Literature Review
for
Three Centres Antenatal Care Consensus Guidelines

Screening for Group B Streptococcus (GBS)

by: Clinical Practice Improvement Unit, The Royal Women's Hospital

Project team members

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April 2005

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Conclusion and recommendations

In pregnant women is screening for GBS using a swab more effective in detecting and improving maternal and perinatal outcomes than risk factor assessment alone?

The Project Team agrees with the SOGC recommendations [1], to:

1. Offer all women screening for group B streptococcal disease at 35 to 37 weeks' gestation with culture done from one swab first to the vagina then to the rectal area.

2. Treat the following women intrapartum at time of labour or rupture of membranes with IV antibiotics:
   - All women positive by GBS culture screening done at 35 to 37 weeks
   - Any women with an infant previously infected with GBS
   - Any women with documented GBS bacteriuria (regardless of level of colony-forming units per mL) in this pregnancy.

3. Treat women in labour at less than 37 weeks' gestation with IV antibiotics unless there has been a negative GBS vaginal/rectal swab culture within 5 weeks.

4. Treat women with intrapartum fever with IV antibiotics (ie chorioamnionitis must be treated, but broader spectrum antibiotics would be advised).

5. If a woman is GBS-positive by culture screening or by history of bacteriuria, with prelabour rupture of membranes at term, treat with GBS antibiotic prophylaxis and initiate induction of labour with IV oxytocin.

6. If GBS culture result is unknown and the woman has ruptured membranes at term for greater than 18 hours, treat with GBS antibiotic prophylaxis.

There is evidence that benefits to mothers regarding reduction in febrile morbidity outweigh the risk of anaphylaxis.

The Project Team notes the evidence regarding the very large number needed to treat to prevent deaths from EOGBS and that this may deter some hospitals from implementing universal screening in favour of a risk based approach. However, cost effectiveness data is not available for morbidity rather than mortality. In the absence of this evidence the Project Team recommend universal screening for reduction in neonatal and maternal morbidity and neonatal mortality from GBS.

This literature review has focused on the antenatal screening for GBS. Literature acknowledges that a significant proportion of women with preterm prelabour rupture of membranes that go on to deliver prematurely will have a neonate affected by GBS sepsis. Therefore the management is directed at ascertainment of GBS status at the time of presentation.

In pregnant women, is screening for GBS after 30 weeks gestation more effective than screening for GBS prior to 30 weeks gestation?

The Project Team agrees with the SOGC recommendations [1], to:

1. Offer all women screening for group B streptococcal disease at 35 to 37 weeks' gestation with culture done from one swab first to the vagina then to the rectal area.

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GBS screening earlier than 35 weeks' gestation is not recommended.

Contents

1. Introduction

The Three Centres Collaboration contracted the Royal Women's Hospital (RWH) Clinical Practice Improvement Unit to conduct a comprehensive search and critical appraisal of publications addressing the topic of screening for Group B Streptococcus (GBS) published between January 2000 and January 2005, to inform the proposed review of the 2001 Three Centres Consensus Guidelines on Antenatal Care.

2. Topics to be addressed

2.1 In pregnant women is screening for GBS using a swab more effective in detecting and improving maternal and perinatal outcomes than risk factor assessment alone?

2.2 In pregnant women, is screening for GBS after 30 weeks gestation more effective than screening for GBS prior to 30 weeks gestation?

3. Methods

3.1 Search strategy

- The OVID interface was used to search the following electronic databases:
  - MEDLINE: 2000 – January 2005
  - CINAHL: 2000 – January 2005
  - EBM Reviews: June 2000 – January 2005
- Cochrane Database: 2005 Issue 1
- Review of article citations and Cochrane Library references for additional citations
- Guidelines developed by specific Colleges of Obstetricians and Gynaecologists were searched including:
  - Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)
  - Royal College of Obstetricians and Gynaecologists (RCOG) , and
  - Society of Obstetricians and Gynaecologists Canada (SOGC).
- Guidelines developed by other groups were searched for via the internet, on the:
  - United States National Guidelines Clearinghouse, and
  - TRIP database

3.2 Search terms

Terms used to identify relevant citations are outlined in Appendix I. The basis of the search was conducted using terms for Group B Streptococcus.

4. Search findings

4.1 Initial search

During the initial search citations were screened and selected using the following inclusion and exclusion criteria:

Inclusion criteria	Exclusion criteria
2000-2005	Guillian-Barre Syndrome
Diagnosis of GBS	Pregnancy infection
Risk factors	Molecular analysis
Antenatal	Group A Streptococcal
	UTI
	Vertical transmission
	Vaginal chlorhexidine in labour
	Dementia
	Alzheimer
	Neonatal infection / management

The initial search retrieved 118 citations and 7 guidelines (Appendix II).

4.2 Key citation selection

The AGREE tool was applied by the Project Team to the following three guidelines which were subsequently used as a basis for answering the first topic.

- Society of Obstetricians and Gynaecologists Canada (SOGC): Clinical Practice Guidelines: The prevention of early-onset neonatal group B streptococcal disease[1].
- Royal College of Obstetricians and Gynaecologists (RCOG): Guideline Number 36: Prevention of early onset neonatal group B Streptococcal disease[2].
- Royal College of Obstetricians and Gynaecologists (RCOG). Clinical Guideline: Antenatal care: routine care for the healthy pregnant woman[3].

In addition, citations with relevant evidence or authoritative opinion were selected to answer the:

- First topic - from the initial search for the period from December 2003.
- Second topic - from the initial search for the period from January 2000.

In addition to the 7 guidelines, 23 publications were retrieved (see Appendix III).

Publications were further screened to identify those studies with respect to quality of methodology and relevance to Australian obstetric practice. This resulted in 17 key citations that were subjected to systematic critical appraisal by the Project Team (Appendix IV).

The evidence within these 17 key citations fell into the following levels (see Appendix IV for definitions):

- Level I evidence: 0 publications
- Level II evidence: 0 publications
- Level III evidence: 8 publications, and
- Level IV evidence: 9 publications.

4.3 Grading recommendations

The Project Team has adapted the Scottish Intercollegiate Guidelines Network (SIGN) system applying the NHMRC Levels of Evidence, to grade recommendations as follows:

A At least one meta analysis, systematic review, or RCT directly applicable to the target population; or Levels I or II evidence.

B A body of evidence including studies rated as Level III-1 or III-2, directly applicable to the target population and demonstrating overall consistency of results.

C A body of evidence including studies rated as III-3 directly applicable to the target population and demonstrating overall consistency of results.

D Evidence Level IV.

5. Results of the critical appraisal process: Commentary on and interpretation of publications reviewed

Early onset GBS (EOGBS) is defined as "GBS occurring in infants less than 1 week old and is acquired through vertical transmission from colonized mothers. Clinical presentations include sepsis, pneumonia and meningitis. The incidence is 1-3/1000 live births (declining to 0.6 per 1000 live births) in active surveillance areas. The death rate for EOGBS is 4.7-9%" [4]. Most recommendations are directed at prevention of EOGBS.

Late onset GBS (LOGBS) is defined as "GBS occurring in infants older than 1 week and is acquired through vertical transmission or through horizontal transmission in the hospital or the community. Meningitis is the most common presentation. The incidence is 0.22 per 1000 total births and the death rate is 2%" [4].

The RANZCOG comment that: "the use of intrapartum prophylaxis with antibiotics (penicillin) given to women at risk of transmission of GBS to their newborns, prevents early onset sepsis and is cost effective. In the USA, intrapartum chemoprophylaxis has led to a 70% decline in the incidence of GBS disease in the past decade" [5]. That is, the incidence has declined from 2-3/1000 to 0.5/1000 with the advent of intrapartum chemoprophylaxis [1].

In Victoria current screening and detection methods for GBS involve vaginal and rectal swabs for culture and sensitivity. Recently, the Food and Drug Authority (FDA) "approved a rapid real-time polymerase chain reaction (RT-PCR) IDI-Strep B assay as a non-culture molecular test (high sensitivity and specificity) with one-hour turnaround time. However, it is not yet available in routine practice in Australia and would require a 24 hour, 7-day week operating molecular biology service" [5].

5.1 In pregnant women is screening for GBS using a swab more effective in detecting and improving maternal and perinatal outcomes than risk factor assessment alone?

The SOGC acknowledge the pivotal randomised controlled trial (RCT) by Boyer and Gotoff in 1985, which demonstrated intrapartum antibiotics reducing the risk of early-onset disease in neonates and less perinatal febrile morbidity in colonized women [1].

Screening approaches

The options for antenatal screening for GBS include:

- Risk assessment
- Universal screening and treating only those who are positive, and
- Universal screening and treating those who are positive in addition to those with a clinical risk factor [2].

All combinations of these approaches have been practiced in Victorian hospitals [6].

SOGC and RCOG guidelines, after the evaluation of evidence, recommend that all women be offered screening for GBS at 35-37 weeks gestation, culture done with one swab first to the vagina then to the rectal area [1, 3]. A key citation supporting this recommendation is based on the greater rates of neonatal GBS when women are managed with a risk factor approach versus a culture based approach of 1.1 per 1000 versus 0 per 1000 (p=0.001) [7]. A large multistate retrospective cohort study reported a 54 percent reduction in EOGBS disease in screened women versus a risk based approach [8]. A retrospective review of infants diagnosed with EOGBS by Pinto et al, found the use of clinical risk factors exclusively will inevitably result in cases where there has been a missed opportunity for intrapartum antibiotic prophylaxis [9].

A review of RCT evidence reports "a highly significant reduction in the risk of GBS sepsis or pneumonia (pooled odds ratio [OR] = 0.17; 95% EI: 0.07, 0.39) with none of

the 368 babies born to treated mothers suffering GBS bacteraemia and only one suffering clinical signs of sepsis / pneumonia" [10:4].

Additional benefits of universal screening include reductions in maternal disease due to clinical chorioamnionitis (from 7.4 percent with the risk based approach compared with 5.2 percent with universal screening) and endometritis (from 4.0 percent with a risk-based approach to 2.8 percent with a screening approach) [1].

Contrary to SOGC guidelines, a technical report by the New Zealand GBS Consensus Working Party recommends the implementation of a GBS risk-based prevention strategy, which aims to ensure the least numbers of women and their babies are exposed to antibiotics, while virtually preventing all deaths from GBS. The Working Party noted that:

"(i) no strategy will prevent all cases of early-onset GBS infection,
(ii) intrapartum antibiotics are associated with rare, but serious, adverse effects,
(iii) concerns remain over developing antibiotic resistance,
(iv) an economic analysis is required to help inform policy,
(v) reliable bedside diagnostic tests for GBS in early labour are not yet available, and
(vi) the most important determinant of effectiveness will be compliance with a single national prevention policy" [11].

Estimated effects of bacteriological screening

The Project Team has applied the SOGC evidence to Victoria's population, where the carriage of GBS is 25 percent. Use of intrapartum antibiotics in screened women with positive GBS reduces the colonization rates to approximately one percent. Ten percent of these colonized women will result in colonized neonates, of which half will develop EOGBS disease. Therefore, approximately 2000 women will need to be screened and 500 treated to prevent one neonate developing EOGBS. Assuming intrapartum antibiotic prophylaxis is 80 percent effective in preventing EOGBS disease, 20,000 women would need to be screened for GBS to prevent one neonatal death from EOGBS. Figures equate with those outlined in the RCOG guidelines[2].

Potential risks of treating women identified as GBS carriers and/or with risk factors

RANZCOG state the risk of anaphylaxis is 0.1 per 1000 [5]. In the United Kingdom using the risk factor based approach approximately 15 percent of all pregnancies would be treated with GBS intrapartum prophylaxis, and using the universal screening approach this figure is closer to 25 percent [2].

Other risks include the possibility of the development of antibiotic resistant organisms and that "exposure to antibiotics in the neonatal perinatal period may affect neonatal faecal flora, with a subsequent impact on immune development and later allergy" [2:4].

Although penicillin is the preferred option for intrapartum antibiotic prophylaxis, Centers for Disease Control and Prevention (CDC) guidelines recommend ampicillin as an acceptable alternative to penicillin [4]. Schuchat reports caution should be taken when using ampicillin instead of penicillin for GBS prophylaxis due to the severity of neonatal ampicillin resistant E coli sepsis and its occurrence after maternal antibiotics [13]. Australian data suggests a reduction in early onset E coli sepsis in all babies secondary to widespread antibiotic use in labour [14].

Project Team Recommendations (A–B)

The Project Team agrees with the SOGC recommendations [1], to:

1. Offer all women screening for group B streptococcal disease at 35 to 37 weeks' gestation with culture done from one swab first to the vagina then to the rectal area.

2. Treat the following women intrapartum at time of labour or rupture of membranes with IV antibiotics:
   - All women positive by GBS culture screening done at 35 to 37 weeks
   - Any women with an infant previously infected with GBS
   - Any women with documented GBS bacteriuria (regardless of level of colony-forming units per mL) in this pregnancy.

3. Treat women in labour at less than 37 weeks' gestation with IV antibiotics unless there has been a negative GBS vaginal/rectal swab culture within 5 weeks.

4. Treat women with intrapartum fever with IV antibiotics (ie chorioamnionitis must be treated, but broader spectrum antibiotics would be advised).

5. If a woman is GBS-positive by culture screening or by history of bacteriuria, with prelabour rupture of membranes at term, treat with GBS antibiotic prophylaxis and initiate induction of labour with IV oxytocin.

6. If GBS culture result is unknown and the woman has ruptured membranes at term for greater than 18 hours, treat with GBS antibiotic prophylaxis.

There is evidence that benefits to mothers regarding reduction in febrile morbidity outweigh the risk of anaphylaxis.

The Project Team notes the evidence regarding the very large number needed to treat to prevent deaths from EOGBS and that this may deter some hospitals from implementing universal screening in favour of a risk based approach. However, cost effectiveness data is not available for morbidity rather than mortality. In the absence of this evidence the Project Team recommend universal screening for reduction in neonatal and maternal morbidity and neonatal mortality from GBS.

This literature review has focused on the antenatal screening for GBS. Literature acknowledges that a significant proportion of women with preterm prelabour rupture of membranes that go on to deliver prematurely will have a neonate affected by GBS sepsis. Therefore the management is directed at ascertainment of GBS status at the time of presentation.

5.2 In pregnant women, is screening for GBS after 30 weeks gestation more effective than screening for GBS prior to 30 weeks gestation?

There is limited data is available specifically pertaining to 30 weeks' gestation.

Haque et al published a retrospective cohort study of Level 2 NICU admissions over a 5 year period. Birth less than 30 weeks' gestation and birth weight less than 1500g were risk factors for sepsis. 50 percent of early onset sepsis was due to GBS (rate 4.2 per 1000 live births). One percent of late onset sepsis (>72 hours old) was due to GBS. Resuscitation at birth and indwelling intravenous catheters were also risk factors for neonatal sepsis. However, the study was not designed to specifically address the issue of whether screening for GBS prior to 30 weeks' gestation would result in either better detection rates for GBS or improved maternal or fetal morbidity or mortality [15].

Lin et al address the issue from the opposite direction. Risk factors in their case-control study for GBS disease 7-180 days of age (LOGBS) include decreasing gestation, black mothers and mothers with GBS carriage. They conclude that these factors are similar to those previously reported for EOGBS but that prematurity is the primary risk factor for LOGBS. The study identified the risk of a 30-week gestation

neonate developing LOGBS disease compared with that of a 37-week gestation neonate is multiplied by a factor of 7.76 (1.34). CDC guidelines state that LOGBS disease is not prevented by intrapartum antibiotic prophylaxis [12]. Lin et al comment this is due to the transplacental transfer of IgG antibodies is inefficient at this gestation and that preterm infants may benefit from prevention strategies to reduce maternal GBS colonization. Although the study was not specifically designed to evaluate screening prior to 30 weeks' gestation and outcomes, it may lend weight to a policy of treating all women with risk factors such as prematurity, regardless of knowledge of GBS status [16].

A more pertinent Sydney study involving a prospective cohort of 500 women attending antenatal clinic was screened using a variety of methods for GBS at 28-32 weeks' gestation. GBS carriage rates were 18-27 percent. The best positive and negative predictive rates for intrapartum carriage were 69 and 92 percent. Five percent of their population delivered prior to 37 weeks' gestation. The authors concluded that neither early antenatal screening nor clinical risk factors are reliable predictors of intrapartum GBS carriage [17].

In addition, "although there is no difference between antenatal and intrapartum carriage rates, the PPV of early antenatal screening for intrapartum carriage was only 69%; 24% of intrapartum carriers were not identified by screening. Based on these data, it is difficult to justify continuation of early antenatal screening. However, PPV and sensitivity can be increased to >85% by screening at 35-37 weeks" [17].

Intrapartum antibiotic prophylaxis based on carriage rates would include 35 percent of women versus 16 percent based on risk factors alone and both strategies would prevent similar proportions of neonatal deaths from GBS sepsis. There was no correlation between carriage and clinical risk factors. More than 50 percent of mothers in their population with infants with GBS sepsis had no risk factors. Compliance with preventive protocols is the most likely determinant of success. Reference is made to earlier work by Rosenstein and Schuchat (1997) in which a review of 245 cases of neonatal GBS sepsis found that 78 percent overall were preventable with a screening based intrapartum antibiotic prophylaxis protocol, compared with 79 percent of cases in preterm and 30 percent term infants with a risk-factor-based protocol [17].

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GBS screening earlier than 35 weeks' gestation is not recommended.

6. Conclusions and recommendations

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Appendix I

Search framework

A structured approach was used to identify an appropriate search strategy for this topic. Using the Patient/Intervention/Compared with/Outcome (PICO) format search terms were listed and entered into the various electronic databases.

P	All pregnant women
I	Swab
	Swab after 30 weeks gestation (is this before or after 30 wks)
C	Risk factor assessment
	Swab prior to 30 weeks gestation
O	Maternal outcomes
	Perinatal outcomes
	Detection of GBS, neonatal sepsis, neonatal mortality
	Cost effectiveness
	Patient satisfaction

Search findings

Term	Medline	Premedline	CINAHL	EBM
Group B Streptococcus / Group B Streptococcal / Group B Streptococci / Streptococcus Group B / Streptococcal Group B / Streptococci Group B / GBS	1444	147	162	81
Screen$ / test$	325695	48318	35275	25829
Group B Streptococcus / Group B Streptococcal / Group B Streptococci / Streptococcus Group B / Streptococcal Group B / Streptococci Group B / GBS and Screen$ / test$	104/348	12/36	26/45	3/25

Cochrane

	Systematic Review	DARE	Central Register
Group B Streptococcus / Group B Streptococcal / Group B Streptococci / Streptococcus Group B / Streptococcal Group B / Streptococci Group B / GBS	2/53	0/1	2/66

Appendix II
Results of Initial Search

1. 1. Maternal screening to prevent neonatal Group B streptococcal disease. *Journal of Medical Screening* 2002;9(4):191.

2. Women's health: new guidelines on group B strep. *Patient Care for the Nurse Practitioner* 2003:7p.

3. Testing for maternal group B streptococci during labor is more cost effective than current screening strategies. *Research* 2003;Activities.(269):8.

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Appendix III
Complete articles retrieved

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Appendix IV
Key Citations

Levels of Evidence Ratings	
I	Evidence obtained from a systematic review of all relevant randomised controlled trials.
II	Evidence obtained from at least one properly-designed randomised controlled trial.
III-1	Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method).
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group.
IV	Evidence obtained from case series, opinions of respected authorities, descriptive studies, reports of expert committees and case studies.

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2.1 In pregnant women is screening for GBS using a swab more effective in detecting and improving maternal and perinatal outcomes than risk factor assessment alone?

Study	Ref.	Population	Intervention	Outcomes	Results	Study type	EL
Main EK and Slagle T 2000	7	California Pacific Medical Center (large private tertiary perinatal referral hospital) San Francisco, USA. Three study periods over 7 years: January 1992 – December 1993 January 1994 – December 1996 January 1997 – December 1998	GBS management protocols	Protocol: • Efficacy to prevent EOGBS disease • Effect of early –onset serious neonatal infections • Usefulness of risk factors • Use of cultures and antibiotics	January 1992 – December 1993 • Less organized approaches to GBS prophylaxis • Focus on antibiotic treatment of preterm labour and intrapartum pyrexia, although antibiotics were used in <50% if cases meeting the criteria. • EOGBS disease rate was 1.1 cases per 1000 births January 1994 – December 1996 – implementation of a risk based approach recommended by CDC and ACOG • EOGBS disease rate was 1.1 cases per 1000 births January 1997 – December 1998 – implementation of a culture based screening protocol between 35 and 37 weeks' gestation as outlined by CDC. • No cases of EOGBS disease • No increases in other early onset infection or antibiotic resistance	Sequential prospective observational study	III-2
Scrag SJ, Zell ER et al 2002	8	Centers for Disease Control and Prevention, USA Eight geographical areas with active surveillance for GBS infection (a stratified random sample of 5144 live births was selected from 629,912 livebirths). 1998-1999	Effectiveness of universal culture screening compared with screening by identification of clinical risk factors.	Prevention of EOGBS disease	• 312 instances of EOGBS. • 52% of mothers had documented antenatal screening. • Risk EOGBS disease was significantly lower in the universal culture screened group than in the group screened by clinical risk (adjusted relative risk, 0.46; 95 percent confidence interval, 0.36 to 0.60). • A secondary analysis was conducted following exclusion of women with risk factors and adequate time for GBS prophylaxis. The relative risk of EOGBS disease was similar—0.48 (95 percent confidence interval, 0.37 to 0.63). Authors conclude that routine antenatal screening for GBS prevents more cases of EOGBS disease than the risk-based approach	Multistate retrospective cohort study	III-2

Schuchat A, Zywicki SS et al 2000	13	Centers for Disease Control and Prevention, USA Eight hospitals for varying periods between: April 1995 – March 1997 52 406 births during surveillance period.	Universal antenatal screening for GBS Risk based strategy for GBS identification	Prevention of EOGBS disease	• 188 infants developed early onset disease (3.5 cases per 1000 live births). • Most infections were caused by GBS (1.4 cases per 1000 births) and Escherichia coli (0.6 cases per 1000 births). • GBS sepsis less often occurred in preterm deliveries compared with other sepsis. • Compared with gestation-matched controls without documented sepsis, GBS disease was associated with intrapartum fever (matched OR, 4.1; CI, 1.2-13.4) and frequent vaginal exams (matched OR, 2.9; CI, 1.1-8. 0). • 49% of GBS cases and 79% of other sepsis had an obstetric risk factor (preterm delivery, intrapartum fever, or membrane rupture >/=18 hours) • Intrapartum antibiotic prophylaxis (IAP) had an adjusted efficacy of 68.2% against any early-onset sepsis. • 69% of E Coli infections had ampicillin resistance. 41% of ampicillin-resistant E coli infections were fatal compared with no deaths in susceptible E coli infections. 91% of infants who developed ampicillin-resistant E coli infections were preterm, and 59% of these infants were born to mothers who had received IAP. Authors conclude that antenatal screening for GBS by culture or risk could potentially prevent a substantial portion of GBS cases. Sepsis caused by other organisms occurs more frequently in premature infants. IAP appears effective against early-onset sepsis. However, caution is advised in the replacing penicillin with ampicillin because of the severity of ampicillin-resistant E coli sepsis and its occurrence after maternal antibiotics for GBS prophylaxis.	Case control study	III-2
Connellan M and Wallace EM 2000	6	Monash Medical Centre, Melbourne Australia 84 hospitals that undertook deliveries of public patients in Victoria, Australia. November 1996 - January 1998.	Postal survey	Clinical protocols for prevention of EOGBS	62 (97%) of hospitals undertook actions to identify and treat pregnant women at risk of EOGBS: • 48 (75%) used bacteriological screening for maternal carriers of GBS: o 15 hospitals used low vaginal swabs o 12 hospitals swabbed before 30 weeks' gestation. o One hospital used low vaginal swab plus anal swab. o Bacteriological screening was more common in metropolitan hospitals than in rural hospitals (100% versus 67%; P = 0.007, Fisher's exact test).	Hospital survey	III-3

		Data included from 64 hospitals representing 42 784 births (68% births in Victoria in 1996)			• 59 (92%) of hospitals targeted prophylaxis by recognised risk factors, including 45 that also undertook screening. There was considerable variation in the specific risk factors used.		
Pinto NM, Soskolne EI et al 2003	9	University of Michigan affiliated nurseries (x2), USA July 1992-December 2001 All infants admitted with culture proven EOGBS.	Initial publication of guidelines for intrapartum chemoprophylaxis	Cases of EOGBS disease	• 92 infants had EOGBS. • 68 of the infants with EOGBS had received no intrapartum prophylaxis. 50% (34) had identifiable risk factors before delivery (32 clinical, two positive maternal culture) and 50% had no risk factors. • Of the 32 with clinical risk factors, 22 were <37 weeks gestation, 12 had ruptured membranes >/=18 hours, nine had intrapartum maternal fever and two had prior GBS bacteriuria. None had a previous infant with EOGBS. 10 had more than one risk factor. • 22 women had antenatal culture for GBS colonization performed. 18 cultures were negative for GBS including 15 obtained using suboptimal culture technique or collected more than 6 weeks before delivery. Neonatal outcomes: No prophylaxis (68): • 14 required extracorporeal membrane oxygenation, and • Three died. Some intrapartum prophylaxis (24): • Nine had received >/=two doses for >/=4 hours immediately before delivery. • two required extracorporeal membrane oxygenation, and • One died. >4 hours of intrapartum prophylaxis:, • no deaths • One infant required extracorporeal membrane oxygenation. Following the publication of CDC guidelines in May 1996, there was a decrease both in the number of cases of EOGBS disease (56 versus 36) as well as in the number with clinical risk factors but no intrapartum prophylaxis (24/56 (43%) versus 5/28 (18%)).	Case series study	III-3

2.2 In pregnant women, is screening for GBS after 30 weeks gestation more effective than screening for GBS prior to 30 weeks gestation?

Study	Ref	Population	Intervention	Outcomes	Results	Study type	EL
Haque KN, Khan MA et al 2004	15	St Helier University Hospital, Surrey, England. 14,767 live births January 1996 – December 2000	Culture for sepsis	Neonatal sepsis. Risk factors of neonatal sepsis • <72 hours old • >72 hours old.	• 1,612 (11%) neonates were admitted to the NICU during the study period. Of those admitted to the NICU 908 were screened for sepsis, including 124 with at least one positive culture (ie sepsis rate of 8.4 per 1,000 live births [1%] or 77 per 1,000 NICU admissions). • 24 neonates had sepsis within 72 hours of birth and 100 developed sepsis after 72 hours of age. Early onset sepsis was most frequently caused by coagulase-negative staphylococci (CoNS) and group B Streptococcus. Late onset sepsis was caused by CoNS and Escherichia coli. **Risk factors** • Risk factors for sepsis were birth before 30 weeks' gestation and birth weight less than 1,500 g. • The key risk factor associated with early onset sepsis was resuscitation at birth. • Late onset sepsis risk factors include respiratory support prior to sepsis, presence of a central or peripheral catheter, and total parenteral nutrition were leading risk factors for late onset sepsis.	Retrospective cohort study	III-2
Lin FYC, Weisman LE et al. 2003	16	Hospitals within 50 mile radius of the Texas Medical Center, Houston, USA. 145 infants treated for LOGBS (23 were excluded, resulting in 122 case patients). July 1995 – June 2000	Culture for sepsis	Maternal and neonatal risk factors for LOGBS (onset of disease or positive culture 7-180 days after birth)	• 145 infants were treated for LOGBS, estimated annual incidence of 0.38 cases / 1000 live births. • Following exclusions, 122 cases were matched with 122 control subjects for hospital of birth and date of birth. • 50% of the case patients were preterm infants, 84% of whom were born at <34 weeks of gestation. The risk for late-onset GBS disease increased by a factor of: o 1.34 (95% confidence interval [CI], 1.15-1.56) for each week of decreasing gestation, o 3.70 (95% CI, 1.35-10.1) for infants of black mothers, and o 4.15 (95% CI, 1.27-13.60) for infants of mothers with a positive GBS screening. Authors conclude prematurity is the major risk factor for late-onset GBS disease, and the risk factors for LOGBS are similar to EOGBS disease.	Case control study	III-2

Gilbert GL, Hewitt MC et al 2002	17	Westmead Hospital (university teaching and tertiary referral hospital ~4300 births per annum) and a community hospital with ~2600 births per annum, New South Wales, Australia. 500 women attending antenatal clinic.	Screen for GBS at 26-32 weeks gestation and at delivery using different screening methods.	Incidence of antenatal anovaginal GBS carriage. Intrapartum clinical risk factors: • predictive values for intrapartum GBS carriage, and • relationship to demographic and obstetric factors.	• GBS carriage rates were similar for antenatal and intra-partum, and varied from 18% to 27%, depending on screening methods. • The best positive and negative predictive values of antenatal GBS culture, for intra-partum carriage, were 69% (95% confidence interval (CI) 64-74) and 92% (95% CI 50-94) respectively. • Clinical risk factors occurred in similar proportions of GBS carriers and non-carriers. Authors conclude that: • Intrapartum GBS carriage cannot be reliably predicted by either early antenatal screening or clinical risk factors. • Intrapartum antibiotic prophylaxis based on GBS carriage or risk factors (when carrier status is unknown) would involve approximately 35% of women, and 16% if based on risk factors alone. Both strategies would prevent similar proportions of neonatal deaths from GBS sepsis. • The most likely determinant of overall effectiveness is compliance with a preventive protocol.	Cohort study	III-2