommended testing strategy, antenatal GBS screening is still a better predictor of GBS carriage in labour than risk factors. Most EOGBS disease occurs in term babies and, while babies born preterm account for a higher proportion of mortality, the major impact of overall morbidity is in babies born at term. Screening would significantly decrease EOGBS disease in term babies while neither screening nor the UK's risk-based strategy would reduce EOGBS infection in babies born preterm. It is unclear why the review document uses a data set different from that published relating to the recent BPSU study, nor why it includes in various places CDC risk factors as well as those described by NICE and RCOG. The report states that screening at 35-37 weeks is not a good predictor of GBS carriage in labour, yet this is a blinkered interpretation of the data, as described above. The report also highlights on more than one occasion how screening at 35-37 weeks would miss preterm births, which are at a higher risk of EOGBS and its most severe consequences. While this is true, the majority of EOGBS occurs in term babies, so the majority would benefit. There would also be an enhance benefit from enhanced healthcare worker and patient awareness of GBS, which may benefit preterm babies as well as term.

129.	GBSS YES	UK NSC Criterion *5. The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed.*	Report finding - Not specifically mentioned.	GBSS view: Met (but why has the UK NSC report failed to address this criterion?) The test is positive or negative. The UK carriage rate is recognised to be 20-25% of women[xxxii].
130.	GBSS YES	UK NSC Criterion *6. The test, from sample collection to delivery of results, should be acceptable to the target population.*	Report finding - Not specifically mentioned.	GBSS view: Met (but why has the UK NSC report failed to address this criterion?) Evidence from other countries shows that sample collection (both self-collected and collected by health professionals) through to the delivery of the results is acceptable[xxxiii], with high rates of take up of antenatal GBS testing. This has also been the case in the UK, most recently during the successful Northwick Park pilot of antenatal GBS screening, and in other research[xxxii]. Women are offered IAP when identified serendipitously as GBS carriers. If detecting GBS carriage changes management, then women should be offered the option to find out whether they are carrying GBS especially if they are choosing to deliver in a low risk, midwifery led setting. If they are not, this is inequitable.
131.	GBSS YES	UK NSC Criterion *7. There should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available*	Report finding - Not specifically mentioned.	GBSS view: Met (but why has the UK NSC report failed to address this criterion?) Existing UK guidelines already recommend offering women intrapartum IV antibiotics when GBS has been detected during the current pregnancy[xxxiv,xxxv].

		to those individuals.		

132.	GBSS YES	UK NSC Criterion *8. If the test is for a particular mutation or set of genetic variants, the method for their selection and the means through which these will be kept under review in the programme should be clearly set out.*	Report finding - Not specifically mentioned.	GBSS view: Not Applicable
133.	GBSS YES	UK NSC Criterion *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*	Report finding - Not met	GBSS view: Met Intravenous antibiotics given in labour to women where GBS has been detected during the current pregnancy are highly effective at reducing EOGBS infection. A population-based study from 2002[iv] found that the screening approach was 50% more effective than the risk-based approach at preventing early-onset GBS infection. Research shows that the incidence of EOGBS infection falls substantially after the introduction of screening, eg in the US by over 80%[xxxvi], in Spain by 86%[xi], in Australia by 82%[xxxvii] and in France by 71%[x]. In these countries, the rates of EOGBS infection are significantly lower than those in the UK. With the current risk based approach, 35% of babies with EOGBS infection have no known risk factors[vii]**Error! Bookmark not defined.**. While the UK NSC review focusses heavily on *potential* harms, the effect or incidence of which are not clear, it focusses less on the *known* benefits; preventing potentially life-threatening infection in

		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.		newborn babies, and all that comes with those infections. Moreover, there are detailed accounts of studies of the effects of the antenatal administration for long periods (up to ten days in the Oracle studies) of broad spectrum/multiple antibiotics. Such studies are of no direct relevance to the administration of penicillin limited to the duration of labour, and create a misleading impression of potential harms. Current NICE guidelines (2011)[xxxviii] on the administration of broad-spectrum antibiotics prior to Caesarean section (incidence currently 27% in the UK) state specifically "no effect on the baby has been demonstrated".

134.	GBSS YES	UK NSC Criterion *10. There should be agreed evidence based policies covering which individuals should be offered interventions and the appropriate intervention to be offered.*	Report finding - Not specifically mentioned.	GBSS view: Met (but why has the UK NSC report failed to address this criterion?) Intravenous antibiotics are already given in labour to women where GBS has been detected during the current pregnancy and this is recognised as being effective at reducing EOGBS infection. See RCOG's Greentop Guideline No 36[xxxv] and NICE CG149[xxxiv].
135.	GBSS YES	UK NSC Criterion *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*	Report finding - Not met	GBSS view: Not Met – and not likely to be The review highlights the lack of RCT evidence but fails to point out that such studies have been proposed for the UK but never funded. This seems a convenient and perennial excuse to do nothing. The original introduction of penicillin was implemented without the benefit of a randomised controlled trial. Evidence from lower quality research in other countries has reported a 71-86% fall in the incidence of EOGBS disease following the introduction of screening. This level of evidence is considered by many to obviate the need for a randomised controlled trial, although we would support such a trial were it to be funded.

		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.		

136.	GBSS YES	UK NSC Criterion *12. There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/ intervention) is clinically, socially and ethically acceptable to health professionals and the public.*	Report finding - Not specifically mentioned.	GBSS view: Met (but why has the UK NSC report failed to address this criterion?) Evidence of the acceptability of screening in other countries, and in the UK studies that involved screening, demonstrates this[vi,xxxiii,xxxix],as does the fact that none of the countries that has introduced antenatal screening has subsequently abandoned it in favour of a risk-based strategy. Bounty has conducted 3 surveys asking women in early pregnancy through to their youngest child being 12 months or less their views about antenatal screening for GBS carriage, which demonstrated that screening was desired and more than simply acceptable[ix,xl,xli]. A petition calling on the Secretary of State for Health, Jeremy Hunt MP, the Chief Medical Officer for England, Prof Dame Sally Davies and the Chief Executive of Public Health England, Dr Duncan Selbie to ensure that information about GBS and screening for GBS carriage are offered to all pregnant women has over 260,000 signatures. Clearly over 260,000 people believe the test is acceptable.
137.	GBSS YES	UK NSC Criterion *13. The benefit gained by individuals from the screening programme should outweigh any harms for example from over-diagnosis, overtreatment, false positives, false reassurance, uncertain findings and*	Report finding - Not specifically mentioned.	GBSS view: Met (but why has the UK NSC report failed to address this criterion?) There is no evidence of significant harm in studies from countries that have adopted screening, for example, recent studies have shown no concomitant increase in other neonatal infections consequent on a reduction in early onset GBS disease[xlii]. There is general acceptance that antibiotics should be offered in labour when GBS carriage is identified during the current pregnancy, because it is recognised that intrapartum antibiotic prophylaxis is highly effective at reducing EOGBS infection. Screening facilitates accurate detection of GBS carriage, and therefore, the ability to optimise the use of antibiotics; which addresses all the challenges cited in the criterion - over-diagnosis, overtreatment, false positives, false reassurance,

		complications.		uncertain findings and complication. Surprisingly, the review gives significant emphasis to the side effects of erythromycin, a broad-spectrum antibiotic, given orally in low dose, and not one of the recommended antibiotics for intrapartum antimicrobial prophylaxis. These side effects cannot be extrapolated either to penicillin G (the first-line drug recommended), or to clindamycin. Despite the review not mentioning them, harms from potentially preventable EOGBS infection are wider than death and disability of the baby. They also include harms caused to the baby's immediate and sometimes extended family both during the acute phase, and in the years following, psychologically and emotionally as well as physically. For example: • Harms during the inpatient treatment during the baby's early hours, days and weeks of life, including emotional, psychological and financial costs • Harms caused by uncertainty around what, if any, damage the baby has sustained from his/her EOGBS infection, including costs (emotional, psychological and financial costs) of follow up consultations and tests • Harms caused by a baby dying from EOGBS infection (emotional, psychological and financial costs) • The effect all or any of the above have on the family during subsequent pregnancies In addition, there are costs associated with the burden of additional care for the family both during the acute period around birth, diagnosis and treatment of infection, and of ongoing follow up/treatment, or around and following a baby's death from potentially avoidable GBS infection. There are also costs associated with the additional support provided to families in subsequent pregnancies, plus costs to society of avoidable deaths and disability. These costs do not seem to have been taken into account and need to be set again the potential harms caused by screening, which are examined in full in the document. No evaluation of the acceptability to parents and/or health professionals of the different potential harms (those of screening and those of potentially avoidable EOGBS infection) seems to have been

				part of the review or indeed considered. Why not? As an obstetrician told us recently, "*I don't want to have to counsel any more bereaved parents when a cheap test and even cheaper antibiotics would have saved their baby.*"

138.	GBSS YES	UK NSC Criterion *14. The opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (value for money). Assessment against this criteria should have regard to evidence from cost benefit*	Report finding – Not met.	GBSS view: Met Previous cost-benefit analyses have demonstrated that antenatal screening is cost-effective and more cost effective than the risk-based strategy[xxvi,xxvii,**Error! Bookmark not defined.**,xxviii]. This report is seeking much more evidence than has been required for other screening decisions, for less common conditions, which have been approved based on less evidence. For example • PKU (prevalence 1 in 10,000) – *'there are only a few well conducted economic evaluations but the evidence suggests that screening all babies for PKU makes sense financially as well as for health and social reasons'* (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/390977/Health_Professional_Handbook_2012_v1.0_December_2012.pdf) • MSUD (prevalence 1 in 116,000) – https://legacyscreening.phe.org.uk/msud - pilot study of these new disorders to screen for 'A pilot should be undertaken to address gaps in our knowledge relevant to the expansion of newborn screening in the UK'. Study in 6 centres. 437,187 samples were analysed and 30 screen positive cases identified. One aim was to 'Help define the costs of screening and undertake cost effectiveness assessment'. This seemed to involve a questionnaire *'which asks parents to give their maximum willingness to pay for an extension in a screening programme'* (http://link.springer.com/article/10.1007/s10545-011-9354-0). *"The mean willingness to pay for the expanded programme was £178 compared to £219 for the hypothetical expanded programme without false positives ($p > 0.05$)".* This compares with the ECM test to detect GBS carriage costed at £11 per pregnancy if rolled out on the NHS.
139.	GBSS YES	UK NSC Criterion *15. Clinical management of the condition and patient outcomes should be optimised in all health care*	Report finding - Not specifically mentioned.	GBSS view: Could easily be met (but why has the UK NSC report failed to address this criterion?) The clinical management that is required is IAP to be offered to mothers who test positive. This is the same treatment that is already in use under the risk-based approach - the difference is that screening will target the antibiotics at women whose babies are most likely to be at risk of developing EOGBS infection, not at women whose babies are unlikely to be affected. There are existing

		providers prior to participation in a screening programme.		guidelines on administering this medication, which would require minimal, if any, updating. Likewise there is already a UK standard for detecting GBS carriage (PHE's UK SMI B58[ii]). There is also existing guidance for what treatment should be given to babies with suspected or proven EOGBS infection (NICE CG149).

140.	GBSS YES	UK NSC Criterion 16. All other options for managing the condition should have been considered (such as improving treatment or providing other services), to ensure that no more cost effective intervention could be introduced or current interventions increased within the resources available.	Report finding - Not specifically mentioned.	GBSS view: Met (but why has the UK NSC report failed to address this criterion?) There is existing guidance on intrapartum antibiotic prophylaxis and on managing EOGBS infection in babies - the RCOG's Greentop guideline No 36[xxxv] on early onset GBS infection was updated in 2012, and NICE CG149 Antibiotics for Neonatal Infection guideline[xxxiv] was also published in 2012, which describe both. Since then, the RCOG has undertaken an audit of UK maternity units and published two reports[i,xliii], which found that the risk factors and indicators for IAP were well embedded in their GBS prevention policies. Despite this, the rate of EOGBS infection continues to increase in the UK.
141.	GBSS YES	UK NSC Criterion *17. There should be a plan for managing and monitoring the screening programme and an agreed set of quality assurance standards.*	Report finding - Not specifically mentioned.	GBSS view: Could Easily be Met (but why has the UK NSC report failed to address this criterion?) The plans for managing and monitoring ECM testing, due for implementation from 1 January 2014 with a U-turn in the decision to implement in late December 2013, could be updated. There is already the PHE's UK SMI B58 for the ECM test process, and IAP is already offered for GBS carriage. These, plus experience of managing and monitoring other antenatal screening programmes, should enable this criterion to be readily met.
142.	GBSS	UK NSC Criterion	Report finding -	GBSS view: Not Addressed (but why has the UK NSC report failed to address this criterion?)

	YES	*18. Adequate staffing and facilities for testing, diagnosis, treatment and programme management should be available prior to the commencement of the screening programme.*	Not specifically mentioned.	Plans made in advance of the expected introduction of ECM testing from 1 January 2014 could be revived, and speed the assessment of requirements for this. In addition, lessons could be learned from maternity units that currently offer ECM testing, plus the experience from Northwick Park Hospital, which undertook a highly successful and well-received pilot of GBS screening in 2014/5.

143.	GBSS YES	UK NSC Criterion *19. Evidence-based information, explaining the purpose and potential consequences of screening, investigation and preventative intervention or treatment, should be made available to potential participants to assist them in making an informed choice.*	Report finding - Not specifically mentioned.	GBSS view: Not Addressed (but why has the UK NSC report failed to address this criterion?) Plans made in advance of the expected introduction of ECM testing from 1 January 2014 could be revived, and speed the assessment of requirements for this. In addition, lessons could be learned from maternity units that currently offer ECM testing, and the experience of Northwick Park Hospital, which undertook a highly successful and well-received pilot of GBS screening in 2014/5, as mentioned above. GBSS already produces high quality patient-information leaflets that are widely used in NHS maternity units and which are undergoing certification for The Information Standard. In addition, the RCOG also provides information, both through its GTG and through the related patient information leaflets.
144.	GBSS YES	UK NSC Criterion 20. *Public pressure for widening the eligibility criteria for reducing the screening interval, and for increasing the sensitivity of the testing process, should be anticipated. Decisions about these parameters should be scientifically justifiable to the*	Report finding - Not specifically mentioned.	GBSS view: Met (but why has the UK NSC report failed to address this criterion?) There are clear parameters for antenatal screening for GBS carriage in other countries, which are scientifically justifiable and readily importable to the UK for the same reasons they were approved in those countries. In addition, these countries have not seen public pressure for widening the eligibility criteria. Public pressure is for informing pregnant women about group B Strep and offering them testing for group B Strep during their pregnancy, as the recent petition (www.change.org/GBS) calling for this, and signed by over 259,000 people attests. Research to improve the sensitivity and specificity of testing would be welcomed. However, until a

		public.		better test is developed, evidence shows testing using the ECM test is better than the current risk-based prevention strategy.

145.	xxxx xxxx ?			To whom it may concern: Our beautiful baby xxxx xxxx xxxx xxxx was born on xxxx xxxx. 17 hours after birth xxxx xxxx was taken to the neonatal unit where xxxx xxxx stayed for 5.5 weeks after contracting GBS meningitis and septicaemia. xxxx xxxx was very very poorly and we were told xxxx xxxx may not survive this infection. xxxx xxxx daddy and I were absolutely heartbroken, the joy of becoming parents was shattered as we wrapped our heads around what was happening. xxxx xxxx was immediately treated for GBS infection and xxxx xxxx first (out of 4) lumbar puncture results confirmed it. xxxx xxxx was connected to so many tubes, cables and machines, it was terrifying. We sat by xxxx xxxx incubator day in and day out, just wishing for a miracle. On day 3 xxxx xxxx began to demand feed and we were allowed to hold xxxx xxxx and change xxxx xxxx nappy etc. xxxx xxxx moved from high dependency to special care within the week and continued on xxxx xxxx three weeks of antibiotics. More lumbar punctures and blood cultures were done and the results were good but not good enough so xxxx xxxx had a further 2 weeks on a new, stronger antibiotic. After 5 weeks it was decided xxxx xxxx would stop xxxx xxxx meds and the doctors would observe xxxx xxxx. 48 hours later we were allowed home. 5.5 weeks, 38 days xxxx xxxx spent in hospital before we got xxxx xxxx home, I didn't leave xxxx xxxx side. I stayed in the hospital for the 5 and a half weeks xxxx xxxx was in there, I refused to leave xxxx xxxx. xxxx xxxx had an MRI scan and it showed xxxx xxxx had a small brain haemorrhage and xxxx xxxx has spots of grey damage to xxxx xxxx brain. Only time will tell if this infection has left a long lasting effect on our xxxx xxxx development but so far xxxx xxxx is passing all of his developmental checks.This infection almost took the life of our little xxxx xxxx but xxxx xxxx is a little warrior and xxxx xxxx fought so hard for xxxx xxxx place on this earth. We got to take xxxx xxxx home on xxxx xxxx. xxxx xxxx is now xxxx xxxx months old and xxxx xxxx is a picture of health, xxxx xxxx so happy, calm and well natured. What xxxx xxxx has been through in xxxx xxxx short little life is horrific but it amazes me how strong our baby has been throughout this whole living nightmare. We have a long way to go but we were just so grateful to be able to bring xxxx xxxx home, sadly too many parents don't get this chance. Something needs to change, tests need to become routine and babies lives need to be saved. I can't understand how people think it's ok to leave it to chance! My xxxx xxxx went though so much unnecessary pain and suffering that was completely avoidable and I will never be able to understand why xxxx xxxx was allowed to go through that pain. If screening for gbs does not become routine in antenatal care then please PLEASE can health professionals at least inform pregnant women about gbs, give out proper information, educate them so they have the knowledge about it and can make a choice to a home test or ask for a test. I had never heard of group b strep until it was too late and I will never forgive the government and nhs for allowing my xxxx xxxx to go

				through this. Why guess when you can test?? Looking at **xxxx xxxx** photos you can see the pain in **xxxx xxxx** face, **xxxx xxxx** suffered so much but **xxxx xxxx** a healthy **xxxx xxxx** month old baby now. Please don't let anymore babies go through this. We can't thank **xxxx xxxx** neonatal unit enough. They saved my **xxxx xxxx** life 🖤🖤🖤

146.	Yvonne Owen YES			As a reflexologist treating many pregnant woman I am amazed at how few women have even heard Group B Strep, let alone know how to test for it. I believe that all women should be given information during their pregnancy about the condition and offered testing as routine at weeks 35-37. This is a preventable condition and to ignore it as not important enough to inform women about is criminal. Those people who were not informed and whose babies have been seriously ill or have died are being let down by the NHS.
147.	Rachel Plunkett YES		Clinical Screening Program- Criteria Not Met	Throughout the document, Criteria Not Met is worded. Not because that there is evidence proving that a screening program would be inefficient but because you have found things wrong with the rials that have occurred. What about the recent trial in NHS North West London who found an 80% reduction in infants poorly with GBS disease in 18 months. http://www.lnwh.nhs.uk/about-us/news-and-media/pressreleases/pilot-shows-that-screening-mothers-for-group-bstrep-gbs-saves-babies/
148.	**xxxx xxxx**			I am not from any organisation and the official comments form baffled me . However, I feel I still have a right to comment on the decision for Strep B screening. My son's girlfriend got the infection last **xxxx xxxx** and it caused her waters to break 15 weeks early. Their baby survived, against all odds (including having caught the infection from his mother). But what followed was 5 months of trauma: stays in 3 hospitals across **xxxx xxxx**, several surgical procedures to fit a permanent shunt in **xxxx xxxx** head that finally worked, emergency laser treatment on **xxxx xxxx** eyes, chest infections, suspected pneumonia.....constant de-sats etc etc. An emotional rollercoaster that we would not wish on anyone!!!!!! All of this could and should have been prevented by a simple screening process....after all: prevention is better than cure, and in many cases of Strep B, there is no cure. Please please please don't sweep this under the carpet any longer. Take action and stop these life-threatening complications (in the lesser cases), and deaths (in the worst).
149.	**xxxx xxxx**			Screening is important. I had Gbs as did my son. I wasn't screened. I had antibiotics too late. my son wasn't screened and ended up in scuba with sepsis. he is 3 now and has gdd and possibly autism. this could of been prevented!

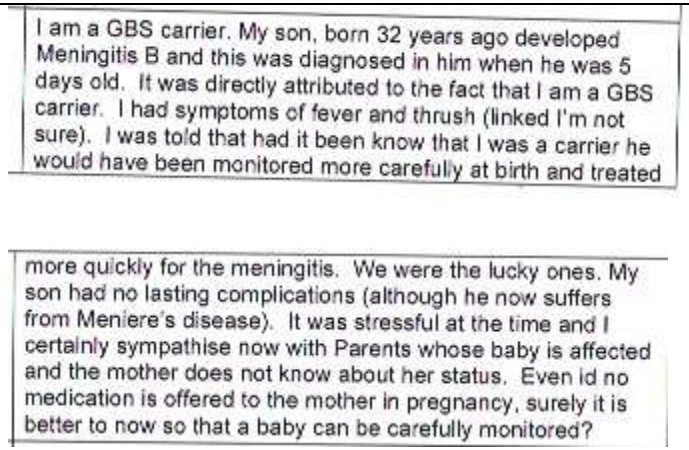
150.	**xxxx xxxx**			I believe and support all that needs to be done to educate and treat women with Group B strep. I lost my son **xxxx xxxx** in 2008, and I was informed after the birth about Group B strep. I had never heard anything about it. If I had known I would of asked for a swab. **xxxx xxxx** lived for 3 weeks, then lost the fight. I now encourage other women about Group B Strep and encourage them to request the test from their Midwives or G.P. It's amazing how many have come back to say they are positive and they had never heard of it before. All women should be made aware of Group B Strep, and all women should be tested and treating as according to National Guidelines.
151.	**xxxx xxxx**			I have read your recommendation that screening for GBS should not be offered to all pregnant women. My daughter was stillborn in **xxxx xxxx** 2007 due to GBS so I naturally disagree with your findings. I also don't believe it is as rare as your report suggests. There was nothing I could do for my daughter but I discussed what happened with pregnant woman with whom I work and without exception each one has been tested and a high number have been positive which is not a surprise given that one third of woman who are thinking about having children would test positive for GBS. I write to you not in hope or expectation that you will magically change your recommendation – although I wish you would – but to ask this. If you will not provide screening will you please do more to make pregnant woman more aware of the existence of GBS are tell them how they can get tested privately. I think better information of what it is, what it can do and what you can do about it would be wonderful. My wife and I were have never heard of GBS when she was pregnant. No-one talked about it and there were no leaflets in the pregnancy pack from the mid wife. I first heard about it when told it had been the cause of the death of my daughter. That cannot be right. Please consider my request.
152.	**xxxx xxxx** NO		Strep B not being routinely tested for	My son died from strep b related infection, it had actually passed through systematically and he died 5 days before he was due. This test is invaluable, this happened in 2009 and I am actually frightened to try again as I dont know whether or not I can trust the NHS to look after me and my unborn child enough, just for the sake of around thirty pounds. What price for a life? Although I was tested at the discretion of my wonderful doctor, I had no idea about Strep B, the risks and whether I could be tested. I was treated with antibiotics but it was too late he was already sick as it had somehow got into my womb. I have been promised a test in future pregnancy, and to be induced at 39 weeks, sorry, its not enough, for my son, that was too late, life is too precious to take the gamble. This test

				must be routinely available and more information given to expectant mothers.

153.	Robert Plumb YES			We are far beyond the point when the NSC can say the best approach is to wait for more evidence. There is plenty of evidence from other countries. Denying pregnant women here the best treatment in order to gather more UK-specific evidence would be unethical. Waiting for a vaccine could mean waiting forever. Using penicillin won't add to antibiotic resistance. The risk of anaphylactic shock is negligible. Studies have shown that screening would result in a net cost savings. Time to act.
154.	**xxxx xxxx**			Dear Evidence Team I am writing to you as the former **xxxx xxxx** of **xxxx xxxx** from **xxxx xxxx** and in my current capacity as the **xxxx xxxx** of a company, **xxxx xxxx**, which I set up to help charities that we are especially passionate about, to grow. In **xxxx xxxx**, I stood outside 10 Downing Street with a placard "Stop the Stillbirth Scandal Campaign" backed by 22,652 signatures and by the Under Secretary of State for Public Health. Thanks to a number of factors, Sands helped to bring about a sea-change in the attitude and approach to stillbirth among policy makers and government officials.Those factors included:- the Sands Reports "Saving Babies' Lives" and "Preventing Babies' Deaths what needs to be done"; the Why? 17 Campaign; the Lancet Report published in April 2011 which placed the UK's stillbirth rates as 33rd out of 35 similar high income countries; the work of the International Stillbirth Alliance in highlighting that countries such as the Netherlands, Norway and Australia had in stark contrast to the UK significantly reduced stillbirth numbers;

				the growing conviction among more and more health professionals that many stillbirths were avoidable; the powerful testimonials of hundreds of bereaved parents devastated by the death of their babies. As a result, all four UK Governments, with the Scottish Government in particular playing a leading role, completely changed their attitude and adopted a collaborative, proactive and committed approach to reducing stillbirths. In my personal view, the refusal to offer all pregnant women routine antenatal screening for group B Strep is no less a scandal and reflects a similar reluctance to take on board the views of many professionals, parents and the successful experiences of other countries who have introduced the offer of a sensitive test for GBS as a routine part of antenatal care. I believe the UK National Screening Committee needs to clearly acknowledge that:- • many countries such as the USA, Canada, France and Germany who routinely offer antenatal GBS testing have seen significant reductions in the number of GBS infections in newborn babies • in contrast, the rate and number of potentially preventable early-onset group B Strep infections have increased, not fallen • the risk-based prevention strategy introduced in 2003 is therefore clearly ineffective • pregnant women have a fundamental right to have information about GBS and to make an informed choice about their care.

				I strongly urge the UKNSC to recommend that all women are given the choice of being tested for GBS carriage at 35-37 weeks of pregnancy and that in doing so, they will play a significant part in helping put an end to the devastating impact on families when one baby a week dies from group B Strep infection, and when one baby every fortnight survives the infection with long-term disabilities - physical, mental or both. Thank you.

155.	xxxx xxxx			I am writing to urge you to change your minds and to please offer Group B strep screening for all pregnancies. This would save the lives of children and prevent people from being disabled with all the costs to society associated with that. As such I believe that it is highly cost effective.
156.	xxxx xxxx		Group B Streptococcus	I strongly agree that all pregnant women should be screened for Group B Streptococcus, as is done in other advanced countries. When one considers the cost of looking after a disabled person for his or her lifetime, universal screening for Group B Streprococcus reveals itself as cost effective.
157.	xxxx xxxx			I would like to submit my opinion that all pregnant woman in the U.K. should be screened for Group B Strep. The recommendation that they should not be screened is wrong.
158.	xxxx xxxx			
159.	xxxx xxxx			Pregnant ladies should be screened for this test ,I have lost a little boy myself and understand the pain and trauma a family go through when losing a child I know of people also who have lost children to this if they had only been screened and given antibiotics this death and trauma would not of happened ,the people who are against this test ,have they lost there own babies???

160.	**xxxx xxxx**			Good Evening, I would like to lodge my comments in relation to the overall 'findings' of this report. I strongly disagree that all pregnant women should not be offered a swab test and if positive, antibiotics in labour for the following reasons: The UK has followed its risk-based approach to prevent group B Strep infections in newborn babies since 2003. Yet both the rate and number of potentially preventable early-onset group B Strep infections (developing in babies aged 0-6 days) have increased, not fallen. Group B Strep remains the most common cause of life-threatening infection in newborn babies and the leading cause of meningitis in babies under three months. On average in the UK: • One baby a day develops group B Strep infection • One baby a week dies from group B Strep infection • One baby a fortnight survives the infection with long-term disabilities – physical, mental, or both If the recommendation that a screening programme to test pregnant women for GBS carriage should not be introduced is accepted by the UK National Screening Committee, many babies will suffer preventable GBS infection – many women carrying GBS won't be identified, and will not receive safe, cheap and effective treatment during labour to prevent early-onset GBS infection in their baby. Yet were these babies born in many other developed countries, including the USA, France, Canada, Germany or Poland, it is almost certain that they and their families would be spared the trauma GBS brings. I am currently 32 weeks pregnant and have tested positive for GBS in my previous pregnancy, that time I was given antibiotics in labour and both myself and my baby were healthy and well. This time I have been told that I will not be offered antibiotics in labour. The knowledge that this now puts my baby in danger of a life threatening infection, that is entirely preventable through antibiotics in labour is terrifying and causing me anxiety and stress. I recommend that all pregnant women be offered a swab test at 35-37 wks and antibiotics in labour.

				Research should continue into even better methods of safeguarding the health and wellbeing of mother and baby.

161.	**xxxx xxxx**			My Baby died of Group B streptococcus infection. He was my first baby. I was 20 years old. It was devastating. Please look carefully at the information submitted by group B Strep Support. Please, at least give women the choice over this. One baby dying each week due to Strep B is unacceptable
162.	**xxxx xxxx**			I believe strep b should be routinely tested in pregnancy for these reasons At 16 weeks pregnant i was taken to hospital due to bleeding.. i was examined and had swaps taken,a few days later i recieved a call from my midwife telling me my results was in amd that i had thrush and strep b, and was advised to do some research and.at my 21 week appointment talk to my midwife regarding whether i wanted the antibiotics or not.. My daughter was born full term (induction) due to my heart going a bit fast and previous history of bleeding throughout pregnancy. I was givin the 4hr antibiotics and had about 4 lots of antibiotics after 3 sweeps .. 2 pessary tablets,they then opted to break my waters.. I had a water birth .. my daughter was born. I was due more antibiotics 20mins before i had but was in full blown labour My daughter was born but i noticed her breathing a bit rapidly,i shared my concerns with the baby doctor who took her straight up to the **xxxx xxxx** unit and put a canula in for antibiotics and also done some blood test and x rays When her xrays come back it showed lots of streak marks going down her chest (which was strep b) .. her bloods come back with her infectious levels being pretty high. I got told that if i had taken my daughter home she would of properly not of made it back in time to the hospital ..

				5 days later with antibiotics working she was aloud home.. every month since then she has either been to the doctors or hospital with chest problems wheeziness which develops to bronchiolitis. She is now **xxxx xxxx** months old and still suffers with these episodes. I plead with you to make strep b routinely tested i could of lost my baby if i wasnt aware that i was a carrier of strep b ... no parent should go through the trauma of watching there baby be so ill and be told that we was extremly luckly we noticed her breathing wasnt right. Let alone the agonising pain other parents go through not knowing they have strep b and watching there perfect bundle of joy sleep forever in there arms A moment thats ment to be they most remarkable day of your life bringing into the world your perfect baby,turning into the most horrendous day watching that baby slip away.. A simple test for pregnant women to diagnosis whether there a carrier or not can help set the ball rolling with the appropriate after care for that baby.. doctors would be more aware that , that baby needs a vigilant eye kept on them incase they show the symptoms of step b. At least that way they could get the care needed

163.	Carolyn Lyle YES			Section and / or page number Text or issue to which comments relate Comment Please use a new row for each comment and add extra rows as required. This is a cheap piece of preventive medicine that saves lives and stops needless heartbreak. Measure the cost of strep B testing against the cost of treating unnecessarily bereaved parents of babies who die and the wider costs to society flowing from adult depression and then factor in the cost of caring for the physical problems and learning difficulties of people who carry lifelong burdens after surviving strep B because they were permanently damaged by the disease. Health and happiness are the good value option. Other countries think so.
164.	**xxxx xxxx**			My daughter died on **xxxx xxxx** she was a hour old, just a hour old, the hospital knew I had strep b and my consultant refused to give me the antibiotics that was needed to save her life, I know have to live with this for the rest of my life, please don't let babies die in vain
165.	**xxxx xxxx**			As a carrier of Group B Strep, a pregnant woman and as a mother who last year lost a baby to Group B Strep I feel my experience of this is more than most. I would therefore like to have a contribution to the consultation for the screening programme. I will begin with a bit of background, I am a healthy **xxxx xxxx** year old female who was classed as a 'low risk' mother, I was encouraged to have my **xxxx xxxx** at the local MLU which we didn't think was fit for purpose (once condemned) and how run down the place was. I wanted to be safe and I opted for a home birth as, 1 I did not feel happy in this place and, 2 I thought I would have better care at home! This was encouraged, I was after all low risk! I was going to get a visit within 24 hours and all would be lovely, a happy, healthy, relaxing homebirth, that is after all what we are promoting these days! This wasn't the case. My **xxxx xxxx** was born, healthy enough, at **xxxx xxxx** and that was it, I was left, with nothing! I would get a visit later that day. **xxxx xxxx** was not interested in feeding, **xxxx xxxx** was just sleepy and a little wingey at times. I didn't get a visit that day, just phone calls, I raised my concerns about feeding, but told that was normal, keep trying and give skin to skin. Which is what I did, still no interest. My concerns grew, in the early hours of the morning my **xxxx xxxx** began to bring up brown

				sticky mucous, I immediately called the local, MLU as directed to do if I had concerns, again these were dismissed as normal. They did not enquire as to any other symptoms or the health of my baby but I was told I would get a visit first thing. At 6am my **xxxx xxxx** began, what I now know as grunting, my baby was dying and I didn't even know it, at 9am I got a telephone call, not the visit I was promised and was again reassured all would be fine and I would get a visit in the early afternoon. At **xxxx xxxx** after I had just redressed my little **xxxx xxxx** **xxxx xxxx** stopped breathing..... nothing could be done to save **xxxx xxxx**, no matter how hard emergency services tried. We had to cradle our newborn baby as **xxxx xxxx** died in our arms only **xxxx xxxx** hours old. The doctors and nurses cried with us. Not knowing what the hell had happened! 3 days later results came back showing **xxxx xxxx** had died of meningitis, pneumonia, sepsis all caused by GROUP B STREP. What makes this worse, **xxxx xxxx** should and could have still been here and up until the early hours of the morning, my **xxxx xxxx** could have been saved. FAILINGS The hospital failed to provide us with any information of signs and symptoms of infection, they failed to recognize themselves the symptoms of a poorly baby and the whole system failed to provide me with information on what Group B Strep is throughout my whole pregnancy! I wasn't a low risk mother, I was a high risk mother but nobody knew that and I was allowed to make a decision to have a homebirth when I was not fully informed of the dangers which put my **xxxx xxxx** life in danger! I have to live with that FOREVER. If I had have known about Group B strep, I'd have happily paid for my own test. Even if I knew what it was I would have been able to research it myself, look for the signs and symptoms but nothing, even the 'professionals' don't have a clue about it! How can we look after our own babies and spot the signs and symptoms if they are not provided to us? How can we seek help for a sick baby when the professionals can't/don't spot the symptoms? Why are we promoting home births/MLU births when training on infections in babies is lacking? WHY THE SILENCE? Why am I called a scaremongerer

				when I try and raise awareness? Why cant we have more information to make our own decisions? WHY IS MY BABY NEEDLESSLY DEAD? If, hypothetically, I had tested positive for Group B Strep and had had my baby in a consultant unit (even if I didn't have antibiotics) with proper monitoring, it is likely that **xxxx xxxx** would still be here so if the antibiotic use is so pivotal for this screening being declined, why couldn't you screen with proper monitoring and proper information. Lives would still be saved and so would money in the long run. We are still years away from getting a vaccine for Group B Strep, what is going to be put into place in the meantime? More training for health professionals? More resources for pregnant women and yes, I know there is information out there but how can you look for something you don't know exists? The UK is one of the worst in developed countries for still birth and neonatal death rates, there are things that can be done and yet we ignore them? The health service is in crisis, they want more focus on midwife led care in the community but don't equip people with the expertise to deal with sick babies, that or care is not provided properly. The relationships and cultures we see today in women and children's services are sick, a real battle between midwives and drs in a headlock over who is the expert! If this is continually left unaddressed then more mothers and their babies will continue to die, more negligence claims will be filed and more Morcombe Bays uncovered. This issue needs more though, more resources and research before it is thrown out again with a death sentence left on unsuspecting babies and their families. Lives are lost and lives are ruined and I get left to speak out for a child who will never get the chance to speak out herself!

166.	**xxxx xxxx** YES			I would like to ask you all, how much money is your child's life worth? £11? More? My 17 day old son **xxxx xxxx** went limp in my arms, we were helpless as we watched our **xxxx xxxx** have a lumbar puncture and have to have **xxxx xxxx** drip placed again and again as **xxxx xxxx** tiny veins kept collapsing. Our **xxxx xxxx** deserved better than this, **xxxx xxxx** was failed. Give our babies a chance.
167.	**xxxx xxxx** YES			Our baby contracted Group B Strep when he was born, after 14 hours of him being born he started 'grunting' he received antibiotics straight away. He was taken to neonatal where he received expert care. He had bloods done and Just over a day later he had a lumbar puncture. Just before the lumbar puncture we were told that he had group b Strep. To say we were devastated is an understatement as I previously knew of group b Strep and had asked my antenatal team if I could be swabbed for this infection and was told 'it wasn't necessary'. My baby had a 1 in 10 chance of dying – they were the statistics that we were left with! He had a chance of brain damage! But instead he fought the infection and is fit and healthy. The statistics are that 1in 4 women carry group b Strep in their gut/vagina. 1 in 2000 babies contract the infection. 1 in 10 babies DIE!! Why on earth can EVERY PREGNANT WOMAN not be screened for group b Strep at 38 weeks and be given antibiotics during labour to stop that baby contracting this awful infection?! It costs pennies to treat with antibiotics. Surely the cost of screening ALL pregnant women is cheaper than 1 in 2000 babies contracting this infection and using neonatal resources for at least 7 days while they at the very least receive a course of antibiotics, a lumbar puncture, blood tests, nurses wages, consultants wages, midwives wages and the overall cost of a weeks stay in an NHS hospital??!!!!!!!! And this is the very least!!! We were lucky! Our baby recovered. 1 in 10 DIE!!! Please do something – please cut the cost of a couple losing their baby, or a baby being permanently brain damaged for the REST of their lives, NO PARENT NEEDS TO GO THROUGH THIS. Most of the modern world screens for this infection, surely we have to too. Please please screen pregnant women for group b Strep – IT IS NECESSARY!
168.	**xxxx xxxx**			The UK NSC's recommendation against routine screening for group B Strep is hugely disappointing and I cannot believe a country such as UK is not doing more to prevent many families suffering the consequences of GBS. Every year, hundreds of newborn babies suffer illness, disability and even death due to group B Strep. My baby suffered the ultimate price, his life. Born a perfectly healthy baby, he caught this infection and within 18 hours he was fighting for his life. As parents we had to watch him suffer and fight with every ounce of being, but ultimately his life was taken away due to an entirely preventable

				infection. How you can recommend that testing is not worth it, I will ever understand. This recommendation would mean future babies will suffer needlessly from infections which could have and should have been prevented – some of these precious babies will die, others will survive with life-long disabilities. Many more families will suffer the lifelong grief we are currently enduring. I cannot understand why the research and evidence from other countries where screening programmes have led to huge reductions in group B Strep infection, is not enough for the NSC, is beyond me. What more would be needed for this to be taken seriously? GBS infections in babies in the UK are rising – we need to be doing more, and hiding behind lack of evidence and doing nothing is no longer acceptable. How many babies have to die before something is done? I have been lucky enough to go to have a daughter. I had another GBS positive pregnancy, I was given antibiotics in labour. I now have a healthy baby girl. She is proof that testing and prevention works! The UK's risk-based prevention strategy has failed to stem the rising tide of group B Strep infection in newborn babies. A safe and effective vaccine is at least a decade away. Screening pregnant women for group B Strep carriage and offering the carriers antibiotics in labour – recognised as international best practice and undertaken for more than a decade in other developed countries – is the best way we currently have to protect our unborn babies.

169.	**xxxx xxxx** YES	Plain English Summary	I disagree in the strongest possible terms with the recommendation of the UK NSC commissioned report not to offer GBS screening..	I wanted to contribute to this consultation by sharing my families experience of the devastating consequences of the current recommendation of the UK NSC report to not offer GBS screening in the UK. The NSC have a considerable advantage over me in that they have known about GBS, and its potentially devastating consequences, for at least 14 years. I only got to hear about it after my **xxxx xxxx**, **xxxx xxxx**, was born on **xxxx xxxx**. **xxxx xxxx** was born perfectly healthy weighing **xxxx xxxx**. **xxxx xxxx** then developed EOGBS. This went unnoticed for 2 days, and **xxxx xxxx** was sent home before having to be rushed back in to the hospital. **xxxx xxxx** suffered considerably (as did we, **xxxx xxxx** family) because of this infection and, as the report states, “unfortunately” (p10) after five days of intensive care, **xxxx xxxx** became one of the “small number” of babies to die from Meningitis and Septicaemia caused by Group B Strep. But really it was known that **xxxx xxxx** was going to die. You didn't know where or when exactly **xxxx xxxx** would die, but you did know that on average 1 baby a week will die from GBS. At the moment the NHS offers antibiotic treatment to women who are known to carry GBS, and testing can be given to those who have risk factors. If it is in fact serious enough to elicit this response when it’s known that a woman is carrying GBS, it is very difficult to understand how you can justify not screening for it. This is not equitable. It is not in-keeping with the core principles of the NHS. And it is certainly not fair to those who remain ignorant of this threat to their child’s life. I feel strongly that it should be up to the mother to decide whether she wishes to be given antibiotics during labour, if she is a carrier of GBS; she should be provided with all of the information available, and be allowed to make an informed decision. While you wait for more research, more babies are dying. You say: “we do not know whether there are any short or long-term harms to the mother or baby from giving antibiotics to the mother during labour, and so do not know how many of the 150,800 treated women and babies might be harmed” (p10); but you do know the consequences of not doing so. On average: • 1 baby a day develops GBS • 1 baby a week dies from GBS • 1 baby a fortnight survives the infection with long term disabilities. • and that, despite the UK's risk based prevention strategy, rates of these infections have increased for more than a decade. And you wait. Professor Dame Sally Davies once said, “why would we continue to let these families suffer when we have it in your hands to do otherwise"; a powerful argument put forward for those affected with

				mitochondrial disease. Surely the same can be said for the babies and families who have suffered, and continue to suffer, due to untreated GBS infection. I would like you to more seriously consider the impact of the loss of even one life, when it may have been preventable. The pain and heartache that has come with knowing **xxxx xxxx** could still be with us is, at times, unbearable. Are these little lives really worth so little? Are these babies not entitled to the same basic human rights the rest of us enjoy? A right to life? A right to equality? **xxxx xxxx** would've been 3 this **xxxx xxxx**. **xxxx xxxx** could have been here with us, enjoying life with **xxxx xxxx** big brother **xxxx xxxx** and **xxxx xxxx** family. **xxxx xxxx** would probably still be here if GBS screening was practiced in the UK.

170.	**xxxx xxxx** YES		Rejection of universal screening programme in the UK for Group B Streptococcus	Having seen the rapid effects of a Group B Strep infection first hand in my own newborn son I would urge that a high quality screening programme is offered to all expectant mothers in late pregnancy using the ECM test and the option for intravenous antibiotics to be administered before delivery to those women found to be carriers.
171.	**xxxx xxxx** YES			I give permission to publish my comments if you choose to do so. My son was born on the **xxxx xxxx**, 4 days past his due date, he was **xxxx xxxx** lbs **xxxx xxxx** oz, and he was my second baby. I had a healthy pregnancy, and kept well, although do believe I had boughts of thrush which I treated myself with a well known over the counter medicine. My labour started at 2pm in the afternoon, lightly, at **xxxx xxxx** pm when I went to hospital I would say my contractions were regular but still not at full strength, my labour continued and was in full swing between 9pm until **xxxx xxxx** when my son was born, my last stages of labour were very fast and I was rushed through to have him, pushed twice and he was with us. My waters were broken by the midwife. At no point was there time to take my temperature in the rush. I tell you this information to be factual and give you the circumstances of my son's birth. Even although we didn't know it My son displayed symptoms of Strep B from the beginning. He was a strange colour, almost jaundiced, but the medical staff kept checking him for jaundice, using a flashing light device, it continued to show negative for jaundice. At his neonatal assessment at approx 10am in the morning, the Dr made a comment when **xxxx xxxx** did the drop test to check his reflexes, "come on little guy, you need to do better than that" immediately I questioned **xxxx xxxx** on what was wrong, **xxxx xxxx** told us, **xxxx xxxx** was testing

				his reflexes and he expected they would be much stronger. I had been told we could leave the hospital that day as this was my second baby. My son also made regular grunting noises, and had great difficulty feeding, he did not feed even though I was very persistent to Breast feed and found it very easy with my daughter. All of these are signs I know now were of his Strep B. I'm not sure why and probably on account of the assessment and the fact he was not feeding the medical staff asked me to stay overnight in the hospital. I had hoped to get out that day as my daughters nativity at her nursery was the following morning. But reluctantly I agreed to stay. I continued to try and feed him, he continued to grunt and appear a strange colour. At approx 3 am that following morning I became distressed with his crying, it wasn't a hungry baby cry, it was a sore and something not right cry, he couldn't settle on his own and stayed in my arms most of the night, while I played him soft classical music, we had a private room. I asked to see a medic who came to see us and did a few tests, they confirmed he was ok. Later on the Dr's told me it was probably mothers intuition, it was also comparison from my first baby, I'm not sure I'd have picked up on it, if he had been my first. In the morning we got up, ready, my husband came in with the car seat and his change of clothes, my son still would not feed and we met a lovely young midwife who came to see us, probably the 8th or 9th medical person we had seen in time in the ward. **xxxx xxxx** name was **xxxx xxxx**, and I later found out **xxxx xxxx** was either training or just finished training. **xxxx xxxx** raised concern, again at the noises he was making, his colour and that he wasn't feeding. **xxxx xxxx** helped him latch on and asked if we had him checked over. We had, **xxxx xxxx** asked if we could stay a while and said **xxxx xxxx** would only be happy to let us go home at lunch time of I could get him to feed.

				A few hours went on, we were excited to be leaving the hospital, our young mid wife came back to see us and still wasn't happy so asked for another medical check. This time yet another Dr, more senior brought the same machines to check him, I believe it was the flash light again and a machine they wrapped round his finger to detect oxygen in the blood. **xxxx xxxx** disappeared very quickly and came back approx 5 minutes later. **xxxx xxxx** was very nice but abrupt, she told we could not leave and she was taking my baby away. **xxxx xxxx** told us she was waiting on a transport crib to take him downstairs. We didn't really know what downstairs was, and were caught a little off guard, thinking my son would be back after they checked him over. We let him go with the medical staff, who told us they would keep us informed, an hour or 2 passed, we chose his name. We want to the gift shop and bought him a teddy bear, and we waited quietly and patiently not wanting to be a burden on the staff or make a fuss, a few times we asked for him and they phoned downstairs and said someone would be up to see us soon. When the nice Dr came back, **xxxx xxxx** asked us to sit down. I remember **xxxx xxxx** name was **xxxx xxxx**. **xxxx xxxx** told us our so was gravely ill, **xxxx xxxx** had tested for oxygen in the blood and could not get a reading, he had sepsis, his organs had started to fail and they would take us down to explain things in more detail and we could see him, but she wanted to prepare us for the sight of him hooked up to the machines and in an incubator, **xxxx xxxx** told us his infection markers were 160 and to make it relative that in a baby his age they should be under 10. Nothing could have prepared us for the sight of him in the little transparent box, by this time we were both in shock. When we went down we saw a team of medics round him. The dr from the assessment, the young dr from the previous night, **xxxx xxxx**, Dr **xxxx xxxx**, Dr **xxxx xxxx**. They explained that he had either Strep B or Ecoli.

				Dr **xxxx xxxx** is obviously a brilliant Dr but was very matter of fact and clinical, **xxxx xxxx** explained that my son had as I say sepsis, and his organs had started to shut down, he had pneumonia, and fluid in his lungs, he has a bleed on his brain, and they wanted to do a lumber puncture to check for meningitis, but none of them thought he would be strong enough. If they couldn't do it, they would try again tomorrow. The medics could obviously tell we were in shock and took us to the relatives room to try and help us understand what was going on. Dr **xxxx xxxx** was very personable and relayed everything we had been told clearly and in layperson terms. **xxxx xxxx** also told us that they didn't think my son would make it through the night and they would make up the family room for us so that my husband could stay in the hospital with us, they said we had to give them some time to clear the room as it was full of equipment apparently they hadn't used it for a number of years. **xxxx xxxx** told us they had started my son on antibiotics straight away, had him on sedatives and asked our permission to intubate him. Who were we to decline, these were the medical people and we wanted them to do everything in their power to save our little boy. At this Dr **xxxx xxxx** popped **xxxx xxxx** head through the door, **xxxx xxxx** confirmed they had managed to get the lumber puncture and the fluid looked clear, which was a good sign. Dr **xxxx xxxx** took time to explain what that all meant in non medical terms. We left him only to try and eat, go to the loo, I prayed, and went to express milk. My son made it through the night, he fought with the intubation tube, he hated it, he fought a great fight and survived. My sons name is **xxxx xxxx** and after all of that he made a full recovery, I told you this story because **xxxx xxxx** is not a statistic or a percentage or something that can be measured in clinical terms. he is a beautiful, vibrant, funny, loving, very strong and very determined boy. He brings us so much joy and laughter and we will never take either of our children forgranted. **xxxx xxxx** spent 5 days in the NICU at **xxxx xxxx** and another 8 in the special baby unit, they confirmed it was Strep B and they had tried to grow cultures to create his own antibiotic.

				He had various and intermittent scans on his organs, and his brain to see how he was recovering, tests everyday that proved his infection markers were reducing consistently. I can only imagine how much his NHS treatment cost not to mention how many times I have had him at A &E, Drs appointments, because I completely neurotic about him. I believe both my husband suffered PTSD quietly and undiagnosed, we constantly worried about his development, read various articles and medical papers on, identifying Cerebral palsy and the other conditions linked with strep B. I believe I have only recently calmed down, he walks well now, he was a late talker, and is still quite a lazy speaker, but he is a perfect little boy. Dr **xxxx xxxx** explained to me about the reason why the NHS didn't screen for Strep B and I didn't question it at the time, probably shock. But I have read numerous articles and information on the subject now, and when I see a news article about another baby dying it breaks my heart and I relive my experience over and over again and blame myself, I could have done something more to help. The U.K. Is so behind on this, there was a paper I think from Canada or the USA with stats on how many babies lives they had saved since introducing screening. It was also confirmed in a paper that the registered cases of Strep B is steadily increasing and not all the attributed infant deaths are recorded properly because we don't test for it routinely, in SIDS, still born babies and other infant mortality rates. This country is allowing babies to die as what? collateral damage. I don't believe your decision is right, to suggest that the NHS do not screen for strep B. At least let mothers to be, decide if they want to be tested and treated, once they are educated enough to understand Strep B, and its consequences. I would like to say I didn't know about Strep B but I did, in fact I had insisted on a test when I was pregnant with my daughter. My mum had seen an episode of this morning where Dr Chris talked

				about and urged pregnant mums to be tested because Strep B can result in death. My test **xxxx xxxx** years ago came back clear and my daughter was a very happy healthy baby. I took it forgranted that my son would be to, and dismissed it when my mum urged me to get tested before his birth. I'm sure you can imagine the guilt I carry around with me and the dread and panic I re-live when I think about how things could have been different for my family. My wider family have also all been affected by what happened to my son. Luckily I got to stay in the hospital all the time my son was there, I believe I was a paranoid and emotional wreck and was so glad I didn't have to come home without him. We thank our lucky stars everyday for our son and that our story ended as it did. All the medical staff and the team at **xxxx xxxx** hospital have to be commended on their, diligence, compassion, care and everything they did for us we all received the best care we could ask for. Even the auxiliary and canteen staff cared for me and my son, showing a real interest and compassion. My sons Strep B could possibly have been detected sooner, however I cannot allow myself to think or wish anything had happened differently because we have **xxxx xxxx**, and if one thing played out differently who's to say our result wouldn't have been different. I have no doubt in my mind however that if we left the hospital a day earlier, our story would have been very different. I appreciate this has been a long read and thank you for taking time to read it. Please stop Strep B infant deaths from happening.....

172.	**xxxx xxxx**			I accidently found out about GBSS 5 yrs ago from my father in law who had been watching TV and called to warn me. I raised the issue and asked for clarification at an antenatal class where I was dismissed. I ended up telling the other Mums about a private test that was available (which I had googled). I myself tested positive and was given 2 courses of antibiotics in labour. My point is that should you once again decide to not test women for this, which in itself is ludacris then at least brief women on what it is and the options available to them i.e private test. Geez you could even do an nhs test option and make money as the main point is saving the babies life and limiting the risks of safe arrival into our world, not ignore the dangers. We are urged to take things like untested swine flu injections as a preventative so why are we not treating something that physically exists and puts our newborns life in danger. It deeply saddens me to hear this week that another baby has died by lack of communication and awareness 5 yrs on. Please make the right decision.
173.	**xxxx xxxx** YES			I would like to inform you that my baby was stillborn at 36 weeks due to Group B Strep. I had a healthy pregnancy and so this came as a huge shock!! I was never informed of GBS or tested for this, had I of- my beautiful daughter would be alive today! I strongly believe that routine screening for GBS would save babies lives, most countries screen for GBS- they can't all be wrong?! Please introduce routine screening.
174.	**xxxx xxxx** YES	ALL	Evidence within The Report	The evidence in the report appears to be inadequately assessed. It's not unreasonable to think that it should be based on more recent research and evidence. It ignores evidence of the sustained benefit of screening in other countries, such as the USA & in Europe, which have had a national policy of screening since 2002. This suggests that the report has been written with conclusions already drawn and agreed, rather than systematically examining all evidence before making conclusions.

175.	**xxxx xxxx** YES My comments are based on the overall Full Report			The methodology used to assess the evidence does not follow best practice guidelines for any questionning, and in places appears to be biased in favour of studies that do not support routine antenatal screening for GBS carriage. This is unfair and unreasonable positioning for questioning.
176.	**xxxx xxxx** YES My comments are based on the overall Full Report			Because there is either little or no information on WHO undertook the study, their qualifications, their roles, and their expertise in relation to GBS. Then it's only reasonable to not have confidence in the conclusions of the UK NSC in relation to question that the quality of the evidence may be in correct. Usually such information is standard practice when reporting the results of systematic reviews – as an endorsement of questioning and research
177.	**xxxx xxxx** YES My comments are based on the overall Full Report			There is some key criteria relating to screening studies that this report does not examine but which are met in other countries where there is a GBS screening programme. . This is unreasonable.
178.	**xxxx xxxx** YES My comments are based on the overall Full Report			This report seeks for much much more evidence than has been required for other screening decisions, or for less common conditions, which have been approved based on much less evidence. Again This suggests a stalling for reasonable conclusions of evidence.
179.	**xxxx xxxx** YES My comments are based on the overall Full Report			As a bereaved mother who lost a baby boy to a LOGBS infection I urge you to continue with effective, thorough and questioning research YET to consider to offer the option for a Screening programme alongside this research till you have concluded screening is actually effective over NOT….& versus the potential NHS/ NICU costs for giving and maintaining care required for any newborn who becomes identified with carrying a GBS infection and beyond.

[i] Tsang C. (2015) Audit of current practice in preventing early-onset neonatal group B streptococcal disease in the UK First report. Available at: https://www.rcog.org.uk/globalassets/documents/guidelines/research--audit/gbs-audit-first-report.pdf

[ii] PHE (2015) UK Standards for Microbiology Investigations B 58 Detection of Carriage of Group B Streptococci. Issue 3 (issued 2006, updated 2014, 2015). Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/438182/B_58i3.pdf

[iii] Fairlie, T., Zell, E. and Schrag, S. (2013) 'Effectiveness of intrapartum antibiotic prophylaxis for prevention of early-onset group B streptococcal disease', Obstetrics and gynecology. 121(3), pp. 570–7.

[iv] Schrag, S., Zell, E., Lynfield, R., Roome, A., Arnold, K., Craig, A., Harrison, L., Reingold, A., Stefonek, K., Smith, G., Gamble, M., Schuchat, A. and Bacterial, A. (2002) 'A population-based comparison of strategies to prevent early-onset group B streptococcal disease in neonates', The New England journal of medicine., 347(4), pp. 233–9.

[v] Schrag, S. and Verani, J. (2012) 'Intrapartum antibiotic prophylaxis for the prevention of perinatal group B streptococcal disease: Experience in the United States and implications for a potential group B streptococcal vaccine', Vaccine. 31.

[vi] Daniels, J., Gray, J., Pattison, H., Hills, R., Khan, K. and Collaborative, G. (2010) 'Intrapartum tests for group B streptococcus: Accuracy and acceptability of screening', BJOG: an international journal of obstetrics and gynaecology. 118(2), pp. 257–65.

[vii] O'Sullivan, C., Lamagni, T., Efstratiou, A., Boyle, M., Meehan, M., Reynolds, A., Doherty, L., Cunney, R. and Heath, P. (2016) 'Group B Streptococcal (GBS) disease in UK and Irish infants younger than 90 days, 2014–2015', Archives of Disease in Childhood, 101(Suppl 1), p. 2. doi: 10.1136/archdischild-2016-310863.3.

[viii] Lord, L.K., Lord, C., Lord, W. and Hodge, R.L. (2015) Montgomery (appellant) v Lanarkshire health board (respondent). Available at: https://www.supremecourt.uk/decided-cases/docs/UKSC_2013_0136_Judgment.pdf

[ix] Bounty Survey 2015 http://gbss.org.uk/wp-content/uploads/2015/05/2015_Bounty_Group_B_Strep_Research.pptx. The Word of Mum research was conducted between 16-31 March 2015 and among 4,673 women in the early stages of pregnancy through to mums with a youngest child aged 12 months.

[x] Albouy-Llaty, M., Nadeau, C., Descombes, E., Pierre, F. and Migeot, V. (2011) 'Improving perinatal group B streptococcus screening with process indicators', Journal of evaluation in clinical practice., 18(4), pp. 727–33.

[xi] Andreu, A., Sanfeliu, I., Viñas, L., Barranco, M., Bosch, J., Dopico, E., Guardia, C., Juncosa, T., Lite, J., Matas, L., Sánchez, F., Sierr, M. and Grupo, de (2003) '[Decreasing incidence of perinatal group B streptococcal disease (Barcelona 1994-2002). Relation with hospital prevention policies]', Enfermedades infecciosas y microbiologia clinica. 21(4), pp. 174–9.

[xii] Daley, A., Isaacs, D. and Study, A. (2004) 'Ten-year study on the effect of intrapartum antibiotic prophylaxis on early onset group B streptococcal and Escherichia coli neonatal sepsis in Australasia', The Pediatric infectious disease journal. 23(7), pp. 630–4.

[xiii] Jordan, H., Farley, M., Craig, A., Mohle-Boetani, J., Harrison, L., Petit, S., Lynfield, R., Thomas, A., Zansky, S., Gershman, K., Albanese, B., Schaffner, W., Schrag, S. and Bacterial, A. (2008) 'Revisiting the need for vaccine prevention of late-onset neonatal group B streptococcal disease: A multistate, population-based analysis', The Pediatric infectious disease journal., 27(12), pp. 1057–64.

[xiv] CDC (2016) Surveillance reports. Group B Streptococcus. Data series online from 1997. Available at: https://www.cdc.gov/abcs/reports-findings/surv-reports.html

[xv] Yancey, M., Schuchat, A., Brown, L., Ventura, V. and Markenson, G. (1996). The accuracy of late antenatal screening cultures in predicting genital group B streptococcal colonization at delivery.

[xvi] Kunze M, Zumstein K, Markfeld-Erol F, et al. Comparison of pre- and intrapartum screening of group B streptococci and adherence to screening guidelines: a cohort study. European Journal of Pediatrics 2015; 174(6): 827-35.

[xvii] Kwatra G, Adrian PV, Shiri T, Buchmann EJ, Cutland CL, Madhi SA. Serotype-specific acquisition and loss of group B streptococcus recto-vaginal colonization in late pregnancy. PLoS ONE 2014; 9(6): e98778.

[xviii] MacKay G, House MD, Bloch E, Wolfberg AJ. A GBS culture collected shortly after GBS prophylaxis may be inaccurate. Journal of Maternal-Fetal and Neonatal Medicine 2012; 25(6): 736-8.

[xix] Scasso S, Laufer J, Rodriguez G, Alonso JG, Sosa CG. Vaginal group B streptococcus status during intrapartum antibiotic prophylaxis. International Journal of Gynecology and Obstetrics 2015; 129(1): 9-12.

[xx] Szymusik I, Kosinska-Kaczynska K, Krolik A, Skurnowicz M, Pietrzak B, Wielgos M. The usefulness of the universal culture-based screening and the efficacy of intrapartum prophylaxis of group B Streptococcus infection. *Journal of Maternal-Fetal and Neonatal Medicine* 2014; **27**(9): 968-70.

[xxi] Libster, R., Edwards, K., Levent, F., Edwards, Rench, M., Castagnini, L., Cooper, T., Sparks, R., Baker, C. and Shah, P. (2012) 'Long-term outcomes of group B streptococcal meningitis', Pediatrics. 130(1).

[xxii] Okike, I., Johnson, A., Henderson, K., Blackburn, R., Muller-Pebody, B., Ladhani, S., Anthony, M., Ninis, N., Heath, P. and Study, neoMen (2014) 'Incidence, etiology, and outcome of bacterial meningitis in infants aged <90 days in the United Kingdom and Republic of Ireland: Prospective, enhanced, national population-based surveillance.' Clinical infectious diseases : an official publication of the Infectious Diseases Society of America., 59(10).

[xxiii] Stoll BJ, Hansen N, Adams-Chapman I, et al 2004. Neurodevelopmental and growth impairment amongst extremely low birth weight infants with neonatal infection. JAMA 292: 2357-2365

[xxiv] Tann, C.J., Nkurunziza, P., Nakakeeto, M., Oweka, J., Kurinczuk, J.J., Were, J., Nyombi, N., Hughes, P., Willey, B.A., Elliott, A.M., Robertson, N.J., Klein, N. and Harris, K.A. (2014) 'Prevalence of bloodstream Pathogens is higher in neonatal Encephalopathy cases vs. Controls using a novel panel of real-time PCR assays', PLoS ONE, 9(5), p. e97259. doi: 10.1371/journal.pone.0097259.

[xxv] Heath, P., Balfour, G., Weisner, A., Efstratiou, A., Lamagni, T., Tighe, H., O'Connell, L., Cafferkey, M., Verlander, N., Nicoll, A., McCartney, A. and Group, P. (2004) 'Group B streptococcal disease in UK and Irish infants younger than 90 days', Lancet (London, England). 363(9405), pp. 292–4.

[xxvi] Colbourn T, Asseburg C, Bojke L, Philips Z, Claxton K, Ades AE et al. Prenatal screening and treatment strategies to prevent group B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses. Health Technol Assess 2007; 11(29):1–226, iii

[xxvii] Kaambwa B, Bryan S, Gray J, Milner P, Daniels J, Khan KS et al. Cost-effectiveness of rapid tests and other existing strategies for screening and management of early-onset group B streptococcus during labour. BJOG 2010; 117(13):1616–1627.

[xxviii] Colbourn TE, Asseburg C, Bojke L, Philips Z, Welton NJ, Claxton K et al. Preventive strategies for group B streptococcal and other bacterial infections in early infancy: cost effectiveness and value of information analyses. BMJ 2007; 335(7621):655.

[xxix] CDC (2010) *ABCs report: Group B Streptococcus, 2002*. Available at: https://www.cdc.gov/abcs/reports-findings/survreports/gbs02.html

[xxx] CDC (2016) *ABCs report: Group B Streptococcus, 2014*. Available at: https://www.cdc.gov/abcs/reports-findings/survreports/gbs14.html

[xxxi] CDC (2010) *ABCs report: Group B Streptococcus, 1997*. Available at: https://www.cdc.gov/abcs/reports-findings/survreports/gbs97.html

[xxxii] Daniels J, Gray J, Pattison H, Roberts T, Edwards E, Milner P et al. Rapid testing for group B streptococcus during labour: a test accuracy study with evaluation of acceptability and cost-effectiveness. Health Technol Assess 2009; 13(42):1–iv.

[xxxiii] Law, K.S.K., Parmar, P., Gregora, M. and Abbott, J. (2013) 'A comparative study assessing the efficacy and acceptability of anorectal swabs for antenatal GBS screening', Journal of Medical Screening, 20(1), pp. 46–48. doi: 10.1177/0969141313482305.

[xxxiv] NICE (2012) Neonatal infection (early onset): Antibiotics for prevention and treatment. Available at: https://www.nice.org.uk/guidance/cg149 (Accessed: 24 January 2017).

[xxxv] Group B Streptococcal disease, early-onset (green-top guideline no. 36). Available at: https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg36/

[xxxvi] Jordan HT, Farley MM, Craig A, Mohle-Boetani J, Harrison LH, Petit S et al. Revisiting the need for vaccine prevention of late-onset neonatal group B streptococcal disease: a multistate, population-based analysis. Pediatr Infect Dis J 2008; 27(12):1057-1064.

[xxxvii] Daley AJ, Isaacs D. Ten-year study on the effect of intrapartum antibiotic prophylaxis on early onset group B streptococcal and Escherichia coli neonatal sepsis in Australasia. Pediatr Infect Dis J 2004; 23(7):630-634.

[xxxviii] NICE (2011) Caesarean section. Available at: https://www.nice.org.uk/guidance/cg132/chapter/1-Guidance#procedural-aspects-of-cs

[xxxix] CDC (2010) Prevention of Perinatal group B Streptococcal disease: Revised guidelines from CDC, 2010. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5910a1.htm

[xl] Bounty Word of Mum survey 2010 http://www.gbss.org.uk/filepool/2010_Bounty_GBS_Survey_Results.pdf

[xli] Bounty Word of Mum survey 2013 http://gallery.mailchimp.com/6599c26deb03ac68f3446cccc/files/2013_Bounty_Group_B_Strep_WOM_Research.pptx

[xlii] (Schrag SJ, Farley MM, Petit S, et al. Epidemiology of Invasive Early-Onset Neonatal Sepsis, 2005 to 2014. Pediatrics. 2016;138(6):e20162013).

[xliii] Tsang, C. (2016) Audit of current practice in preventing early-onset neonatal group B streptococcal disease in the UK Second report. Available at: https://www.rcog.org.uk/globalassets/documents/guidelines/research--audit/gbs-audit-second-report-january-2016.pdf