Modelling the effect of the introduction of antenatal screening for group B Streptococcus (GBS) carriage in the UK

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ABSTRACT

Objectives To estimate the potential impact of the addition of culture-based screening for group B streptococcus (GBS) carriage in pregnancy to a risk-based prevention policy in the UK. We aimed to establish agreement within a multidisciplinary group of key stakeholders on the model input parameters.

Design Deterministic model using a consensus approach for the selection of input parameters.

Setting and participants A theoretical annual cohort of 711,999 live births in the UK (excluding births by elective caesarean section).

Interventions Culture-based screening for GBS at 35–37 weeks of pregnancy added to the recommended risk-based prevention policy in place on the date of modelling.

Outcome measures Outcomes assessed included use of intrapartum antibiotic prophylaxis (IAP), early onset GBS (EOGBS), EOGBS mortality, severe EOGBS-related morbidity and maternal penicillin anaphylaxis.

Results With no prophylaxis strategy, the model estimated that there would be 421 cases of culture positive EOGBS in a year (0.59/1000 live births). In the risk-based prophylaxis scenario, 30,666 women were estimated to receive IAP and 70 cases of EOGBS were prevented. Addition of screening resulted in a further 96,260 women receiving IAP and the prevention of an additional 52 to 57 cases of EOGBS. This resulted in the prevention of three EOGBS deaths and four cases of severe disability. With screening, an additional 1,675 to 1,854 women receive IAP to prevent one EOGBS case and 24,065 to 32,087 receive IAP to prevent one EOGBS death.

Conclusions The evidence base available for a broad range of model input parameters was limited, leading to uncertainty in the estimates produced by the model. Where data was limited, the model input parameters were agreed with the multidisciplinary stakeholder group, the first time this has been done to our knowledge. The main impact of screening is likely to be on the large group of low-risk women where the clinical impact of EOGBS tends to be less severe. This model suggests that the reduction in mortality and severe disability due to EOGBS with antenatal GBS screening is likely to be very limited, with a high rate of overdetection and overuse of antibiotics.

INTRODUCTION

Group B Streptococcus (GBS) is a bacterium which can be commonly found in the digestive system and female reproductive tract. It can be transmitted from a pregnant carrier to her newborn, typically during vaginal delivery.1

While the bacterium does not usually cause harm, in some cases it can cause early onset infection in the newborn’s first week of life. This is termed early onset GBS (EOGBS) disease. In the UK, GBS is the most common cause of neonatal sepsis and meningitis.2,3

Comprehensive surveillance established an overall rate of EOGBS at 0.48 per 1000 live births in the UK and Ireland in 2000–2001.4 Since then, routine laboratory surveillance has shown a fluctuation in incidence of culture positive EOGBS with slight increases between 2000 and 2010.5 Preliminary national surveillance data from 2014 to 2015 suggests that the overall incidence of EOGBS was 0.57 per 1000 live births in the UK and Ireland.6 Clindamycin had been used as the main alternative to penicillin prophylaxis in women with penicillin allergy; however, since 2000 there has been a marked increase.
in resistance to clindamycin in patients of all ages. As a result, the most recent guidance from the Royal College of Obstetricians and Gynaecologists (RCOG), published in 2017, has recommended that clindamycin should no longer be used for this purpose. Vancomycin is now recommended by the RCOG as the antibiotic of choice for women with severe allergy to penicillin.

In the UK, the mortality rate in term newborns with EOGBS is estimated to be between 6% and 10.6%, with a similar proportion left with severe morbidity. In pre-term newborns with EOGBS, the mortality rate is reported to be higher.

**Antenatal screening for GBS**

Pregnant women can be screened for GBS carriage in late pregnancy. Screening involves the collection of specimens using vaginal and rectal swabs which are processed using selective culture media. The purpose of screening is to identify a group of women who are eligible for intravenous intrapartum antibiotic prophylaxis (IAP) as a means of preventing EOGBS disease. The mainstay of IAP is benzylpenicillin.

In the UK, currently there is agreement between the guidance issued by the UK National Screening Committee (UK NSC), the National Institute for Health and Care Excellence (NICE) and the RCOG that routine screening for GBS carriage should not be offered.

A number of maternal risk factors for EOGBS have been identified. These include having a baby with GBS in a previous pregnancy, incidentally detected maternal GBS carriage, prematurity, prolonged membrane rupture and suspected infection in labour. In the UK, at the time of this modelling exercise (2014–2015), GBS IAP was recommended for women with either of the first two listed risk factors and broad spectrum antibiotics, with an agent active against GBS, recommended for women with suspected infection in labour. Since the completion of the modelling exercise, the RCOG has updated its guideline on GBS. The main change is that they now recommend offering GBS IAP to all women in confirmed pre-term labour. This is due to the increased risk of EOGBS and mortality in pre-term infants compared with term infants.

In 2017, the UKNSC completed the process of reviewing the evidence on antenatal GBS screening as part of its triennial review process. This review concluded that the recommendation not to implement screening in the UK should not be changed. This was because the committee considered there to be insufficient evidence on the balance of benefits and harms from culture-based screening and treating women with positive results with IAP.

The discussion on antenatal screening for GBS has taken place in a UK policy context shaped by the Maternity Review, ‘National Health Service Outcomes Frameworks’ and the Antimicrobial Resistance Strategy. These major policy drivers emphasise issues ranging from patient choice and experience, place of birth, reduction of neonatal deaths, antibiotic stewardship and reduction of antibiotic usage. The potential impact of screening on these issues, therefore, needs to be considered.

The charity, Group B Strep Support (GBSS), has campaigned for screening since the 1990s. The controversy surrounding the screening policy is reflected in journal debate, and politicians from the main parties in the four UK countries have signed petitions, raised parliamentary questions and led delegations on this issue. A petition in favour of screening, with over 250,000 signatures, was delivered to the ministers and senior officials in January 2017.

In part, this interest is stimulated by the implementation of antenatal screening for maternal GBS carriage in a number of developed countries. With few exceptions, retrospective cohort studies from these countries report a decline in the rate of culture positive EOGBS following the introduction of screening. For example, surveillance data from the USA reports reduced rates of EOGBS following implementation of each new policy change. The retrospective and observational design of these studies makes it difficult to ascertain if the data are complete, or if the reduction is conclusively attributable to screening alone.

In addition, the absence of reports on the effect of screening on the rate of culture-negative sepsis presumed to be due to EOGBS disease limits interpretation further. The difficulty in extrapolating data from different geographical settings has also been noted in relation to EOGBS. However, the absence of suitably powered UK studies necessitates the use of available data from the UK and other countries, to estimate the potential impact of screening in the UK.

The UK NSC therefore convened a multidisciplinary, multi-agency expert group in 2014 to consider the available evidence to inform the development of a model to estimate the preventive potential of screening when added to current clinical practice. A pivotal aim of the process was to establish a shared set of assumptions among key stakeholders on a controversial topic.

**METHODS**

**Model structure**

A pragmatic deterministic model was developed in Microsoft Excel 2010 to simulate two scenarios in a 1-year UK pregnancy cohort. The first scenario was based on the risk-based management pathway recommended in the UK at the time of the model development (2014–2015). The second scenario was the screening and risk-based scenario. In this scenario, antenatal culture-based screening for GBS was offered at 36 weeks of pregnancy to women not already identified as being at risk through the risk-based strategy. This scenario was based broadly on the screening strategy recommended by the US Centers for Disease Control and Prevention and the existing UK risk-based approach. This meant that women with known risk factors who should already be offered...
IAP under UK guidelines continued to be offered IAP without screening. Women without these risk factors were offered screening. Women giving birth pre-term, before 37 weeks, were assumed not to receive screening. This was due to the timing of the screening test at 36 weeks and the logistics of transport and laboratory processing time.

Within both scenarios, women were sequentially divided into mutually exclusive groups based on various clinical parameters.

In scenario one, the existing risk-based approach, the clinical characteristics on which the sequential divisions were based were as follows:
► Mode of birth (elective caesarean section or not).
► Presence of antenatal risk factors for EOGBS (a previous baby with EOGBS, incidental detection of GBS carriage or no risk factors).
► Timing of birth (term or pre-term).
► Presence of intrapartum risk factors for EOGBS (pre-term pre-labour rupture of membranes, suspected infection during labour, or ‘uncomplicated birth’, that is, no intrapartum risk factors).

This resulted in the population being divided into 15 ‘clinical risk groups’. These are depicted in figure 1.

In scenario 2, the screening and risk-based approach, women who had no antenatal risk factors for EOGBS and who gave birth at term were eligible for screening. The population eligible for screening is depicted in figure 2 and was divided into groups based on:
► Receipt of screening (yes or no).
► Result of screening (positive or negative for GBS).
► GBS status at delivery (positive or negative for GBS).
► Presence of intrapartum risk factors for EOGBS (infection during labour or uncomplicated birth).

This resulted in 23 clinical risk groups in scenario two, comprising the 13 groups from scenario one which would not be eligible for screening plus an additional 10 groups resulting from screening. Risks for EOGBS and related outcomes had been agreed in advance and were applied to these groups to obtain the numbers of affected individuals. The agreed risks are summarised in tables 1 and 2.

Figure 3 depicts the model structure for IAP and outcomes from the model.

To ensure a fair comparison, model outputs were checked to make sure that the number of EOGBS cases was equivalent in both scenarios if no antibiotic prophylaxis was given. In order to achieve this, the GBS
colonisation transition rates in the model needed to be adjusted to ensure that there was no overall change in GBS carriage rates between the time of screening and the time of delivery.

**Consensus building approach**

Members of the expert group are listed in [table 3](#). They comprised representatives from UK organisations responsible for the development of guidance, policy and patient advocacy relating to EOGBS, as well as experts with experience in clinical practice fields related to EOGBS, microbiology, epidemiology or statistics.

Members of the group were given the opportunity to comment on the structure of the model and individual model parameters.

Evidence identified in the UK NSC’s 2012 triennial review of antenatal GBS screening policy and national guidance documents were used to inform data used in the model.6 13 14 25 These were supplemented by a broad search in September 2014 for papers published since the 2012 NSC evidence review (see online supplementary information for details). Relevant national data was also identified from sources such as the Office for National Statistics.

Higher quality evidence, such as systematic reviews28 29 and randomised clinical trials, were prioritised as sources of data, as were studies from the UK.14 A summary of up to five potential values for each input parameter, based on the best available and most relevant evidence identified, was provided to the expert group. Where no evidence regarding an input parameter was identified, this was also noted.

Through a two part survey, the group was asked to consider the relevance of each input parameter, the most appropriate source of the parameter value, and the applicability of the source-study findings to a UK population. Group members could also suggest alternative sources of data. In the absence of suitable published data for a parameter, the expert group selected a figure based on clinical experience and opinion.

All parameters and assumptions that received over 70% agreement were included in the model unchanged. Those that did not meet this threshold were refined and resubmitted to the expert group. Those that received over 50% agreement in the second round were included in the model. A small number of assumptions went forward to the second round. These focused on the details of the modelled IAP strategy. This included the timing and duration of IAP, whether second-line antibiotics should be included for analysis in the model, the schedule for those receiving IAP and subsequently developing fever in labour and whether IAP uptake and optimum duration should vary by risk group. All proposed changes received 70% or more, except for one which received 65%.

The survey results informed two meetings of the expert group. The first meeting reviewed and agreed about the model structure and input parameters. The second received and discussed the outputs of the model.

**Patient and public involvement**

Representatives of GBSS were involved as members of the expert group in all stages of the group’s work. This included individual discussion with the project lead (DB) regarding the consensus building approach to agreeing to the model’s parameters, priorities and outcomes. It also included participation in the two-part survey and workshops to discuss the model.

Results of the model were disseminated to all members of the expert group in the form of a draft report of the modelling project. Comments received from GBSS raised a number of concerns about the outcomes of the model. These concerns centred on the emerging results of an enhanced surveillance study which suggested that the rate of EOGBS had increased.

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**Figure 2** Flow of screening eligible women through the screening scenario. Group B Streptococcus (GBS), intrapartum antibiotic prophylaxis (IAP) against early onset GBS (EOGBS).
and that mortality had decreased. GBSS suggested that the model should be re-run with the new data and that greater emphasis on EOGBS in term women was needed. It was not possible to address all the concerns without reconvening the expert group in a new modelling exercise. However, GBSS’s concern prompted a post hoc analysis in term women with no risk factors indicating IAP. This is the most important group in the context of screening and the post hoc analysis is briefly reported later in this paper.

Outcomes
Outcomes for each scenario were evaluated in a hypothetical UK maternity cohort, over a 1-year period. The outcomes were total culture positive EOGBS infections, EOGBS mortality and severe morbidity (eg, severe motor, intellectual, visual, hearing or other neurological impairment that meant the child was not able to attend mainstream school), use of IAP and maternal penicillin anaphylaxis. These outcomes were combined to explore the number of additional women needed to be treated with IAP to prevent additional EOGBS cases, deaths and severe disability.

The expert group noted that some of the model input parameters were based on low quality or inconclusive evidence. In order to explore the effect these data may have on outcomes, one-way sensitivity analyses were

| Parameter | Input data | Data source |
|-----------|------------|-------------|
| Maternity population characteristics | England and Wales – 718,235, Scotland – 57,202, Northern Ireland – 24,890, Total – 800,327 | Office for National Statistics 2012 live birth data[^38] Information Services Division Scotland 2012–2013 data[^39] and National Records of Scotland 2012 data[^40] Northern Ireland Statistics and Research Agency 2012[^41] |
| Elective caesarean section rate | England – 10.7%, Wales – 11.7%, Scotland – 12.8%, Northern Ireland – 15.3%, Total –11.04%* | Hospital Episode Statistics (HES) 2012–2013 data[^42] Stats Wales 2012–2013 data[^43] ISD Scotland 2012-2013 data[^39] Department of Health, Social Services and Public Safety Northern Ireland 2012–2013 data[^41] |
| Pre-term birth rate | 8.2% | HES 2012–2013 data[^42] |

Proportion of the population with antenatal risk factors for EOGBS

| Parameter | Input data | Data source |
|-----------|------------|-------------|
| Previous infant with EOGBS | 0.03% of model cohort | Colbourn et al, 2007[^7] |
| Incidental group B S *streptococcus* detection | 5.0% of model cohort | Expert group consensus agreement based on Colbourn et al, 2007[^7] and Daniels et al, 2011[^44] |

Proportion of the term population with intrapartum risk factors

| Parameter | Data source |
|-----------|-------------|
| Rate of maternal intrapartum infection in term deliveries | Daniels et al, 2011[^44] |
| Rate of maternal intrapartum infection in pre-term deliveries | Daniels et al, 2011[^44] |
| Rate of pre-labour rupture of membranes (PROM) in pre-term deliveries | Royal College of Obstetricians and Gynaecologists (RCOG) Pre-term PROM Green-top guideline 44, 2010[^45] |

EOGBS mortality and morbidity outcomes

| Parameter | Data source |
|-----------|-------------|
| Mortality in pre-term babies with EOGBS | RCOG, 2012[^14] [derived from Heath et al, 2004[^4]] |
| Mortality in term babies with EOGBS | RCOG, 2012[^14] [derived from Heath et al, 2004[^4]] |
| Morbidity in pre-term babies with EOGBS | Expert group consensus agreement [based on Colbourn et al, 2007[^7]] |
| Morbidity in term babies with EOGBS | Expert group consensus agreement [based on Colbourn et al., 2007[^7]] |

[^4]: Excludes stillbirths, miscarriages and terminations; multiple births are only counted once.
carried out to look at the impact of varying the following input parameters:

- Screening uptake rate.
- Antibiotic delivery in screen positive women.
- Effectiveness of IAP in preventing EOGBS.
- Transition rates for GBS status from screening to delivery.

The sensitivity analyses were run using a plausible lower and higher estimate, based on ranges agreed by the expert group. Individual parameters were changed one at a time, leaving all other parameters unchanged to provide discrete analyses of their impact. Input parameter values and data sources are presented in tables 1, 2, 4 and 5.

**Results**

The model’s key results are presented in table 6.

Based on the inputs 800 327 live births were included in the model. Current guidance recommends that women with intact membranes undergoing elective caesarean should not receive GBS IAP in the absence of labour.

As such, live births by elective caesarean were excluded, reducing the number included in the analysis to 711 999. Without IAP, there were an estimated 421 cases of culture positive EOGBS, a rate of 0.59/1000 live births. The modelled estimate of deaths and severe disability caused by EOGBS without IAP was 42 and 29 respectively.

In the risk based scenario, 30 666 women were estimated to receive antibiotics in labour and 70 cases of EOGBS prevented. In the screening scenario, a further 96 260 women received IAP on the basis of the screening result. This resulted in the prevention of an additional 52 to 57 cases of EOGBS (range in sensitivity analyses: 40 to 67) which included the prevention of three deaths (range in sensitivity analyses: two to four) and four cases of severe disability (range in sensitivity analyses: 3 to 5). This means that with screening, an additional 1675 to 1854 women receive IAP to prevent one EOGBS case and 24 065 to 32 087, to prevent one EOGBS death. Maternal anaphylaxis remained an extremely rare event in both scenarios, with 0.3 cases in the risk based scenario and 1.7 cases in the screening scenario.

Among women receiving IAP in the model, 8% received clindamycin due to reported penicillin allergy. It was assumed that treatment failure due to clindamycin resistance would be avoided by susceptibility testing in screen-positive women.

The sensitivity analyses did not have a large impact on results (see ranges above). An additional, post hoc analysis, focusing on term women with no risk factors indicating IAP, was undertaken. All parameters remained the same as those described above. However, an increase in

| Risk group | Input data | Data source |
|------------|------------|-------------|
| Background incidence/risk group | 0.2 per 1000 births | Royal College of Obstetricians and Gynaecologists (RCOG), 2012 |
| Suspected maternal infection at term | 5.29 per 1000 births | RCOG, 2012 |
| Pre-term birth | 2.30 per 1000 births | RCOG, 2012 |
| Suspected maternal infection at pre-term | 5.29 per 1000 births | Expert group consensus agreement based on RCOG, 2012 |
| Pre-term pre-labour rupture of membranes | 2.30 per 1000 births | Expert group consensus agreement based on RCOG, 2012 |
| Previous baby with EOGBS with no other risk factors | 50 per 1000 births | Expert group consensus agreement |
| Incidence rate/1000 births | 100 per 1000 births | Expert group consensus agreement |
| Incidental group B Streptococcus detection | 2.30 per 1000 births | Expert group consensus agreement based on RCOG, 2012 |
| GBS carrier in labour with no other antenatal or intrapartum risk factors, delivering at term | 0.91 per 1000 births | Expert group consensus agreement based on available data |
| GBS carrier in labour with suspected maternal infection, delivering at term | 24.0 per 1000 births | Expert group consensus agreement based on available data |
| Not a GBS carrier in labour, delivering at term (with or without suspected maternal infection) | 0 per 1000 births | Expert group consensus agreement |

| Background colonisation rate | 22% [Sensitivity analysis: 20%–30%] | Expert group consensus agreement |
the rate of EOGBS in carriers in this group along with a decrease in mortality was assumed. When the rate of EOGBS was double that used in the model, the additional number of women receiving IAP to prevent a case of EOGBS was 844 to 926. The reduced mortality rate meant that the number of women receiving IAP to prevent a death from EOGBS remained the same as the model’s main estimate of 24 065 to 32 087.

**DISCUSSION**

The key outcomes of the model are summarised in box 1. This model suggests that the additional reduction in mortality and severe disability due to EOGBS with culture-based screening for maternal GBS carriage added to the current risk-based approach is likely to be, numerically, very limited in the UK. The addition of screening to the modelled risk-based prevention strategy increased the prevention of EOGBS cases from approximately 16% with the risk-based prevention strategy alone to approximately 25% of the modelled total. Similarly, the proportion of deaths prevented increased from approximately 12% to 19%.

There are a number of reasons for this limited numerical impact. The distribution of EOGBS across the risk groups and the clustering of its worst effects in groups outside the screening population limit the benefits that can be expected. In the model, 54% of the EOGBS cases and 75% of deaths occurred in groups which were not eligible for screening, notably in the groups of women who already have known risk factors for EOGBS prior to 36 weeks or who give birth pre-term. In addition, not all women carrying GBS at labour would be correctly identified by the test. The model estimated that between 20 916 and 30 726 women who screened negative at 36 weeks gestation would be GBS positive at delivery. This group comprised women whose GBS carriage status was estimated to change from negative at the point of screening to positive at the time of labour. This number includes women truly transitioning in carriage status and also those receiving false negative screening test results.

Expert consensus and examples of non-UK based screening programmes suggest that attrition along the pathway should be expected and that uptake of both screening and IAP would be less than 100%. In addition, the delivery of IAP for sub-optimum durations is thought to reduce its prophylactic effect and was factored into the model. However, it should be noted that estimates of effectiveness are not well grounded in clinical trial evidence, and the evidence base exploring duration of administration and prophylactic effect is limited to observational studies.

Prevention of EOGBS as a result of screening has to be considered in relation to the impact on the population as a whole. The likelihood of having a baby affected by
EOGBS appears to be low in women delivering at term with no known risk factors; a rate of about 0.2/1,000 live births was used in the model. These are the women who would be eligible for screening. Studies of antenatal GBS screening test accuracy mainly focus on accuracy for predicting maternal GBS carriage at delivery, and rarely report on neonatal outcomes or ability of the test to predict these. The positive predictive value of screening in late pregnancy for the outcome of EOGBS has recently been estimated as approximately 0.2% (2 cases of EOGBS per 1000 screen-detected carriers). This would be the level of risk reported to women who screen positive. Overdetection is a constant concern about screening, and its high rate in this context means that the ability of GBS screening to provide high quality post-test information may need to be questioned.

Overtreatment is a consequence of overdetection. A number of factors contribute to the high rate of overuse of IAP as a consequence of screening. The model estimated that between 16,382 and 24,065 screen positive women would receive antibiotics when they are no longer carrying the bacterium during labour. In addition, a large proportion of carriers in labour do not transmit the bacterium to the neonate during delivery. Among colonised neonates, only 3% develop EOGBS.

The absence of a diagnostic or risk refinement strategy, to follow a screen-positive result means that many thousands of women would receive GBS IAP to manage a very low risk of EOGBS affecting their baby.

Reports of GBS organisms with reduced susceptibility, or resistance to penicillin, have caused concern despite being very rare and of uncertain clinical significance. While clindamycin has previously been recommended for IAP in women with penicillin allergy, the increase in resistance to this antibiotic has led to RCOG recommending that it should no longer be used for this purpose. In addition to this, the possibility has been raised that intrapartum antibiotics may have long-term effects on the infant gut flora and research into this is in the early stages.

The difficulty in quantifying the harm of GBS IAP may make screening appear to be a harm-free intervention. However, the use of antibiotics in such a large group of women, the vast majority of whom will not experience benefit, means its fit with the current policy emphasis on prudent antibiotic prescribing goals may be difficult. This is because, as modelled, screening would do little to reduce antibiotic usage in the clinical risk groups who already receive IAP, there is low risk of EOGBS in the screened population, limited impact of screening on the worst outcomes, a lack of evidence to estimate whether outcomes are different for screen-detected and clinically-detected babies with EOGBS and

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Table 3  Members of the expert group

| Expert group member                  | Position                                                                 |
|-------------------------------------|--------------------------------------------------------------------------|
| Professor Catherine Peckham (Chair) | National Health Service (NHS), NHS Infectious Diseases in Pregnancy Screening Programme, Executive Lead/Institute for Child Health |
| Dr Alison Bedford-Russell           | Neonatologist, Birmingham Women’s Hospital/Group B Strep Support (GBSS)  |
| Professor Peter Brocklehurst        | Director, Birmingham Clinical Trials Unit, University of Birmingham/Royal College of Obstetricians and Gynaecologists (RCOG)/Greentop Guideline |
| Professor Androulla Efstratiou      | Head, WHO Global Reference Centre for Diphtheria & Streptococcal Infections and European Centre for Disease Prevention and Control, UK Scientific Coordinator |
| Professor Paul Heath                | Consultant in paediatric infectious diseases, St George’s University Hospitals NHS Trust, London: BPSU study/RCOG/Greentop Guideline |
| Dr Rhona Heath                      | Obstetrician, Edinburgh/RCOG/Greentop Guideline                          |
| Dr Theresa Lamagni                 | Senior Epidemiologist and Section Head, Healthcare-Associated Infection & Antimicrobial Resistance Division, National Infection Service, Public Health England (PHE) |
| Dr Anne Mackie                      | Director of Screening & Screening Quality Assurance, PHE                  |
| Mr John Marshall                    | Evidence Lead, UK National Screening Committee                           |
| Dr Rachel Moll                      | National Medical Director’s Fellow, PHE                                  |
| Mrs Jane Plumb                      | Chief Executive, GBSS                                                    |
| Dr Julie Robotham                   | Statistics, Modelling and Economics Department, PHE                      |
| Ms Farah Seedat                     | PhD student, University of Warwick                                       |
| Dr Nan Shetty                       | Consultant Microbiologist and Training Lead, Reference Microbiology Services, PHE |
| Professor Helen Spiby               | Professor of Midwifery, University of Nottingham                         |
| Professor Phillip Steer             | Emeritus Professor of Obstetrics & Gynaecology, Imperial College/GBSS     |
| Professor Ben Stenson               | Neonatologist, Royal Infirmary of Edinburgh/RCOG/Greentop Guideline       |
| Professor Mark Turner               | Neonatologist, Liverpool Women’s NHS Foundation Trust                    |

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a high rate of overtreatment. In addition, the large number of additional women receiving GBS IAP will need to do so in a setting where the antibiotics can be delivered intravenously. This may reduce the choice of birth setting for these women by removing the option of home birth.
Strengths and limitations
Antenatal screening for GBS is a controversial topic, and one of the strengths of this study was the use of a multidisciplinary stakeholder group encompassing a wide range of viewpoints, to gain consensus on the model structure and inputs. To our knowledge, this is the first

Table 5  Screening test uptake and colonisation status transitions between screening and delivery

| Parameter | Input data | Data source |
|-----------|------------|-------------|
| Screening uptake rate | 90% [Sensitivity analysis – 75%–95%] | Expert group consensus agreement |

Colonisation status transition

- Transition rate † from group B Streptococcus (GBS+) at 36 weeks to GBS- at delivery
  - Base case 1: 25% [Sensitivity analysis 11.7%–40%] by Valkenburg-van den Berg et al. 2010,28 Di Renzo et al 201552 and expert group consensus agreement

- Transition rate † from GBS- at 36 weeks to GBS+ at delivery
  - Base case 1: 7.1% [Sensitivity analysis 3.3%–12%] by Valkenburg-van den Berg et al. 2010,28 Di Renzo et al 201552 and expert group consensus agreement

*NB: Based on the data available, it is not possible to distinguish between women who have an incorrect screening result (ie, false positive or false negative) and whose true colonisation status remains unchanged at delivery, and those who had a correct screening result (true positive or true negative) and then transition to a different colonisation status at delivery.

Table 6  Model results

| Risk group | Outcomes before application of either prevention scenario (baseline) | Scenario 1 (risk-based prevention) | Scenario 2 (risk-based plus screening-based prevention) |
|------------|---------------------------------------------------------------|-----------------------------------|-----------------------------------------------------------|
| Number of women in risk group | Early onset GBS (EOGBS) cases | Number of women receiving antibiotics | Antibiotic type offered | Number of women receiving antibiotics |
| Neonate affected by EOGBS in a previous pregnancy | 214 | 12 | IAP and broad spectrum* | 192 | IAP and broad spectrum* | 192 |
| Incidental detection of maternal GBS carriage | 35600 | 84 | IAP and broad spectrum* | 17005 | IAP and broad spectrum* | 17005 |
| Pre-term delivery without the above risk factors | 55446 | 134 | Broad spectrum* | 3041 | Broad spectrum* | 3041 |
| Suspected intrapartum infection at term without the above risk factors | 13036 | 69 | Broad spectrum* | 10428 | Broad spectrum* in all, preceded by IAP in 2065 screen-positive women | 10428 |
| Term women with no antenatal or intrapartum risk factors indicating intrapartum antibiotic prophylaxis (IAP) (without screening) | 607703 | 122 | N/A | 0 | IAP for women who screen group B Streptococcus GBS positive | 96260 |

Summary

| Totals for each scenario | Baseline | Scenario 1 | Scenario 2 |
|-------------------------|----------|------------|------------|
| Population EOGBS cases | 800327 | 30666 | 126926 |
| Deaths from EOGBS | 42 | 70 | 122–127 |
| Severe disability from EOGBS | 29 | 5 | 8–9 |

*Broad spectrum antibiotics given to those with suspected intrapartum infection. N/A, not applicable.
time this approach has been taken to inform a model of antenatal GBS screening.

Data sources were identified through the use of UK National Screening Committee evidence reviews and broad systematic searches for subsequently published evidence. Higher quality evidence, such as published systematic reviews were used where available, as well as national sources including guidance and national statistics. However, systematic reviews to support each model input were not feasible. In addition, the expert group provided input on realistic input values in the absence of relevant evidence.

Limited evidence was available for many model parameters. This includes the rate of penicillin anaphylaxis and the proportion of pregnant women reporting allergy to penicillin. Research to inform these and other inputs would improve future modelling exercises. Research into factors which impact EOGBS risk in babies born to women colonised by GBS could be valuable in the development of a post-screening risk refinement strategy to narrow the pool of women receiving antibiotics. Apart from this group, the number of women receiving antibiotics and the type of antibiotic used remained constant in both strategies in the women with risk factors.

CONCLUSION
This is the first time a consensus-based assessment of the evidence has been developed within a UK-based expert group. A very limited evidence base was encountered and important issues such as the impact of screening on culture-negative disease or on women’s birth experience could not be addressed. However, consensus was achieved on the structure of the model and the parameters required for an estimate of the preventive potential of screening.

The resulting outputs focus attention on a hypothetical screening programme which was estimated to combine a low impact, in terms of preventing the worst aspects of EOGBS, with a high impact, in terms of the volume of women categorised as high risk and treated with prophylactic antibiotics in labour.

Expectations about the benefits of interventions, including screening interventions, can be overestimated by both patients and health professionals.36 37 The modelling work steered by this expert group provides a useful sense of perspective on antenatal screening for maternal GBS carriage.

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alone, and has not been reviewed by the expert group, and may not represent those of all expert group members. DB and JM lead the work to define the model's aims, organise the expert group and to manage the process. AW was responsible for producing the model and provided advice throughout the project's life cycle. AW and AB are employees of Bazian Ltd. which received payment to develop the model through contracts with the UK National Screening Committee. All authors contributed to interpretation of the results. JM, DB, and AW drafted the end of project report and this publication, with critical review by all authors. JM acts as guarantor for the paper.

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**Competing interests** CP chaired the expert group. JM and DB were both employees of the UK National Screening Committee at the time of preparation of the model. An is an employee of Bazian Ltd. who received payment to develop the model and write up the project through contracts with the UK National Screening Committee. Bazian Ltd. have also been paid to carry out other literature searches, reviews and models for the National Screening Committee, including reviews of the evidence on antenatal GBS screening. Bazian Ltd is part of The Economist Group, and holds contracts with public and private organisations within the healthcare industry.

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