Queensland Clinical Guidelines

Translating evidence into best clinical practice

Maternity and Neonatal **Clinical Guideline**

Early onset Group B Streptococcal disease

Queensland Government

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- Ensuring informed consent is obtained prior to delivering care
- Meeting all legislative requirements and professional standards
- Applying standard precautions, and additional precautions as necessary, when delivering care
- Documenting all care in accordance with mandatory and local requirements

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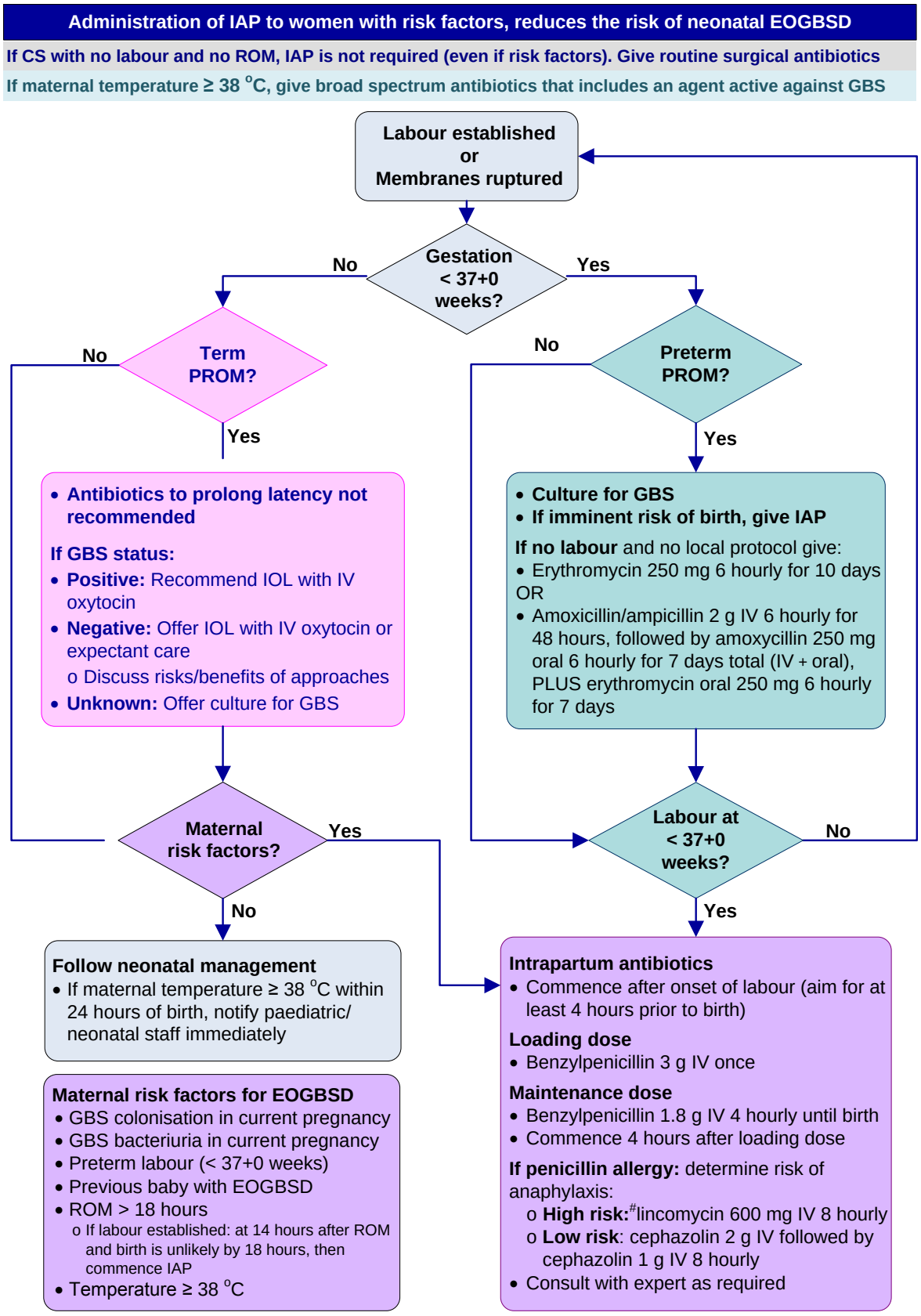
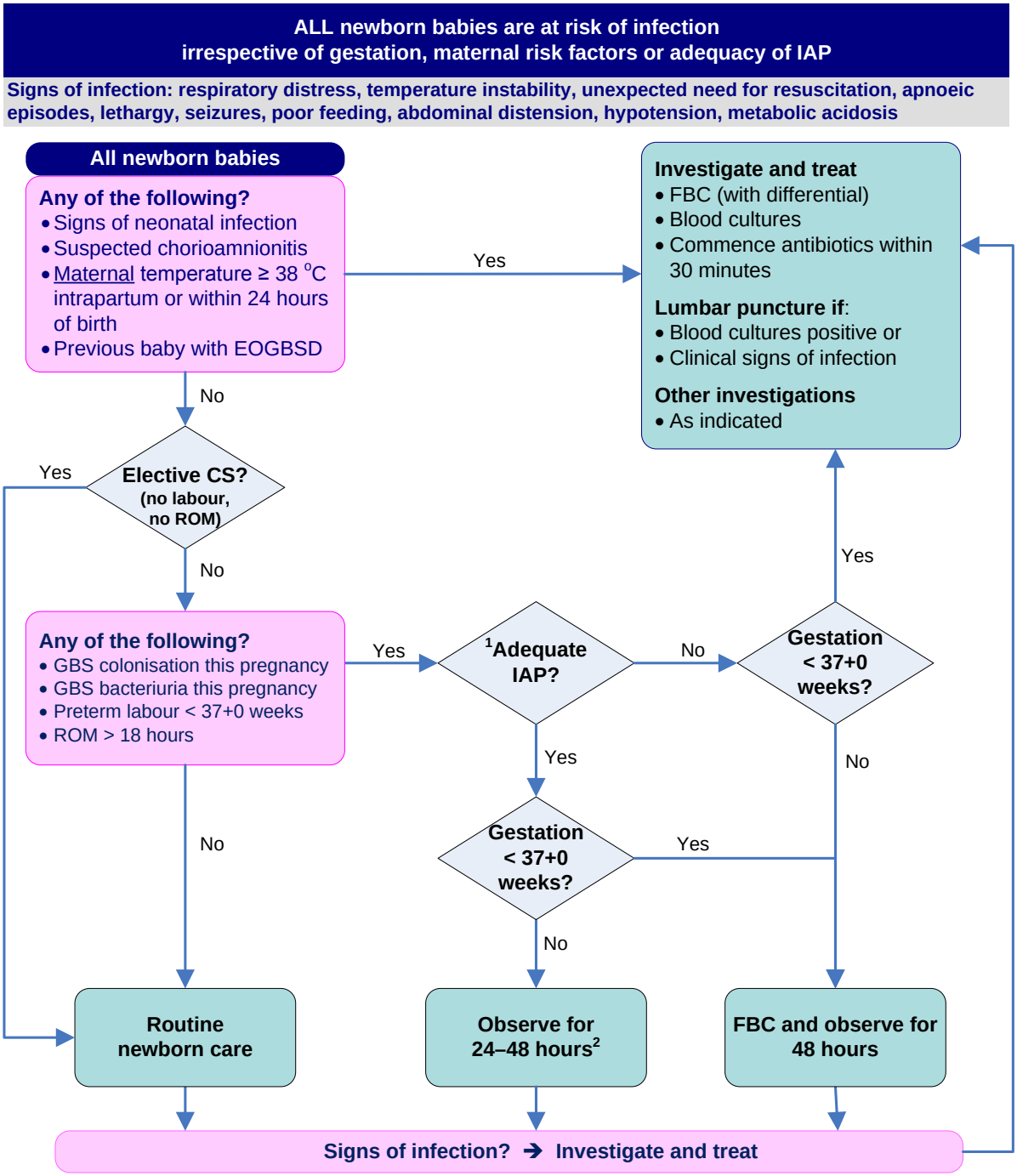
Flow Chart: Maternal management of early onset Group B Streptococcal disease (EOGBSD)



Queensland Clinical Guidelines: EOGBSD Flowchart version F16.20-1-V3-R21

EOGBSD: early onset Group B Streptococcal disease, **GBS:** Group B Streptococcus, **IAP:** intrapartum antibiotic prophylaxis, **IV:** intravenous, **IOL:** induction of labour, **PROM:** prelabour rupture of membranes **ROM:** rupture of membranes, **>:** greater than, **<:** less than
#clindamycin may be substituted for lincomycin

Flow Chart: Neonatal management of early onset Group B Streptococcal disease



Antibiotics as per local protocols; if no protocols
- Benzylpenicillin 60 mg/kg IV every 12 hours **OR**
- Ampicillin/amoxicillin 50 mg/kg IV every 12 hours

AND Gentamicin IV (Gent regimen 1 **OR** Gent regimen 2)

Gestation	Gent regimen 1	Gent regimen 2
<30 weeks	2.5 mg/kg 36 hourly	5 mg/kg 48 hourly
30–34^{+6} weeks	2.5 mg/kg 24 hourly	4.5 mg/kg 36 hourly
≥ 35 weeks	2.5 mg/kg 24 hourly	4 mg/kg 24 hourly

[1] **Adequate intrapartum antibiotics** = Intrapartum antibiotics given more than 2 hours before birth

[2] **Discharge** after 24 hours if usual readiness for discharge criteria met and parents can understand and follow instructions (recognise signs of infection, contact help via telephone, transport baby for care if required)

Queensland Clinical Guidelines: EOGBSD Flowchart F16.20-2-V3-R21

CS: caesarean section, **EOGBSD:** early onset Group B Streptococcal disease, **FBC:** full blood count, **GBS**: Group B Streptococcus, **IAP:** intrapartum antibiotic prophylaxis, **IV:** intravenous, **ROM:** rupture of membranes, **T:** temperature, **>:** greater than, **<:** less than, **≥:** greater than or equal to

Abbreviations

CI	Confidence interval
CS	Caesarean section
CRP	C-reactive protein
EOGBSD	Early onset Group B Streptococcus disease
FBC	Full blood count
GBS	Group B Streptococcus
IAP	Intrapartum antibiotic prophylaxis
IOL	Induction of labour
IV	Intravenous
LOD	Late onset disease
PMC	Primary maternity carer
PPROM	Preterm prelabour rupture of membranes
PROM	Prelabour rupture of membranes
PTL	Preterm labour
RANZCOG	Royal Australian and New Zealand College of Obstetricians and Gynaecologists
RCT	Randomised controlled trial
RDS	Respiratory distress syndrome
ROM	Rupture of membranes
RR	Relative risk

Definition of terms

Colonised	The presence of microorganisms at levels that provoke neither symptoms nor immune response.
Early onset GBS	Occurs within the first week of life. Most commonly within 72 hours of birth.
Expectant management	Non-intervention at any particular point in the pregnancy, allowing progress to a future gestational age. Intervention occurs only when clinically indicated.[1]
Imminent risk of preterm birth	Substantial risk of birth within 24 hours as clinically determined by the woman's health care provider.
Late onset GBS	Occurring after the first seven days of life.
Latency	Time from prelabour rupture of membranes (PROM) to birth.
Shared decision making	Shared decision making involves the integration of a woman's values, goals and concerns with the best available evidence about benefits, risks and uncertainties of treatment, in order to achieve appropriate health care decisions. It involves clinicians and the woman making decisions about the woman's management together. In partnership with their clinician, women are encouraged to consider available screening, treatment, or management options and the likely benefits and harms of each, to communicate their preferences, and help select the course of action that best fits these.[2]
Threatened preterm labour	Preterm contractions without dilatation of the cervix and without substantial risk of imminent birth (within 24 hours) as clinically determined by the woman's health care provider.

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1 Introduction

Streptococcus *agalactiae* or Group B Streptococcus (GBS) is the most frequent cause of early onset neonatal sepsis.[3,4] Maternal colonisation of the lower genital tract with GBS during pregnancy increases the risk of neonatal infection by vertical transmission.[4] Administration of intrapartum antibiotic prophylaxis (IAP) to women at risk of transmitting GBS to their baby can substantially reduce the rate of (but not totally prevent) early onset GBS disease (EOGBSD).[5] IAP does not prevent late onset GBS disease.

1.1 Universal screening versus risk factor approach

There is limited high quality scientific evidence and a lack of expert consensus on whether a risk based or a screening approach should be used.[6] Queensland recommends a risk based approach for the identification of women for whom IAP is indicated. This is based on an assessment of the rate of EOGBSD in Queensland (in the context of a risk based approach), the likely cost effectiveness of both strategies, the quality of the evidence in support of both approaches (Level III-2) and issues of current practice, compliance and uptake.[7] In the absence of compelling new evidence, this guideline continues to advocate such an approach (i.e. decision to treat based on identification of maternal risk factors). The Statewide Maternity and Neonatal Clinical Network and the Clinical Excellence Division, Queensland Health, have endorsed the risk factor approach for use in Queensland. For further details of rationale, refer to Appendix A: Rationale for risk factor approach in Queensland.

1.2 Burden of disease

Table 1. Burden of illness

Aspect	Considerations
Incidence of EOGBSD	• There is no single source of Queensland or Australian data • Incidence has declined world-wide since the introduction of IAP[5,8,9] o 1991–1993: 2 cases/1000 live births (Australia)[7] o 1995–1997: 0.5 cases/1000 live births (Australia)[7] o 1999–2007: 0.29 cases/1000 live births (Australia)[7] o 2000–2004: 0.34 cases/1000 live births (Queensland)[7] o 2002–2011: 0.43 cases/1000 live births (North Queensland)[10] o 2005–2008: 0.38 cases/1000 live births (Australia)[11] o 2009–2011: 0.26 cases/1000 live births (New Zealand)[12] o 2005–2014 0.32 cases/1000 live births (Queensland)[13]
Maternal colonisation	• Colonisation rates vary, estimated prevalence 10–30%[4,14] • Colonisation may be transient, intermittent or persistent[4] • Detection of GBS is dependent on valid and reliable sampling and culture techniques • The intensity of maternal colonisation is directly related to the risk of transmission to the baby[15] • Babies born to women with GBS bacteriuria (any colony count) during pregnancy are more frequently and more heavily colonised with GBS, increasing the risk of EOGBS[8] • There is an increased prevalence of GBS colonisation amongst women giving birth preterm[16-18]
Early onset Group B Streptococcus disease (EOGBSD)	• Leading cause of neonatal sepsis pneumonia or meningitis[4] • 40–50% of babies born to GBS positive mothers will become colonised with GBS in the absence of IAP[6,15] • 1–2% of all colonised babies are infected by Streptococcus *agalactiae*[6,19] o Preterm babies are four times more likely to develop EOGBSD than term babies[20] • 50% of EOGBSD cases show signs of disease at birth[19] • Mortality from EOGBSD is estimated to be 6%[11] • 65% of deaths are in babies weighing less than 2500 grams[19] • Estimated that 70% of EOGBSD cases have at least one of the following: low birth weight (less than 2500 g), rupture of membranes (ROM) greater than 18 hours duration or maternal intrapartum fever[15,21]

1.3 Clinical standards

Table 2. Clinical standards

Aspect	Considerations
Consent	• Discuss EOGBSD and IAP with women during the antenatal period in a manner that supports informed decision making • Document the discussion and decisions about IAP in the healthcare records (including handheld pregnancy health record) • Confirm decision prior to any healthcare intervention as per routine practice
Routine screening for GBS	• Queensland Health recommends a risk factor based approach for the identification of women for IAP, therefore in this context routine screening for antenatal GBS carriage is not recommended in Queensland • If requested, GBS screening at 35–37 weeks gestation may be appropriate for individual women o Offer information about the implications of the GBS screening test o If GBS negative and risk factors are present at the onset of labour, then recommend IAP [refer to section 2 Risk factors]
Future developments	• Although not yet common in clinical practice there is potential for development of a vaccine for pregnant women (similar to pertussis and influenza)[9] • Rapid testing is a new technology and may be useful in screening for GBS in the future. The currently available assays do not have the performance characteristics required. Use these tests only in an evaluation or research setting in Queensland
Health care systems for risk reduction[9]	• Increased compliance to a single approach is likely to achieve a greater reduction in the incidence of EOGBSD than either using both approaches together or changing the approach[12] • Routinely provide written information about GBS and EOGBSD to women during the antenatal period o Refer to Queensland Clinical Guidelines parent information about EOGBSD • Systematically promote adherence to recommended clinical practices through clinician education • Establish and promote systematic processes to identify women for whom IAP is recommended (e.g. incorporate into routine antenatal and early labour assessments and into health care record documentation) • Collect specimens according to recommended technique • Audit care so opportunities for further risk reduction can be identified • Establish systematic data collection regarding EOGBSD incidence in Queensland (and Australia) to evaluate effectiveness of prevention strategies
GBS isolates	• GBS isolates are characterised according to capsular polysaccharide (CPS) serotype, of which 10 are recognized: Ia, Ib, II–IX [22] • An increase of disease caused by serotype IV isolates and concurrent emergence of lincomycin resistance within this serotype has been reported[23] o Large proportions of type IV isolates reported among GBS isolates in United Arab Emirates, Turkey and Zimbabwe • When penicillin, ampicillin, or cephazolin cannot be used (e.g. due to penicillin hypersensitivity), consider testing GBS isolates for inducible lincomycin resistance and antimicrobial drug-resistant isolates of all serotypes[4,8,24] o Refer to Table 6. Penicillin hypersensitivity o Seek expert advice

2 Risk factors

Risk factors for EOGBSD include[4,8,24]:

- Preterm labour (PTL) at less than 37+0 weeks (spontaneous or induced)
- Rupture of membranes (ROM) greater than or equal to 18 hours prior to birth
- Maternal temperature greater than or equal to 38 ^{o}C intrapartum or within 24 hours of giving birth
- GBS colonisation in the current pregnancy
- GBS bacteriuria in the current pregnancy (any colony count)
- Previous baby with EOGBSD

2.1 Risk reduction

Reliable and systematic identification of women for whom IAP is indicated, is an important opportunity for risk reduction. In Queensland, the proportion of women with risk factors who do not receive IAP is unknown. One study reported that in 48 cases of EOGBSD, risk factors were present in 67% and adequate IAP was given to only six of these mothers (19%).[25]

Table 3. Risk reduction

Aspect	Considerations
Information	• Use the principles of shared decision making to discuss GBS and EOGBSD with the woman during pregnancy [refer to Definition of terms] • Routinely provide written information about GBS and EOGBSD, (including risk factors and risk and benefits of IAP to themselves and their baby)
History	• Assess for risk factors during pregnancy • Document the presence/absence of risk factors in the health record • If there is a history of penicillin allergy, document in the health record and advise the woman to alert health care providers [refer to Table 6.] • Review history at the onset of labour to identify indications for IAP
Measures not recommended	• Vaginal disinfection with chlorhexidine in labour for the prevention of EOGBS morbidity in preterm or term babies does not reduce vertical transmission or the risk of EOGBSD[26] • Antenatal treatment of GBS carriage is not recommended as it does not reduce the likelihood of GBS colonisation at the time of birth[3]
Breastfeeding	• Breastfeeding/breast milk is safe in women who are GBS positive[27] and has not be reported in association with EOGBSD • GBS has been cultured from breast milk and reported in association with late onset disease and recurrent neonatal infections with GBS[28] o Refer to section 6.1 Late onset GBS disease • Refer to Queensland Clinical Guideline: *Establishing breastfeeding*[29]

2.2 Specimen collection

Table 4. Specimen collection

Aspect	Considerations
Context	• Detection of GBS is increased by up to 25% by collecting an anorectal swab in addition to a low vaginal swab[4,8] • Detection of GBS from vaginal-perianal swab is not significantly different from the detection rate from vaginal-rectal swab[30-32] • Women report experiencing less discomfort from vaginal-perianal than from vaginal–rectal collection methods[32-34]
Specimen collection technique	• Swabs may be self-collected by the woman[33] • When specimen collection for GBS is clinically indicated, recommend either a vaginal-rectal swab OR a vaginal-perianal swab: • Use one single dry swab stick, insert into vaginal introitus and then: o For vaginal-anorectal : insert into anus (through the anal sphincter)[4] o For vaginal-perianal: swab the perianal surface without penetration through the anal sphincter o Place into standard bacterial transport medium (e.g. Amies or Stuart's) o Label specimen clearly with 'GBS screening in pregnancy'

3 Intrapartum antibiotic prophylaxis

Recommend IAP to women with one or more risk factors who are in active labour. Refer to an Australian pharmacopeia for full details of all drugs.

Table 5. Intrapartum antibiotic prophylaxis

Aspect	Recommendation
Context	• The IAP regimen in previous versions of this guideline (i.e. loading dose of benzylpenicillin 1.2 g IV, then 600 mg IV 4 hourly), aligned with the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) (2009)[35] recommendations o A specific IAP regimen is no longer recommended by RANZCOG[24] • Penicillin 5 million units IV (approximately 3 g) loading dose and then penicillin 2.5 million units IV (approximately 1.8 mg) every 4 hours until birth, has been recommended by the Centre for Disease Control (CDC) since 1996[36] • In the CDC update (2010)[4],the maintenance regimen was changed to 2.5–3 million units, primarily to accommodate available preparations • Good quality evidence is lacking to identify the lowest dose IAP regimen required to exceed the minimum inhibitory concentration for GBS AND achieve a clinically relevant reduction in EOGBSD • The IAP regimen outlined below is consistent worldwide[3,4,8,37-40]
Drug of choice	• Benzylpenicillin intravenous (IV) is the antibiotic of choice for IAP[8,39] • Erythromycin is not recommended for IAP due to increasing rates of resistance (up to 32% or more for invasive isolates)[41,42] • Oral antibiotics are not recommended and are insufficient for IAP[4]
Regimen	• Benzylpenicillin 3 g IV at the onset of labour[39] followed 4 hours later by benzylpenicillin 1.8 g IV every 4 hours until birth[39]
Effectiveness	• In a case control analysis of women with obstetric risk factors, adjusted effectiveness of IAP in preventing EOGBSD was 86% (95% CI, 0.66 to 0.94%)[43] • When the first dose of IAP was given two or more hours before birth, the effectiveness was 89% (95% CI, 0.70to 0.96)[43] • Effectiveness was lowest if there was intrapartum fever (72%, 95% CI, 0.09 to 0.93) or if administration occurred less than two hours before birth (71%, 95% CI, 0.08 to 0.93)[43]
Adequacy of IAP	• Due to the rapidity of some labours, especially in multiparous women, it can be difficult to confidently estimate the time-to-birth interval • Four hours prior to birth is commonly recommended as the interval required for adequate prophylaxis[3,4,24] but there is evidence that adequate fetal concentrations may be reached earlier (within 1–2 hours)[15,44-46] • In order to maximise the window for administration of IAP, this guideline recommends aiming for administration at least 4 hours prior to birth while recognising administration two hours prior to birth as adequate prophylaxis in determining neonatal management • If birth is anticipated in less than two hours, administer IAP as benefit may still occur[16,45]

3.1 Penicillin hypersensitivity

Table 6. Penicillin hypersensitivity

Aspect	Consideration
Context[39]	• Anaphylaxis from penicillin estimated 1–4 cases per 10,000 courses with up to 10% of these reactions being fatal • 2.5% of patients with a confirmed penicillin allergy also had a cephalosporin allergy • Clinical history is the single most important component of diagnosis of antimicrobial hypersensitivity
High risk of anaphylaxis[39]	• Where there is a history of immediate reaction to penicillins (characterised by development of urticaria, angioedema, bronchospasm or anaphylaxis within 1–2 hours of drug administration) administer: o #Lincomycin (or clindamycin) 600 mg IV every 8 hours until birth
***Lower risk of anaphylaxis**[39]	• Where there is a history of a delayed type (non-immediate) reaction to penicillins (i.e. no history of immediate reaction) characterised by macular, papular or morbilliform rash occurring several days after starting treatment administer: o Cephazolin 2 g IV followed by: o Cephazolin 1 g IV every 8 hours
Complex circumstances	• Consult with a medical microbiologist or infectious diseases physician as required, especially if there is allergy to both clindamycin and penicillin • Consider isolate susceptibility testing as appropriate to the clinical circumstances

*Excludes delayed type reactions due to serum sickness, drug rash with eosinophilia and systemic symptoms (DRESS) and Steven-Johnson syndrome/toxic epidermal necrolysis: In these cases avoid penicillins, cephalosporins and carbapenems
Lincomycin is listed on the Queensland Health List of Approved Medicines (LAM) and is the accepted alternative to clindamycin

3.2 IAP not required

IAP is not required in the following circumstances:

- Elective caesarean section (no labour, no rupture of membranes) irrespective of GBS carriage[3,24] or gestational age
- Routine surgical antibiotic prophylaxis for CS is indicated
- GBS carriage detected in a previous pregnancy[3] (even if GBS status is unknown in the current pregnancy)
- Threatened preterm labour with intact membranes where the risk of imminent birth is low

4 Specific condition management

Table 7. Specific conditions

Aspect	Considerations
GBS positive in the current pregnancy	• A finding during pregnancy of vaginal and/or rectal GBS does not require treatment in the antenatal period[39] • Specimen collection *before* 35 weeks is less predictive of GBS status at term[24] than collection between 35–37 weeks gestation • If GBS is detected at any gestation of pregnancy in an incidentally collected vaginal swab, recommend IAP o Repeat swab is not required
GBS bacteriuria	• If there is GBS urinary tract infection (UTI) at any gestation in the current pregnancy (usually where quantitative count is greater than or equal to 10^5 cfu/m) recommend treatment at the time of diagnosis *and* IAP[3,4,23] • If there is GBS bacteriuria, a GBS vaginal swab is not required as the woman is presumed to be GBS colonised
Preterm labour (intact or ruptured membranes)	• If there is imminent risk of preterm birth, with or without ruptured membranes, give IAP • If preterm labour (PTL) ensues, continue IAP irrespective of GBS or membrane status • If PTL does not establish and membranes intact, cease IAP • If PTL does not establish and membranes ruptured, refer to section 4.1 Prelabour rupture of membranes
Temperature greater than or equal to 38 ^oC	• Replace GBS specific antibiotic prophylaxis with broad spectrum antibiotic therapy that includes an agent active against GBS[3] • If there is maternal pyrexia (intrapartum or within 24 hours of birth), immediately notify medical (paediatric/neonatal)l staff as it may have implications for neonatal management • Advise women to seek advice from health care professionals if maternal temperature is greater than or equal to 38 ^oC within 24 hours of birth (especially if discharged within 24 hours of birth) • If there is prelabour rupture of membranes (PROM) or preterm prelabour rupture of membranes (PPROM) refer to section 4.1
Obstetric procedures if GBS positive	• Provided women with GBS risk factors are treated with IAP, there is insufficient evidence to recommend either avoidance of, or alterations of technique, in obstetric procedures (e.g. membrane sweeping, amniotomy, fetal scalp blood sampling or fetal scalp electrode) on the basis of positive GBS status[24,37]
Chorioamnionitis	• Do not inhibit labour, but consider hastening birth under broad spectrum intravenous antibiotic cover o Collect low and high vaginal swabs for culture o Recommend IOL • Optimal antibiotic regimen not established. If no local protocols exist suggested regimen: o Ampicillin (or amoxicillin) 2 g IV initial dose, then 1 g IV every 6 hours o Gentamicin 5 mg/kg IV daily o Metronidazole 500 mg IV every 12 hours o Continue antibiotic treatment after birth o Consider oral antibiotics once afebrile and tolerating oral medication • Request placental histology to inform review of extent/severity of infection and for quality assurance purposes

4.1 Prelabour rupture of membranes

Table 8. Prelabour rupture of membranes

Aspect	Consideration
Context	• GBS colonisation in pregnancy is not associated with increased risk of PROM[47]
IAP	• IAP not required prior to the onset of established labour (even if membranes have been ruptured for more than 18 hours)
Care decisions	• Discuss the risks and benefits of immediate versus expectant management in a manner that supports shared decision making • Individualise recommendations taking into account, gestational age, fetal wellbeing, maternal health and wellbeing, maternal preferences and the ability to provide ongoing surveillance o Refer to Queensland Clinical Guideline: *Induction of labour*[48] o Refer to Queensland Clinical Guideline: *Preterm labour and birth* • If term prelabour rupture of membranes, refer to Table 9. Term prelabour rupture of membranes • If preterm prelabour rupture of membranes, refer to Table 10. Preterm prelabour rupture of membranes

4.1.1 Term prelabour rupture of membranes

Table 9. Term prelabour rupture of membranes

Aspect	Consideration
Context	• There is no difference in incidence of early onset neonatal sepsis, maternal or neonatal infectious morbidity, mortality or stillbirth when routine use of antibiotics is compared with placebo or no antibiotics (N= 2639, 4 studies) for PROM at or near term[49,50] • Reduced infectious morbidity has been reported when labour is established and IAP is administered for term PROM greater than 12 hours duration[51]
IAP for term PROM	• **Irrespective of GBS status, when labour establishes (not before) commence IAP if:** o Duration of ROM is greater than or equal to18 hours at the onset of established labour o During established labour, the duration of ROM reaches or exceeds 14 hours and birth is assessed as unlikely before duration of ROM equals18 hours (i.e. do not wait for duration of ROM to equal 18 hours before commencing IAP)
Expectant management versus immediate birth	• If known positive GBS status or there are other risk factors, recommend induction of labour (IOL) with IV oxytocin and IAP[52-54] • If known negative GBS status and no other risk factors, offer expectant management or IOL with IV oxytocin[54] • If unknown GBS status offer swabbing for GBS culture • Expectant management more than 96 hours is associated with higher risk of neonatal sepsis[55] o If expectant management at home, advise women when to seek assistance from a health care practitioner (e.g. signs of infection, decreased fetal movements) o If inpatient expectant management, follow local protocols (and according to clinical circumstances) for monitoring maternal and fetal health and wellbeing (e.g. cardiotocograph (CTG), maternal observations)
Antibiotics prior to the onset of labour	• Routine antibiotic administration is not recommended for women with PROM at or near term prior to the onset of labour[40,49]

4.1.2 Preterm prelabour rupture of membranes

Table 10. Preterm prelabour rupture of membranes

Aspect	Consideration
IAP for PPROM	• When labour ensues (or CS), recommend IAP regardless of GBS status • If labour/birth ensues while antibiotics to prolong latency are being administered, amoxicillin/ampicillin 2 g IV once, followed by 1 g every 6 hours for 48 hours is adequate as IAP[4] o Oral antibiotics alone are not adequate for IAP[4,8]
Expectant management versus immediate birth	• Recommend specimen collection for detection of GBS[17] • For PPROM less than 24 weeks gestation counsel about the risks and benefits including neonatal morbidity and mortality and individualise care[56] o Refer to Queensland Clinical Guideline: *Perinatal care at the threshold of viability*[57] • For PPROM 24–33 weeks gestation, recommend expectant management until 33 completed weeks, then reassess • For PPROM greater than or equal to 34+0 weeks gestation consider individual risks and benefits relevant to the clinical circumstances[54,58,59] o One RCT (N=1839) of PPROM at 34 to 36+6 weeks gestation[58]: ▪ Reported no significant difference in neonatal sepsis between immediate birth and expectant management (RR 0.8; 95% CI 0.5 to 1.3) ▪ Recommended (in the absence of overt signs of infection or fetal compromise) expectant management with appropriate surveillance of maternal and fetal wellbeing for PPROM close to term
Antibiotics prior to the onset of labour	• Antibiotics following PPROM is associated with a statistically significant reduction in (22 trials, 6872 women and babies)[60]: o Chorioamnionitis (RR 0.66, 95% CI 0.46 to 0.96) o Numbers of babies born within 48 hours (RR 0.71;95% CI 0.58 to 0.87) and 7 days (RR 0.79; 95% CI 0.71 to 0.89) o Neonatal infection in babies (RR 0.67; 95% CI 0.52 to 0.85) o Number of babies with an abnormal cerebral ultrasound scan prior to discharge from hospital (RR 0.81; 95% CI 0.68 to 0.98) • There is no evidence that antibiotic prophylaxis in PPROM alters perinatal mortality or longer term outcomes[60] • The optimal antibiotic regimen to prolong latency in the setting of PPROM is unclear because multiple regimens have demonstrated benefit[60-63] • The two largest RCTs used the following regimens: o Ampicillin 2 g IV every 6 hours and erythromycin 250 mg IV every 6 hours for 48 hours followed by amoxicillin 250 mg orally every 8 hours and erythromycin 333 mg orally every 8 hours for 5 days (N=614, gestational age 24–32 weeks)[64] o Erythromycin 250 mg orally every 6 hours for 10 days (N=4826, gestational age 23–36 weeks)[65] • Therapeutic Guidelines[39] (evidence unreported) recommend: o Amoxicillin/ampicillin 2 g IV every 6 hours for 48 hours, followed by amoxicillin 250 mg oral, every 8 hours for a total of 7 days (IV+oral), PLUS erythromycin 250 mg oral every 6 hours for 7 days • Gestational age (i.e. later versus earlier preterm gestation) may influence the choice and duration of antibiotic regimen[66]
Regimen to prolong latency	• In the absence of good quality evidence, if no local protocols exist, recommend either: o Erythromycin 250 mg oral 6 hourly for 10 days[65] **OR** o Amoxicillin/ampicillin 2 g IV every 6 hours for 48 hours, followed by amoxicillin 250 mg oral, every 8 hours for a total of 7 days (IV+oral), PLUS erythromycin 250 mg oral every 6 hours for 7 days[39] • Amoxicillin/clavulanic acid is not recommended as it is associated with an increased risk of neonatal necrotising enterocolitis (RR 4.72, 95% CI 1.57 to 14.23)[60]

CI: confidence interval, **RCT:** randomised controlled trial, **RR:** relative risk, **N:** number

5 Newborn care

All newborn babies are at risk of infection irrespective of gestational age, maternal risk factors or intrapartum antibiotic treatment.

5.1 Signs of sepsis

Clinical signs of sepsis can be non-specific and subtle and a high index of suspicion is required as delay in initiating treatment may significantly increase neonatal mortality and morbidity.

Table 11. Signs of sepsis

Aspect	Considerations
Context	• 90% EOGBSD occurs during the first 24 hours of life[4] usually evident as[5]: o Respiratory disease (54%) o Generalised sepsis (27%) o Meningitis (15%) • GBS is the most common causative pathogen of neonatal bacterial meningitis[67,68]
General features	• Pallor • Jaundice • Hypothermia, fever, temperature instability • Poor tolerance to handling • Hypoglycaemia or hyperglycaemia • Metabolic and/or respiratory acidosis
Respiratory	• Unexpected need for resuscitation • Respiratory distress: o Tachypnoea o Apnoeic episodes o Grunting o Cyanosis o Nasal flaring o Chest recession
Cardiovascular	• Tachycardia • Bradycardic episodes • Poor perfusion • Hypotension
Gastrointestinal	• Poor feeding • Vomiting • Abdominal distension • Feed intolerance • Bilious aspirates/vomits • Loose stools
Central nervous system	• Lethargy • Irritability • Meningeal inflammation • Seizures

5.2 Investigation of sepsis

Any baby with clinical signs of sepsis requires a full diagnostic evaluation and empirical antibiotic therapy started (within 30 minutes[69]) regardless of adequacy of IAP, other obstetrical risk factors or maternal GBS status.

Table 12. Investigation of sepsis

Aspect	Considerations
Indications for investigation	• Clinical signs of infection[4] o Refer to Table 11. Signs of sepsis • Maternal chorioamnionitis is suspected[4] (temperature greater than or equal to 38 ^{o}C intrapartum or within 24 hours of birth) • The woman has had a previous baby with EOGBSD • Gestational age is less than 37+0 weeks *and* there was inadequate IAP o Refer to Table 5. Intrapartum antibiotic prophylaxis
Minimum investigations	• Prior to antibiotics: o Full blood count (FBC) with differential o Blood cultures—ideally, collect 1 mL of blood[41]
Lumbar puncture	• Recommended (where local capabilities permit) where there is[4,41]: o Positive blood culture *or* o Clinical signs suggestive of sepsis (as babies with meningitis may have sterile blood cultures[4]) *or* o Insufficient improvement in response to antimicrobial therapy[41] • Collect a serum glucose concomitantly
Other Investigations	• Consider chest x-ray if respiratory signs[4] o Pulmonary infection may be radiographically indistinguishable from respiratory distress syndrome (RDS). The presence of neutropenia, unexplained severe apnoea, poor peripheral vascular perfusion and shock, and lower peak inspiratory pressures on a ventilator than are usually present with RDS, may aid differentiation • Endotracheal culture may be of value if obtained immediately after endotracheal tube placement[41] • C-reactive protein (CRP) rises approximately 12 hours after onset of sepsis and returns to normal within 2–7 days of successful treatment o CRP raised in 85% of episodes of confirmed sepsis and therefore can be normal in cases of true sepsis o CRP can also be increased in the absence of infection o Single values may give false positive or negative results o Serial CRP may be useful to guide duration of treatment
Routine use not recommended	• Due to suboptimal sensitivity and specificity and poor predictive value for infection, routine use of urine antigen, cultures of mucous membranes, gastric aspirate and surface swabs not recommended[41]

5.3 Antibiotic therapy

Commence antibiotic therapy within 30 minutes where a baby has clinical signs of sepsis.

Table 13. Antibiotic therapy

Aspect	Considerations
Context	• Use broad-spectrum antibiotics which provide cover against EOGBSD as well as other common pathogens • The type and duration of antibiotic treatment is determined by the clinical indications and may be modified by results of the investigations
Administration	• If peripheral intravenous access cannot be established, consider antibiotic administration via umbilical vein catheter • The intramuscular route may be used as an interim measure if other routes unavailable o Administer all recommended antibiotics at the same dose o Seek further advice but do not delay initiation of treatment
Empirical antibiotic therapy	• Where local guidelines for antibiotics do not exist, suggested empirical antibiotic therapy is[41]: o Benzylpenicillin 60 mg/kg IV every12 hours o **Or** amoxicillin/ampicillin 50 mg/kg IV every 12 hours o **PLUS** gentamicin IV [refer to Table 14. Gentamicin dosing regimen]
GBS sepsis	• If GBS infection confirmed by culture and meningitis is excluded, use a susceptible narrower spectrum penicillin and discontinue aminoglycoside
GBS meningitis[39]:	• If GBS meningitis is diagnosed o 0–7 days of age: benzylpenicillin 60 mg/kg IV every 12 hours for 14–21 days o 8–28 days of age: benzylpenicillin 60 mg/kg IV every 6 hours for 14–21 days
Duration of therapy	• Varies depending on results of cultures and clinical course; discuss with a paediatrician or infectious diseases physician • If GBS sepsis is proven or suspected then continue antibiotics for 7–10 days or longer as indicated • If blood cultures are negative, white count is normal, symptoms resolve and baby is known to be well then discontinue antibiotics after 36–48 hours[69]

5.3.1 Gentamicin regimens

Two gentamicin-dosing regimens are in common use in Queensland. Where local guidelines for gentamicin do not exist, consistently use (throughout the service) either gentamicin regimen one or gentamicin regimen two outlined in Table 14. Gentamicin dosing regimens. Also, refer to Table 15. Serum concentration monitoring.

Table 14. Gentamicin dosing regimens by gestation

Gentamicin regimen one[69]	**Dose (IV)**	**Dose frequency**
Less than 30 weeks	2.5 mg/kg	36 hourly
Greater than or equal to 30 weeks	2.5 mg/kg	24 hourly
Gentamicin regimen two[39]	**Dose (IV)**	**Dose frequency**
Less than 30 weeks	5.0 mg/kg	48 hourly
30–34^{+6} weeks	4.5 mg/kg	36 hourly
Greater than or equal to 35 weeks	4.0 mg/kg	24 hourly

5.3.2 Gentamicin monitoring

Table 15. Serum concentration monitoring

Aspect	Consideration
Context[70]	• Serum concentration monitoring avoids both excessive and sub-therapeutic concentrations thus preventing toxicity and ensuring efficacy • All neonates require serum aminoglycoside concentration monitoring • Collect serum trough levels just before the next dose is administered
Regimen one monitoring[70]	• Collect trough levels prior to third dose o If oliguric or poor renal function, collect trough level and wait for result prior to administering second dose • Aim for trough level less than 2 mg/L • If greater than or equal to 2 mg/L then extend the dosage interval by 12 hours • If dose or dose interval is altered, recheck trough levels prior to the third dose of the new order • If more than three doses administered, aim for trough level less than 1 mg/L
Regimen two monitoring[71]	• Trough levels required only when treating for more than 48 hours o Collect earlier if clinically indicated (e.g. active cooling or poor renal function) • Aim for trough levels 0.5 to 1 mg/L • If trough level higher than 0.5 to 1 mg/L, lengthen the dosing interval • If trough level lower than 0.5 to 1 mg/mL, shorten the dosing interval

5.4 Postnatal care for asymptomatic well baby

Undertake newborn observations according to clinical assessment, rather than protocol alone. Determine care location (postnatal ward or newborn unit) based on clinical indications and the service capabilities of the facility.

Table 16. Asymptomatic well baby

Well baby	Recommendation
All (with or without maternal risk factors)	• Routine newborn care that includes clinical surveillance for signs of sepsis (e.g. observation of colour, temperature, heart rate, respiratory rate) as is appropriate to the clinical circumstances
Elective CS (no labour no ROM)	• As for all well babies • Term babies do not require routine investigation or monitoring regardless of maternal GBS status • In the absence of other clinical indications, admission to newborn unit not required
Term with maternal risk factors, and **adequate IAP**	• As for all well babies and: o Clinical surveillance for 48 hours • Discharge may occur at 24 hours after birth if the home care is suitable o Refer to section 6 Discharge • In the absence of other clinical indications, admission to newborn unit not required
Term with maternal risk factors and **inadequate IAP**	• As for all well babies and: o Clinical surveillance for signs of sepsis for 48 hours (discharge before 48 hours not recommended) o Full blood count • In the absence of other clinical indications, admission to newborn unit not usually required
Preterm with **adequate IAP**	• As for all well babies and: o Clinical surveillance for signs of sepsis for 48 hours and: o Full blood count • Maintain a high index of awareness that preterm babies are more susceptible to infection • If baby is well, there are no other clinical indications, and there is sufficient experienced staff to provide clinical surveillance, admission to a newborn unit may not be required
Preterm with **inadequate IAP**	• Investigate [refer to Table 12. Investigation of sepsis] • Treat with antibiotics [refer to Table 13. Antibiotic therapy] • Admission to newborn unit usually required due to prematurity

6 Discharge

Table 17. Discharge

Aspect	Considerations
Criteria	• Consider usual discharge criteria to inform readiness for discharge[4] • Consider parental ability to understand and follow instructions including[4]: o Recognise and respond appropriately to signs of infection in the baby o Communicate with healthcare providers by telephone o Transport the baby promptly to an appropriate healthcare facility if required
Future pregnancy advice	• If this baby has had EOGBSD, advise the woman: o IAP is recommended during the next labour o The next baby has an increased risk of EOGBSD o To inform health care providers in the next pregnancy that a previous baby has had EOGBSD • If the woman has had GBS colonisation in this pregnancy but without infection in the baby, birth management is not affected in the next pregnancy
Follow-up	• Inform the woman's primary maternity carer (PMC) and general practitioner (if not PMC) in writing that there is a risk of recurrence of GBS in the baby, and of GBS infection in babies in future pregnancies

6.1 Late onset GBS disease

Table 18. Late onset Group B Streptococcal disease

Aspect	Consideration
Risk factors	• The use of IAP for EOGBSD has had no notable effects on the occurrence of late onset disease (LOD)[15,72] • LOD more common in babies with low birth weight and in the early preterm, postulated to be related to[72]: o Immature immune response o Longer inpatient status with exposure to invasive devices and increased administration of broad spectrum antibiotics after day three • Most common clinical presentation of LOD is sepsis, followed by meningitis[15]: o Term babies present earlier than preterm o Babies without IAP exposure present earlier than babies with IAP exposure o The earlier LOD presents, the higher the risk for meningitis and death
Information for parents	• At discharge, offer parents of babies at increased risk of LOD, advice about: o Signs of sepsis in the newborn o Importance of seeking medical assistance if baby unwell

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Appendix A: Rationale for risk factor approach in Queensland

Refer to *References* for works cited in this Appendix.

Uniform adherence with a single approach is likely to be the major determinant in making further reductions in EOGBSD.[42]

Aspect	Comment
Approach description	**Screening approach** • Universal antenatal screening for GBS carriage at 35–37 weeks gestation and treat all women with positive cultures, women with a preterm birth where GBS carriage status is unknown or previous infant with EOGBSD with intrapartum antibiotics **Risk factor approach** • No universal antenatal screening, treat all women with risk factors for EOGBSD with intrapartum antibiotics
Rate of EOGBSD in Queensland	• The overall rate of EOGBSD in Queensland has declined from 0.34/1000 live births in 2000–2004 to 0.32/1000 live births during 2005–2014[13] • A risk based approach has been advocated in Queensland throughout this time
Evidence by approach	**Universal screening** • Largely based on one retrospective study[73] that reported antenatal culture-based strategy when compared to risk factors based policy, was 50% more effective in preventing EOGBSD (0.33/1000 versus 0.59/1000 live births). This study reported: o 30–40% of women colonized with Group B Streptococci without obstetric factors who were identified by screening were ignored by the risk-based approach o Women with a prenatal screening culture positive for GBS were more likely to receive IAP than women with obstetric risk factors o Obstetric risk factors were also present in non-colonized women, so the risk factor-based approach lacked specificity and unnecessarily exposed many women to intrapartum chemoprophylaxis
	Risk based approach • There is a lack of a well-designed randomized control trial or systematic reviews (of RCTs or other study designs) evaluating the effectiveness of universal versus risk-based GBS screening. The available evidence (including Schrage et al) includes significant bias and confounds limiting their applicability[6] • An association between the introduction of universal screening guidelines and a decline in the EOGBSD rate[5] does not imply cause and effect[6] o The decline in USA EOGBSD rates antedated implementation of widespread screening o A decline in EOGBSD rates has occurred in New Zealand under a risk factor based approach[12] (0.24 per 1000 live births is lower than target rate of 0.25 per 1000 live births set by Centre for Disease Control USA)
Number needed to treat (NNT)	• RCOG estimated the following NNT[3] o Screening approach:750 women who screened positive to GBS would need to be treated to prevent one case of GBS disease and 7034 women treated to prevent one neonatal death o Risk factor based approach:625 women with a GBS risk factor would need to be treated to prevent one case of GBS disease and 5882 women treated to prevent one neonatal death • An Australian study reports NNT of 1191 GBS carrier women and to screen 5704 women in order to prevent one case of EOGBSD[74] • A Canadian study reports that 3449 women would require universal screening to prevent a single case of EOGBSD that would be missed using a risk-based approach; and that the number increases to 68,966 to prevent a single death[75]
Cost-effectiveness	• Attempts to evaluate the cost-effectiveness of the strategies have produced differing results • A 2013 economic analysis 'Cost-effectiveness of strategies to prevent infection of Group B Streptococcus in neonates from maternal colonisation' commissioned by the Australia's Commonwealth Department of Health and Ageing, reported*:* *"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….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"*

Limitations by approach

Aspect	Consideration
Limitations of universal screening approach	• 52–78% of EOGBSD cases are born to women who screen negative in the third trimester and do not receive IAP[76-78] • 10% of women GBS negative at screening were GBS positive during labour (and did not receive IAP)[79] • 50% of women GBS positive at screening were GBS negative during labour[79] • In women who do not receive IAP due to false negative results, and the transient nature of GBS colonisation, an adverse neonatal outcome (e.g. infection, death) may occur • Estimated that 70% of EOGBSD cases have one of: low birth weight (less than 2500 g) rupture of membranes (ROM) greater than 18 hours' duration or maternal intrapartum fever[15,21] • Women with a positive result may be excluded from some models of care (e.g. homebirth, midwifery led) and the impact compounded by timing which is usually in the last weeks of pregnancy[6] • May lead to further medicalisation of labour and require more counselling and a higher level of care for many more women, increasing costs and the risk of obstetrical intervention[6] • Positive culture (known GBS colonisers or false positive result) may lead to maternal anxiety and stress during pregnancy • Increases the chances of anaphylaxis with exposure to IAP • Babies exposed to IAP increased by 5% with introduction of universal screening[78] o There is increasing recognition of the importance of antenatal colonisation of the neonatal gut microbiome[80] with exposure to IAP occurring just as babies are about to establish penicillin-susceptible anaerobic gut microbiome
Limitations of risk factor based approach	• 25–40% of EOGBSD cases are born to women without risk factors[8,81,82] • In women without risk factors (who do not receive IAP), an adverse neonatal outcome (e.g. infection, death) may occur

Approach by organisation

		Approach Type			
Organisation	**Year**	**Risk factor**	**Universal screening**	**Either**	**Not stated**
Royal College of Obstetricians and Gynaecologists	2012	✓			
National Institute for Clinical Excellence	2012	✓			
New Zealand GBS Consensus Working Party	2014	✓			
Northern Ireland	2015	✓			
Centre for Disease Control and Prevention	2010		✓		
The Society of Obstetricians and Gynaecologists of Canada	2013		✓		
European Consensus Conference	2012		✓		
The American College of Obstetricians and Gynaecologists	2011		✓		
Australian Health Ministers' Advisory Council 2014, Clinical Practice Guidelines: Antenatal Care – Module II	2014			✓	
Royal Australian and New Zealand College of Obstetricians and Gynaecologists	2012			✓	
Australasian Society for Infectious Diseases	2014			✓	
Queensland (Qld Health)	2010	✓			
South Australia (SA Health)	2012		✓		
*Western Australia (KEMH)	2010		✓		
*Australian Capital Territory (ACT Health Shared Care Guidelines)	2010		✓		
*New South Wales (NSW Health)	2005			✓	
Victoria (3 Centres Collaboration)	2006			✓	
*Tasmania	-				No guideline
*Northern Territory					No guideline

* Source: Homer CS, Scarf V, Catling C, Davis D. Culture-based versus risk-based screening for the prevention of Group B Streptococcal disease in newborns: a review of national guidelines. Women Birth. 2014; 27(1):46-51.

Appendix B: Normal laboratory reference ranges for a term baby

- Consider the result in the context of the entire clinical picture
- Laboratory tests are only useful if they guide management
- Normal values for preterm may differ—seek expert advice
- Where possible, use local laboratory reference ranges
- Consider laboratory error if spurious results are returned for a well-baby

Cerebral Spinal Fluid (CSF)

CSF	Unit of measure	Age		With bacterial meningitis
Leucocytes	$x10^6$/L	≤ 25 (predominately mononuclear)		Elevated
Protein	mg/L	**< 1 week** 200–1700	**1 week–3 months** 200–1000	Elevated
Glucose	mmol/L	**0–12 years** 3.3–4.5		Decreased (but may be normal)
Glucose **(CSF: blood ratio)**	ratio	≥ 0.6 (normally 2/3 of plasma glucose)		Decreased (but may be normal)

Haematology

		Age				
Full Blood Count (venous)	Unit of measure	< 1 day	1day– < 3 days	3 days– < 1 week	1 week – < 2 weeks	With bacterial infection
Hb	g/L	135–226	145–226	135–226	125–206	
Hct	%	0.42–0.67	0.50–0.67	0.42–0.67	0.39–0.63	
MCV	fL	95–121	95–121	88–126	86–126	
MCH	pg	31–37	31–37	28–37	290–380	
MCHC	g/L	290–370	290–370	290–380	280–380	
Platelets	10^9/L	150–400	150–400	150–400	150–400	Decreased
WBC	$x10^9$/L	9.0–34.0	10.0–26.0	7.0–23.0	5.0–21.0	Elevated or decreased (decrease associated with worse prognosis)
Neutrophil	$x10^9$/L	5.0–21.0	4.0–14.0	1.5–10.0	1.0–10	Generally elevated
Band (immature)	$x10^9$/L	<1.2	<1.2x	<1.2x	<1.2	Elevated
I:T ratio [Band/total neutrophils] < 0.2						
I:M ratio [immature/mature] < 0.25						
Eosinophil	$x10^9$/L	< 0.8	0.1–1.0	0.1–2.0	0.1–2.0	
Basophil	$x10^9$/L	< 0.1	< 0.1	< 0.1	< 0.1	
Lymphocyte	$x10^9$/L	2.0–11.0	3.0–8.0	2.0–17.0	2.0–17.0	
Monocytes	$x10^9$/L	< 1.9	0.5–2.0	0.1–1.7	0.1–1.7	
CRP	mg/L	< 5	< 5	< 5	< 5	Elevated Serial rise more significant Single result may not exclude or confirm infection

Hb: haemoglobin, **Hct:** haematocrit, **MCV:** mean corpuscular volume, **MCH:** mean corpuscular haemoglobin, **MCHC:** mean corpuscular haemoglobin concentration, **WBC:** white blood cell, **CRP:** C reactive protein

Source: Reference ranges from Pathology Queensland 2015

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