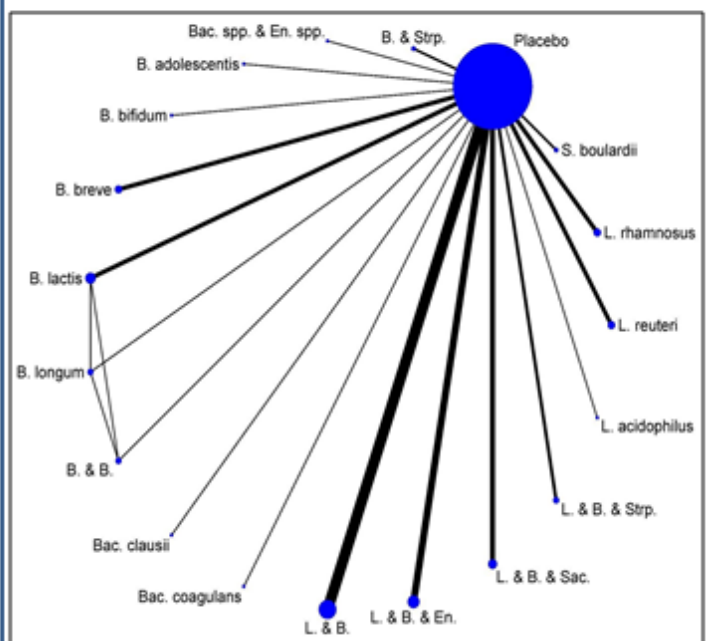


- Systematic review of 63 Randomized controlled trials
- Outcome measures: Mortality, necrotizing enterocolitis  $\geq$ stage II, culture positive sepsis, feed intolerance, reduction in days to reach full feeds and reduction in days of hospitalization
- Median of average birth weight : 1204 g (IQR 1062-1433)
- Median of average gestational age: 30.1 weeks (IQR, 28.7-31.3)

## Network of eligible comparisons for all-cause mortality



# ACADEMIC P.E.A.R.L.S

Pediatric Evidence And Research Learning Snippet



## Probiotics in Preterm Newborns

Probiotics Reduce Mortality and Morbidity in Preterm, Low-Birth-Weight Infants: A Systematic Review and Network Meta-analysis of Randomized Trials. *Gastroenterology* 2020

	All-cause Mortality OR (95% CI)	NEC (stage $\geq$ II) OR (95% CI)	Culture proven sepsis OR (95% CI)	Feed intolerance OR (95% CI)	Reduction in days to reach full feed MD (95% CI)	Reduction in days of hospitalization MD (95% CI)
<b>Lactobacillus spp and Bifidobacterium spp</b>	<b>0.56 (0.39,0.80)</b>	<b>0.35 (0.20,0.59)</b>	0.87 (0.60,1.27)	-	<b>-2.15 (-3.78,-0.51)</b>	-2.84 (-6.21,0.54)
<b>Bifidobacterium animalis subsp. lactis</b>	0.43 (0.16,1.15)	<b>0.31 (0.13,0.74)</b>	0.73 (0.38,1.43)	0.10 (0.00,2.29)	-	<b>-13.00 (-22.71,-3.29)</b>
<b>Lactobacillus reuteri</b>	0.77 (0.51,1.17)	<b>0.55 (0.34,0.91)</b>	0.71 (0.41,1.26)	0.26 (0.06,1.10)	<b>-2.62 (-4.53,-0.71)</b>	<b>-7.89 (-11.60,-4.17)</b>
<b>Lactobacillus rhamnosus</b>	0.84 (0.33,2.12)	<b>0.44 (0.21,0.90)</b>	0.84 (0.45,1.57)	0.75 (0.11,5.35)	0.02 (-3.29,3.32)	-1.85 (-7.62,3.91)
Lactobacillus spp and Bifidobacterium spp and Enterococcus spp	0.78 (0.23,2.62)	<b>0.28 (0.16,0.49)</b>	0.43 (0.17,1.07)	0.23 (0.02,3.07)	-	-6.00 (-19.53,7.53)
Bifidobacterium spp and Streptococcus salivarius subsp. thermophilus	0.84 (0.51,1.40)	<b>0.38 (0.19,0.75)</b>	1.04 (0.52,2.06)	-	-1.35 (-4.66,1.95)	-2.75 (-10.00,4.50)
Bacillus spp and Enterococcus spp	0.95 (0.02,48.18)	<b>0.23 (0.08,0.63)</b>	-	-	-	-
<b>Lactobacillus spp and Bifidobacterium spp and Saccharomyces boulardii</b>	1.05 (0.51,2.17)	0.73 (0.29,1.85)	0.54 (0.28,1.04)	0.47 (0.04,5.04)	<b>-3.30 (-5.91,-0.69)</b>	-3.20 (-8.38,1.98)
Lactobacillus spp and Bifidobacterium spp and S. salivarius subsp. thermophilus	0.40 (0.12,1.30)	0.42 (0.16,1.13)	0.68 (0.35,1.30)	0.68 (0.06,7.70)	5.75 (-0.33,11.83)	7.25 (-5.83,20.33)
Bacillus clausii	0.83 (0.37,1.87)	0.98 (0.14,7.10)	0.70 (0.20,2.45)	0.81 (0.06,11.00)	-	-
Bifidobacterium breve	0.92 (0.63,1.34)	0.92 (0.64,1.32)	0.87 (0.48,1.55)	-	-1.53 (-4.30,1.24)	1.18 (-5.88,8.24)
S. boulardii	1.01 (0.46,2.23)	0.81 (0.42,1.55)	0.77 (0.40,1.45)	0.53 (0.08,3.40)	-1.02 (-3.64,1.61)	-1.86 (-6.65,2.92)

High or moderate certainty evidence	Among the most effective	Inferior to the most effective, but superior to placebo	No more effective than placebo
Low or very low certainty evidence	May be among the most effective	May be inferior to the most effective, but superior to placebo	May be no more effective than placebo

### Conclusion:

Combination of lactobacillus and bifidobacterium species reduced all cause mortality.

Combination of Bacillus and Enterococcus; Bifidobacterium and Strep salivarius cause largest reduction in NEC development.

Combination of Lactobacillus, Bifidobacterium, Saccharomyces reduces time to full feeding.

### EXPERT COMMENT

“Lactobacillus & Bifidobacterium species may be beneficial to reduce mortality and NEC in pre-term infants. Probiotic strains and dosages should be carefully chosen. Doses between  $1 - 5 \times 10^9$  colony forming units/g can be used safely & effectively. RCTs with single strain probiotics should be performed in India to make a general recommendation”



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### Reference

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