

Laura Folgori<sup>1</sup>, Chiara Tersigni<sup>1,2</sup>, Julia Bielicki<sup>1,3</sup>, Yingfen Hsia<sup>1</sup>, Paul Heath<sup>1</sup>, Mike Sharland<sup>1</sup>

<sup>1</sup>Paediatric Infectious Disease Research Group, Institute for Infection and Immunity, St George's University of London, London, UK; <sup>2</sup>Department of Health Sciences, University of Florence, Pediatric Infectious Diseases Division, Anna Meyer Children's University Hospital, Italy; <sup>3</sup>Paediatric Pharmacology, University Children's Hospital Basel, Basel, Switzerland; <sup>4</sup>Paediatric Infectious Diseases Unit, St George's University Hospitals NHS Foundation Trust, London UK

## BACKGROUND

- Babies admitted to Neonatal Intensive Care Units (NICU) are at significant risk of developing bloodstream infections (BSIs).
- Gram-negative bacteria (GNB) can cause both colonisation and BSI, but the association between these entities is unclear.

## AIMS

Systematic literature review aiming to evaluate:

- the relationship between GNB colonisation and subsequent concordant infection in neonates (baby level)
- the correlation between GN colonisation pressure and the burden of GN sepsis at unit-level.

## METHODS

- Medline – Embase - Cochrane Library
- Strengthening the Reporting of Observational Studies in Epidemiology for Newborn Infection* (STROBE- NI)

## Inclusion criteria

- cohort studies
- published between 2000-2016
- reporting :
  - total number of neonates (0-28 days)
  - colonised with GNB
  - assessed by rectal/skin swab culture
  - total number of babies infected by GNs (same bacteria)

Author, year	Age in days at screening	n of screened babies	n of colonised babies	n of non-colonised babies	n of colonised infected babies	n of non-colonised infected babies	concordant GN-BSI in colonised babies (%)
Akturk H, 2016	nr	1,671	44	1,627	8	nr	18.2
Almuneef MA, 2001	median 2	239	89	150	10	0	11.2
Biran V, 2010	nr	nr	46	nr	3	nr	6.5
Boo NY, 2005	median 9	368	80	288	5	4	6.2
Graham PL, 2007	nr	nr	221	nr	19	nr	8.6
Gundes S, 2005	nr	49	8	41	2	5	25.0
Mamma C, 2008	median 13	210	36	174	0	nr	0.0
Mustapa M, 2014	nr	161	11	150	4	nr	36.4
Oteo J, 2013	nr	413	7	406	3	4	42.8
Parm U, 2011	nr	278	154	124	16	51	10.4
Pessoa-Silva CL, 2003	nr	380	219	161	9	4	4.1
Singh N, 2002	42 ±3 SEM	1,410	240	1,170	9	nr	3.7
Smith A, 2010	nr	698	625	73	59	0	9.4
Suviste J, 2012	nr	2,101	45	2,056	1	9	2.2
Velasco C, 2009	nr	443	159	284	9	8	5.7

Table 1: Rate of colonisation and BSIs in studies included in the baby-level analysis

## RESULTS

- 27 studies fulfilled our inclusion criteria, 15 for the baby-level and 12 for the unit-level analysis.
- High study heterogeneity, with suboptimal overall quality of reporting assessed by the STROBE-NI statement (44.8%).
- Neonates colonised with GNB were significantly more at risk of developing BSIs than non-colonised babies (RR 3.9; 95%CI 1.04-14.57).
- A positive linear correlation was observed between colonisation pressure and BSI rate at the unit-level (Pearson's coefficient (r) 0.7964; p=0.001).

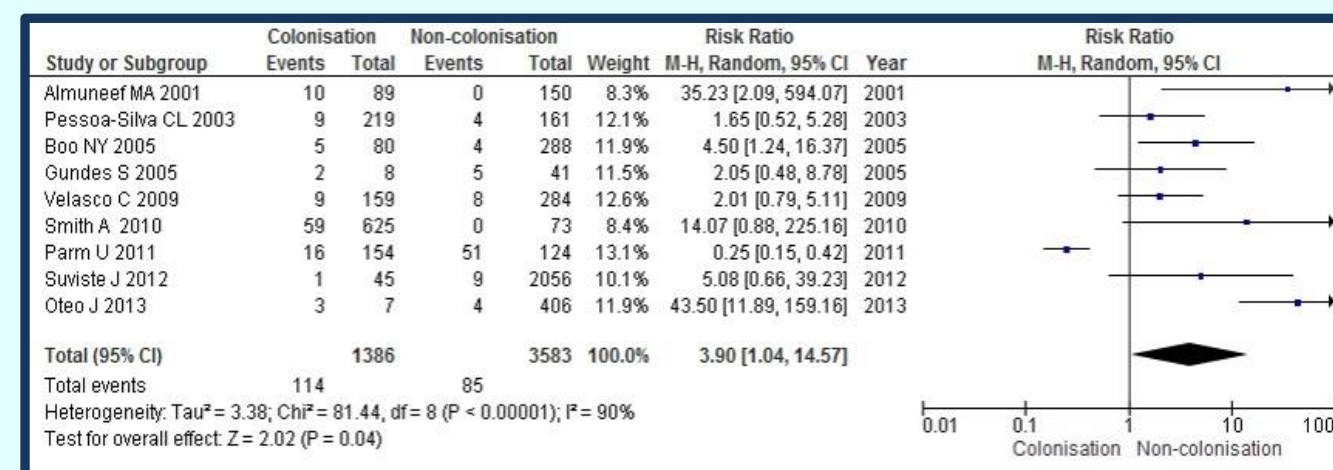


Figure 1: Prevalence of concordant BSIs in colonised and non-colonised babies

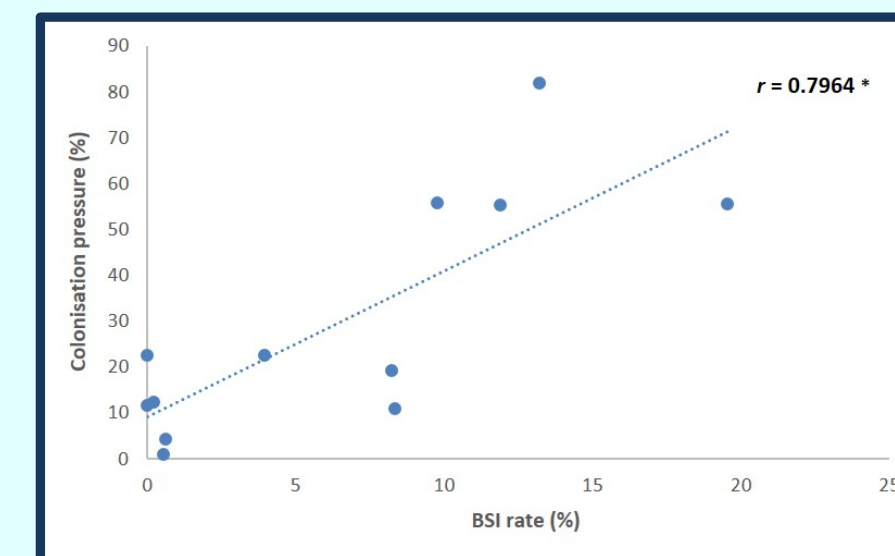


Figure 2: Pearson's correlation (r) between colonisation pressure and rate of BSI at unit level (\*p=0.001)

Author, year	n of screened babies	n of colonised babies	colonisation pressure (%)	n of infected babies (in the same period)	BSI rate (%)
Cassettari VC, 2009	120	27	22.5	7	5.8
Das P, 2011	242	198	81.8	32	13.2
Gbaguidi-Haore H, 2008	735	166	22.6	29	3.9
Gupta A, 2004	73	14	19.2	6	8.2
Haase R, 2014	635	27	4.3	4	0.6
Litzow JM, 2009	1,831	1,017	55.5	358	19.6
Macnow T, 2013	1,475	15	1.0	8	0.5
Mamma C, 2007	210	116	55.2	25	11.9
Parm U, 2011	276	154	55.8	27	9.8
Rettedal S, 2013	469	58	12.4	1	0.2
Richards C, 2004	69	8	11.6	0	0.0
Roy S, 2010	228	25	11.0	19	8.3

Table 2: Colonisation pressure and rate of BSIs in studies included in the unit-level analysis

## CONCLUSION

- The analysis of large cohorts of colonised neonates with clinical outcomes is still needed to define the major determinants leading from colonisation to infection.
- If a correlation between gut colonisation and GN-BSI is confirmed, rectal swabs could be used as a proxy at either patient- or unit-level to guide empirical antibiotic treatment and potentially conserve broad spectrum antibiotics use.