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Group B streptococci and other serious neonatal infections

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Types of neonatal infection

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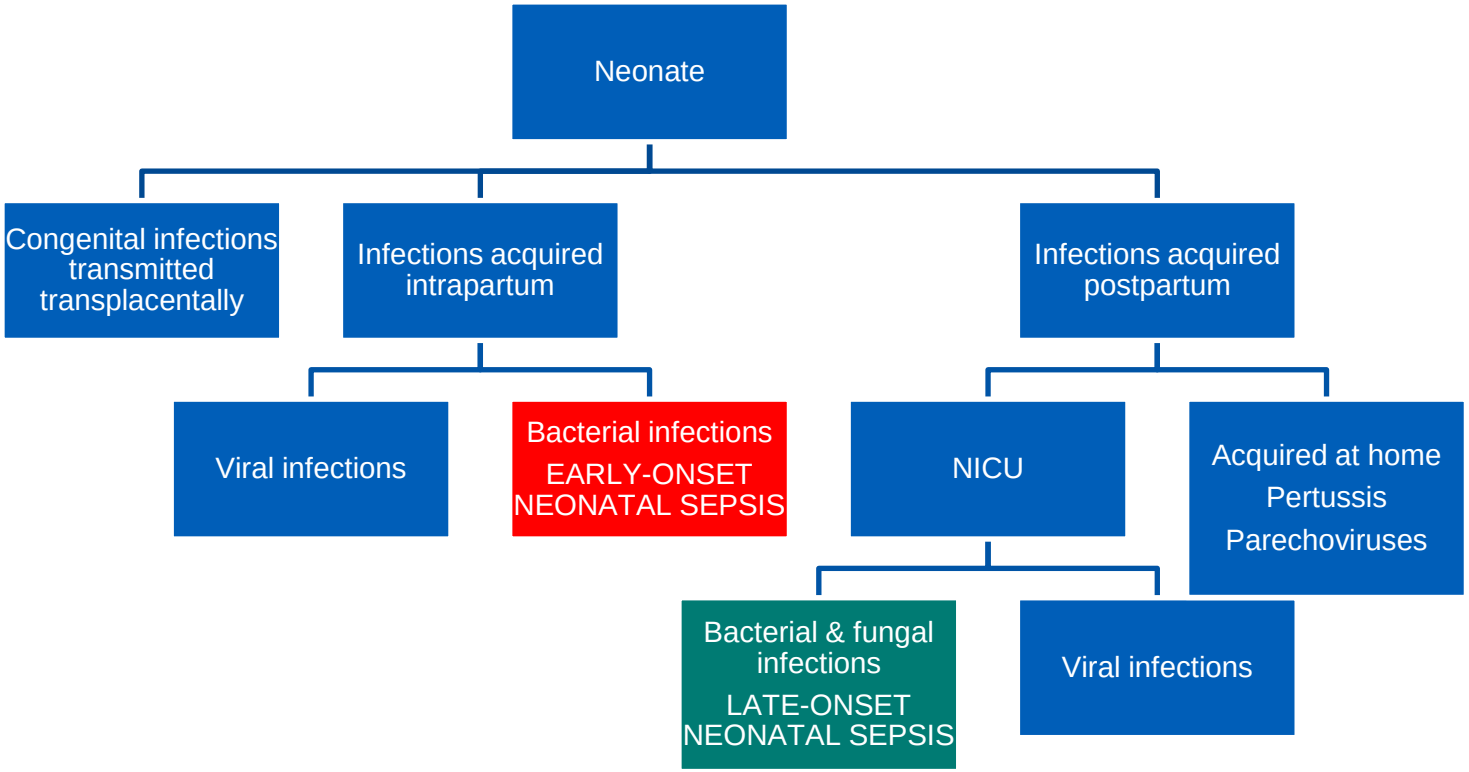

Microbial causes of very early-, early- & late-onset infections in the NICU

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Species	<24h	1-7d	>7d
CNS	<5%	33%	50-60%
Enterococci	<5%	<5%	<5%
GBS	40-60%	<5%	<5%
S aureus	<5%	10-20%	15-20%
Enterobacteriaceae	10-30%	30-50%	10-15%
Other GNB	5-10%	<10%	5-15%
Candida	0%	<5%	5-10%

Causes of community-acquired BSI in general paediatric patients age <3 m

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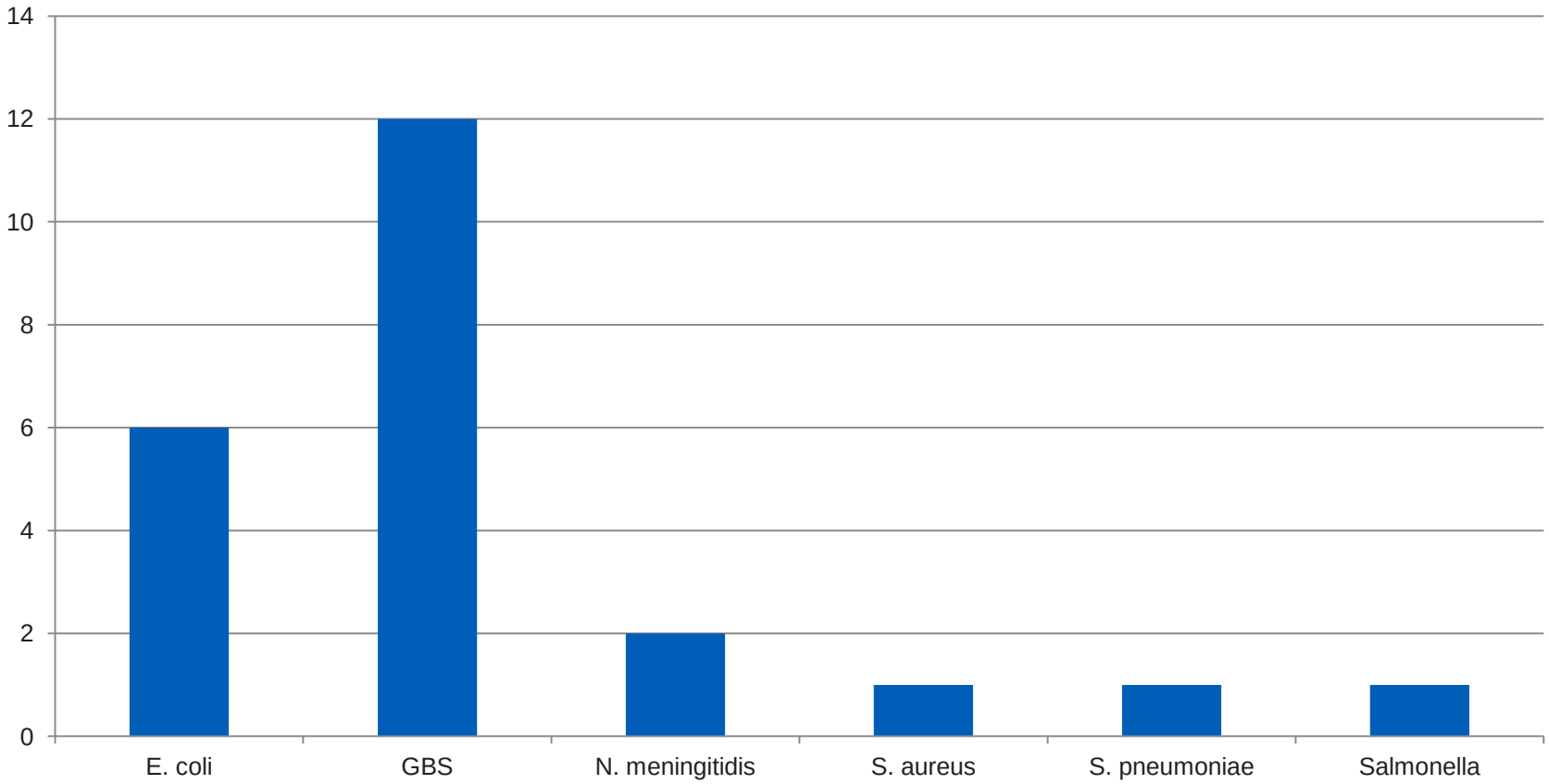

Guidelines relating to neonatal bacterial infections

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- RCOG Green-top Guideline No. 36. Group B Streptococcal Disease, Early-onset
  - Published: 13/09/2017
- NICE Clinical Guidelines
  - CG 149: Early-onset neonatal sepsis
  - CG 160: Fever in under 5s: assessment and initial management
  - CG 102: Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management
  - NG 51: Sepsis: recognition, diagnosis and early management

Overview

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- GBS
- Multidrug-resistant Gram-negative bacteria

Group B streptococcus

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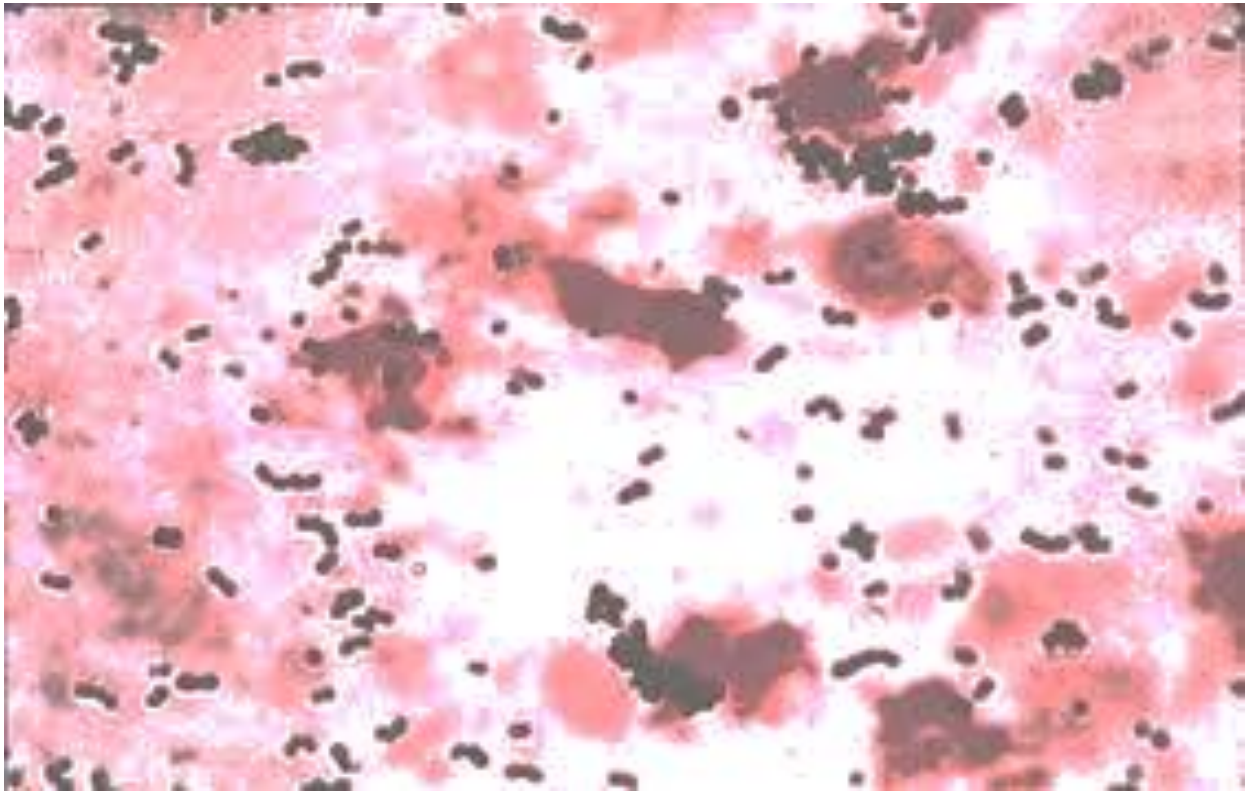
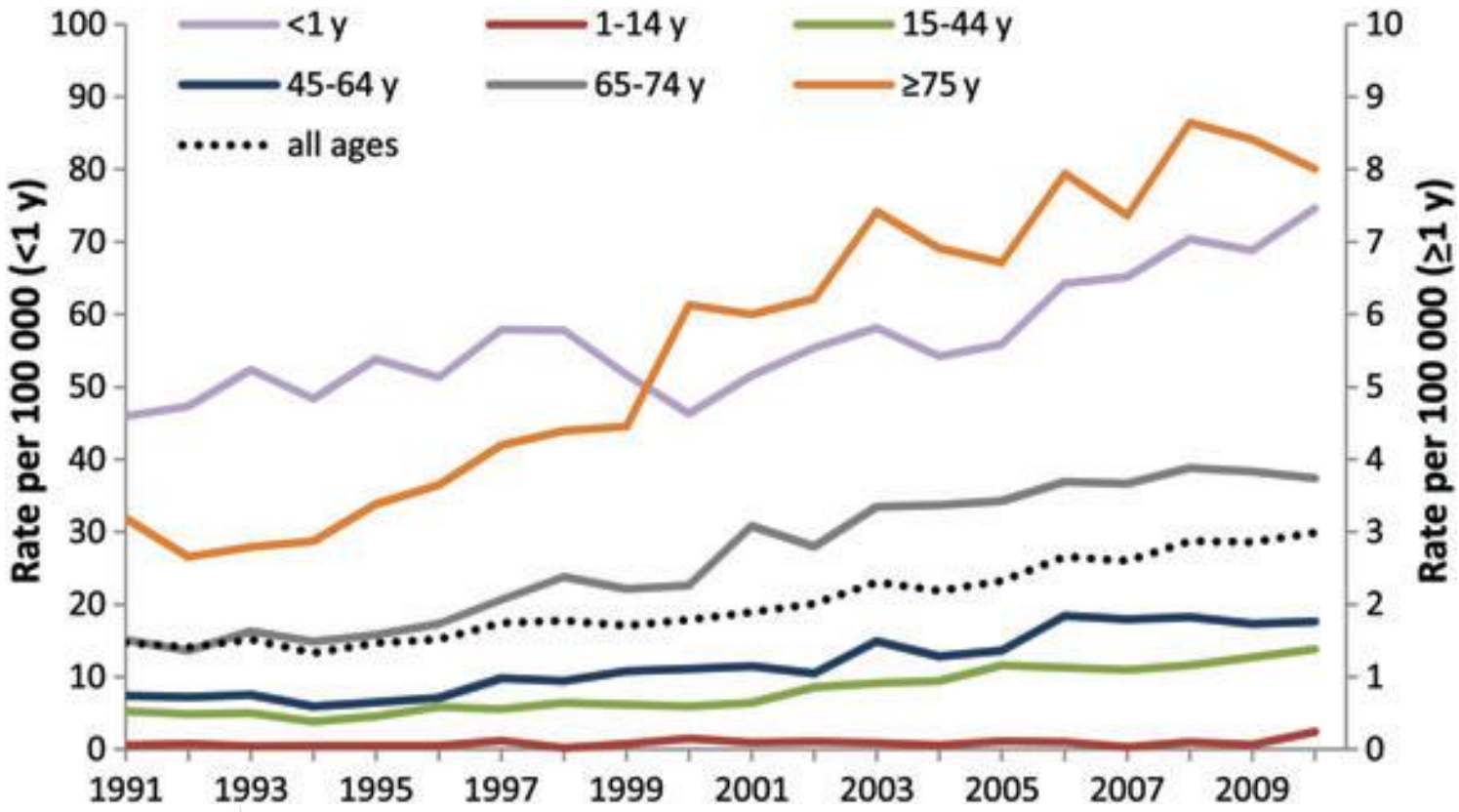


The commonest cause of serious early-onset neonatal sepsis

Group B streptococcus



Age-specific rates of invasive group B streptococcal (GBS) infection,
England and Wales, 1991–2010

Neonatal GBS

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- Early-onset (EOGBS)
  - Cases with onset in first 7 days
    - 30-40% cases & up to 80% deaths occur in pre-term infants
    - >90% within the first 24 h
    - 50% of cases present within first 1 h of life
- Late-onset (LOGBS)
  - Cases presenting age 7 days-3 months
  - Immunisation is only feasible preventative strategy

Preventing EOGBS

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- Cochrane review of five RCTs (all of poor quality) found that IAP decreased rates of culture-proven EOGBS neonatal sepsis by 83%, 95%CI 61% to 93%)

Intrapartum antibiotic prophylaxis

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- Theoretical basis
  - Antibiotics active against GBS given **as soon as possible after onset of labour**
  - Therapeutic concentrations of antibiotics in cord blood within one hour of administration to mother
  - The baby receiving prophylaxis against, or in some cases early treatment for, GBS disease

Does IAP work?

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- US experience
  - Incidence of GBS decreased from 1.7/1000 births in early 1990s to 1.0/1000 births before IAP introduced
  - After IAP incidence continued to fall to a low of 0.34/1000 births, then increased slightly to 0.4/1000 births

Does IAP work?

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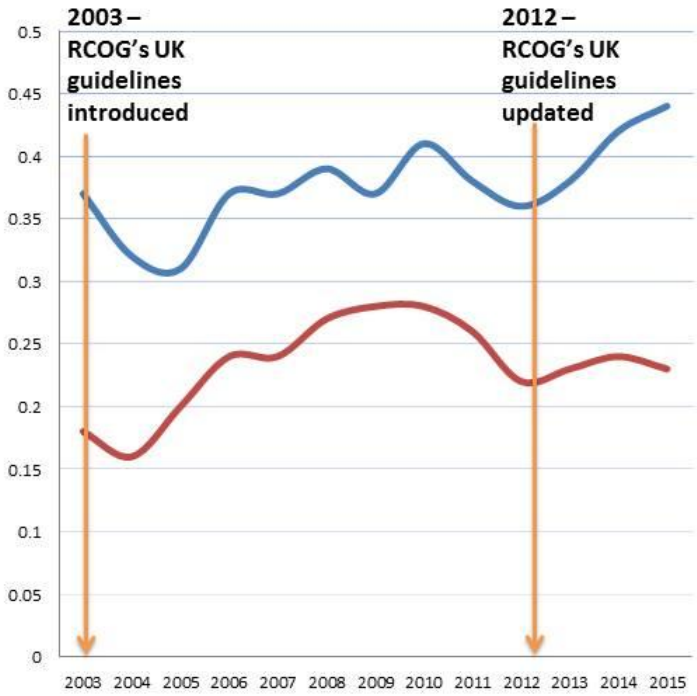
Proven Group B Strep Bacteraemia in Babies 2003-15
England, Wales & Northern Ireland, Voluntary Surveillance*



"Data collection is based on voluntary reporting systems and as such it is important to note that regional and temporal incidence rates can be affected by completeness of and local variations in reporting."

PHE's Health Protection Report Volume 10 Number 41. 25 November 2016

Rate of babies reported with proven early-onset GBS bacteraemia (0-6 days) per 1000 live births

Rate of babies reported with proven late-onset GBS bacteraemia (7-90 days) per 1000 live births

Series online. Data published by Public Health England
https://www.gov.uk/government/publications/pyogenic-and-non-pyogenic-streptococcal-bacteraemia-annual-data-from-voluntary-surveillance

How should need for IAP be determined?

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- Risk factor-based approach
- GBS detection-based approach
  - Screen women at 35-37 weeks gestation
    - Vagino-rectal swabs
    - Enrichment culture or PCR
- Stakeholders continually lobbying to change UK policy

GBS detection strategies

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	Day 1	Day 2	Day 3
Enrichment culture, followed by subculture	Inoculate broth	Subculture broth onto solid medium	Report result
Enrichment culture, followed by PCR	Inoculate broth + perform PCR direct on broth after incubation + report result		
PCR	Report result in <1 hour		

Modelling universal culture-based screening

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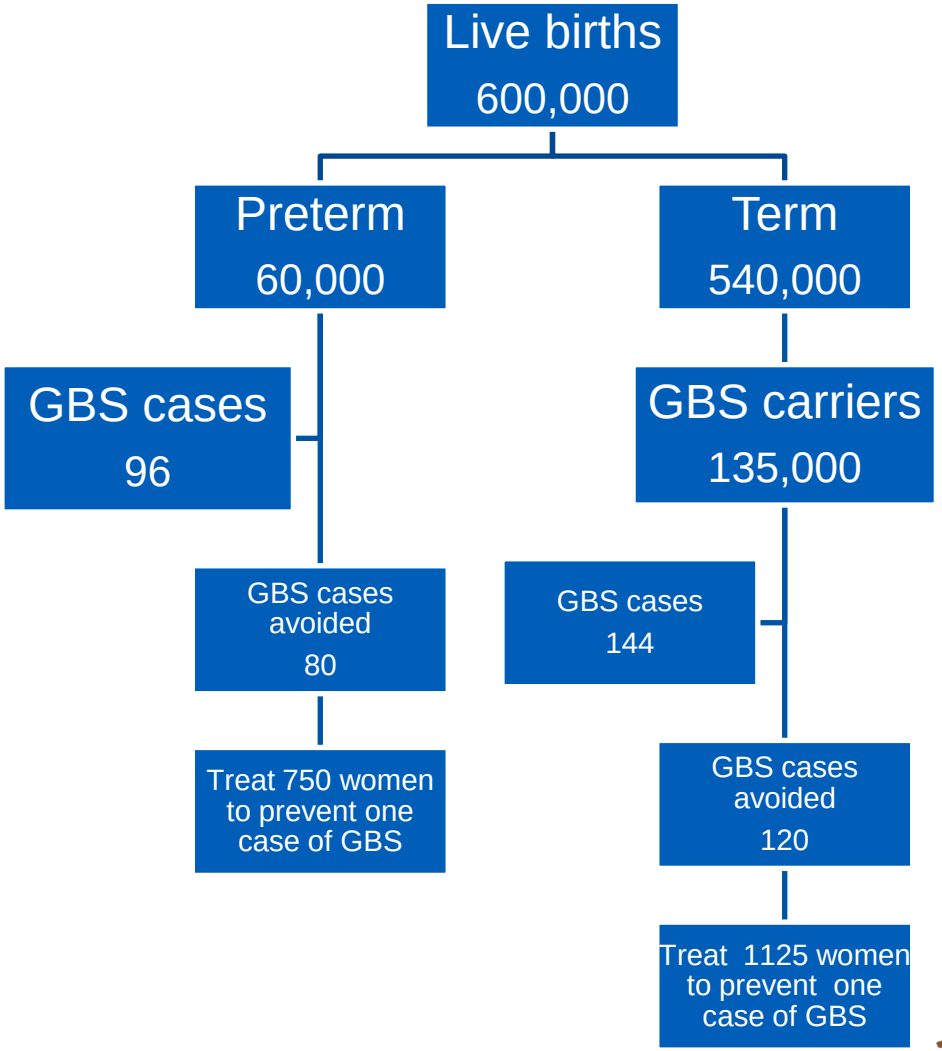

Impact of a culture-based screening programme

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- Number of women screened: 540,000
- Number of women offered IAP: 195,000
- Number of cases of GBS prevented: 200
- Number of women & babies exposed to antibiotics that would be of no benefit: 194,800

Adopting a testing in labour screening programme

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- Number of women screened: 600,000
- Number of women offered IAP: 150,000
- Number of cases of GBS prevented: 200
- Number of women & babies exposed to antibiotics that would be of no benefit: 149,800
- 45,000 fewer women get antibiotics

The problem of MDR-GNB

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- Kent A *et al*. Neonatal gram-negative infections, antibiotic susceptibility and clinical outcome: an observational study.
  - *Arch Dis Child Fetal Neonatal Ed* doi:10.1136/archdischild-2015-309554
- 118 episodes of GNB BSI in 116 patients in 8 NNUs
  - ESBL producers 13.8%
  - Increasing aminoglycoside MIC associated with increased mortality

Screening neonatal admissions for Gram-negative bacteria

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- Reasons for screening
  - Infection prevention & control
  - Clinical: choice of antibiotics
- At BWC we have been screening for over 8 years
  - Frequency of screening: at least weekly
  - Screen for:
    - ESBL producers
    - Gentamicin-resistant Enterobacteriaceae
    - *Serratia* spp.
    - *Pseudomonas aeruginosa*
    - *Acinetobacter baumannii*

What have we learned?

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- 10-20% of babies will have ≥1 of these bacteria during their admission
  - Isolation policy has changed
    - No longer isolate acinetobacter or gentamicin-resistant Enterobacteriaceae
    - Permit cohort isolation of other babies with some different bacteria on a hierarchical basis
- Only a small proportion of babies who acquire these bacteria become infected with them
  - Real challenge for antibiotic stewardship

GNB 'of interest'
April 2016-December 2016

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	Colonisation	BSI
ESBL	43	1
Gentamicin-resistant	37	3
Serratia	78	0
Pseudomonas aeruginosa	49	1
Acinetobacter baumannii	27	0
TOTAL	234	5 (2.1% of colonised babies; 33.3% of babies with Gram-negative sepsis))
Other GNB	-	10

In summary

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- Having started screening, it is very difficult to stop
- Original reason for screening was IPC
- Become more clinically important in selecting empiric antibiotics for septic babies
  - Need tight stewardship
    - Indications for starting very broad-spectrum antibiotics
    - De-escalation

Conclusion

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- Two screening programmes:
  - One local programme screening babies for GNB
    - (Relatively) expensive
    - We don't know whether we are doing any good, but we can't stop
  - A national programme (GBS)
    - We need to be careful to resistant pressure to change practice without evidence
    - If we do we will not know that we are doing more good than harm, but we may not be able to stop