COMMERCIAL IN CONFIDENCE

FINAL REPORT

Cost-effectiveness of strategies to prevent infection of group B streptococcus in neonates from maternal colonisation

Economic evaluation to support national evidence based antenatal care guidelines

Prepared for
Commonwealth Department of Health and Ageing

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THE CENTRE FOR INTERNATIONAL ECONOMICS
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Summary

Economic analysis of screening (in some cases in conjunction with providing intrapartum antibiotic prophylaxis) to prevent early onset group B streptococcus disease does not provide support for broad based intervention measures.

Based on measurable benefits, none of the strategies examined are cost effective relative to 'doing nothing' — that is, the benefits do not outweigh the costs involved. This is because of the relatively low number of neonates affected and the absence of robust data on severe/long-term health effects in the event of infection.

That said, it is acknowledged that the low number of neonates affected could be the product of screening practices, and without screening this could possibly change over time.

Of the three strategies examined, routine screening (and to a lesser extent screening and treatment for risk factors) appears to be most cost effective, however, the result is not necessarily definitive enough to guide clinical choice.

Purpose of this study

In 2002, the Centre for Disease Control and Prevention recommended routine screening of all pregnant women to prevent early-onset group B streptococcus disease (EOGBSD) in neonates.

In Australia today, most institutions adopt either a

- *risk-factor approach* to screening, whereby women with certain risk-factors are given intrapartum antibiotic prophylaxis (IAP) to prevent transmission, or a
- *routine* screening approach where women are tested for GBS colonisation at 35-37 weeks. For the latter, women who are preterm and have not been screened will be given IAP, whilst women with fever will be given IAP regardless of colonisation status.

This economic evaluation assesses the cost-effectiveness of these prevention strategies to support national evidence based antenatal care guidelines.

Clinical outcomes largely relate to EOGBSD cases avoided

The principle measured health outcome adopted in international studies is the cost of EOGBSD cases avoided.

Other outcomes that could be examined have proved difficult to quantify under the screening strategy, such as the increased use of antibiotics, restriction of birthing options and maternal stress associated with test results.

Modelling results

Economic analysis of screening (with or without providing intrapartum antibiotic prophylaxis (IAP) in the presence of risk factors) does not support the cost effectiveness of intervention to prevent early onset group B streptococcus disease.

This is because of the relatively low number of neonates affected and the absence of valid data on severe/long-term health effects in the event of infection.

Of the three strategies examined, economic modelling shows that routine screening only is slightly more cost-effective than routine screening with treatment for certain risk factors when the comparator is 'doing nothing'.

- **Routine screening has an ICER of $71 600 per EOGBSD case avoided while routine screening with IAP for certain risk factors has an ICER of $73 500 per EOGBSD case avoided compared to the 'do nothing' alternative.**
- **When comparing total benefits and total costs, the benefit cost ratio ranges from 0.15-0.21 across the strategies. That is, costs are considerably higher than the benefits across all strategies examined. This reflects the low proportion of neonates that have colonisation, and the (only) partial effectiveness of IAP in preventing transmission.**
- **However, the economic analysis excludes any long-term costs associated with disability from EOGBSD due to the lack of consistent clinical evidence on disability impacts. If evidence of long effects emerged, these results would need to be revisited.**
- **Sensitivity testing to reflect the range of costs in the literature changes the order of magnitude of the results, but does not change the ultimate finding that quantifiable costs outweigh quantifiable benefits.**

2 Background

Early-onset group B streptococcus (GBS) disease can be prevented in neonates through intrapartum antibiotic prophylaxis (IAP) in pregnant women. Current Australian recommendations are that women receive IAP on the basis of risk factors or a positive culture result.

There are no Australian-specific studies in the economic literature, however international literature suggests that a risk-based approach to care is more cost-effective than routine screening.

Group B Streptococcus infection risk for neonates

Group B streptococcus (GBS) is a type of bacteria that can colonise the lower genital tract of women. It normally does not cause disease, however, there is a risk of vertical transmission (mother-to-child) if the woman is pregnant.

If a neonate (newborn less than one month) contracts GBS, this can lead to poor health outcomes including early-onset GBS disease, leading to meningitis or at worst, death.

GBS maternal colonisation is not uncommon, with estimated prevalence ranging from 6.5 to 36 per cent over 13 European countries.[1]

The chance of vertical transmission for an untreated women with GBS ranges from 36.4 to 50 per cent depending on the source.[2]

While prevalence is relatively high, there is a low chance of a child with GBS developing early-onset GBS disease (1 to 2 per cent).[3]

The recommended intervention to prevent the transmission of GBS from the mother to neonates is intrapartum antibiotics prophylaxis (IAP), which is the intravenous treatment of women in labour with antibiotics to prevent the transmission of GBS during birth.

Current Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) guidelines recommend giving intrapartum antibiotics when:

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[1] Barcaite E, Bartusevicius A, Tameliene R, Kliucinskas M, Maleckiene L, Nadisauskiene R. 2008, Prevalence of maternal group B streptococcal colonisation in European countries. Acta Obstetricia et Gynecologica Scandinavica;87:260–71.

[2] Colbourn, T. Gilbert, R. 2007. An overview of the natural history of early onset group B streptococcal disease in the UK, Early human development, 83.

[3] Centers for Disease Control and Prevention, 2010 Prevention of perinatal group B streptococcal disease, MMWR 2010;59(No. RR-10).

1 A women has a positive result from a GBS culture test

2 A women presents with the following risk factors:
   a) GBS bacteriuria (bacteria in urine) in current pregnancy
   b) history of previous neonate with early-onset GBS disease
   c) preterm labour at less than 37 weeks
   d) rupture of membranes greater than 18 hours prior to birth, or
   e) maternal fever greater or equal to 38°C[4]

IAP does not guarantee the prevention of early-onset GBS disease in neonates.

However, it does greatly reduce the chances of the disease developing. There are risks involved with IAP including:

- maternal anaphylaxis and other allergic reaction
- the increased exposure of antibiotics to the mother and child can lead to
  - antibiotic resistance
  - influencing the child's immune system including developing allergies[5]

Group B streptococcus universal screening and culture testing

The Centers for Disease Control and Prevention (CDC) recommended universal screening over risk-based screening in 2002 for the prevention of perinatal GBS disease. In 2010, the CDC revised their guidelines to expand on their recommendation on universal screening including laboratory testing methods and treatment algorithms.[6]

GBS colonisation in pregnant women can be confirmed through culture testing. The specimen is collected from the lower genital tract, preferably a vaginal-rectal swab and sent to the pathology unit for culture testing. A midwife can perform the collection or the woman can self-collect if she chooses.

The culture test takes at least 24 hours to get a result and the result is valid for 5 weeks.[7]

A positive result can inform the mother and midwife about preventative options including IAP. However, it is possible that women may be restricted in their birthing options including homebirths.[8]

A negative result can inform the mother and clinician that there is no need for IAP due to no GBS colonisation.

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[4] The Royal Australian and New Zealand College of Obstetricians and Gynaecologists, November 2012, C-Obs 19: Maternal Group B Streptococcus in Pregnancy: screening and management.

[5] King Edward Memorial Hospital, September 2010, Clinical guidelines Section B: Obstetrics and midwifery guidelines: Group B streptococcal disease, Western Australia.

[6] Centers for Disease Control and Prevention, 2010 op. cit.

[7] ibid.

[8] Sheehy, A. Davis, D. and Homer, C. S. E. 2013, Assisting women to make informed choices about screening for Group B Streptococcus in pregnancy: A critical review of the evidence, Women and Birth, 26.

Issues of specificity and sensitivity

With all testing, there is a chance of obtaining false-positive and false-negative results:

- a false positive occurs when the result indicates that the mother has GBS colonisation, but in reality she does not, and can result in women receiving antibiotics they do not need, increasing exposure of antibiotics to the mother and neonate, and
- a false-negative indicates that there is no GBS colonisation when in reality there is and can result in women not receiving the antibiotics or care they need, putting their neonate at risk of acquiring early-onset GBS disease.

Overview of the economic literature

There appear to be no *Australian* economic studies of early-onset group B streptococcus disease (EOGBSD) prevention and screening strategies.

International economic studies are of interest although there are none that are wholly relevant to this evaluation. These are evaluated more fully in Appendix A and include:

- Kaambwa, et al. 2010, Cost-effectiveness of rapid tests and other existing strategies for screening and management of early-onset group B streptococcus during labour.

  A cost-effectiveness study that compares the strategies of universal screening (culture or PCR), risk-factors approach, universal IAP and a 'do nothing' nothing approach to prevent EOGBSD cases in the UK. Many inputs and variables were derived from a United Kingdom Health Technology Assessment (HTA) by Daniels et al, 2009, so there was limited reporting on data sources. The measured outcomes was EOGBS diseases and deaths avoided. The authors found that universal screening was the most cost-effective, however, after removing the assumption that preterm women did not receive IAP, then the risk-factor approach became the most cost-effective.
- Turrentine, et al. 2009, Cost-effectiveness of universal prophylaxis in pregnancy with prior group B streptococci colonization.

  A cost-utility study comparing the strategies of universal screening and universal IAP to prevent EOGBSD and the QALYs gained, specifically for women who had GBS colonisation in a previous pregnancy. The U.S study restricted the analysis to these women and excluded women with risk factors, hence a risk factors approach was not considerered. Previous GBS colonisation is not considered a risk factor in the Australian context. Authors found that universal IAP for these women was more cost-effective that rescreening them.
- Colbourn, et al 2007, 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.

  An economic evaluation for a United Kingdom HTA. This is a cost-utility study comparing various strategies to prevent both EO GBS and non-GBS disease in neonates in the UK. The strategies included current practice, risk factors approach, routine screening (culture based and PCR) and hypothetical strategies based on vaccination. The authors collected their inputs from the perspective of the National Health Service (NHS) and had access to hospital costs hence a number of inputs and

variables were collected for this study. This study did not include prolonged ruptures of the membranes (PROM) as a risk factor. The authors found that the risk-factor based approach was cost-effective, whilst the most cost-effective option was to screen all low risk women and treat all preterm and other high risk women. Universal screening either by culture testing or PCR was not cost-effective.

- Van den Akker-van Marle, et al. 2005, Cost-effectiveness of different treatment strategies with intrapartum antibiotic prophylaxis to prevent early-onset group B streptococcal disease.

  A cost-utility study comparing the prevention strategies of risk-based, universal screening, a combined strategy and the current Dutch guidelines in the Netherlands. The costs and utilities associated with EOGBD were not calculated clearly and may be subject to bias as they were collected from parents of children who had GBS disease. The authors found that the risk-based and combined strategies were the most cost-effective compared to universal screening or the Dutch guideline strategy. The costs of care for pregnancy is different as the percentage of homebirths in the Netherlands is 30 per cent compared to 1 per cent in Australia.

- Stan et al. 2001, Choosing a strategy to prevent neonatal early-onset group B streptococcal sepsis: economic evaluation.

  A cost-effectiveness study comparing prevention strategies to prevent neonatal streptococcal sepsis in Switzerland. The authors found that the risk-factors approach to care was more cost-effective compared to their current policy and routine screening.

- Benitz et al. 1999, Preventing early-onset Group B streptococcal sepsis: Strategy development using decision analysis.

  A cost-effectiveness study comparing the prevention strategies to determine the cost of a prevented EOGBSD case in U.S. The strategies included risk-factors, universal screening (either 28 or 35-37 weeks) with IAP for positive results and risk factors and universal IAP. The findings were that the risk factors strategy had the lowest cost per prevented case. Price years were not reported.

Table 2.1 summarises the similarities and differences between the studies published in economic literature.

2.1 Comparison of economic evaluations

	Kaambwa, 2010	Turrentine, 2009	Colbourn, 2007	Van den Akker-van Marle, 2005	Stan, 2001	Benitz, 1999
Patient group						
All pregnant women	✓	×	✓	✓	✓	✓
Comparator						
Universal Screening (culture)	✓	✓	✓	✓	✓	✓
Risk-factors approach	✓	×	✓	✓	✓	✓
Other comparators (e.g. PCR screening or universal IAP)	✓	✓	✓	✓	✓	✓
Measured outcome						
EOGBSD cases avoided	✓	✓	×	×	×	✓
Cost QALY gained	×	✓	✓	✓	×	×
Other outcome	×	×	×	×	✓	×
Findings						
Universal screening more cost-effective than risk-factor?	✓	×	×	×	×	×
Risk-factor approach more cost-effective than universal screening?	✓ (assumptions changed)	×	✓	✓	✓	✓
Other finding	×	✓	✓	✓	×	×

Source: The CIE

The two studies that were most relevant to the Australian system were Colbourn et al. 2007 and Kaambwa, B. et al. 2010, as the maternity care system in Australia is more similar to the UK or NZ that the United States.[9] These studies are also more recent, lending to the improved validity of cost estimates and other parameters.

[9] Homer, C. Scarf, V. and Davis, D. 2012. Review of evidence for guidelines for minimisation of early onset group B Streptococcal (EOGBS) infection, University of Technology Sydney (not publicly available).

3 Economic framework

The two main approaches to preventing EOGBSD is a risk-factors or screening result. Under the routine screening strategy is it normal to give unscreened preterm women and those with fever IAP.

The resource use in a screening strategy include the cost of screening (materials and staff time) and treatment (IAP and costs of allergic reaction). The measured health outcome is the cost of EOGBSD cases avoided. A number of outcomes that would be difficult to quantify under the screening strategy include the increase use of antibiotics, restriction of birthing options and maternal stress form test results.

The two main clinical options adopted in Australian institutions include risk-based strategy and routine screening with IAP for certain risk factors. This review evaluates the cost-effectiveness of strategies in addition to routine screening to inform national clinical guidelines.

Alternative prevention strategies for GBS infection in neonates

The Department of Health and Ageing (the Department) post-consultation draft Clinical Practice Guidelines Antenatal Care-Module II recommendations include:

- 'Offer either routine antenatal screening for Group B streptococcus colonisation or a risk factor-based approach to prevention, depending on organisational policy (Grade C)'
  - 'If offering antenatal screening, arrange for testing to take place at 35-37 weeks gestation (Grade B)'
- 'Encourage women to self-collect vaginal-rectal specimens for culture testing for Group B streptococcus and offer information about how to do this (Grade C)'

Both clinical practices are in use in Australia, and this depends on jurisdictional guidelines and organisational policy.[10]

This leaves open two prevention strategies (risk-based treatment and routine screening) and this evaluation assesses the relative economic impact of each.

10 The Royal Australian and New Zealand College of Obstetricians and Gynaecologists, November 2012, C-Obs 19: Maternal Group B Streptococcus in Pregnancy: screening and management. Queensland Maternity and Neonatal Clinical Guidelines Program, November 2010, Early onset Clinical guidelines Section B: Obstetrics and midwifery guidelines:Group B streptococcal disease, Queensland. King Edward Memorial Hospital, September 2010, Group B streptococcal disease, Western Australia.

Option 1: Risk factor based approach to prophylactic treatment of GBS colonisation in pregnant women

In the risk factor approach, women receive IAP if they present with:

- preterm labour at less than 37 weeks
- rupture of membranes greater than 18 hours prior to birth
- maternal fever greater or equal to 38°C during labour
- GBS bacteriuria (bacteria in urine) in current pregnancy, and/or
- history of previous neonate with early-onset GBS disease.[11]

The first three risks occur when the woman is in labour and decisions regarding prophylaxis must be made swiftly as there usually is not enough time to perform GBS screening.

The recommended dosage is a loading dose at least four hours before birth, followed by maintenance doses every four to six hours until birth. However, it has been accepted that IAP given at least two hours before birth is still beneficial.[12]

Option 2: routine/universal antenatal screening for GBS colonisation in pregnant women at 35-37 week gestation

In the routine screening approach, all women would be screened for GBS at gestation of 35-37 weeks.

This option results in more women with GBS colonisation being treated than the risk factor-based approach.

This means that there would be increased IAP and thus antibiotic exposure to both the mother and neonate, and increase the risks associated with this exposure.

Option 2a: routine/universal antenatal screening for GBS colonisation in pregnant women at 35-37 week gestation with IAP for certain risk factors

Under a universal screening approach, not all women will necessarily be screened. For instance, women who give birth preterm may miss out on the opportunity to be screened, and women will most likely be given IAP. Similarly, women who present on admission with a fever are generally given IAP regardless of colonisation status.

This highlights the limitations of screening with respect to timing, including, the time it takes to perform the test (> 24 hours) and that results are valid for 5 weeks, thus screening cannot occur earlier.

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11 The Royal Australian and New Zealand College of Obstetricians and Gynaecologists, November 2012, C-Obs 19: Maternal Group B Streptococcus in Pregnancy: screening and management.

12 Queensland Maternity and Neonatal Clinical Guidelines Program, November 2010, Early onset Group B streptococcal disease, Queensland.

Cost and consequences of alternative approaches

Each strategy has differing costs and consequences, table 3.1 illustrates the various resources used and the subsequent health outcomes of these options.

Although the three strategies have many of the same types of costs and consequences, the **amount or magnitude** differ between them. Some costs or consequences are also avoided under the different options.

The risk factor-based approach avoids the costs involved with screening (specimen collection and testing), and less women are given IAP reducing the cost of antibiotics and IV drip.

The universal screening approach includes the costs of screening, increased antibiotic use and exposure. This increased exposure can lead to flow-on effects such as antibiotic resistance, increase chances of anaphylaxis and immune impacts on the newborn. However, it is possible that the rate of early-onset GBS disease and death in neonates will fall.

3.1 Costs and consequences of strategies to prevent EOGBSD in neonates

Item	Risk-factor approach	Routine screening	Routine screening with IAP for certain risk factors
Cost (resource use)			
▪ Cost of screening – consultation to educate women on self-collection or collection by clinician – cost of specimen analysis by pathology unit ▪ cost of consultation with clinician to discuss results and options	×	✓	✓
▪ Cost of treatment – cost of intravenous antibiotics (penicillin, clindamycin, IV drip) – cost of staff time (midwife time during IAP administration)	✓	✓	✓
Cost of maternal adverse reactions from antibiotics	✓	✓	✓
Consequences (health outcomes)			
Measured health outcome			
Cases of early-onset GBS disease	✓	✓	✓
Other health outcomes			
Restrict access to women wishing to have a home birth or within a birth clinic	✓	✓	✓
Emotional/psychological impacts on women	×	✓	✓
Antibiotic resistance	×	✓	✓
Antibiotic exposure to mother and child (impacts on immune system)	×	✓	✓

Source: The CIE

4 Model of options for Australia

Three clinical pathways are modelled in this evaluation. This includes the following.

1) a risk-factor approach to prevention, where women are deemed as either having risk factors or not having risk factors on admission to hospital due to labour, and women with risk factors are given IAP

2) a routine screening strategy, where all women are screened at 35-37 week gestation through a rectal vaginal swab. If the result is positive (or false positive), then she is given IAP, and if the result is negative (or false negative), then she is not given IA, and

3) a combined strategy (screening plus risk based treatment), where institutions that routinely screen women at 35-37 week gestation give IAP to women who are preterm and their colonisation status is unknown or present with fever regardless of colonisation status.

To help identify the most appropriate recommendation for antenatal care with respect to GBS screening, the key economic questions include:

- What is the relative cost-effectiveness of preventing early-onset group B streptococcus Disease (EOGBSD) in neonates through the universal antenatal screening of GBS colonisation in women, a risk factor-based approach to prevention or a combined routine screening approach with IAP given for certain risk factors?
  - What are the resource costs associated with each option?
  - What are the health outcomes associated with each option?

Prevention strategies and outcomes to be measured

To determine the cost effectiveness of the three preventative strategies, the costs and consequences of relevent clinical event pathways needs to be identified.

Chart 4.1 illustrates the decision tree of the three clinical options and can include the probabilities of clinical events and their associated costs. The intervention is IAP and this is based on either a positive result from the culture test, or the presentation of certain risk factors.

Alternative strategies to prevent EOGBSD

In the risk-factor approach to prevention, women are deemed as either having risk factors or not having risk factors on admission to hospital due to labour. These risk factors include preterm birth, fever of 38ºC or more, prolonged rupture of membranes (PROM) for 18 hours or more, having a previous baby colonised with GBS and GBS bacteriuria.

Women are given IAP if they present with risk factors, consequently, there is a reduced chance of the neonate being colonised, and there is a small chance of the neonate developing EOGBSD.

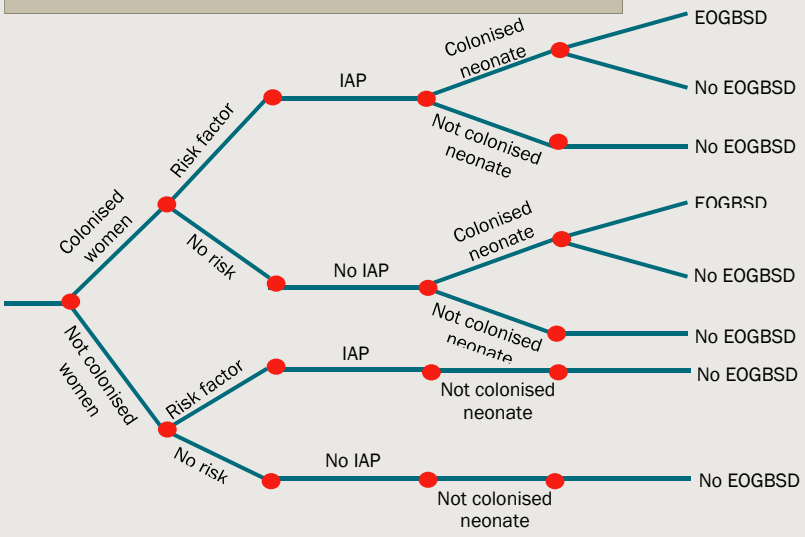
In the routine screening strategy, all women are screened at 35-37 week gestation through a rectal vaginal swab. If the result is positive (or false positive), then she is given IAP, similarly, if the result is negative (or false negative), then she is not given IAP. The IAP should reduce the chance of infection of neonate and consequently the number of EOGBSD cases, women who received a false negative screen are not given IAP regardless of risk factors.

In the combined strategy (screening plus risk based treatment), institutions that routinely screen women at 35-37 week gestation give IAP. Women who are preterm are given IAP if their colonisation status is unknown, that is, they have not been screened, or if they received a positive result. Women who present with fever will be given IAP regardless of colonisation status.

4.1 Alternative prevention strategies to address early-onset GBS disease in neonates

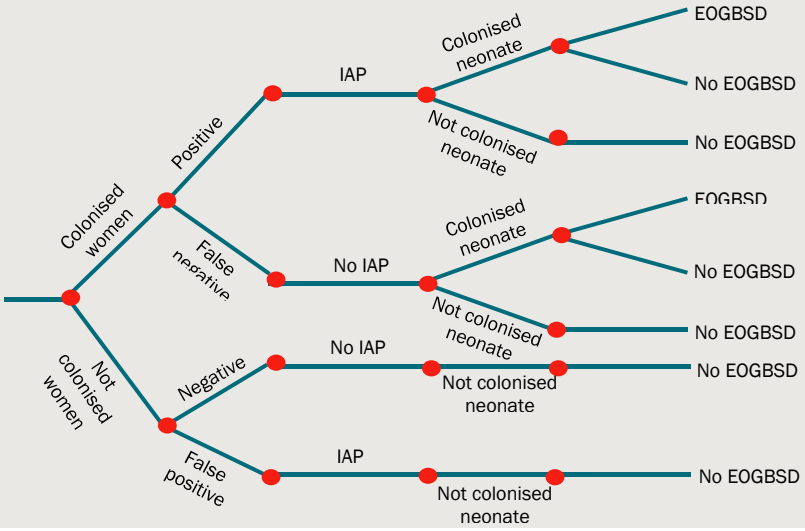
1

Risk-factor prevention strategy
- IAP given to woman during labour if they present with risk factors
- Recommendation Grade C



2

Routine screening strategy
- IAP given to woman with positive result from screen performed at 35-37 week gestation
- Recommendation Grade C



Key consideration:
- Sensitivity and specificity of test:
  - false positive
  - false negative
- Prevalence of risk factors
- Probability of occurrence:
  - probability of maternal colonisation
  - probability of vertical transmission
  - probability of IAP in the prevention of colonisation
  - probability of adverse event from antibiotic
- Probability of outcomes including EOGBSD from colonised neonate
- Cost of intervention:
  - culture testing
  - antibiotic administration
  - cost of adverse events
- Cost of EOGBSD

Continued on next page

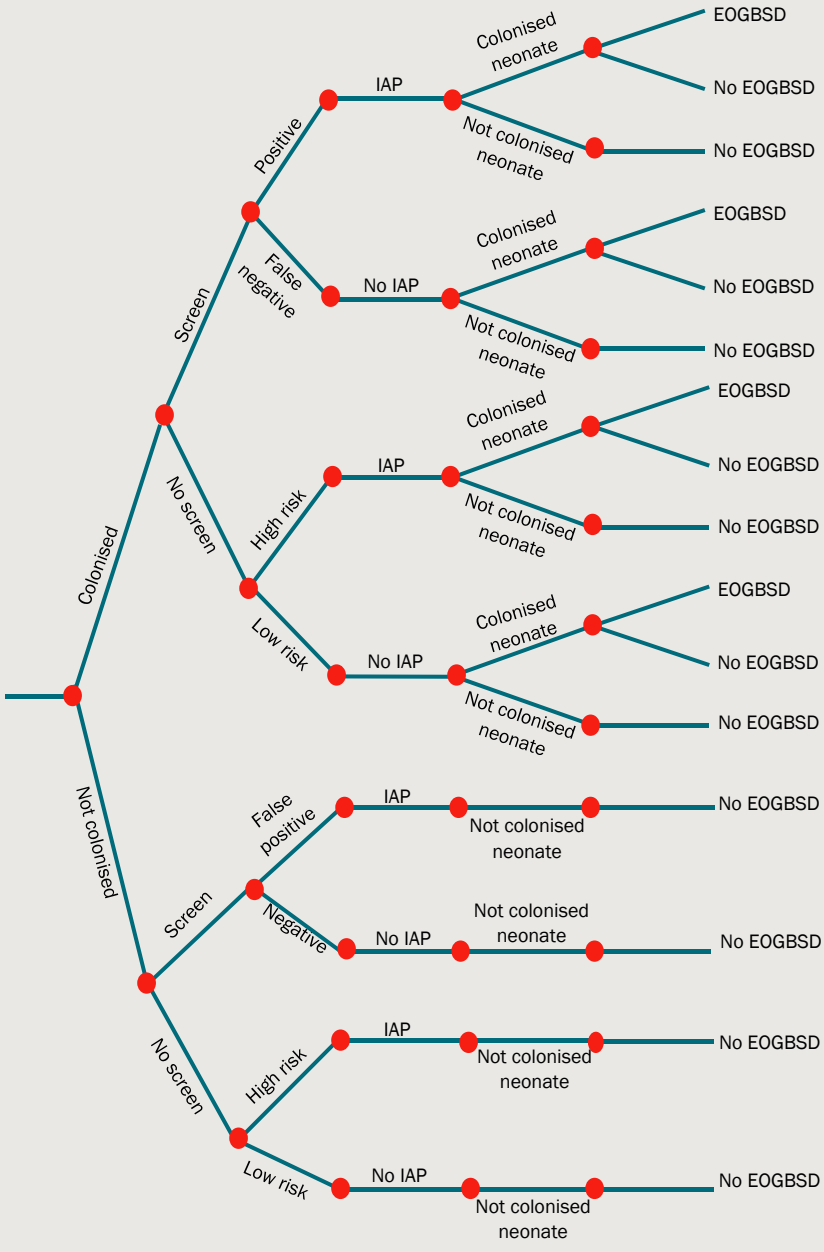
Key

IAP	*Intrapartum antibiotic prophylaxis*
EOGBSD	*Early–onset Group B streptococcus disease*

2a

Routine screening with IAP for certain risk factors

- Current practice for institutions offering routine screening at 35-37 week gestation, IAP given to unscreened preterm women and women with fever during labour



Key consideration:

- Sensitivity and specificity of test:
  - false positive
  - false negative
- Prevalence of risk factors
- Probability of IAP given:
  - preterm unscreened
  - fever
- Probability of occurrence:
  - probability of maternal colonisation
  - probability of vertical transmission
  - probability of IAP in the prevention of colonisation
  - probability of adverse event from antibiotic
- Probability of outcomes including EOGBSD from colonised neonate
- Cost of intervention:
  - culture testing
  - antibiotic administration
  - cost of adverse events
- Cost of EOGBSD

Source: The CIE

Key

IAP *Intrapartum antibiotic prophylaxis*

EOGBSD *Early–onset Group B streptococcus disease*

The clinical event pathways developed for this evaluation make various assumptions about risk factors and adoption of different strategies and associated outcomes. These are set out in box 4.2.

4.2 Assumptions underpinning alternative screening strategies

1 Only colonised women can give birth to colonised neonates. This is dependent on the rate of vertical transmission and impact of IAP (if relevant).

2 In the routine screening strategy, assume that there is 100 per cent compliance rate, that is, all women are screened, and all women who are indicated for IAP (that is, have a positive result) receive it. Similarly, it is assumed that all women are screened at the relevant time, that is, at 35-37 week gestation, not earlier (so that results may be invalid) or at admission (where screening results may not be used). These conditions are not likely to hold in practice, hence, the combined strategy takes into account the fact that unscreened preterm women are given IAP.

3 Cost of EOGBSD is based on the short-term costs of care, that is, neonatal intensive care unit costs. Main outcome measured is the cost per avoided case of EOGBSD, so model does not take into account any long-term costs associated with disability from EOGBSD.

Understanding the economic footprint of alternative strategies

The key data requirements for the model include the prevalence of maternal GBS colonisation and subsequent probability of vertical transmission and EOGBSD in neonates. Other parameters include the prevalence of risk factors and the cost and effectiveness of IAP along with the probability of and cost of allergic reaction. For the screening strategies test characteristics required include the specificity, sensitivity, compliance to screening and cost.

Parameters of prevalence of disease and probabilities of events

Table 4.3 summarises available prevalence data collected for the model.

Rates and probabilities were derived from the systematic literature review on cost-effectiveness studies. Where possible, Australian specific studies on the clinical effectiveness of the studies were sought, also, the studies referenced by the economic evaluations were reviewed. The numbers used in the model are in the base case estimate column.

The prevalence of maternal GBS colonisation ranges from 6.5 to 36 per cent based on a literature review of 13 European countries, another review identified a colonisation rate between 10 to 20 per cent.[13]

[13] Barcaite E, Bartusevicius A, Tameliene R, Kliucinskas M, Maleckiene L, Nadisauskiene R. 2008, Prevalence of maternal group B streptococcal colonisation in European countries. Acta Obstetricia et Gynecologica Scandinavica 2008;87:260–71. Trijbels-Smeulders, M. A. Kollee,L. A. Adriaanse,A. H. Kimpen, J. L. and Gerards, L. J. 2004. Neonatal group B streptococcal infection: incidence and strategies for prevention in Europe, Pediatr Infect Dis J, 23:172–173.

4.3 Parameters for the model

Item	Base case estimate	Range	Reference
	%	%	
Prevalence of maternal GBS colonisation in labour	24	6.5 - 36	Angstetra, 2007. Barcaite, 2008. Conellen, 2000. Hiller, 2005. Hassan, 2011.
Probability of vertical transmission to the neonate from a colonised mother	36.4	36.4-50	Colbourn, 2007. Stan, 2001
Probability of colonised neonate developing EOGBSD	1.5	1 - 2	CDC, 2010. Boyer, 1985. Turrentine, 2006
Prevalence of risk factors	20.9, 31.35 (colonised) and 1.93 (not colonised)	16 - 22	Colbourn, 2007. Gilbert, 2002. Daniels, 2011. Stan, 2001
Prevalence of women who have the risk factors preterm or fever	8.94, 13.41 colonised and 5.96 not colonised	8.94-9.6	Colbourn, 2007. ABS, 2007.
Effectiveness of IAP in the prevention of EOGBSD in neonates	86	80 - 89	Lin, 2001. Schrag,2002. Benitz, 1999.
Rates of compliance (screening)	85	84.7 - 85	Van Dyke, 2009. Goins, 2010
Sensitivity of culture testing	81	30 - 90.8	Hiller, 2005 . Van den Akker-van, Marle, 2005. Stan, 2005. Colbourn, 2007.
Specificity of culture testing	93	88.9 - 95	Stan, 2001. Colbourn, 2007. Hiller, 2005. Benitz,1999 (Risk factors).
Probability of allergic reaction with penicillin (maculopapular rash)	5	0.7 - 5	Stan, 2001. Colbourn, 2007. CDC, 2010, Petri, 2006
Probability of severe allergic reaction with penicillin	0.001		Stan, 2001. Colbourn, 2007

Source: The CIE

Two Australian cohort studies have identified a colonisation rate of 24 per cent (2004) and 20 per cent (1998-99), however, earlier studies have identified a colonisation rate between 12 to 15 per cent (published 1989-1995).[14]

The colonisation rate of 24 per cent was chosen as this was based on more recent sampling. The probability of vertical transmission from a colonised mother without IAP

[14] Angstetra D, Fergusen D, Giles W. Institution of universal screening for group B stretococcus (GBS) from a risk management protocol results in reduction of early-onset GBS disease in a tertiary obstetric unit. Australian and New Zealand Journal of Obstetrics and Gynaecology 2007;47:378–82. Hiller, J. E. McDonald, H. M. Darbyshire, P. and Crowther, C. A. 2005. Antenatal screening for Group B Streptococcus: A diagnostic cohort study, BMC Pregnancy and Childbirth, 5(12). Connellan, M. and Wallace, E. M. 2000.Prevention of perinatal group B streptococcal disease: screening practice in public hospitals in Victoria. MJA. 172.

is 36.4 per cent based on a pooled estimate from 6 studies ranging from 1975 to 1985.[15] Stan, 2001 used 50 per cent.

The chance of a colonised neonate developing EOGBSD is between 1 and 2 per cent, the midpoint of 1.5 per cent was used in the base case analysis.[16]

A small Australian cohort study found that risk factors occur in 16 per cent of women, however international studies have identified the incidence to be 17.7 per cent, 20.9 per cent and 22 per cent.[17] The risk factors incidence rate of 20.9 per cent was used in the base case analysis. Colbourn, 2007 found that colonised women had a 1.5 odds ratio of having risk factors, hence it was estimated that 31.35 per cent of colonised women had risk factors, whilst, 13.93 per cent of uncolonised women had risk factors.

It is assumed that only 85 per cent of the population are screened, the remaining 15 per cent are given IAP in the combined strategy if they present with risk factors, these are preterm birth with colonisation unknown, and fever regardless of colonisation status.[18] It is assumed that the percentage of women with preterm births is 7.34 per cent based on Colbourn, 2007, however this is similar to 8 per cent as seen in Australia in 2004.[19] The proportion of women with fever is assumed to be 1.6 per cent.[20] This makes the proportion of unscreened women with risk factors to receive IAP at 8.94 per cent. However, it has also been suggested that 49.7 per cent of preterm women are unscreened.[21] In the sensitivity analysis it was assumed that having risk factors preterm birth and fever also had a 1.5 odds ratio of being colonised.

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15 Colbourn, T. Gilbert, R. 2007. An overview of the natural history of early onset group B streptococcal disease in the UK, Early human development, 83

16 Centers for Disease Control and Prevention, 2010 Prevention of perinatal group B streptococcal disease, MMWR 2010;59(No. RR-10)

17 Gilbert, G. L. Hewitt, M. C. Turner, C. M. and Leeder, S. R. 2002. Epidemiology and predictive values of risk factors for neonatal group B streptococcal sepsis, Australian and New Zealand Journal of Obstetrics and Gynaecology, 42(5). Daniels, J. P. Gray, J. Pattison, H. Gray, R, Hills, R. Khan, K. 2011. Intrapartum tests for group B streptococcus: accuracy and acceptability of screening, BJOG, 118. Stan, C. M. Boulvain, M. Bovier, P. A. et al. 2001. Choosing a strategy to prevent neonatal early-onset group B streptococcal sepsis: economic evaluation. 180. Colbourn, T. Asseburg, C. Bojke, L. et al. 2007. Prenatal screening and treatment strategies to prevent gtoup B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses. Health Technology Assessment. 11(29).

18 Van Dyke, M. K. Phares, C. R. Lynfield, R. et al. 2009.Evaluation of universal antenatal screening for group B streptococcus, The New England Journal of Medicine, 360(25).

19 Colbourn, T. Asseburg, C. Bojke, L. et al. 2007. Prenatal screening and treatment strategies to prevent gtoup B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses. Health Technology Assessment. 11(29). ABS, Australia Social Trends, 2007. 4102.0

20 Colbourn, T. Asseburg, C. Bojke, L. et al. 2007. Prenatal screening and treatment strategies to prevent gtoup B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses. Health Technology Assessment. 11(29)

21 Van Dyke, M. K. Phares, C. R. Lynfield, R. et al. 2009.Evaluation of universal antenatal screening for group B streptococcus, The New England Journal of Medicine, 360(25)

IAP is 80 to 89 per cent effective in preventing the transmission of GBS to neonates.[22] We used the rate of 86 per cent as Van den Akker-van Marle, 2005, also cited this.

The sensitivity of culture testing ranged from 33 to 90.8 per cent and the specificity of culture testing ranges from 88.9 to 95 per cent.[23] We used 81 per cent for sensitivity rate and 93 per cent for the specificity rate in the model as this was based on an Australian study.[24]

The probability of a mild maternal antibiotic reaction was 5 per cent and a severe reaction of 0.01 per cent.[25] The risk of developing any allergic reaction (either mild or severe) was 0.7 to 4 per cent, whilst the risk of anaphylaxis by penicillin ranged from 4/10000 to 4/100000.[26]

Cost estimates

Table 4.4 lists the cost estimates used for the base case analysis. All prices were adjusted to 2012 Australian dollars, prices were inflated according to healthcare and social assistance inflation rate and converted to Australian dollars.

Culture screen

The cost of a culture screen has been estimated at $34.34, after adjusting for the rate of receiving positive and negative screens (where the latter avoids an additional discussion with a midwife). This includes costs of the consumables for testing including gloves,

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22 Benitz, W. E. Gould, J. B. and Druzin, M. L. 1999. Antimicrobial prevention of early-onset Group B streptococcal sepsis: estimates of risk reduction based on a critical literature review, Pediatrics, 103. Centers for Disease Control and Prevention, 2010 Prevention of perinatal group B streptococcal disease, MMWR 2010;59(No. RR-10). Schrag SJ, Zell ER, Lynfield R, et al. A population-based comparison of strategies to prevent early-onset group B streptococcal disease in neonates. N Engl J Med 2002;347:233–9. Lin FY, Brenner RA, Johnson YR, et al. The effectiveness of risk-based intrapartum chemoprophylaxis for the prevention of early-onset neonatal group B streptococcal disease. Am J Obstet Gynecol 2001;184:1204–10.

23 Hiller, J. E. McDonald, H. M. Darbyshire, P. and Crowther, C. A. 2005. Antenatal screening for Group B Streptococcus: A diagnostic cohort study, BMC Pregnancy and Childbirth, 5(12). Van den Akker-van Marle ME, Rijnders ME, Dommelen P, Fekkes M, Wouwe JP, Amelink-Verburg MP, Verkerk PH. Cost-effectiveness of different treatment strategies with intrapartum antibiotic prophylaxis to prevent early-onset group B streptococcal disease. BJOG. 2005 Jun;112(6):820-6. Stan, C. M. Boulvain, M. Bovier, P. A. et al. 2001. Choosing a strategy to prevent neonatal early-onset group B streptococcal sepsis: economic evaluation. 180. Colbourn, T. Asseburg, C. Bojke, L. et al. 2007. Prenatal screening and treatment strategies to prevent gtoup B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses. Health Technology Assessment. 11(29)

24 Hiller, J. E. McDonald, H. M. Darbyshire, P. and Crowther, C. A. 2005. Antenatal screening for Group B Streptococcus: A diagnostic cohort study, BMC Pregnancy and Childbirth, 5(12).

25 Stan, C. M. Boulvain, M. Bovier, P. A. et al. 2001. Choosing a strategy to prevent neonatal early-onset group B streptococcal sepsis: economic evaluation. 180.

26 Centers for Disease Control and Prevention, 2010 Prevention of perinatal group B streptococcal disease, MMWR 2010;59(No. RR-10)

swabs, transport medium, plates and broth and 10 minutes of pathologists' time,[27] a 10 minute consultation with a midwife to educate women regarding self-collection, and if the test returned positive, another 10 minute consultation with a.[28]

This estimate is at the lower bound of results reported in in the literature, which ranged from $20.83 to $80.11,[29] and should be considered conservative.

IAP

The cost of IAP consists of the consumables for treatment including a cannula, saline flush (5ml), 5ml syringe, saline for injection (20ml) and the cost of 15 minutes of a midwifes time.[30]

The cost of intravenous antibiotics is based on the cost of initial doses and 2 subsequent doses of benzylpenicillin or clindamycin depending if the women is allergic to beta lactam. The cost of an initial dose of 1.2mg IV benzylpenicillin is $99.06 and two subsequent doses of 600mg IV benzylpenicillin of $99.06.[31] The cost of an initial dose of clindamycin of 600mg is $10.97 and for two subsequent doses at 600mg each is $21.94.[32]

This brings the total cost of IAP adjusting for treatment with either benzylpenicillin or clindamycin to $198.60, which is high compared to the literature where the cost of IAP ranges from $23.90 to $133.58.[33]

Antibiotic reaction

The cost of a mild antibiotic reaction is estimated to be $102.02 and for a severe antibiotic reaction at $1 352.18. Multiplied by the probability of each event occurring, this amounts to $5.21 per patient.[34] However, it should be recognised that probabilities and costs are from an older, non-Australian study.

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27 Colbourn, 2007.Pathology technician grade 1 accessed 18 September <http://www.fairwork.gov.au/2006payscalesummaries/AP783872.pdf>

28 Average cost of midwife at Grade 5 in NSW, QLD and VIC, accessed 18 September 2013 <http://www0.health.nsw.gov.au/policies/ib/2011/pdf/IB2011_009.pdf>, <http://www.health.qld.gov.au/hrpolicies/wage_rates/nursing.asp>, <http://docs.health.vic.gov.au/docs/doc/E167F91430C2F660CA257A2F0018CFA7/$FILE/Final%20signed%20Nurses%20and%20Midwives%20Agreement.pdf>

29 Colbourn, 2007. Kaambwa, 2007. Turrentine, 2009. Stan, 2001.

30 Colbourn, 2007

31 Benzylpenicillin 600mg IV DPMQ 1775K, PBS Online, accessed 18 September 2013

32 University of Pennsylvania, hospital costs, accessed 18 September 2013 <http://www.uphs.upenn.edu/bugdrug/antibiotic_manual/antibiotic%20costs.htm>

33 Colbourn, 2007. Kaambwa, 2007. Stan, 2001

34 Stan, 2001

Cost of EOGBSD

We assumed the cost of treating neonatal morbidity is $1320.98 per bed days with severe cases such as meningitis costing 8 bed days and a mild case such as bacteraemia costing 5 bed days.[35] Assuming 15 per cent of cases are severe and the remaining are mild amounts to $7 199.36 to treat EOGBSD.

This is similar to the Colbourn, 2007 study which costed severe cases at $1 200.71 per bed day and $727.12 per bed day for mild cases.

4.4 Cost estimates for baseline model

Item	Base case estimate	Range	References
	$		
Cost of culture screen (positive)	26.13		Colbourn, 2007. NSW Health, QLD Health, VIC Health, Fairwork Australia
Cost of culture screen (negative)	20.01		Colbourn, 2007. NSW Health, QLD Health, VIC Health, Fairwork Australia
Cost of culture screen	21.53	10.9 - 80.11, average from literature is 44.66	Colbourn, 2007. NSW Health, QLD Health, VIC Health, Fairwork Australia, . Kaambwa, 2007. Turrentine, 2009. Stan, 2001
Costs of IAP	198.60	23.90-133.58, average from literature is 58.97	Colbourn, 2007. NSW Health, QLD Health, VIC Health, PBS online, University of Pennsylvania`, Kaambwa, 2007. Stan, 2001
Cost of antibiotic reaction	5.21		Stan, 2001
Cost of IAP adjusting for antibiotic reaction	203.81	29.11-138.79	Colbourn, 2007. NSW Health, QLD Health, VIC Health, PBS online, University of Pennsylvani. Stan, 2001.
Cost of severe EOGBSD	10567.86	9 605.65 to 10 567.89	Lain, (article in press, eHUB, 2013), Colbourn, 2007
Cost of mild EOGBSD	6604.91	3 635.58 to 6 604.91	Lain, (article in press, eHUB, 2013), Colbourn, 2007
Cost of EOGBSD	7199.36	4531.09-7199.36	Lain, (article in press, eHUB, 2013). QLD Maternity guidelines, Colbourn, 2007

Note: Prices adjusted to 2012 $AUD. Prices were inflated according to healthcare and social assistance inflation rate and converted to Australian dollars. According to the model there were 24.76 per cent positive results and 75.24 per cent negative results. Assumed that 90 per cent of wome are treated with benzylpenicillin and 10 per cent with clindamycin. Assumed that the proportion of neonates with severe EOGBSD is 15 per cent and with mild EOGBSD is 85 per cent.

Source: The CIE. Lain, S. J. Nassar, N. Bowen, J. R. and Roberts, C. L. Article in press. Risk factors and costs of hospital admissions in first year of life: A hospital population-based study, The Journal of Pediatrics. Queensland Maternity and Neonatal Clinical Guidelines Program, November 2010, Early onset Clinical guidelines Section B: Obstetrics and midwifery guidelines: Group B streptococcal disease, Queensland

[35] Lain, S. J. Nassar, N. Bowen, J. R. and Roberts, C. L. Article in press. Risk factors and costs of hospital admissions in first year of life: A hospital population-based study, The Journal of Pediatrics.

Cost-effectiveness of alternative strategies

Incremental cost-effectiveness ratio

The incremental cost effectiveness ratio (ICER) is used to determine the cost-effectiveness of the different strategies. The ICER is calculated by dividing the relative cost an intervention by the relative benefit of the intervention. That is:

$$ICER = (Cost_{Strategy} - Cost_{Comparator})/(Health\ outcome_{Strategy} - Health\ outcome_{Comparator})$$

The health outcome is calculated as the EOGBSD cases avoided from the strategy compared to the comparator. The cost of the strategy is the cost of resources (either IAP and/or screening) minus the costs of saved from that strategy. The costs saved from the strategy is the cost of consequences of the strategy (treatment of EOGBSD cases) minus the costs of consequences from the comparator:

$$Cost\ of\ strategy = (Cost\ of\ resources_{Strategy} - (Cost\ of\ consequences_{Strategy} - Cost\ of\ consequences_{Comparator}))$$

The three prevention strategies were compared to a hypothetical case of no screening or treatment, which had no costs of resources but resulted in 13.11 EOGBSD cases per 10 000 women.

Table 4.5 shows that all three strategies have high ICERs compared to the comparator of no screening or treatment.

With the routine screening and screening with IAP for risk factors around $60 000 per EOGBSD case avoided.

The risk-factor approach to care has the highest ICER of over $96 591 per EOGBSD case avoided.

4.5 ICER of strategies compared to no 'do nothing' alternative, per 10 000 women

Strategy	EOGBSD cases avoided per 10 000	Costs of resources	Costs of consequences	Cost savings	Cost of strategy, adjusted for savings	ICER
		$'000	$'000	$'000	$'000	$'000
No screening or treatment	-	0	94.34	-	-	-
Risk based strategy	3.53	368.57	68.91	25.44	34.31	97.12
Routine screening strategy	9.13	719.19	28.62	65.72	65.35	71.59
Routine screening with treatment for risk factors	7.91	628.60	37.40	56.95	58.17	73.53

Source: The CIE

Considering that most Australian institutions either follow a risk-based strategy, routine screening or a combined screening approach, ICERs were calculated against the risk-based strategy as this had the highest cost-effective ratio compared to no treatment.

Table 4.6 shows the incremental cost of preventing an extra EOGBSD case under the routine screening strategy was $55 464 compared to the risk-based screening strategy.

The routine screening with IAP for certain risk factors was more cost-effective with an ICER of $54 491per EOGBSD case avoided.

4.6 ICERs compared to strategy of routine based screening, per 10 000 women

Strategy	EOGBSD cases avoided per 10 000	Costs of resources	Costs of consequences	Cost savings	Cost of strategy, adjusted for savings	ICER
		$'000	$'000	$'000	$'000	$'000
Risk based strategy	-	388.57	68.91	-	368.57	-
Routine screening strategy	5.6	717.19	28.62	40.28	678.91	55.46
Routine screening with treatment for risk factors	4.38	638.60	37.40	31.51	607.09	54.49

Source: The CIE

Other factors that affect cost-effectiveness

The ideal time to test is after 35-37 week gestation. However, in some cases only 50 per cent of women tested in this time period.[36]

This is to ensure adequate preparation for prophylaxis, if the test is performed too early then the result could be invalid as GBS colonisation can occur later in pregnancy. If the testing is performed too late, that is, during admission, then there may not be enough time to get the results, particularly if the time between admission and delivery is less than 24 hours.

There can be issues with the collection of the specimen, taking the swab can be considered invasive leading to avoidance by women. Further, there are issues with self-collection, clinicians should explain to the woman how to self-collect using diagrams or pictures if necessary. Language or communication barriers can make this difficult leading to inadequate specimen collection and possibly inaccurate results.

The model did not distinguish between the five risk factors and women are likely to have more than one risk factor, for instance, bacteriuria and preterm labour. Another limitation is that under a routine screening strategy, some women may present with suspected preterm labour, fail to progress and deliver at term with no risk factors.

Finally, compliance rates for treatment under the risk-based approach was assumed to be at 100 per cent. It is possible that in some institutions, there may be women who are indicated for treatment (have risk factors) but do not receive IAP.

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36 Van Dyke, M. K. Phares, C. R. Lynfield, R. et al. 2009.Evaluation of universal antenatal screening for group B streptococcus, The New England Journal of Medicine, 360(25)

5 Key findings

Routine screening (and to a lesser extent routine screening and treatment for risk factors) is expected to be more cost effective than a risk based approach, although the results are not strong enough to meaningfully guide clinical choice. Routine screening has an ICER of $71 588 per EOGBSD case avoided while routine screening with IAP for certain risk factors has an ICER of $73 532 per EOGBSD case avoided compared to the 'do nothing' alternative.

Sensitivity analysis on the resource and consequences costs does not change this outcome — adjusting costs to upper or lower bounds of the literature changes the magnitude of the ICER but not the ranking of strategies.

The difference in results across the strategies examined reflects differences in identifying, treating and avoiding EOGBSD.

Based on measurable costs and benefits, none of the strategies examined are cost effective relative to 'doing nothing' — the benefits do not outweigh the costs involved. This is because of the relatively low number of neonates affected and the absence of valid data on severe/long-term health effects in the event of infection.

That said, it is acknowledged that the low number of neonates affected could be the product of screening practices, and without screening this could possibly change over time.

Costs and consequences of current practice in Australia

Current practice in Australian institutions is to adopt either a risk-factors strategy or provide routine screening with IAP given to preterm women with unknown colonisation and women with fever regardless of colonisation status.

Under the risk-factor strategy, for every 10 000 women, there would be 9.57 cases of EOGBSD costing $68 905.29. The cost of resources would be $368 573.

Under the routine screening strategy, 3.98 cases of EOGBSD would occur in every 10 000 women, costing $28 622.88. The cost of implementing the strategy would be $719 191.

Under the screening strategy with IAP for certain risk factors, there would be 5.19 cases of EOGBSD for every 10 000 women. This would cost $37 393 in hospital care while the cost of the implementing the strategy would be $638 603.

Economic feasibility

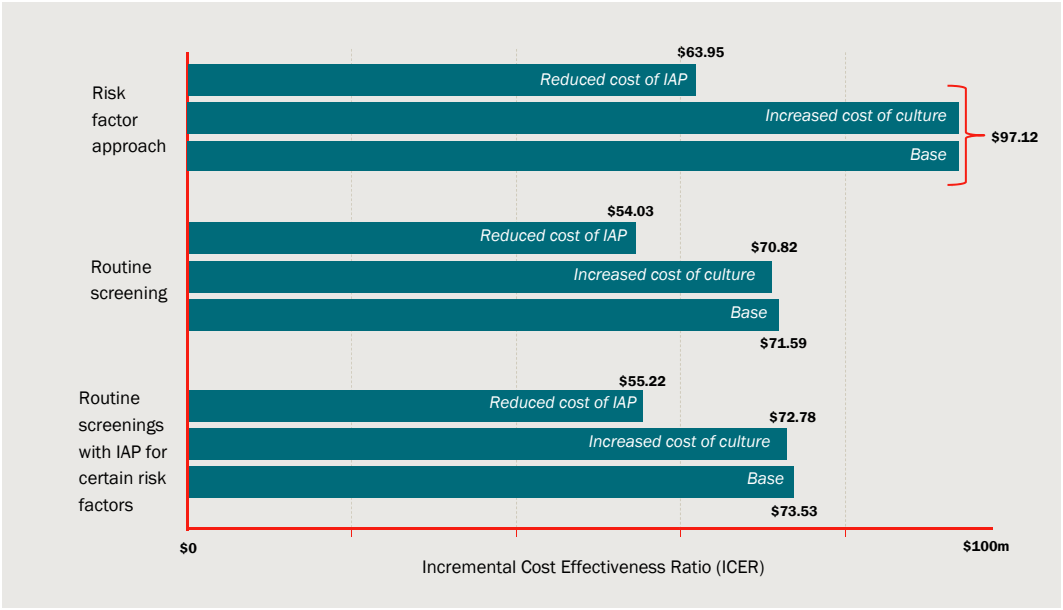
Sensitivity analysis

All parameters including costs were changed under a one-way sensitivity analysis to determine if the findings in the model were robust.

The parameters that the model were most sensitive to include that costs of screening, cost of IAP and the test characteristics such as sensitivity and specificity, as shown in Table 5.2.

The cost estimates that the model was most sensitive to were the cost of IAP and culture testing, when using values from the literature, this changed the ICERs and their rankings as seen in chart 5.1.

5.1 Alternative strategies to prevent early onset GBS Disease



Note: The cost of IAP reduced to $138.79 per women and the cost of culture screen increased to $20.83 per women as per literature.
Data source: The CIE.

Under the model the routine screening with IAP for certain risk factors strategy was more cost-effective compared to the routine screening strategy, against the risk-factor strategy as the comparator, at an ICER of ~$55 500 per EOGBSD case avoided.

An increase in the cost of culture screening from $21.53 to $44.66 (middle value found in the literature) brings the ICERs of the screening strategies to >$95 000.

Reducing the cost of IAP from $203.81 to the highest cost found in the literature of $138.79 showed that the ICERs ranking was lowest for the routine screening strategy against both the 'do nothing' and risk-factor strategy comparators, this also brought the ICER of the risk-factor strategy to $64 000 compared to the 'do nothing' comparator.. If the cost of IAP was reduced to $29.11 (lower end of the literature values), then the risk-factor approach was most cost-effective compared to the do nothing alternative,

further, the ICERs of the screening strategy dropped to around $24 000 per EOGBSD case avoided.

The remaining changes in the parameters including prevalence of GBS colonisation, probability of transmission, and development of EOGBSD left the ICER rankings unchanged. However, if the probability of the colonised neonate developing EOGBSD fell from 1.5 per cent to 1 per cent, the ICERs of the screening strategies against the risk factor approach increased to over $85 000. Changes to the prevalence of risk factors in either the risk-factor approach or combined routine screening and risk-factor strategies did not change the ICER rankings. Similarly, small increases and decreases in the effectiveness of IAP did not affect the ICER rankings.

If the sensitivity of the culture testing was as low as 30 per cent as suggested in the literature, the risk-factors approach was more cost-effective compared to the do nothing scenario. If the sensitivity of testing increased to 90.8 per cent, the ICER rankings remained the same.

The model was sensitive to both small increases and decreases to specificity of the culture test from 93 per cent. A fall in specificity to 89.9 per cent showed that the routine screening strategy was more cost-effective compared to both comparators.

If the specificity of culture testing increased from 93 to 95 per cent, then the routine screening with IAP for certain risk factors strategy was the most cost-effective when compared to the do nothing alternative and risk-factor based approach.

Barriers to implementation

Screening presents a barrier to women's access to other models of delivery, that is, homebirth or at a birth clinic. Women who receive a positive result can be excluded from many publicly funded homebirth models. As this occurs in the last weeks of pregnancy, the impact on women and her family is multiplied.[37] The proportion of women who give birth in planned homebirths (and unexpected births in other settings) or birth clinics made up 0.9 per cent and 2.2 per cent, respectively, in 2010.[38]

Similarly a positive GBS screening result may preclude women from continuing care led by a midwife, as they would then be cared for by an obstetrician.

There is also a possibility that a positive culture result will lead to maternal anxiety and stress during the pregnancy. Women who are known GBS colonisers (or received a false positive result) can experience stress about the impacts of this on their neonate and upcoming IAP during delivery.

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[37] Sheehy, A. Davis, D. and Homer, C. S. E, 2013, Assisting woment to make informed choices about screening for Group B Streptococcus in pregnancy: A critical review of the evidence, Women and Birth, 26 (2)

[38] Australian Institute of Health and Welfare, Li Z. Zeki, R. Hilder, L. and Sullivan, E.A, 2012. Australia's mothers and babies 2010. Perinatal statistics series no. 27. Cat. No. PER 57. Canberra: AIHW National Perinatal Epidemiology and Statistics Unit.

5.2 Sensitivity analysis: ICERs for strategies compared to do nothing and routine screening strategies

		ICER 1 vs. N	ICER 2 vs. N	ICER 3 vs. N	ICER 2 vs. 1	ICER 3 vs. 1	Ranking compared to base analysis
	Sensitivity values	**97124.47**	**71588.04**	**73532.89**	**55463.82**	**54491.27**	
	$						
Cost of culture screen	44.66	97124.47	96926.97	98387.72	96802.26	99497.35	Compared to do nothing alternative, risk-factor approach is the most cost-effective. Compared to risk-factor approach, routine screening is more cost-effective than combined screening
Cost of culture screen	80.11	97124.47	135762.46	136481.27	160159.27	168247.59	Compared to do nothing alternative, risk-factor approach is the most cost-effective. Compared to risk-factor approach, routine screening is more cost-effective than combined screening
Cost of IAP adjusting for antibiotic reaction	29.11	7723.1	24282.74	24174.77	34738.84	37453.54	Compared to do nothing alternative, risk-factor approach is the most cost-effective. Compared to risk-factor approach, routine screening is more cost-effective than combined screening
Cost of IAP adjusting for antibiotic reaction	138.79	63947.5	54033.00	55216.05	47772.76	48168.55	Same
Cost of EOGBSD	4531.09	99792.74	74256.31	76201.16	58132.09	57159.54	Same
Prevalence of maternal GBS colonisation in labour	6.5	313158.26	177105.77	186323.43	91199.53	83950.37	Same
Prevalence of maternal GBS colonisation in labour	36	70377.43	58523.93	59568.35	51039.40	50843.95	70377.43
Prevalence of vertical transmission to the neonate from a colonised mother	50	68748.39	50157.86	51573.72	38419.44	37711.42	68748.39
Probability of colonised neonate developing EOGBSD	1	149286.38	110981.73	113899.02	86795.42	85336.58	Same
Probability of colonised neonate developing EOGBSD	2	71043.51	51891.19	53349.83	39798.03	39068.61	Same
Prevalence of risk factors if maternal colonisation	24	115800.59	71588.04	73532.89	52972.22	51571.37	Same

		ICER 1 vs. N	ICER 2 vs. N	ICER 3 vs. N	ICER 2 vs. 1	ICER 3 vs. 1	Ranking compared to base analysis
	Sensitivity values	**97124.47**	**71588.04**	**73532.89**	**55463.82**	**54491.27**	
	$						
Prevalence of risk factors if maternal colonisation	33	94075.30	71588.04	73532.89	56128.04	55305.38	Same
Prevalence of risk factors if no maternal colonisation	10.66	82808.94	71588.04	73532.89	64502.93	66045.85	Same
Prevalence of risk factors if no maternal colonisation	14.66	100320.29	71588.04	73532.89	53445.92	51911.80	Same
Prevalence of preterm birth risk factor	9.6	97124.47	71588.04	73673.53	55463.82	54793.54	97124.47
Effectiveness of IAP in the prevention of EOGBSD in neonates	80	104948.75	77497.09	79587.81	60163.56	59118.07	Same
Effectiveness of IAP in the prevention of EOGBSD in neonates	89	93607.93	68932.28	70811.58	53351.58	52411.81	Same
Rates of compliance (screening)	84.7	97124.47	71588.04	73628.75	55463.82	54558.36	Same
Sensitivity of culture testing	30	97124.47	131847.63	133922.94	-660102.71	-107529.36	Risk-factors was the most cost-effective against a do nothing alternative. However, the routine screening was more cost-effective compared to the combined strategy when the comparator was risk-factors.
Sensitivity of culture testing	90.8	97124.47	67762.28	69566.15	52278.60	51250.80	Same
Specificity of culture testing	88.9	97124.47	71588.04	80347.15	55463.82	66805.56	Routine screening more cost-effective than combined strategy compared to risk-factor approach
Specificity of culture testing	95	97124.47	71588.04	70208.87	55463.82	48484.30	Combined screening strategy is the most cost-effective when compared to do nothing and to risk-factor based approach

Note :1 = Risk-factor strategy, 2 = Routine screening, 3 = Routine screening with IAP for certain risk factors and N= do nothing alternative

Source: The CIE

A Collection and appraisal of economic literature

Search strategy

A number of databases were searched for peer-reviewed literature on the cost-effectiveness or economic evaluations of the two main prevention strategies for GBS infection in neonates. The search terms used were developed in collaboration with the Department and included 'cost', 'pregnancy', 'group B streptococcus' and 'antibiotic'.

The databases searched were Medline, CINAHL, Cochrane Library, Embase, EconLit and Science Direct.

Table A.1 lists the results of the searches.

A.1 Results of literature search strategy

Database	Terms	Results	Date
Medline	cost AND pregnancy AND group B streptococcus AND antibiotic	60	6 August 2013
Cochrane Library	cost AND pregnancy AND group B streptococcus AND antibiotic	8	7 August 2013
Science Direct	cost AND pregnancy AND group B streptococcus AND antibiotic excluding non-relevant journals	419	7 August 2013
CINAHL	cost AND pregnancy AND group B streptococcus AND antibiotic	4	8 August 2013
Embase	cost AND pregnancy AND group B streptococcus AND antibiotic	17	8 August 2013
EconLit	cost AND pregnancy AND group B streptococcus AND antibiotic	5	8 August 2013

Source: The CIE

The results of the searches were analysed by reviewing the abstracts and published full reports of studies that were identified as potentially relevant. These studies were assessed for inclusion in the literature review against a predetermined set of inclusion criteria.

Inclusion criteria and reasons for exclusion

The inclusion criteria is designed to assess whether the study is relevant to the issue being evaluated. Table A.2 illustrates the criteria developed for inclusion of studies that are to be critically appraised. The criteria is based on the format that The Cochrane Collaboration use for their systematic reviews of the literature.[39]

[39] Higgins, J.P.T. Green, S. C. Cochrane Handbook for Systematic Reviews of Interventions 4.2.6 (updated September 2006); In: The Cochrane Library, Issue 4, 2006. Chichester, UK: John Wiley & Sons, Ltd.

Only economic evaluations that included an intervention of IAP for prevention of EOGBSD were included, also, at least one relevant comparator was required.

Studies that did not evaluate cost effectiveness but rather clinical effectiveness were not included in the review.

A.2 Inclusion and exclusion criteria for economic evaluations of strategies to prevent EOGBSD in neonates

Group	Inclusion criteria	Example reasons for exclusion
Types of studies	Economic evaluations such as cost-effectiveness studies	No relevant or useable data on cost or consequences
Participants	Pregnant women at 35-37 weeks gestation	Very specific patient group, which excludes any relevant group
Intervention	▪ Risk-factor approach to prevention: – assessment of risk factors during labour and provision of IAP ▪ Routine screening: – culture testing of recto-vaginal swab pre-labour followed by IAP during labour	▪ Inappropriate intervention: – culture testing at a different time point – risk factors assessed are different to those in current Australian guidelines – PCR or rapid antigen based test only
Comparison	Risk-factor approach to prevention of GBS disease in neonates vs. routine/universal screening of GBS colonisation in pregnant women prior to labour	▪ Inappropriate comparator: – Comparator is risk-based screening
Outcome measures	Incremental cost per avoided GBS sepsis or early-onset GBS disease in neonates	Effectiveness or health outcomes are not measured and linked back to cost

Source: The CIE

The cost-effectiveness studies to be included for appraisal are listed in table A.3. Table A.4 lists the studies excluded from the critical appraisal and reasons for exclusion. Studies that evaluated different interventions, for instance, earlier studies evaluated culture testing at 26-28 week gestation were excluded. Other studies may have used rapid tests such as PCR based tests or rapid antigen tests as part of their universal screening approach.

A.3 Economic evaluations to be included for critical appraisal

Title	Author	Year	Country	Outcome measure
Choosing a strategy to prevent neonatal early-onset group B streptococcal sepsis: economic evaluation	Stan, C. M. Boulvain, M. Bovier, P. A. et al.	2001	Switzerland	Cost per averted sepsis case
Cost-effectiveness of different treatment strategies with intrapartum antibiotic prophylaxis to prevent early-onset group B streptococcal disease	Van den Akker-van Marle M. E. Rijnders ME, Dommelen P, et. al.	2005	Netherlands	ICER per QALY gained
Preventing early-onset Group B streptococcal sepsis: Strategy development using decision analysis	Benitz, W. E. Gould, J. B. and Druzin, M. L.	1999	United States of America	Cost per averted sepsis case
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	Colbourn, T. Asseburg, C. Bojke, L. et al. Both HTA and BMJ article.	2007	United Kingdom	Health service costs per QALY
Cost-effectiveness of universal prophylaxis in pregnancy with prior group B streptococci colonization	Turrentine, M.A. Ramirez, M.M. Mastrobattista, J.M.	2009	United States of America	Cost per averted sepsis case and cost per QALY gained
Cost-effectiveness of rapid tests and other existing strategies for screening and management of early-onset group B streptococcus during labour	Kaambwa, B. Bryan, S. Gray, J. Milner, P. 2010	2010	United Kingdom	Cost per avoided EOGBS infection, cost per avoided EOGBS related death and cost per QALY gained

Source: The CIE

A.4 Studies to be excluded from review

Title	Author	Year	Country	Reason for exclusion
Streptococcus colonisation in pregnancy: prevalence and prevention strategies of neonatal sepsis	Rausch, A-V. Gross, A. Droz, S. Bodmer, T. and Surbek, D.	2009	Switzerland	Only included the costs of different strategies Did not link these costs back to effectiveness of interventions, not a true economic evaluation
A trial of preventing early- and late-onset Group B streptococcal sepsis with combined intrapartum chemoprophylaxis and universal neonatal screening	Bertini, G. Dani. C. Cianciulli, D. Rubaltelli, F.F. and Nicoletti, P.	2006	Italy	Only included the cost of screening strategies Did not link these costs back to effectiveness of interventions or the comparators, not a true economic evaluation
Prevention of neonatal group B streptococcal sepsis: is routine antenatal screening appropriate	Gilbert, G.L. Isaacs, D. Burgess, M.A. et al.	1995	Australia	Only included the costs of different strategies Did not link these costs back to effectiveness of interventions, not a true economic evaluation

Title	Author	Year	Country	Reason for exclusion
An analysis of the cost-effectiveness of selected protocols for the prevention of neonatal group B streptococcal infection	Yancey, M.K. Duff, P.	1994	United States of America	Screening at 26-28 weeks
Comparison of prevention strategies for neonatal group B streptococcal infection. A population-based economic analysis	Mohle-Boetani JC, Schuchat A, Plikaytis BD,	1993	United States of America	Screening at 26-28 weeks
Cost-effectiveness of intrapartum screening and treatment for maternal group B streptococci colonization	Strickland, D. M. Yeomans, E. R. and Hankins, G. D.	1990	United States of America	Intrapartum screening using rapid tests (<2 hours) instead of culture testing
Rapid testing for group B streptococcus during labour: a test accuracy study with evaluation of acceptability and cost-effectiveness	Daniels, J. Gray, J. Pattison, H. et al.	2009	United Kingdom	Interventions are rapid tests not culture based

Source: The CIE

Critical appraisal

Once relevant studies have been identified for inclusion into the review, they must be critically appraised for internal and external validity. The National Health and Medical Research Council (NHMRC) developed the appraisal items and grading system used.[40]

The critical appraisal is performed to determine if the study design and its findings are valid and if these results are generalisable or transferable to the Australian setting.

An assessment of internal validity addresses the issue of whether the results in the study are valid in its own setting. External validity or generalisability is a measure of whether the findings of the study are transferable to the current Australian health care system.

Value judgements are required in assessing internal and external validity and any points of contention were discussed and resolved with the Department and Expert Advisory Committee.

Checklist for appraising economic evaluation studies

Table A.5 provides the checklist for critical appraisals, along with grading criteria and example reasons for a poor grading.

[40] National Health and Medical Research Council, July 2001, How to compare the costs and benefits: evaluation of the economic evidence. Handbook series on preparing clinical practice guidelines, Canberra

A.5 Critical appraisal framework for internal and external validity

Appraisal item or issue	Reason(s) for poor grading
Appraisal item for internal validity	**Y = item is clearly demonstrated, ? = some concern the item may not have been appropriately carried out, ?? = clear concerns about the item, NA = item is not applicable in the context**
Was the study question well defined?	Viewpoint for the evaluation is not clearly stated
Were appropriate health care options chosen and clearly described?	It is unclear who did what, to whom, where and how often for each health care option
Was an appropriate study type used?	Type of evaluation is unclear or incorrect
Was the effectiveness of the health care options established?	There is no evidence or there is weak evidence of the effectiveness of the health options and interventions
Were the cost estimates related to the baseline population risk?	Cost estimates are related to only a specific group, for instance, a high risk group
Were all the relevant costs and consequences identified for each health care option?	Relevant costs are not included in the evaluation
Were costs and consequences measured accurately?	▪ No allocation of shared resources such as hospital overheads ▪ Resource use not measured accurately
Were costs and consequences valued credibly?	▪ Pricing of resources is inaccurate, for instance, may be an inaccurate proxy ▪ Prices are not adjusted for inflation
Was differential timing considered?	Future costs and consequences have not been discounted
Was incremental analysis performed?	No incremental analysis included
Was a sensitivity analysis performed?	No sensitivity analysis included
Were modelling techniques used in a clear and reasonable way?	Assumptions in the model are not clear or explicit
Appraisal issue for external validity	**A = study is generalisable to the proposed guideline setting with regard to this issue, B = some concerns relating to generalisability for this issue, C = study is not transferable to proposed guideline setting sufficient concern about this issue**
Patient group	The study focused on a different or specific population group with differing resource consumption
Health system setting	Health system setting is not comparable, in particular: ▪ older studies can include equipment no longer being in use ▪ health care institution differs in size or type of experience across personnel ▪ setting is not applicable to the rural and urban mix in Australia ▪ health care option cannot be transferred due to supply constraints in Australia ▪ differences in incentive structures to health care professionals, institutions or patients
Health care option	Differences in: ▪ treatment options (types of medication or procedure) ▪ time spent as inpatient versus ambulatory care

Appraisal item or issue	Reason(s) for poor grading
Resource costs	▪ Resource costs have not been disaggregated enough so that prices in international studies can be adjusted to Australian dollars ▪ Resource consumption due to differing health care options leads to costs that cannot be transferred to the Australian setting
Marginal versus average cost	Inappropriate use of marginal or average costing depending on what is being evaluated
Other specific issues relating to the guideline	There may be specific issues or drivers that would prevent the transferability of a study to the current Australian context

Source: National Health and Medical Research Council, July 2001, How to compare the costs and benefits: evaluation of the economic evidence. Handbook series on preparing clinical practice guidelines, Canberra

Table A.6 shows the validity assessment of the cost-effectiveness studies included for review.

A.6 Critical appraisal of economic evaluation of strategies to prevent EOGBSD in neonates

Appraisal item or issue	Grade
Stan, C. M. et al. 2001	
Internal validity	
Was the study question well defined?	Y
Were appropriate health care options chosen and clearly described?	Y
Was an appropriate study type used?	Y
Was the effectiveness of the health care options established?	Y
Were the cost estimates related to the baseline population risk?	Y
Were all the relevant costs and consequences identified for each health care option?	Y
Were costs and consequences measured accurately?	Y
Were costs and consequences valued credibly?	Y
Was differential timing considered?	NA
Was incremental analysis performed?	Y
Was a sensitivity analysis performed?	Y
Were modelling techniques used in a clear and reasonable way?	Y
The cost-effectiveness study aimed to determine the most cost-effective strategy to prevent neonatal streptococcal sepsis in Switzerland, based on Swiss current policy, universal screening (CDC) and risk factors strategy. Costs included culture testing, IAP, mild and severe antibiotic reaction. The measured consequence is episodes of streptococcal sepsis rate. Found that risk factors strategy was the more cost-effective option compared to current policy and routine screening.	
Internally valid?	**Yes**
External validity	
Patient group	A

Appraisal item or issue	Grade
Health system setting	C
Health care option	C
Resource costs	B
Marginal versus average cost	A
The patient group is pregnant women, the costs and rates are based on university hospitals in Geneva, Switzerland. It is unlikely that the care and resource consumption is transferable to the Australia context. Cost estimates have been adjusted to 1999 prices, and from Swiss francs to £. Prices can be adjusted to current AUD, but validity may be an issue due to the age of the prices	
Externally valid?	**No, sufficient concern that the results are not generalisable.**
Van den Akker-van Marle, M. E. et al. 2005	
Internal validity	
Was the study question well defined?	Y
Were appropriate health care options chosen and clearly described?	Y
Was an appropriate study type used?	Y
Was the effectiveness of the health care options established?	Y
Were the cost estimates related to the baseline population risk?	Y
Were all the relevant costs and consequences identified for each health care option?	Y
Were costs and consequences measured accurately?	?
Were costs and consequences valued credibly?	?
Was differential timing considered?	Y
Was incremental analysis performed?	?
Was a sensitivity analysis performed?	Y
Were modelling techniques used in a clear and reasonable way?	Y
The cost-utility study aims to determine the costs and effects of different strategies to prevent EOGBSD, including, risk-based strategy, universal screening strategy, combined strategy and the Dutch guidelines. Costs included screening, hospital admission (low risk vs. high risk pregnancies attract different resources),cost of EOGBSD (hospitalisation, medical aids and education). Quantities and cost were not measured or reported separately, cost of GBS cases derived from survey of a parent group with children that had EOGBSD. Likely that this group will be biased towards severe cases, that is, overstatement of costs and understatement of QoL. Price years not reported. Sensitivity analysis was not reported on resource use or short-term costs. The measured outcomes was cost per QALY gained. The authors found that the risk-based and combined risk-based strategies were the most cost-effective, compared to universal screening and the current Dutch strategy.	
Internally valid?	**Issues with the measurement and credibility of the costs and consequences**
External validity	
Patient group	A
Health system setting	C

Appraisal item or issue	Grade
Health care option	C
Resource costs	C
Marginal versus average cost	A
Patient group are pregnant women in the Netherlands. The Netherlands have a unique obstetric system whereby pregnancies are rated either low risk (homebirth, birth clinic or hospital with midwife) or high risk (hospital with obstetrician). The percentage of homebirths in the Netherlands is30 per cent, in Australia it is 1 per cent, thus the cost and type of care is different.[1] Unlikely that resources consumption and costs of care are transferable to the Australian context. Price years are not reported, thus adjusting to current AUD impossible.	
Externally valid?	**No, sufficient concern that the study results are not generalisable.**
Benitz, W. E. et al. 1999	
Internal validity	
Was the study question well defined?	Y
Were appropriate health care options chosen and clearly described?	Y
Was an appropriate study type used?	Y
Was the effectiveness of the health care options established?	Y
Were the cost estimates related to the baseline population risk?	Y
Were all the relevant costs and consequences identified for each health care option?	Y
Were costs and consequences measured accurately?	Y
Were costs and consequences valued credibly?	Y
Was differential timing considered?	NA
Was incremental analysis performed?	?
Was a sensitivity analysis performed?	Y
Were modelling techniques used in a clear and reasonable way?	Y
Cost-effectiveness study of strategies to prevent EOGBSD, strategies includes risk factors, universal screening (either 28 or 35-37 weeks) and IAP for positive results and risk factors and universal IAP. Costs included screening, IAP, adverse reaction to antibiotics. Consequences include cost of GBS cases. Measured outcome is the cost per case prevented. Findings were that risk factors strategy had the lowest cost per prevented case and that even universal IAP did not prevent all cases of EOGBSD Marginal cost per prevented case not explicitly reported in the text, results are shown in a chart.	
Internally valid?	
External validity	
Patient group	A
Health system setting	C
Health care option	B
Resource costs	C

Appraisal item or issue	Grade
Marginal versus average cost	A
The patient group is pregnant women at the Lucile Packard Children's Hospital in the US. It is unlikely that resource consumption and cost of care is transferable to the Australian context. Price years are not reported adjusting to current AUD is impossible. Further, the study was published in 1999, given the age of the study this may impact on the generalisability of the findings.	
Externally valid?	**No, sufficient concern over the transferability of the results.**
Colbourn, T. E. et al. 2007	
Internal validity	
Was the study question well defined?	Y
Were appropriate health care options chosen and clearly described?	Y
Was an appropriate study type used?	Y
Was the effectiveness of the health care options established?	Y
Were the cost estimates related to the baseline population risk?	Y
Were all the relevant costs and consequences identified for each health care option?	Y
Were costs and consequences measured accurately?	Y
Were costs and consequences valued credibly?	Y
Was differential timing considered?	Y
Was incremental analysis performed?	Y
Was a sensitivity analysis performed?	Y
Were modelling techniques used in a clear and reasonable way?	Y
Cost-utility study on the costs and consequences of different strategies to prevent EO GBS-and non-GBS (*E. coli*) disease in neonates in the UK. The strategies included current practice, RCOG recommendation (risk factors approach), screening (culture based and PCR) and hypothetical strategies based on vaccination. A total of 713 preventions strategies were modelled, 170 strategies remained after the removal of vaccinations. Costs included admission costs, screening, IAP and adverse events. Consequences included utilities based on disability, meningitis, bacteraemia, death, still-births and life expectancy. The measured outcome was healthcare cost per QALY gained. Findings were that universal screening, either by PCR or culture test was not cost-effective, however, the risk-factor based approach was cost-effective. A combined strategy of culture screening with IAP for preterm and high risk women was cost-effective.	
Internally valid?	**Yes**
External validity	
Patient group	A
Health system setting	B
Health care option	C
Resource costs	A
Marginal versus average cost	A
Other specific issues relating to the guideline	B

Appraisal item or issue	Grade
Patient group is pregnant women in the UK health care system. It is unlikely that the care and resource use will be transferable to the Australian context. Health care option differs with PROM not being evaluated, in the Australian guidelines, PROM is considered a risk factor. Prices are disaggregated and provided as 2005 £. Adjustment to current AUD is possible.	
Externally valid? **Concern over the transferability to the Australian context**	
Turrentine, et al. 2009	
Internal validity	
Was the study question well defined?	Y
Were appropriate health care options chosen and clearly described?	Y
Was an appropriate study type used?	Y
Was the effectiveness of the health care options established?	Y
Were the cost estimates related to the baseline population risk?	Y
Were all the relevant costs and consequences identified for each health care option?	Y
Were costs and consequences measured accurately?	Y
Were costs and consequences valued credibly?	Y
Was differential timing considered?	Y
Was incremental analysis performed?	Y
Was a sensitivity analysis performed?	Y
Were modelling techniques used in a clear and reasonable way?	Y
Cost-utility analysis of strategies to prevent EOGBSD in women who were previously colonised with GBS. Strategies included screening or universal IAP. Costs include screening, IAP, neonatal blood culture and complete blood count, maternal anaphylaxis. Consequences include GBS cases. Measured outcome is cost per prevented case of EOGBSD. Findings of the study were that universal IAP for women who were previously colonised with GBS was more cost effective than re-screening women.	
Internally valid?	**Yes**
External validity	
Patient group	C
Health system setting	C
Health care option	B
Resource costs	B
Marginal versus average cost	A
Patient group is very specific, second child or greater with previous maternal colonisation with GBS. Excludes women with risk factors such as preterm, previous baby with EOGBSD and GBS bacteriuria based in the US. It is unlikely that resource use and cost of care will be transferable to the Australian context. Health care option differs as in Australia having been colonised by GBS in a previous pregnancy is not considered a risk factor that warrants IAP. It is unlikely that these women will be given IAP unless they presented with risk factors (which were excluded from the model). A do nothing comparator would have been useful.	

Appraisal item or issue	Grade
Costs are provided in 2008 US$, prices can be adjusted to current AUD.	
Externally valid? **No, sufficient concern over the transferability to the Australian context.**	
Kaambwa, B. et al. 2010	
Internal validity	
Was the study question well defined?	Y
Were appropriate health care options chosen and clearly described?	Y
Was an appropriate study type used?	Y
Was the effectiveness of the health care options established?	Y
Were the cost estimates related to the baseline population risk?	Y
Were all the relevant costs and consequences identified for each health care option?	?
Were costs and consequences measured accurately?	?
Were costs and consequences valued credibly?	?
Was differential timing considered?	Y
Was incremental analysis performed?	Y
Was a sensitivity analysis performed?	Y
Were modelling techniques used in a clear and reasonable way?	Y
Cost-effectiveness study for a range of strategies to prevent EOGBSD, including screening (PCR or culture), risk factors, universal IAP and do nothing. Costs included screening, IAP, cost of delivery and EOGBSD. Cost of adverse events was not included. The effectiveness data were derived from another study, mainly, Daniels, J. et al. 2009. Rapid testing for group B streptococcus during labour: a test accuracy study with evaluation of acceptability and cost-effectiveness, Health Technology Assessment, 13(42). In general, there was limited reporting on cost sources. Measured outcome was cost per EOGBS disease avoided and EOGBS death avoided. Findings were that universal IAP was the most cost-effective option. However, once this was removed, culture screening was the most cost-effective under certain conditions. If the assumptions that women who were preterm and did not get screened and receive IAP, or if there was a small increase in the cost of a test, then the risk-facto approach was most cost-effective.	
Internally valid? **Yes, although, some concern over reporting of data, hence accuracy and validity of cost estimates.**	
External validity	
Patient group	A
Health system setting	B
Health care option	B
Resource costs	A
Marginal versus average cost	A
The patient group is pregnant women in the UK. It is unlikely that the cost of care and resource use will be transferable to the Australian context. The study under its base assumptions assume under universal screening, women who are preterm do not receive IAP, making this strategy the most cost-effective. However, when this assumption is removed, it made the risk factors strategy most cost-effective. It is current practice for Australian institution to provide IAP to preterm women	

Appraisal item or issue	Grade
when colonisation status is unknown. Cost are provided in 2005 £, adjusting current AUD possible.	
Externally valid?	**No, concern over the transferability to the Australian context.**

Note: Internal validity grades include: Y = item is clearly demonstrated, ? = some concern the item may not have been appropriately carried out, ?? = clear concerns about the item, NA = item is not applicable in the context. External validity grades include: A = study is generalisable to the proposed guideline setting with regard to this issue, B = some concerns relating to generalisability for this issue, C = study is not transferable to proposed guideline setting sufficient concern about this issue. Appraisal guidelines from National Health and Medical Research Council, July 2001, How to compare the costs and benefits: evaluation of the economic evidence. Handbook series on preparing clinical practice guidelines, Canberra. Abbreviations: CDC (Centers for Disease Control and Prevention), EOGBSD (early-onset Group B Streptococcus disease), GP (general practitioner), HTA (Health Technology Assessment, UK), IAP (intrapartum antibiotic prophylaxis), ICER (incremental cost-effectiveness ratio),IV (Intravenous),, PROM (prolonged rupture of membranes), QALY (quality adjusted life years), RCOG (Royal College of Obstetricians) and RCT (randomised controlled trial).

Source: The CIE. [1] Australian Institute of Health and Welfare, Li Z. Zeki, R. Hilder, L. and Sullivan, E.A, 2012. Australia's mothers and babies 2010. Perinatal statistics series no. 27. Cat. No. PER 57. Canberra: AIHW National Perinatal Epidemiology and Statistics Unit

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