

Supplementary file 2. GRADE Evidence Profile [15] for NDI in NEC.

Quality assessment							No. of patients		Effect		Quality
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Cases	Controls	Relative (95% CI)	Absolute (95% CI)	
NDI in NEC vs. No NEC							NEC	No NEC			
19	OS	Moderate ^a	Substantial	Not serious	Serious ^b	None	942/ 2,137 (44%)	9,275/ 29,624 (31%)	RR 1.56 (1.39, 1.74)	130 more per 1000 (from 90 more to 172 more)	⊗⊗ LOW
Cerebral palsy in NEC vs. no NEC							NEC	No NEC			
13	OS	Moderate ^a	Considerable	Not serious	Serious ^b	None	325/ 1,903 (17%)	1,984/ 27,715 (7%)	RR 1.84 (1.38, 2.45)	100 more per 1000 (from 45 more to 173 more)	⊗⊗ LOW
Blindness in NEC vs. no NEC							NEC	No NEC			
6	OS	Moderate ^a	Substantial	Not serious	Serious ^b	None	41/ 1,481 (2.8%)	133/ 18,179 (0.7%)	RR 3.36 (1.60, 7.02)	21 more per 1000 (from 5 more to 54 more)	⊗⊗ VERY LOW
Hearing impairment in NEC vs. no NEC							NEC	No NEC			
6	OS	Moderate ^a	Low	Not serious	Serious ^b	None	39/ 1,261 (3.1%)	190/ 12,744 (1.5%)	RR 2.00 (1.41, 2.83)	16 more per 1000 (from 7 more to 29 more)	⊗⊗ LOW
NDI in surgical NEC in NEC vs. medical NEC							Surgical NEC	Medical NEC			
10	OS	Moderate ^a	Low	Not serious	Serious ^b	None	317/ 733 (43%)	204/ 761 (27%)	RR 1.60 (1.34, 1.90)	160 more per 1000 (from 91 more to 240 more)	⊗⊗ LOW
IVH in NEC vs. no NEC							NEC	No NEC			
10	OS	Moderate ^a	Low	Not serious	Serious ^b	None	246/ 1,147 (21%)	2,142/ 12,813 (17%)	RR 1.38 (1.15, 1.66)	40 more per 1000 (from 16 more to 69 more)	⊗⊗ LOW
PVL in NEC vs. no NEC							NEC	No NEC			
6	OS	Moderate ^a	Moderate	Not serious	Serious ^b	None	97/ 1,013 (10%)	606/ 12,394 (5%)	RR 1.87 (1.29, 2.71)	50 more per 1000 (from 17 more to 98 more)	⊗⊗ LOW
ROP in NEC vs. no NEC							NEC	No NEC			
6	OS	Moderate ^a	Substantial	Not serious	Serious ^b	None	174/ 384	875/ 1,743	RR 1.41 (0.95,	50 fewer per 1000 (from 135 fewer to 6	⊗⊗ VERY

							(45%)	(50%)	2.11)	more)	LOW
IVH in surgical NEC in NEC vs. medical NEC							Surgical NEC	Medical NEC			
4	OS	Moderate ^a	Substantial	Not serious	Serious ^b	None	41/ 286 (20%)	45/ 463 (25%)	RR 1.49 (0.70, 3.20)	50 fewer per 1000 (from 224 fewer to 31 more)	⊗OOO VERY LOW

NDI: neurodevelopmental impairment; **NEC:** necrotizing enterocolitis; **IVH:** Intraventricular hemorrhage; **PVL:** periventricular leukomalacia;

ROP: retinopathy of prematurity; **OS:** observational study; **CI:** confidence interval; **RR:** risk relative.

^a Bias due to possible confounding; ^b OIS not met

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.