

Appendix F – GRADE tables

No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	Effect size (95%CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
C-reactive protein (≤ 10 mg/l): Sample at time of blood culture										
14	13 cross-sectional	2083	0.80 (0.68, 0.88)	0.71 (0.63, 0.78)	LR+ 2.77 (2.33, 3.29)	Serious ¹	Not serious	Very serious ⁵	Not serious	Very low
					LR- 0.29 (0.19, 0.41)	Serious ¹	Not serious	Very serious ⁵	Not serious	Low
C-reactive protein (10 mg/l): Sample at time of blood culture										
5	Cross-sectional	928	0.62 (0.50, 0.73)	0.73 (0.59, 0.83)	LR+ 2.33 (1.55, 3.49)	Very serious ²	Not serious	Serious ⁶	Serious ⁸	Very low
					LR- 0.53 (0.38, 0.69)	Serious ¹	Not serious	Serious ⁶	Serious ⁹	Very low
C-reactive protein (≥ 10 mg/l): Sample at time of blood culture										
3	Cross-sectional	325	0.77 (0.56, 0.90)	0.69 (0.38, 0.89)	LR+ 2.93 (0.95, 7.75)	Serious ¹	Not serious	Very serious ⁵	Very serious ¹⁰	Very low
					LR- 0.40 (0.12, 1.08)	Serious ¹	Not serious	Very serious ⁵	Very serious ¹¹	Very low
C-reactive protein (≤ 10 mg/l): Sample taken 12-24 hours after blood culture										
2	Cross-sectional	257	0.88 (0.59, 0.97)	0.91 (0.38, 0.99)	LR+ not calculable	Serious ¹	Not serious	Serious ⁶	N/A ¹⁶	Low
					LR- 0.23 (0.03, 0.99)	Serious ¹	Not serious	Serious ⁶	Serious ⁹	Very low
C-reactive protein (10 mg/l): Sample taken 24 hours after blood culture										
1 (Beltempo 2018)	Cross-sectional	416	0.84 (0.76, 0.90)	0.70 (0.65, 0.75)	LR+ 2.82 (2.32, 3.39)	Serious ¹	Serious ³	N/A ⁷	Not serious	Moderate
					LR- 0.23 (0.14, 0.34)	Serious ¹	Serious ³	N/A ⁷	Not serious	Moderate

Neonatal infection: antibiotics for prevention and treatment evidence reviews for investigations before starting treatment for late-onset neonatal infection FINAL (April 2021)

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C-reactive protein (10 mg/l): Sample taken 48 hours after blood culture										
1 (Beltempo 2018)	Cross-sectional	416	0.73 (0.66, 0.80)	0.79 (0.74, 0.84)	LR+ 3.52 (2.72, 4.52)	Serious ¹	Serious ³	N/A ⁷	Not serious	Moderate
					LR- 0.34 (0.26, 0.44)	Serious ¹	Serious ³	N/A ⁷	Not serious	Moderate
C-reactive protein (from urine sample – 9.4 ng/ml): Sample taken when infection was diagnosed										
1 (Ozdemir 2020)	Cross-sectional	66	0.52 (0.35, 0.68)	0.80 (0.64, 0.90)	LR+ 2.58 (1.22, 5.44)	Serious ¹	Not serious	N/A ⁷	Serious ⁸	Low
					LR- 0.62 (0.39, 0.88)	Serious ¹	Not serious	N/A ⁷	Serious ⁹	Low
Procalcitonin (lower threshold) (≤ 10 ng/ml)										
7	Cross-sectional	535	0.76 (0.67, 0.84)	0.65 (0.57, 0.72)	LR+ 2.21 (1.64, 2.91)	Serious ¹	Not serious	Not serious	Serious ⁸	Low
					LR- 0.37 (0.24, 0.54)	Serious ¹	Not serious	Serious ⁶	Serious ⁹	Very low
Procalcitonin (higher threshold) (1000 ng/ml)										
1 (Blommen dahl 2002)	Cross-sectional	169	0.77 (0.50, 0.92)	0.62 (0.54, 0.70)	LR+ 2.02 (1.40, 2.91)	Very serious ²	Serious ³	N/A ⁷	Serious ⁸	Very low
					LR- 0.37 (0.14, 1.01)	Very serious ²	Serious ³	N/A ⁷	Very serious ¹¹	Very low
Neutrophil count (>5000 / ≤ 1800 ≥ 5400 / age-adjusted count)										
3	Cross-sectional	329	0.60 (0.48, 0.70)	0.62 (0.51, 0.72)	LR+ 1.61 (1.05, 2.37)	Serious ¹	Not serious	Serious ⁵	Serious ⁸	Very low
					LR- 0.66 (0.44, 0.95)	Serious ¹	Not serious	Very serious ⁶	Serious ⁹	Very low
Neutrophils (I:T ratio) (>0.07 , >0.12 / >0.2 / >0.65)										
6	Cross-sectional	961	0.70	0.55	LR+ 1.62 (1.03, 2.81)	Serious ¹	Not serious	Very serious ⁵	Serious ⁹	Very low

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No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	Effect size (95%CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
			(0.39, 0.89)	(0.26, 0.81)	LR- 0.58 (0.28, 0.96)	Serious ¹	Not serious	Very serious ⁵	Serious ⁹	Very low
White blood cell count (blood culture) (<5000 cells/mm ³ / <5000 >20000 cells/mm ³)										
3	Cross-sectional	526	0.46 (0.32, 0.60)	0.87 (0.66, 0.96)	LR+ 4.37 (1.10, 12.70)	Serious ¹	Not serious	Very serious ⁵	Serious ⁸	Very low
					LR- 0.64 (0.43, 0.95)	Serious ¹	Not serious	Serious ⁶	Serious ⁹	Very low
White blood cell count (CSF culture) (>19.5 cells/mm ³ / >20 cells/mm ³)										
2	Cross-sectional	6462	0.94 (0.31, 1.00)	0.93 (0.52, 0.99)	LR+ Not calculable	Serious ¹	Serious ⁴	Very serious ⁵	N/A ¹⁶	Very low
					LR- 0.21 (0.00, 1.33)	Serious ¹	Serious ⁴	Very serious ⁵	Very serious ¹¹	Very low
Platelet count (100 cells/mm ³ / 150 cells/mm ³)										
2	Cross-sectional	150	0.53 (0.34, 0.71)	0.63 (0.19, 0.92)	LR+ 2.13 (0.48, 8.15)	Serious ¹	Not serious	Very serious ⁵	Very serious ¹⁰	Very low
					LR- 0.98 (0.34, 3.00)	Serious ¹	Not serious	Very serious ⁵	Very serious ¹¹	Very low
Surface swabs (anal cleft)										
1 (Puri 1995)	Cross-sectional	31	0.07 (0.02, 0.26)	0.46 (0.22, 0.71)	LR+ 0.13 (0.03, 0.67)	Serious ¹	Not serious	N/A ⁷	Serious ¹²	Low
					LR- 2.03 (1.08, 3.79)	Serious ¹	Not serious	N/A ⁷	Serious ¹³	Low
Surface swabs (axilla)										
1 (Puri 1995)	Cross-sectional	31	0.45 (0.26, 0.66)	0.46 (0.22, 0.71)	LR+ 0.84 (0.41, 1.68)	Serious ¹	Not serious	N/A ⁷	Very serious ¹⁴	Very low
					LR- 1.19 (0.58, 2.47)	Serious ¹	Not serious	N/A ⁷	Very serious ¹⁵	Very low
Surface swabs (cubital fossa)										

No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	Effect size (95%CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
1 (Puri 1995)	Cross-sectional	31	0.02 (0.00, 0.19)	0.29 (0.11, 0.57)	LR+ 0.03 (0.00, 0.53)	Serious ¹	Not serious	N/A ⁷	Serious ¹²	Low
					LR- 3.35 (1.38, 8.10)					
Surface swabs (ear)										
1 (Puri 1995)	Cross-sectional	31	0.55 (0.34, 0.74)	0.79 (0.51, 0.93)	LR+ 2.63 (0.82, 8.46)	Serious ¹	Not serious	N/A ⁷	Very serious ¹⁰	Very low
					LR- 0.57 (0.33, 0.99)					
Surface swabs (external genitalia)										
1 (Puri 1995)	Cross-sectional	31	0.02 (0.00, 0.19)	0.62 (0.35, 0.84)	LR+ 0.06 (0.00, 1.08)	Serious ¹	Not serious	N/A ⁷	Serious ¹²	Low
					LR- 1.56 (1.00, 2.43)					
Surface swabs (gastric aspirate)										
1 (Puri 1995)	Cross-sectional	31	0.45 (0.26, 0.66)	0.71 (0.43, 0.89)	LR+ 1.55 (0.57, 4.21)	Serious ¹	Not serious	N/A ⁷	Very serious ¹⁰	Very low
					LR- 0.77 (0.45, 1.32)					
Surface swabs (inguinal fold)										
1 (Puri 1995)	Cross-sectional	31	0.02 (0.00, 0.19)	0.38 (0.16, 0.65)	LR+ 0.04 (0.00, 0.61)	Serious ¹	Not serious	N/A ⁷	Serious ¹²	Low
					LR- 2.60 (1.25, 5.42)					
Surface swabs (lumbar area)										
1 (Puri 1995)	Cross-sectional	31	0.02 (0.00, 0.19)	0.29 (0.11, 0.57)	LR+ 0.03 (0.00, 0.53)	Serious ¹	Not serious	N/A ⁷	Serious ¹⁴	Low
					LR- 3.35					

No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	Effect size (95%CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
					(1.38, 8.10)					
Surface swabs (nasal swab)										
1 (Puri 1995)	Cross-sectional	31	0.50 (0.30, 0.70)	0.71 (0.43, 0.89)	LR+ 1.71 (0.64, 4.57)	Serious ¹	Not serious	N/A ⁷	Very serious ¹⁰	Very low
					LR- 0.71 (0.40, 1.24)	Serious ¹	Not serious	N/A ⁷	Very serious ¹¹	Very low
Surface swabs (neckfold)										
1 (Puri 1995)	Cross-sectional	31	0.02 (0.00, 0.19)	0.29 (0.11, 0.57)	LR+ 0.03 (0.00, 0.53)	Serious ¹	Not serious	N/A ⁷	Serious ¹²	Low
					LR- 3.35 (1.38, 8.10)	Serious ¹	Not serious	N/A ⁷	Serious ¹³	Low
Surface swabs (palms)										
1 (Puri 1995)	Cross-sectional	31	0.12 (0.04, 0.32)	0.29 (0.11, 0.57)	LR+ 0.17 (0.05, 0.57)	Serious ¹	Not serious	N/A ⁷	Serious ¹²	Low
					LR- 3.02 (1.23, 7.40)	Serious ¹	Not serious	N/A ⁷	Serious ¹³	Low
Surface swabs (pharynx)										
1 (Puri 1995)	Cross-sectional	31	0.45 (0.26, 0.66)	0.54 (0.29, 0.78)	LR+ 0.99 (0.45, 2.14)	Serious ¹	Not serious	N/A ⁷	Very serious ¹⁴	Very low
					LR- 1.01 (0.53, 1.94)	Serious ¹	Not serious	N/A ⁷	Serious ¹³	Low
Surface swabs (popliteal space)										
1 (Puri 1995)	Cross-sectional	31	0.02 (0.00, 0.19)	0.29 (0.11, 0.57)	LR+ 0.03 (0.00, 0.53)	Serious ¹	Not serious	N/A ⁷	Serious ¹²	Low
					LR- 3.35 (1.38, 8.10)	Serious ¹	Not serious	N/A ⁷	Serious ¹³	Low
Surface swabs (scalp: occipital)										
		31	0.07	0.38	LR+ 0.11	Serious ¹	Not serious	N/A ⁷	Serious ¹²	Low

No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	Effect size (95%CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	Quality
1 (Puri 1995)	Cross-sectional		(0.02, 0.26)	(0.16, 0.65)	(0.02, 0.57)	Serious ¹	Not serious	N/A ⁷	Serious ¹³	Low
					LR- 2.48 (1.18, 5.19)					
Surface swabs (soles)										
1 (Puri 1995)	Cross-sectional	31	0.02 (0.00, 0.19)	0.29 (0.11, 0.57)	LR+ 0.03 (0.00, 0.53)	Serious ¹	Not serious	N/A ⁷	Serious ¹²	Low
					LR- 3.35 (1.38, 8.10)					
Surface swabs (umbilicus)										
1 (Puri 1995)	Cross-sectional	31	0.60 (0.39, 0.77)	0.79 (0.51, 0.93)	LR+ 2.86 (0.90, 9.10)	Serious ¹	Not serious	N/A ⁷	Very serious ¹⁰	Very low
					LR- 0.51 (0.28, 93)					
Tip of the IV long line (longitudinal split method) (Culture of tip yielded ≥15 colony forming units of the same colony type)										
1 (Martin-Rabdn 2017)	Cross-sectional	277	0.97 (0.91, 0.99)	0.88 (0.84, 0.92)	LR+ 8.41 (6.06, 11.67)	Serious ¹	Not serious	N/A ⁷	Not serious ¹⁰	Moderate
					LR- 0.04 (0.01, 0.11)					
Tip of the IV long line (qualitative method) (Culture of tip yielded ≥15 colony forming units of the same colony type)										
1 (Marconi 2008)	Cross-sectional	85	0.99 (0.89, 1.00)	0.60 (0.45, 0.73)	LR+ 2.48 (1.72, 3.60)	Serious ¹	Not serious	N/A ⁷	Serious ⁸	Low
					LR- not calculable					
Tip of the IV long line (roll plate method) (Culture of tip yielded ≥15 colony forming units of the same colony type)										
3	Cross-sectional	387	0.73 (0.50, 0.88)	0.80 (0.53, 0.93)	LR+ 3.96 (1.68, 8.99)	Serious ¹	Not serious	Very serious ⁵	Serious ⁸	Very low
					LR- 0.36 (0.18, 0.60)					

1. >33.3% of weight of meta-analysis at moderate or high risk of bias. Quality downgraded 1 level
2. Single study at high risk of bias. Quality downgraded 2 levels
3. Single study which is partially directly applicable. Quality downgraded 1 level
4. >33.3% of weight of meta-analysis from partially directly applicable studies. Quality downgraded 1 level
5. $I^2 >66.7\%$. Quality downgraded 2 levels
6. $I^2 >33.3\%$ but $<66.7\%$. Quality downgraded 1 level
7. Single study. Inconsistency not applicable
8. Positive likelihood ratio crossed 1 end of the defined MIDs (1 or 2). Quality downgraded 1 level
9. Negative likelihood ratio crossed 1 end of the defined MIDs (0.5 or 1). Quality downgraded 1 level
10. Positive likelihood ratio crossed both ends of the defined MIDs (1 and 2). Quality downgraded 2 levels
11. Negative likelihood ratio crossed both ends of the defined MIDs (0.5 and 1). Quality downgraded 2 levels
12. Positive likelihood ratio crossed 1 end of the defined MIDs for negative likelihood ratio (0.5 or 1). Quality downgraded 1 level
13. Negative likelihood ratio crossed 1 end of the defined MIDs for positive likelihood ratio (1 or 2). Quality downgraded 1 level
14. Positive likelihood ratio crossed both ends of the defined MIDs for negative likelihood ratio (0.5 and 1). Quality downgraded 2 levels
15. Negative likelihood ratio crossed both ends of the defined MIDs for positive likelihood ratio (1 and 2). Quality downgraded 2 levels
16. Likelihood ratio not calculable. Imprecision not applicable