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PROBIOTICS FOR THE PREVENTION OF NECROTIZING ENTEROCOLITIS: META-ANALYSIS OF SURGICAL OUTCOMES

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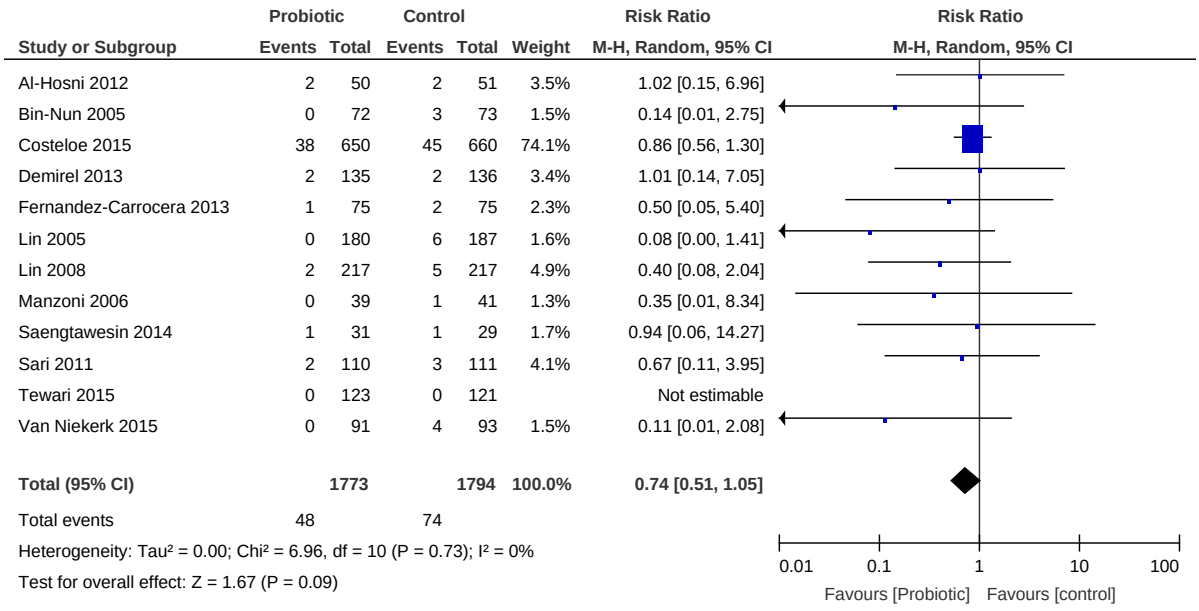
Aim of the Study: Probiotic administration to preterm infants has the potential to prevent necrotizing enterocolitis (NEC). Data from randomized controlled trials (RCTs) are conflicting but in meta-analysis seem to support probiotic administration. To date, these analyses have not focused on surgical outcomes. We aimed to determine the effect of probiotic administration to preterm infants on surgical outcomes of NEC.

Methods: A systematic review of RCTs of probiotic administration to preterm infants was performed. Studies were included if outcomes included any of (i) Bell's Stage III NEC; (ii) surgery for NEC; (iii) deaths attributable to NEC. Article selection and data extraction was performed independently by two authors; conflicts were adjudicated by a third author. Data were meta-analysed using Review Manager 5.3. A random effects model was decided on a priori because of the heterogeneity of study design; data are risk ratio (RR) with 95%CI.

Main Results: Thirty-three RCTs reported NEC as an outcome. However, only 16 reported predefined surgical outcomes; all were included. A variety of probiotic products was administered across studies. Description of surgical outcomes in most studies was poor. Only 6/16 specifically reported incidence of surgery for NEC, 12 reported Bell's stage III and 13 reported NEC-associated mortality. Although there was a trend towards probiotic administration reducing stage III NEC, this was not significant (RR 0.74 [0.52-1.05], p=0.09, Figure). There was no effect of probiotics on the RR of surgery for NEC (RR 0.84 [0.56-1.25], p=0.38). Probiotics did, however, reduce the risk of NEC-associated mortality (RR 0.56 [0.34-0.93], p=0.03).

Conclusion: Despite 33 RCTs on probiotic prevention of NEC, evidence for prevention of surgical NEC is not strong, partly due to poor outcome reporting. In studies included in this meta-analysis, probiotic administration was associated with a reduction in NEC related mortality.



Study or Subgroup	Probiotic Events	Probiotic Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Al-Hosni 2012	2	50	2	51	3.5%	1.02 [0.15, 6.96]
Bin-Nun 2005	0	72	3	73	1.5%	0.14 [0.01, 2.75]
Costeloe 2015	38	650	45	660	74.1%	0.86 [0.56, 1.30]
Demirel 2013	2	135	2	136	3.4%	1.01 [0.14, 7.05]
Fernandez-Carrocera 2013	1	75	2	75	2.3%	0.50 [0.05, 5.40]
Lin 2005	0	180	6	187	1.6%	0.08 [0.00, 1.41]
Lin 2008	2	217	5	217	4.9%	0.40 [0.08, 2.04]
Manzoni 2006	0	39	1	41	1.3%	0.35 [0.01, 8.34]
Saengtawesin 2014	1	31	1	29	1.7%	0.94 [0.06, 14.27]
Sari 2011	2	110	3	111	4.1%	0.67 [0.11, 3.95]
Tewari 2015	0	123	0	121		Not estimable
Van Niekerk 2015	0	91	4	93	1.5%	0.11 [0.01, 2.08]
Total (95% CI)		**1773**		**1794**	**100.0%**	**0.74 [0.51, 1.05]**
Total events	48		74			

Heterogeneity: Tau² = 0.00; Chi² = 6.96, df = 10 (P = 0.73); I² = 0%

Test for overall effect: Z = 1.67 (P = 0.09)