Supplementary appendices

Single or multiple strain probiotics for prevention of mortality and morbidity in preterm infants: a systematic review and network meta-analysis of randomized trials

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Online Supplementary Contents

Appendix 1: Search strategies

MEDLINE – from 1946

# ▲	Searches
1	enterocolitis, necrotizing/
2	(necroti?ing enterocolitis or enterocolitis necroticans or nec or typhlitis or pneumatosis intestinalis).tw.
3	1 or 2
4	randomized controlled trial.pt.
5	controlled clinical trial.pt.
6	randomized.ab.
7	placebo.ab.
8	drug therapy.fs.
9	randomly.ab.
10	trial.ab.
11	groups.ab.
12	or/4-11
13	exp animals/ not humans.sh.
14	12 not 13
15	3 and 14

Embase Classic and Embase – from 1947

# ▲	Searches
1	enterocolitis, necrotizing/
2	(necroti?ing enterocolitis or enterocolitis necroticans or nec or typhlitis or pneumatosis intestinalis).tw.
3	1 or 2
4	crossover-procedure/
5	double-blind procedure/
6	randomized controlled trial/
7	single-blind procedure/
8	((doubl* adj blind*) or (singl* adj blind*) or allocat* or assign* or cross over* or crossover* or factorial* or placebo* or random* or volunteer*).tw.
9	or/4-8
10	exp Animals/ not humans/
11	9 not 10
12	3 and 11

Cochrane Central Register of Controlled Trials

# ▲	Searches
1	enterocolitis, necrotizing/
2	(necroti?ing enterocolitis or enterocolitis necroticans or nec or typhlitis or pneumatosis intestinalis).tw.
3	**1 or 2**

Science Citation Index Expanded (SCI-EXPANDED) – from 1900
Social Sciences Citation Index (SSCI) – from 1956

Set	
# 5	#3 NOT #4 *Indexes=SCI-EXPANDED, SSCI Timespan=All years*
# 4	TS=(rat or rats or mouse or mice or pig or pigs or piglet or piglets or porcine or animal) *Indexes=SCI-EXPANDED, SSCI Timespan=All years*
# 3	#2 AND #1 *Indexes=SCI-EXPANDED, SSCI Timespan=All years*
# 2	TS=((doubl* NEAR blind*) or (singl* NEAR blind*) or allocat* or assign* or "cross over*" or crossover* or factorial* or placebo* or random* or volunteer*) *Indexes=SCI-EXPANDED, SSCI Timespan=All years*
# 1	TS=("necrotising enterocolitis" or "necrotizing enterocolitis" or "enterocolitis necroticans" or "nec" or "typhlitis" or "pneumatosis intestinalis") *Indexes=SCI-EXPANDED, SSCI Timespan=All years*

BIOSIS Previews 1980 to present (Oct 22, 2014)

Set	
# 5	#3 NOT #4 *Indexes=BIOSIS Previews Timespan=All years*
# 4	TS=(rat or rats or mouse or mice or pig or pigs or piglet or piglets or porcine) *Indexes=BIOSIS Previews Timespan=All years*
# 3	#2 AND #1 *Indexes=BIOSIS Previews Timespan=All years*
# 2	TS=((doubl* NEAR blind*) or (singl* NEAR blind*) or allocat* or assign* or "cross over*" or crossover* or factorial* or placebo* or random* or volunteer*) *Indexes=BIOSIS Previews Timespan=All years*
# 1	TS=("necrotising enterocolitis" or "necrotizing enterocolitis" or "enterocolitis necroticans" or "nec" or "typhlitis" or "pneumatosis intestinalis") *Indexes=BIOSIS Previews Timespan=All years*

CINAHL (EBSCOHost)

#	Searches
S17	S3 AND S16
S16	S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15
S15	TX allocat* random*
S14	(MH "Quantitative Studies")
S13	(MH "Placebos")
S12	(MH "Placebos")
S11	TX placebo*
S10	TX random* allocat*
S9	(MH "Random Assignment")
S8	TX randomi* control* trial*

S7	TX ((singl* n1 blind*) or (singl* n1 mask*)) or TX ((doubl* n1 blind*) or (doubl* n1 mask*)) or TX ((tripl* n1 blind*) or (tripl* n1 mask*)) or TX ((trebl* n1 blind*) or (trebl* n1 mask*))
S6	TX clinic* n1 trial*
S5	PT Clinical trial
S4	(MH "Clinical Trials+")
S3	S1 OR S2
S2	TX ("necrotising enterocolitis" or "necrotizing enterocolitis" or "enterocolitis necroticans" or "nec" or "typhlitis" or "pneumatosis intestinalis")
S1	(MH "Enterocolitis, Necrotizing")

Scopus

((TITLE-ABS-KEY ("necrotising enterocolitis" OR "necrotizing enterocolitis" OR "enterocolitis necroticans" OR "nec" OR "typhlitis" OR "pneumatosis intestinalis")) AND (TITLE-ABS-KEY ((doubl* W/1 blind*) OR (singl* W/1 blind*) OR allocat* OR assign* OR "cross over*" OR crossover* OR factorial* OR placebo* OR random* OR volunteer*))) AND NOT (TITLE-ABS-KEY (rat OR rats OR mouse OR mice OR pig OR pigs OR piglet OR piglets OR porcine OR animal))

ProQuest Dissertations & Theses Full Text

(TI,AB,FT("necrotising enterocolitis" OR "necrotizing enterocolitis" OR "enterocolitis necroticans" OR "typhlitis" OR "pneumatosis intestinalis") AND TI,AB,FT((doubl* NEAR/1 blind*) OR (singl* NEAR/1 blind*) OR allocat* OR assign* OR "cross over*" OR crossover* OR factorial* OR placebo* OR random* OR volunteer*)) NOT TI,AB,FT(rat OR rats OR mouse OR mice OR pig OR pigs OR piglet OR piglets OR porcine OR animal)

Google scholar

("necrotizing enterocolitis" OR "necrotising enterocolitis" OR "enterocolitis necroticans" OR "typhlitis" OR "pneumatosis intestinalis") AND (random AND trial)

WHO International Clinical Trials Registry Platform (search covers: Australian New Zealand Clinical Trials Registry; Chinese Clinical Trial Registry; EU Clinical Trials Register (EU-CTR); The Netherlands National Trial Register; Brazilian Clinical Trials Registry (ReBec); Clinical Trials Registry – India, Korea, Cuba, Iran, Thailand,…)

("necrotizing enterocolitis" OR "necrotising enterocolitis" OR "enterocolitis necroticans" OR "typhlitis" OR "pneumatosis intestinalis")

The ISRCTN registry

("necrotizing enterocolitis" OR "necrotising enterocolitis" OR "enterocolitis necroticans" OR "typhlitis" OR "pneumatosis intestinalis")

clinicaltrials.gov

("necrotizing enterocolitis" OR "necrotising enterocolitis" OR "pneumatosis intestinalis") | Interventional Studies

("necrotizing enterocolitis" OR "necrotising enterocolitis" OR "pneumatosis intestinalis") AND (random* OR placebo OR trial)

Appendix 2: References to trials included in the network meta-analysis

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Appendix 3: Characteristics of participants of trials included in the network meta-analysis

Ref #	Study (year)	LN	BW (g)	GA (wks)	APGAR M5	% C-Sec	% MV	% IUGR	% SGA	% MM fed	% FM fed
1	Al-Hosni (2012)	EN	778.5	25.7	7.5	51.5	-	-	0.0	-	0.0
2	Arora (2017)	EN	1700.0	32.9	-	82.0	-	9.3	22.7	100.0	0.0
3	Bin-Nun (2005)	EN	1131.4	29.5	8.0	78.0	-	-	20.0	61.4	24.1
4	Braga (2011)	EN	1173.7	29.4	8.0	51.5	-	-	23.0	-	0.0
5	Chowdhury (2016)	EN	1324.0	31.5	-	-	-	-	-	-	0.0
6	Chrzanowska-Lisiewska (2012)	EN	1257.8	29.5	6.6	72.3	-	-	100.0	0.0	100.0
7	Costalos (2003)	EN	1648.1	31.4	-	44.8	-	15.0	-	0.0	100.0
8	Costeloe (2016)	EN	1041.0	28.0	-	52.7	-	-	-	46.1	34.1
9	Dani (2002)	EN	1334.9	30.8	-	79.3	45.5	17.3	-		35.0
10	Dashti (2014)	EN	1406.4	31.2	9.2	82.4	50.0	-	-	34.6	5.9
11	Demirel (2013)	EN	1147.4	29.3	6.0	80.4	-	-	-	-	-
12	Deng (2010)	CHN	1628.7	32.8	-	-	-	-	-	-	-
13	Di (2010)	CHN	-	33.0	-	-	-	-	-	-	-
14	Dilli (2015)	EN	1204.3	28.7	7.0	34.5	-	-	-		21.8
15	Dongol Singh (2017)	EN	-	-	-	-	-	-	-	-	-
16	Dutta (2014)	EN	1323.3	30.9	8.9	32.9	29.5	-	-	-	7.4
17	Fernández-Carrocera (2013)	EN	1130.0	31.1	-	-	2.0	-	78.0	-	-
18	Fujii (2006)	EN	1427.7	31.3	-	-	-	-	-	-	-
19	Hariharan (2016)	EN	959.2	29.0	-	-	36.7	-	-	-	-
20	Hays (2016)	EN	1170.0	29.2	-	78.2	51.8	-	-	-	0.5
21	Hernandez-Enriquez (2016)	SPN	1293.3	31.4	-	72.3	13.6	-	-	-	0.0
22	Hikaru (2010)	EN	1036.4	28.3	-	-	-	-	-	-	
23	Hua (2014)	CHN	1786.6	33.1	-	60.3	-	-	23.0	24.1	75.9
24	Huang (2009)	CHN	1100.0	30.1	-	-	-	-	-	-	-
25	Indrio (2017)	EN	1439.1	-	-	85.0	-	-	0.0	0.0	100.0
26	Jacobs (2013)	EN	1055.5	27.9	8.0	67.0	-	-	-	50.8	-
27	Kanic (2015)	EN	1064.2	28.5	7.5	-	77.5	-	-	31.3	-
28	Ke (2008)	CHN	-	33.5	-	-	-	-	-	-	-
29	Kitajima (1997)	EN	1026.0	28.2	-	-	-	-	13.2	-	0.0

30	Lin (2005)	EN	1087.2	28.3	-	55.6	-	-	22.6	-	0.0
31	Lin (2008)	EN	1053.1	-	-	65.7	-	-	21.4	65.4	0.0
32	Manzoni (2014)	EN	1134.8	29.6	7.4	78.1	-	-	-	28.0	17.9
33	Mihatsch (2010)	EN	863.4	26.7	7.9	69.4	-	-	10.0	17.2	67.2
34	Millar (1993)	EN	1472.5	30.3	-	40.0	-	-	-	-	-
35	Mohan (2008)	EN	1425.3	31.2	8.1	88.4	-	-	-	-	15.9
36	Oncel (2014)	EN	1059.5	28.1	8.0	78.8	-	-	8.2	15.0	13.5
37	Patole (2014)	EN	1060.2	28.5	-	69.9	-	-	25.2	-	1.3
38	Punnahitananda (2006)	EN	1135.8	29.2	-	-	-	-	-	-	
39	Qiao (2016)	EN	1623.0	32.3	-	-	28.3	-	-	0.0	100.0
40	Ren (2010)	CHN	1700.0	31.0	-	-	-	-	-	-	-
41	Reuman (1986)	EN	1371.5	30.6	7.1	-	-	-	-	-	-
42	Rojas (2012)	EN	1522.9	32.0	9.0	82.9		-	28.9	2.8	40.5
43	Romeo (2011)	EN	1961.7	33.5	-	91.0	-	-	-	-	-
44	Rouge (2009)	EN	1084.8	28.1	8.9	67.0	-	4.3	-	-	-
45	Roy (2014)	EN	1130.5	32.1	-	80.4	9.8		-	-	0.0
46	Sadowska-Krawczenko (2012)	POL	973.1	29.5	7.0	65.5	-	41.8	-	-	0.0
47	Saengtawesin (2014)	EN	1229.6	30.8	-	65.0	-	-	8.3	-	0.0
48	Samanta (2009)	EN	1191.4	30.1	-	47.8	-	-	34.4	100.0	0.0
49	Sari (2011)	EN	1254.5	29.6	-	71.5	-	-	7.2	28.1	0.0
50	Serce (2013)	EN	1144.0	28.8	7.5	84.6	-	-	11.0	-	-
51	Shadkam (2015)	EN	1407.5	30.9	-	-	-	-	-	100.0	0.0
52	Shashidhar (2017)	EN	1223.0	31.1	8.0	62.5	-	-	35.6	45.2	0.0
53	Sinha (2015)	EN	2262.0	-	-	5.8	-	-	-	-	0.0
54	Stratiki (2007)	EN	1500.0	30.8	9.0	36.0	13.3	-	-	0.0	100.0
55	Tewari (2015)	EN	1363.0	30.0	-	60.7	-	13.2	-	-	0.0
56	Totsu (2014)	EN	1007.7	28.6	7.5	68.6	-	-	-	-	-
57	van Neikerk (2014)	EN	1009.0	28.7	-	78.0	-	25.7	-	0.0	0.0
58	van Neikerk (2015)	EN	972.0	28.7	-	74.0	-	18.2	-	100.0	0.0
59	Wejryd (2018)	EN	733.0	25.5	-	-	-	-	-	-	0.0
60	Xiao-yuan (2007)	CHN	1745.0	31.0	-	-	-	-	-	-	4.0
61	Xu (2016)	EN	1951.9	33.0	-	-	-	-	-	0.0	100.0

62	Yang (2011)	CHN	-	-	-	-	-	-	-	0.0	100.0
63	Zhou (2012)	CHN	1891.3	34.3	-	-	-	-	-	-	-

Footnote: LN = Language, EN = English, CHN = Chinese, POL = Polish, SPN = Spanish, BW = birth weight, GA = gestational age (weeks), APGAR M5 = APGAR score at 5-minute, % C-Sec = percent infants delivered by caesarean section, % MV = percent infants with mechanical ventilation support, % IUGR = percent infants with intrauterine growth restriction, % SGA = percent infants small for gestational age, % MM fed = percent infant exclusively fed with mother's milk, % FM fed = percent infant exclusively fed with formula milk.

Appendix 4: Treatment characteristics of trials and outcomes included in the network meta-analysis

Ref #	Study (year)	Arm 1	n	Probiotic formulation	Trt duration (weeks)	Arm 2	n	Probiotic formulation	Trt duration (weeks)	Arm 3	n	Probiotic formulation	Trt duration (weeks)	Arm 4	n	Outcomes
1	Al-Hosni (2012)	Multi-strain probiotics	50	*L. rhamnosus* ATCC 53103 *B. longum* subsp. *infantis*	up to 34 wks PMA or discharge	Control/No treatment	51	NA	-	-	-	-	-	-	-	ACM, NEC, LOS
2	Arora (2017)	Multi-strain probiotics	75	*L. rhamnosus; L. acidophilus* *B. longum* subsp. *longum* *S. boulardii*	2	Control/No treatment	75	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF, HOS
3	Bin-Nun (2005)	Multi-strain probiotics	72	*B. longum* subsp. *infantis; B. bifidum* *S. salivarius* subsp. *thermophilus*	up to 36 wks PMA	Placebo	73	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF
4	Braga (2011)	Multi-strain probiotics	119	*L. casei* *B. breve*	4	Control/No treatment	112	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF
5	Chowdhury (2016)	Multi-strain probiotics	52	*L. rhamnosus; L. acidophilus; L. casei* *B. longum* subsp. *infantis; B. bifidum;* *B. longum* subsp. *longum*	until discharge	Control/No treatment	50	NA	-	-	-	-	-	-	-	NEC, TFF, HOS
6	Chrzanowska-Lisiewska (2012)	Single strain probiotics	21	*L. rhamnosus* ATCC 53103	6	Preterm Formula	26	NA	-	-	-	-	-	-	-	NEC, LOS, HOS
7	Costalos (2003)	Single strain probiotics	51	*S. boulardii*	≥ 4	Preterm Formula	36	NA	-	-	-	-	-	-	-	NEC, LOS, FIT, TFF
8	Costeloe (2016)	Single strain probiotics	650	*B. breve* YIT4010	up to 36 weeks PMA or discharge	Placebo	660	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF, HOS
9	Dani (2002)	Single strain probiotics	295	*L. rhamnosus* ATCC 53103	until discharge	Placebo	290	NA	-	-	-	-	-	-	-	ACM, NEC, LOS
10	Dashti (2014)	Multi-strain probiotics	69	*L. acidophilus; L. rhamnosus; L. delbrueckii* subsp. *bulgaricus; L. casei*	NR	Placebo	67	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF

				B. breve; B. longum subsp. *longum* *S. salivarius* subsp. *thermophilus*												
11	Demirel (2013)	Single strain probiotics	135	*S. boulardii*	until discharge	Control/No treatment	136	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, FIT, TFF, HOS
12	Deng (2010)	Multi-strain probiotics	63	*L. acidophilus* *B. longum* subsp. *longum* *E. faecalis*	2	Control/No treatment	62	NA	-	-	-	-	-	-	-	ACM, NEC
13	Di (2010)	Multi-strain probiotics	182	*Bacillus subtilis* *E. faecium*	until discharge	Control/No treatment	173	NA	-	-	-	-	-	-	-	ACM, NEC
14	Dilli (2015)	Single strain probiotics	100	*B. animalis* subsp. *lactis*	8	Synbiotics	100	*B. animalis* subsp. *lactis* plus *inulin*	8	FOS	100	NA	8	Placebo	100	ACM, NEC, LOS, FIT, TFF, HOS
15	Dongol Singh (2017)	Single strain probiotics	37	*L. rhamnosus* LCR 35	Until full enteral feeding	Placebo	35	NA	-	-	-	-	-	-	-	ACM, NEC
16	Dutta (2014)	Multi-strain probiotics (high dose)	38	*L. rhamnosus; L. acidophilus* *B. longum* subsp. *longum* *S. boulardii*	3	Multi-strain probiotics (high dose)	38	*L. rhamnosus; L. acidophilus* *B. longum* subsp. *longum* *S. boulardii*	2	Multi-strain probiotics (low dose)	38	*L. rhamnosus; L. acidophilus* *B. longum* subsp. *longum* *S. boulardii*	3	Placebo	35	ACM, NEC, LOS
17	Fernández-Carrocera (2013)	Multi-strain probiotics	75	*L. rhamnosus; L. acidophilus; L. casei; L. plantarum* *B. longum* subsp. *infantis* *S. salivarius* subsp. *thermophilus*	until discharge	Control/No treatment	75	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF, HOS
18	Fujii (2006)	Single strain probiotics	11	*B. breve* M-16V	until discharge	Placebo	8	NA	-	-	-	-	-	-	-	NEC, LOS, HOS
19	Hariharan (2016)	Multi-strain probiotics	93	*L. acidophilus* *B. bifidum* *S. boulardii*	6	Control/No treatment	103	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, FIT, TFF
20	Hays (2016)	Multi-strain probiotics	47	*B. animalis* subsp. *lactis; B. longum* subsp. *longum*	4 to 6	Single strain probiotics	48	*B. longum* subsp. *longum*	4 to 6	Single strain probiotics	50	*B. animalis* subsp. *lactis*	4 to 6	Placebo	52	ACM, NEC, LOS, TFF

21	Hernandez-Enriquez (2016)	Single strain probiotics	24	*L. reuteri* DSM 17938	3	Control/No treatment	20	NA	-	-	-	-	-	-	-	NEC, TFF, HOS
22	Hikaru (2010)	Single strain probiotics	108	*B. breve* M-16V	Until discharge	Placebo	100	NA	-	-	-	-	-	-	-	ACM, LOS, TFF, HOS
23	Hua (2014)	Multi-strain probiotics	119	*L. delbrueckii* subsp. *bulgaricus* *B. longum* subsp. *longum* *S. salivarius* subsp. *thermophilus*	2	Control/No treatment	138	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, FIT
24	Huang (2009)	Single strain probiotics	95	*B. adolescentis*	1 to 2	Control/No treatment	88	NA	-	-	-	-	-	-	-	ACM, NEC
25	Indrio (2017)	Single strain probiotics	30	*L. reuteri* DSM 17938	4	Placebo	30	NA	-	-	-	-	-	-	-	TFF, HOS
26	Jacobs (2013)	Multi-strain probiotics	548	*B. longum* subsp. *infantis* DSM 33361; *B. animalis* subsp. *lactis* DSM 15954 *S. salivarius* subsp. *thermophilus* TH-4	term corrected age/until discharge	Placebo	551	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF, HOS
27	Kanic (2015)	Multi-strain probiotics	40	*L. gasseri* PTA-5845 *B. longum* subsp. *infantis* PTA-5843 *E. faecium* PTA-5844	until discharge	Control/No treatment	40	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF, HOS
28	Ke (2008)	Multi-strain probiotics	438	*L. acidophilus* *B. longum* subsp. *longum* *E. faecalis*	until discharge	Control/No treatment	446	NA	-	-	-	-	-	-	-	ACM, NEC
29	Kitajima (1997)	Single strain probiotics	45	*B. breve* YIT4010	4	Control/No treatment	46	NA	-	-	-	-	-	-	-	ACM, NEC, LOS
30	Lin (2005)	Multi-strain probiotics	180	*L. acidophilus* *B. longum* subsp. *infantis*	until discharge	Control/No treatment	187	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, HOS
31	Lin (2008)	Multi-strain probiotics	222	*L. acidophilus* *B. bifidum*	6	Placebo	221	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF, HOS

32	Manzoni (2014)	Synbiotics	238	*L. rhamnosus* ATCC 53103	4 to 6	Lactoferrin	247	NA	4 to 6	Placebo	258	-	-	-	-	ACM, NEC, LOS, TFF, HOS
33	Mihatsch (2010)	Single strain probiotics	91	*B. animalis* subsp. *lacti s* DSM 15954	until discharge	Placebo	89	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF
34	Millar (1993)	Single strain probiotics	10	*L. rhamnosus* ATCC 53103	2 wks	Placebo	10	NA	-	-	-	-	-	-	-	LOS, FIT
35	Mohan (2008)	Single strain probiotics	37	*B. animalis* subsp. *lacti s* DSM 15954	3 wks	Placebo	32	NA	-	-	-	-	-	-	-	NEC
36	Oncel (2014)	Single strain probiotics	200	*L. reuteri* DSM 17938	4 wks	Placebo	200	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, FIT, TFF, HOS
37	Patole (2014)	Single strain probiotics	79	*B. breve* M-16V	corrected age of 37 wks	Placebo	80	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF
38	Punnahitanand a (2006)	Multi-strain probiotics	89	*L. acidophilus* *B. longum* subsp. *infantis*	4/until discharge	Placebo	85	NA	-	-	-	-	-	-	-	ACM
39	Qiao (2016)	Multi-strain probiotics	30	*L. acidophilus* *B. longum* subsp. *longum* *E. faecium*	2 wks	Placebo	30	NA	-	-	-	-	-	-	-	FIT
40	Ren (2010)	Multi-strain probiotics	80	*B. longum* subsp. *infantis* *L. acidophilus* *Bacillus cereus* *E. faecalis*	1 to 2 wks	Control/No treatment	70	NA	-	-	-	-	-	-	-	ACM, NEC
41	Reuman (1986)	Single strain probiotics	15	*L. acidophilus*	4 wks	Placebo	15	NA	-	-	-	-	-	-	-	ACM, NEC, HOS
42	Rojas (2012)	Single strain probiotics	372	*L. reuteri* DSM 17938	until discharge	Placebo	378	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, FIT, HOS
43	Romeo (2011)	Single strain probiotics	83	*L. reuteri* ATCC 55730	6/until discharge	Single strain probiotics	83	*L. rhamnosus* ATCC 53103	6/until discharge	Control/ No treatment	83	-	-	-	-	LOS, FIT, TFF, HOS
44	Rouge (2009)	Multi-strain probiotics	45	*L. rhamnosus* ATCC 53103 *B. longum* subsp. *longum* Reut er ATCC BAA-999	until discharge	Placebo	49	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, HOS

45	Roy (2014)	Multi-strain probiotics	56	*L. acidophilus* *B. bifidum; B. animalis* subsp. *lacti s; B. longum* subsp. *longum*	6/until discharge	Placebo	56	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF, HOS
46	Sadowska-Krawczenko (2012)	Single strain probiotics	30	*L. rhamnosus* ATC A07FA	Until discharge	Placebo	25	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, HOS
47	Saengtawesin (2014)	Multi-strain probiotics	31	*L. acidophilus* *B. bifidum*	6/until discharge	Control/No treatment	29	NA	-	-	-	-	-	-	-	ACM, NEC, NRM, LOS, TFF, HOS
48	Samanta (2009)	Multi-strain probiotics	91	*L. acidophilus* *B. longum* subsp. *infantis; B. animalis* subsp. *lactis; B. longum* subsp. *longum*	until discharge	MBM	95	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF, HOS
49	Sari (2011)	Single strain probiotics	121	*Bacillus coagulans*	until discharge	Placebo	121	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, FIT, TFF, HOS
50	Serce (2013)	Single strain probiotics	104	*S. boulardii*	until discharge	Placebo	104	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF, HOS
51	Shadkam (2015)	Single strain probiotics	30	*L. reuteri* DMS 17938	Until full enteral feeding	Placebo	30	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF
52	Shashidhar (2017)	Multi-strain probiotics	48	*L. acidophilus; L. rhamnosus* *B. longum* subsp. *longum* *S. boulardii*	4	Placebo	48	NA	-	-	-	-	-	-	-	ACM, NEC, TFF, HOS
53	Sinha (2015)	Multi-strain probiotics	668	*L. acidophilus; L. plantarum; L. casei; B. breve; B. longum* subsp. *infantis; B. longum* subsp. *longum* *S. salivarius* subsp. *thermophilus*	4	Placebo	672	NA	-	-	-	-	-	-	-	ACM, LOS
54	Stratiki (2007)	Single strain probiotics	41	*B. animalis* subsp. *lactis*	until discharge	Preterm Formula	36	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF

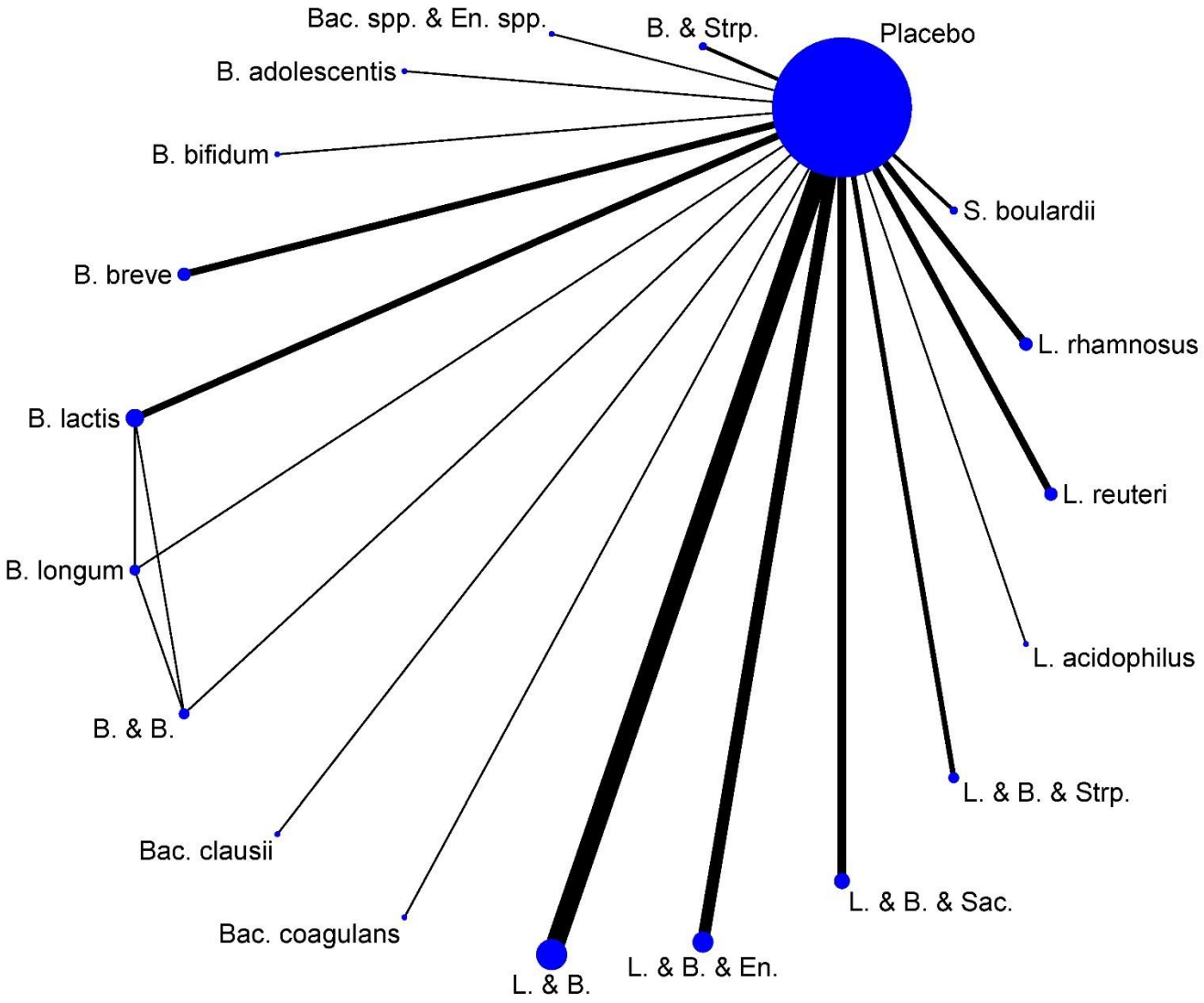
55	Tewari (2015)	Single strain probiotics	123	*Bacillus clausii*	6	Placebo	121	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, FIT
56	Totsu (2014)	Single strain probiotics	153	*B. bifidum*	until weight reach 2 kg	Placebo	130	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF, HOS
57	van Neikerk (2014)	Multi-strain probiotics	37	*L. rhamnosus* ATCC 53103 *B. longum* subsp. *infantis*	4	Placebo	37	NA	-	-	-	-	-	-	-	ACM, NEC, NRM, LOS, TFF
58	van Neikerk (2015)	Multi-strain probiotics	54	*L. rhamnosus* ATCC 53103 *B. longum* subsp. *infantis*	4	Placebo	54	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF
59	Wejryd (2018)	Single strain probiotics	68	*L. reuteri* DSM 17938	4	Placebo	66	NA	-	-	-	-	-	-	-	ACM, NEC, LOS, TFF
60	Xiao-yuan (2007)	Multi-strain probiotics	276	*L. acidophilus* *B. longum* subsp. *infantis* *E. faecalis*	until discharge	Control/No treatment	248	NA	-	-	-	-	-	-	-	ACM, NEC, LOS
61	Xu (2016)	Single strain probiotics	51	*S. boulardii*	4/until discharge	Control/No treatment	49	NA	-	-	-	-	-	-	-	NEC, LOS, HOS
62	Yang (2011)	Multi-strain probiotics	31	*L. acidophilus* *B. longum* subsp. *longum* *E. faecalis*	Until full enteral feeding	Preterm Formula	31	NA	-	-	-	-	-	-	-	ACM, NEC, TFF
63	Zhou (2012)	Multi-strain probiotics	75	*L. acidophilus* *B. longum* subsp. *infantis* *E. faecalis* *Bacillus cereus*	1	Control/No treatment	50	NA	-	-	-	-	-	-	-	ACM, NEC

Footnote: n = number analyzed (as reported in study publication); wks = weeks

Appendix 5: Networks of treatment comparisons

e-figure 1: Network of eligible comparisons for all-cause mortality

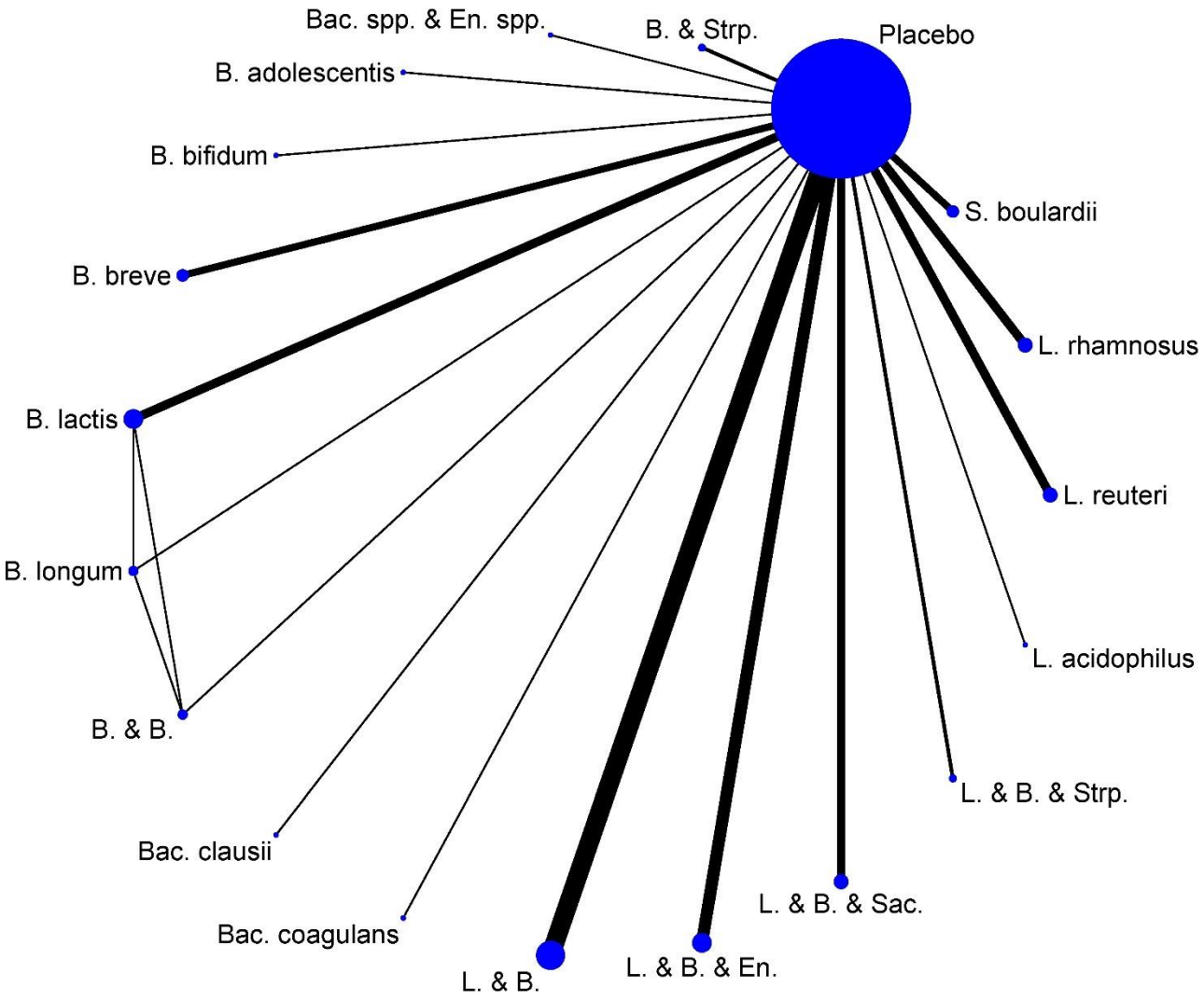
The size of the node corresponds to the number of infants randomized to that intervention. The interventions directly compared are linked with a line; the thickness of the line corresponds to the number of studies that assessed the comparison.



Footnote: Two of the seven studies included to construct the L. & B. & En. node included an additional bacterial genus and species, *Bacillus cereus*, that after running the analysis and assessment of heterogeneity we decided to merge into a single node. *B. adolescentis: Bifidobacterium adolescentis; B. & B.: Bifidobacterium animalis* subsp*. lactis & Bifidobacterium longum* subsp*. longum; B. coagulans: Bacillus coagulans; Bac & En.: Bacillus* spp*. & Enterococcus* spp*.; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; B. clausii: Bacillus clausii; L. acidophilus: Lactobacillus acidophilus; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-figure 2: Network of eligible comparisons for severe NEC

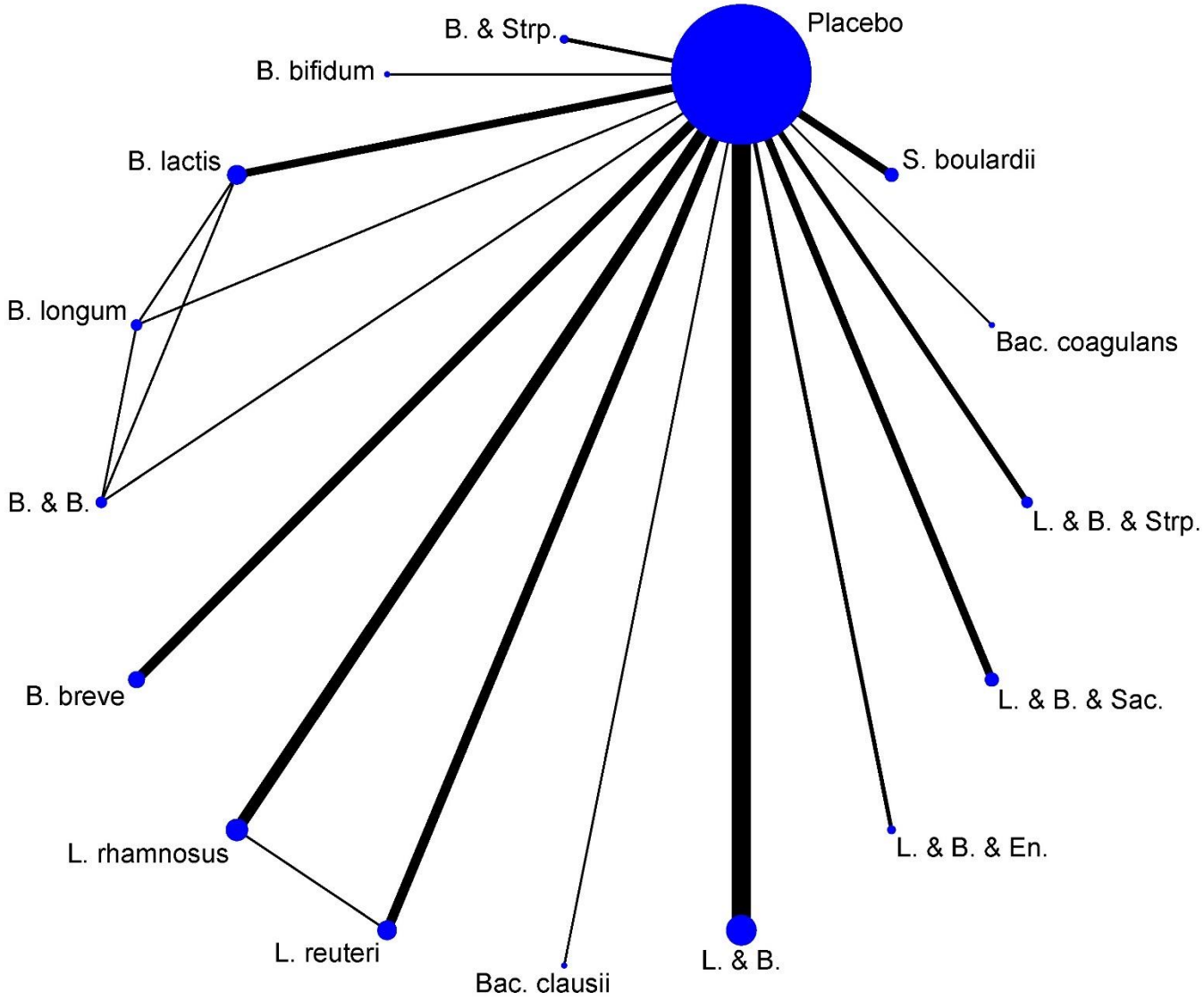
The size of the node corresponds to the number of infants randomized to that intervention. The interventions directly compared are linked with a line; the thickness of the line corresponds to the number of studies that assessed the comparison.



Footnote: Two of the seven studies included to construct the L. & B. & En. node included an additional bacterial genus and species, *Bacillus cereus*, that after running the analysis and assessment of heterogeneity we decided to merge into a single node. *B. adolescentis: Bifidobacterium adolescentis; B. & B.: Bifidobacterium animalis* subsp*. lactis & Bifidobacterium longum* subsp*. longum; Bac. coagulans: Bacillus coagulans; Bac & En.: Bacillus* spp*. & Enterococcus* spp*.; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; B. clausii: Bacillus clausii; L. acidophilus: Lactobacillus acidophilus; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-figure 3: Network of eligible comparisons for late-onset sepsis

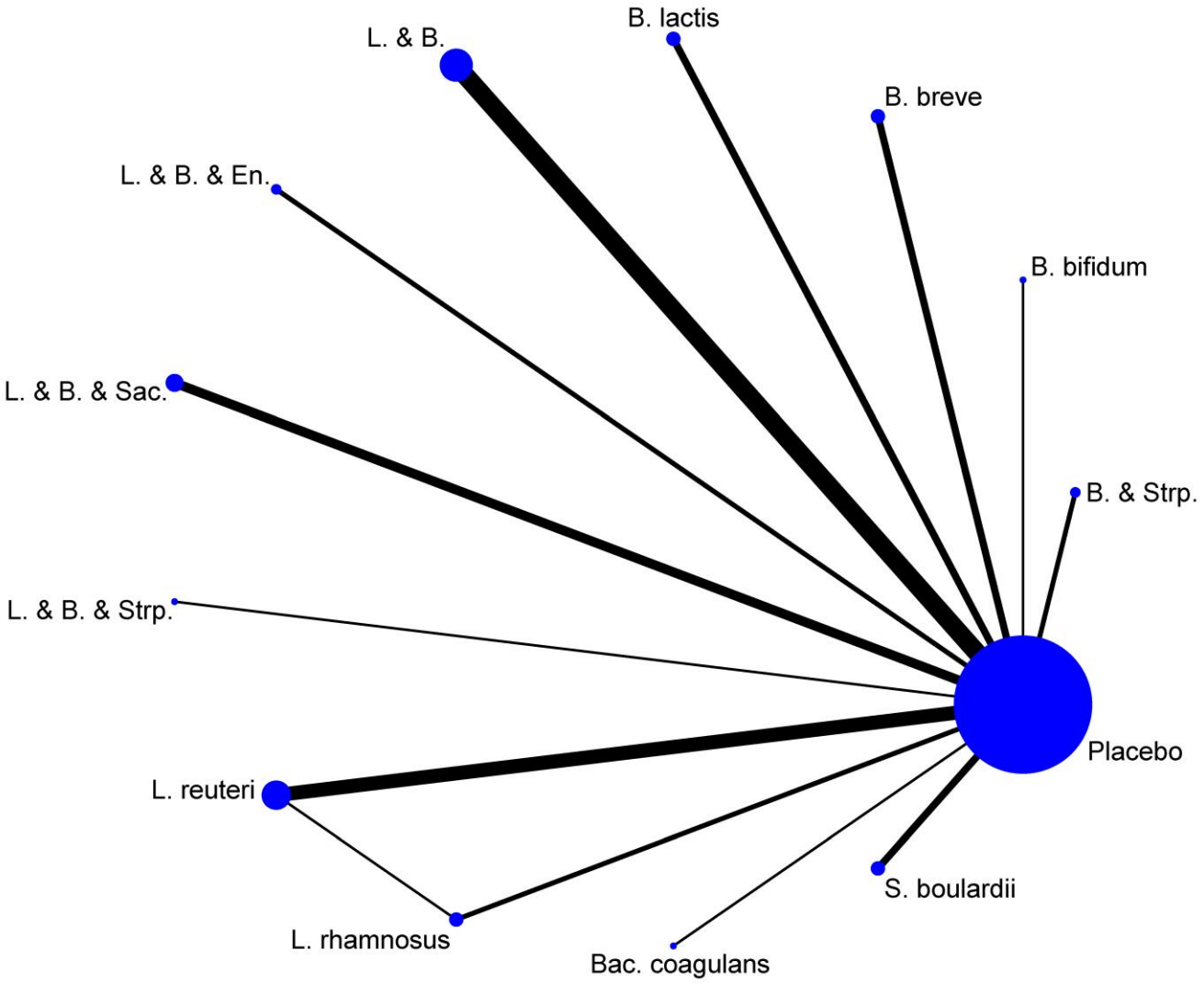
The size of the node corresponds to the number of infants randomized to that intervention. The interventions directly compared are linked with a line; the thickness of the line corresponds to the number of studies that assessed the comparison.



B. & B.: Bifidobacterium animalis subsp*. lactis & Bifidobacterium longum* subsp*. longum; Bac. coagulans: Bacillus coagulans; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; Bac. clausii: Bacillus clausii; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-figure 4: Network of eligible comparisons for duration of time to reach full enteral feeding

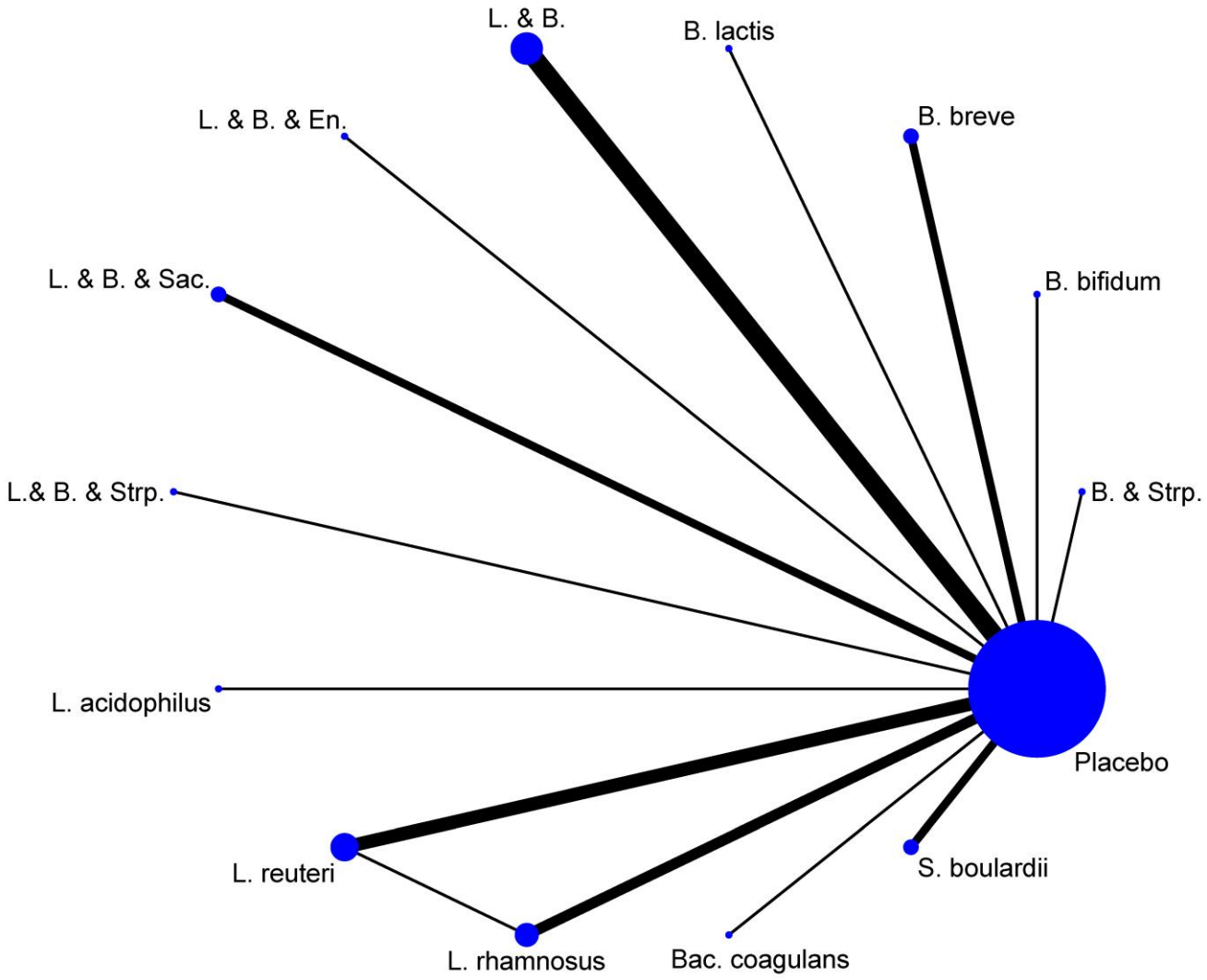
The size of the node corresponds to the number of infants randomized to that intervention. The interventions directly compared are linked with a line; the thickness of the line corresponds to the number of studies that assessed the comparison.



Bac. coagulans: Bacillus coagulans; B. & Strp.: Bifidobacterium spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. breve: Bifidobacterium breve; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-figure 5: Network of eligible comparisons for hospital stay

The size of the node corresponds to the number of infants randomized to that intervention. The interventions directly compared are linked with a line; the thickness of the line corresponds to the number of studies that assessed the comparison.



Bac. coagulans: Bacillus coagulans; B. & Strp.: Bifidobacterium spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. lactis: Bifidobacterium animalis* subsp*. lactis; B. breve: Bifidobacterium breve; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. acidophilus: Lactobacillus acidophilus; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

Appendix 6: Summary of risk of bias assessments for included trials

Ref #	Study (year)	Sequence generation	Allocation concealment	Parents blinded	Health care providers blinded	Data collectors/ outcome assessors blinded	Missingness (> 5%: high)	Funding
1	Al-Hosni (2012)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
2	Arora (2017)	Low Risk	High Risk	High Risk	High Risk	High Risk	Low Risk	no funding
3	Bin-Nun (2005)	Low Risk	High Risk	Low Risk	Low Risk	Low Risk	Low Risk	non-industry
4	Braga (2011)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
5	Chowdhury (2016)	High Risk	High Risk	High Risk	High Risk	High Risk	High Risk	no funding statement
6	Chrzanowska-Lisiewska (2012)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
7	Costalos (2003)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
8	Costeloe (2016)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	non-industry
9	Dani (2002)	Low Risk	Low Risk	High Risk	High Risk	Low Risk	Low Risk	no funding statement
10	Dashti (2014)	High Risk	High Risk	Low Risk	Low Risk	High Risk	Low Risk	no funding statement
11	Demirel (2013)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
12	Deng (2010)	High Risk	High Risk	High Risk	High Risk	High Risk	Low Risk	no funding
13	Di (2010)	High Risk	High Risk	Low Risk	Low Risk	High Risk	Low Risk	no funding
14	Dilli (2015)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
15	Dongol Singh (2017)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
16	Dutta (2014)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	any industry
17	Fernández-Carrocera (2013)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
18	Fujii (2006)	Low Risk	Low Risk	High Risk	High Risk	High Risk	Low Risk	non-industry
19	Hariharan (2016)	Low Risk	High Risk	High Risk	High Risk	High Risk	Low Risk	no funding statement
20	Hays (2016)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	any industry
21	Hernandez-Enriquez (2016)	High Risk	Low Risk	High Risk	High Risk	High Risk	Low Risk	no funding statement
22	Hikaru (2010)	Low Risk	Low Risk	Low Risk	Low Risk	High Risk	Low Risk	any industry
23	Hua (2014)	Low Risk	High Risk	Low Risk	Low Risk	High Risk	Low Risk	non-industry
24	Huang (2009)	High Risk	High Risk	High Risk	High Risk	High Risk	Low Risk	no funding
25	Indrio (2017)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	any industry
26	Jacobs (2013)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	non-industry
27	Kanic (2015)	High Risk	High Risk	Low Risk	High Risk	High Risk	Low Risk	no funding statement
28	Ke (2008)	High Risk	High Risk	Low Risk	Low Risk	High Risk	Low Risk	no funding

29	Kitajima (1997)	Low Risk	High Risk	High Risk	High Risk	High Risk	Low Risk	no funding statement
30	Lin (2005)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	non-industry
31	Lin (2008)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	non-industry
32	Manzoni (2014)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	any industry
33	Mihatsch (2010)	Low Risk	Low Risk	Low Risk	High Risk	High Risk	Low Risk	no funding statement
34	Millar (1993)	High Risk	High Risk	Low Risk	Low Risk	Low Risk	Low Risk	any industry
35	Mohan (2008)	Low Risk	Low Risk	Low Risk	Low Risk	High Risk	Low Risk	any industry
36	Oncel (2014)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
37	Patole (2014)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	non-industry
38	Punnahitananda (2006)	High Risk	High Risk	High Risk	High Risk	High Risk	Low Risk	no funding statement
39	Qiao (2016)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
40	Ren (2010)	Low Risk	High Risk	High Risk	High Risk	High Risk	Low Risk	no funding
41	Reuman (1986)	High Risk	High Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
42	Rojas (2012)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	non-industry
43	Romeo (2011)	Low Risk	High Risk	High Risk	High Risk	High Risk	Low Risk	no funding statement
44	Rouge (2009)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	non-industry
45	Roy (2014)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
46	Sadowska-Krawczenko (2012)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
47	Saengtawesin (2014)	Low Risk	Low Risk	High Risk	High Risk	High Risk	Low Risk	non-industry
48	Samanta (2009)	Low Risk	High Risk	Low Risk	Low Risk	High Risk	Low Risk	no funding statement
49	Sari (2011)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	High Risk	no funding statement
50	Serce (2013)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	any industry
51	Shadkam (2015)	Low Risk	Low Risk	Low Risk	Low Risk	High Risk	Low Risk	non-industry
52	Shashidhar (2017)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	High Risk	no funding
53	Sinha (2015)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	non-industry
54	Stratiki (2007)	High Risk	Low Risk	Low Risk	Low Risk	High Risk	High Risk	any industry
55	Tewari (2015)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	no funding statement
56	Totsu (2014)	Low Risk	Low Risk	High Risk	Low Risk	Low Risk	High Risk	no funding
57	van Neikerk (2014)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	any industry
58	van Neikerk (2015)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	any industry
59	Wejryd (2018)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	non-industry
60	Xiao-yuan (2007)	High Risk	High Risk	High Risk	High Risk	High Risk	Low Risk	no funding

61	Xu (2016)	Low Risk	High Risk	Low Risk	Low Risk	High Risk	High Risk	no funding
62	Yang (2011)	High Risk	High Risk	High Risk	High Risk	High Risk	Low Risk	no funding
63	Zhou (2012)	High Risk	High Risk	High Risk	High Risk	High Risk	Low Risk	no funding

Appendix 7: Results of the direct pairwise comparisons and GRADE assessments for all outcomes

e-Table 1: Results of direct pairwise comparisons with number trials and events for each trial arm and certainty of evidence (CoE) for all-cause mortality

Comparison	OR (95% CI)	# trials	# events C 1	n C 1	# events C 2	n C 2	I^2	P-bias*	GRADE CoE	Imprecision	Indirectness	Inconsistency	Overall RoB
***S. boulardii* vs PLC**	1.01 (0.46, 2.23)	2	13	242	13	244	0.0	-	Moderate	Serious	Not serious	Not serious	Not serious
***Bacillus coagulans* vs PLC**	0.91 (0.38, 2.15)	1	11	121	12	121	-	-	Low	Serious	Not serious	Not serious	Serious
***L. rhamnosus* vs PLC**	0.84 (0.33, 2.12)	4	9	401	11	391	0.0	-	Moderate	Serious	Not serious	Not serious	Not serious
***L. reuteri* vs PLC**	0.77 (0.51, 1.17)	4	43	670	55	674	0.0	-	Moderate	Serious	Not serious	Not serious	Not serious
***L. acidophilus* vs PLC**	0.29 (0.03, 3.12)	1	1	15	3	15	-	-	Low	Very serious	Not serious	Not serious	Serious
***L. & B. & Strp* vs PLC**	0.40 (0.12, 1.30)	3	4	862	12	885	0.0	-	Moderate	Serious	Not serious	Not serious	Not serious
***L. & B. & Sac* vs PLC**	1.05 (0.51, 2.17)	5	21	399	16	328	0.0	-	Low	Serious	Not serious	Not serious	Serious
***L. & B. & En* vs PLC**	0.78 (0.23, 2.62)	7	2	1003	3	947	0.0	-	Very Low	Very serious	Not serious	Not serious	Very serious
***L. & B.* vs PLC**	**0.56 (0.39, 0.80)**	11	59	976	101	984	0.0	0.697	High	Not serious	Not serious	Not serious	Not serious
***B. longum* subsp. *longum* vs PLC**	2.22 (0.19, 25.27)	1	2	48	1	52	-	-	Moderate	Very serious	Not serious	Not serious	Not serious
***B. animalis* subsp. *lactis* vs PLC**	0.52 (0.13, 2.08)	4	7	282	17	277	38.5	-	Moderate	Serious	Not serious	Serious	Not serious
***Bac. clausii* vs PLC**	0.83 (0.37, 1.87)	1	12	123	14	121	-	-	Moderate	Serious	Not serious	Not serious	Not serious
***B. breve* vs PLC**	0.75 (0.34, 1.68)	4	54	880	62	882	10.5	-	Moderate	Serious	Not serious	Not serious	Not serious
***B. bifidum* vs PLC**	4.31 (0.20, 90.52)	1	2	153	0	130	-	-	Low	Very serious	Not serious	Not serious	Serious
***B. adolescentis* vs PLC**	0.93 (0.02, 47.20)	1	0	95	0	88	-	-	Very Low	Very serious	Not serious	Not serious	Very serious
***Bac & Ent* vs PLC**	0.95 (0.02, 48.18)	1	0	182	0	174	-	-	Very Low	Very serious	Not serious	Not serious	Very serious
***B. & Strp.* vs PLC**	0.72 (0.29, 1.77)	2	30	620	36	624	44.5	-	Low	Serious	Not serious	Serious	Not serious
***B. & B.* vs PLC**	1.11 (0.07, 18.24)	1	1	47	1	52	-	-	Moderate	Very serious	Not serious	Not serious	Not serious

B. & B.* vs *B. longum* subsp. *longum	0.50 (0.04, 5.56)	1	1	47	2	48	-	-	Moderate	Very serious	Not serious	Not serious	Not serious
B. & B.* vs *B. animalis* subsp. *lactis	0.52 (0.05, 5.88)	1	1	47	2	50	-	-	Moderate	Very serious	Not serious	Not serious	Not serious
B. animalis* subsp. *lactis* vs *B. longum* subsp. *longum	0.96 (0.13, 7.09)	1	2	50	2	48	-	-	Moderate	Very serious	Not serious	Not serious	Not serious

*P-value of Harbord's test for small-study effects. Footnotes: Results are Odds Ratio (95% CIs) from DerSimonian and Laird random-effects meta-analysis. Numbers underlined in bold represent statistically significant results. "n" is number of infants randomized to each arm. C = comparison; RoB = overall risk of bias. Two of the seven studies included to construct the L. & B. & En. node included an additional bacterial genus and species, *Bacillus cereus*, that after running the analysis and assessment of heterogeneity we decided to merge into a single node. *B. adolescentis: Bifidobacterium adolescentis; B. & B.: Bifidobacterium animalis* subsp*. lactis & Bifidobacterium longum* subsp*. longum; Bac. coagulans: Bacillus coagulans; Bac & En.: Bacillus* spp*. & Enterococcus* spp*.; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; B. clausii: Bacillus clausii; L. acidophilus: Lactobacillus acidophilus; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Table 2: Results of direct pairwise comparisons with number trials and events for each trial arm and certainty of evidence (CoE) for severe NEC

Comparison	OR (95% CI)	# trials	# events C 1	n C 1	# events C 2	n C 2	I^2	P-bias*	GRADE CoE	Imprecision	Indirectness	Inconsistency	Overall RoB
***S. boulardii* vs PLC**	0.81 (0.42, 1.55)	4	18	341	20	325	0.0	-	Moderate	Serious	Not serious	Not serious	Not serious
***Bacillus coagulans* vs PLC**	0.58 (0.20, 1.65)	1	6	121	10	121	-	-	Moderate	Serious	Not serious	Not serious	Serious
***L. rhamnosus* vs PLC**	**0.44 (0.21, 0.90)**	5	12	422	25	417	0.0	-	Moderate	Serious	Not serious	Not serious	Not serious
***L. reuteri* vs PLC**	**0.51 (0.26, 0.98)**	5	27	694	49	694	34.5	-	Moderate	Not serious	Not serious	Not serious	Serious
***L. acidophilus* vs PLC**	1.00 (0.02, 53.66)	1	0	15	0	15	-	-	Very low	Very serious	Not serious	Not serious	Serious
***L. & B. & Strp* vs PLC**	0.42 (0.16, 1.13)	2	6	194	14	213	0.0	-	Moderate	Serious	Not serious	Not serious	Serious
***L. & B. & Sac* vs PLC**	0.74 (0.25, 2.19)	5	13	399	14	328	21.0	-	Low	Serious	Not serious	Not serious	Serious
***L. & B. & En* vs PLC**	**0.28 (0.16, 0.49)**	7	18	1003	60	947	0.0	-	Low	Not serious	Not serious	Not serious	Very serious
***L. & B.* vs PLC**	**0.35 (0.20, 0.59)**	11	19	937	59	941	0.0	0.597	High	Not serious	Not serious	Not serious	Not serious
***B. longum* subsp. *longum* vs PLC**	0.35 (0.03, 3.46)	1	1	48	3	52	-	-	Low	Very serious	Not serious	Not serious	Not serious
***B. animalis* subsp. *lactis* vs PLC**	**0.34 (0.11, 1.00)**	5	8	319	29	309	33.1	-	Moderate	Serious	Not serious	Not serious	Serious
***B. clausii* vs PLC**	0.98 (0.14, 7.10)	1	2	123	2	121	-	-	Low	Very serious	Not serious	Not serious	Not serious
***B. breve* vs PLC**	0.92 (0.64, 1.32)	4	61	785	67	794	0.0	-	Moderate	Serious	Not serious	Not serious	Not serious
***B. bifidum* vs PLC**	0.85 (0.02, 43.14)	1	0	153	0	131	-	-	Very low	Very serious	Not serious	Not serious	Serious
***B. adolescentis* vs PLC**	0.13 (0.01, 2.51)	1	0	95	3	88	-	-	Very low	Very serious	Not serious	Not serious	Serious
***Bac & Ent* vs PLC**	**0.23 (0.08, 0.63)**	1	5	182	19	173	-	-	Moderate	Serious	Not serious	Not serious	Serious
***B. & Strp* vs PLC**	0.27 (0.06, 1.21)	2	12	620	34	624	53.6	-	Low	Serious	Not serious	Serious	Serious
***B. & B.* vs PLC**	1.94 (0.44, 8.62)	1	5	47	3	52	-	-	Low	Very serious	Not serious	Not serious	Not serious
B. & B.* vs *B. longum* subsp. *longum	5.11 (0.57, 45.37)	1	5	47	1	48	-	-	Low	Very serious	Not serious	Not serious	Not serious
B. & B.* vs *B. animalis* subsp. *lactis	2.86 (0.53, 15.50)	1	5	47	2	50	-	-	Low	Very serious	Not serious	Not serious	Not serious

B. animalis* subsp. *lactis* vs *B. longum* subsp. *longum	1.96 (0.17, 22.33)	1	2	50	1	48	-	-	Low	Very serious	Not serious	Not serious	Not serious

*P-value of Harbord's test for small-study effects. Footnotes: Results are Odds Ratio (95% CIs) from DerSimonian and Laird random-effects meta-analysis. Numbers underlined in bold represent statistically significant results. "n" is number of infants randomized to each arm. C = comparison; RoB = overall risk of bias. Two of the seven studies included to construct the L. & B. & En. node included an additional bacterial genus and species, *Bacillus cereus*, that after running the analysis and assessment of heterogeneity we decided to merge into a single node. *B. adolescentis: Bifidobacterium adolescentis; B. & B.: Bifidobacterium animalis* subsp*. lactis & Bifidobacterium longum* subsp*. longum; Bac. coagulans: Bacillus coagulans; Bac & En.: Bacillus* spp*. & Enterococcus* spp*.; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. animalis* subsp*. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; B. clausii: Bacillus clausii; L. acidophilus: Lactobacillus acidophilus; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Table 3: Results of direct pairwise comparisons with number trials and events for each trial arm and certainty of evidence (CoE) for culture proven sepsis

Comparison	OR (95% CI)	# trials	# events C 1	n C 1	# events C 2	n C 2	I^2	P-bias*	GRADE CoE	Imprecision	Indirectness	Inconsistency	Overall RoB
***S. boulardii* vs PLC**	0.79 (0.51, 1.21)	4	46	341	55	325	0.0	-	Moderate	Serious	Not serious	Not serious	Not serious
***Bacillus coagulans* vs PLC**	1.15 (0.63, 2.10)	1	29	121	26	121	-	-	Moderate	Serious	Not serious	Not serious	Serious
***L. rhamnosus* vs PLC**	0.86 (0.53, 1.38)	6	46	478	53	475	0.0	-	Moderate	Serious	Not serious	Not serious	Not serious
***L. reuteri* vs PLC**	0.64 (0.32, 1.31)	5	67	753	84	757	66.9	-	Low	Serious	Not serious	Serious	Serious
***L. & B. & Strp* vs PLC**	0.71 (0.50, 1.01)	3	82	862	106	885	0.0	-	Moderate	Serious	Not serious	Not serious	Serious
***L. & B. & Sac* vs PLC**	0.46 (0.16, 1.27)	4	66	351	83	280	76.7	-	Low	Serious	Not serious	Serious	Serious
***L. & B. & En* vs PLC**	0.44 (0.14, 1.31)	2	23	316	37	288	60.2	-	Low	Serious	Not serious	Serious	Serious
***L. & B.* vs PLC**	0.87 (0.60, 1.28)	10	191	885	212	891	54.7	0.655	Moderate	Not serious	Not serious	Serious	Serious
***B. longum* subsp. *longum* vs PLC**	0.84 (0.30, 2.34)	1	8	48	10	52	-	-	Low	Very serious	Not serious	Not serious	Not serious
***B. animalis* subsp. *lactis* vs PLC**	0.79 (0.50, 1.24)	4	45	282	55	277	0.0	-	Low	Serious	Not serious	Not serious	Serious
***Bac. clausii* vs PLC**	0.70 (0.27, 1.79)	1	8	123	11	121	-	-	Moderate	Serious	Not serious	Not serious	Not serious
***B. breve* vs PLC**	0.87 (0.49, 1.53)	5	102	893	112	894	45.8	-	Low	Serious	Not serious	Serious	Serious
***B. bifidum* vs PLC**	0.49 (0.17, 1.39)	1	6	153	10	130	-	-	Low	Serious	Not serious	Not serious	Serious
***B. & Strp* vs PLC**	1.03 (0.54, 1.97)	2	103	620	113	624	67.6	-	Low	Serious	Not serious	Serious	Serious
***B. & B.* vs PLC**	0.86 (0.31, 2.41)	1	8	47	10	52	-	-	Low	Very serious	Not serious	Not serious	Not serious
B. & B.* vs *B. longum* subsp. *longum	1.02 (0.35, 2.94)	1	8	48	8	47	-	-	Low	Very serious	Not serious	Not serious	Not serious
B. & B.* vs B. *animalis* subsp. *lactis	0.95 (0.34, 2.65)	1	8	47	9	50	-	-	Low	Very serious	Not serious	Not serious	Not serious
B. animalis* subsp. *lactis* vs *B. longum* subsp. *longum	1.10 (0.39, 3.13)	1	9	50	8	48	-	-	Low	Very serious	Not serious	Not serious	Not serious
L. reuteri* vs *L. rhamnosus	0.49 (0.04, 5.55)	1	1	83	2	83	-	-	Very low	Very serious	Not serious	Not serious	Serious

*P-value of Harbord's test for small-study effects. Footnote: Results are Odds Ratio (95% CIs) from DerSimonian and Laird random-effects meta-analysis. Numbers underlined in bold represent statistically significant results. "n" is number of infants randomized to each arm. C = comparison; RoB = overall risk of bias; PLC = Placebo. *B. & B.: Bifidobacterium animalis* subsp*. lactis & Bifidobacterium longum* subsp*. longum; Bac. coagulans: Bacillus coagulans; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. animalis* subsp*. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; B. clausii: Bacillus clausii; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Table 4: Results of direct pairwise comparisons with number trials and events for each trial arm and certainty of evidence (CoE) feed intolerance

Comparison	OR (95% CI)	# trials	# events C 1	n C 1	# events C 2	n C 2	I^2	P-bias*	GRADE CoE	Imprecision	Indirectness	Inconsistency	Overall RoB
***S. boulardii* vs PLC**	0.42 (0.18, 1.00)	2	33	186	64	172	26.0	-	Moderate	Serious	Not serious	Not serious	Not serious
***Bacillus coagulans* vs PLC**	**0.47 (0.27, 0.81)**	1	49	110	70	111	-	-	Low	Serious	Not serious	Not serious	Serious
***L. rhamnosus* vs PLC**	0.47 (0.10, 2.26)	2	29	98	39	96	35.8	-	Low	Serious	Not serious	Not serious	Serious
***L. reuteri* vs PLC**	**0.32 (0.12, 0.89)**	3	85	655	155	661	87.2	-	Low	Serious	Not serious	Serious	Serious
***L. & B. & Strp* vs PLC**	0.68 (0.33, 1.43)	1	13	119	21	138	-	-	Low	Serious	Not serious	Not serious	Serious
***L. & B. & Sac* vs PLC**	**0.47 (0.26, 0.83)**	1	35	93	58	103	-	-	Moderate	Not serious	Not serious	Not serious	Serious
***L. & B. & En* vs PLC**	0.23 (0.07, 0.76)	1	5	30	14	30	-	-	Moderate	Serious	Not serious	Not serious	Not serious
B. *animalis* subsp. *lactis* vs PLC	**0.10 (0.01, 0.82)**	1	1	100	9	100	-	-	Moderate	Serious	Not serious	Not serious	Not serious
***Bac. clausii* vs PLC**	0.81 (0.24, 2.74)	1	5	123	6	121	-	-	Moderate	Serious	Not serious	Not serious	Not serious
L. reuteri* vs *L. rhamnosus	0.07 (0.02, 0.24)	1	3	83	29	83	-	-	Very low	Very serious	Not serious	Not serious	Serious

* P value of Harbord's test for small-study effects. Footnote: Results are Odds Ratio (95% CIs) from DerSimonian and Laird random-effects meta-analysis. Numbers underlined in bold represent statistically significant results. "n" is number of infants randomized to each arm. C = comparison; RoB = overall risk of bias; PLC = Placebo. *B. adolescentis: Bifidobacterium adolescentis; B. & B.: Bifidobacterium animalis* subsp*. lactis & Bifidobacterium longum* subsp*. longum; Bac. coagulans: Bacillus coagulans; Bac & En.: Bacillus* spp*. & Enterococcus* spp*.; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. animalis* subsp*. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; B. clausii: Bacillus clausii; L. acidophilus: Lactobacillus acidophilus; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Table 5: Results of direct pairwise comparisons with number trials and events for each trial arm and certainty of evidence (CoE) for time to reach full enteral feed (days)

Comparison	MD (95% CI)	# trials	n comparison 1	n comparison 2	I^2	P-bias*	GRADE CoE	Imprecision	Indirectness	Inconsistency	Overall RoB
***S. boulardii* vs PLC**	-0.94 (-2.03, 0.15)	3	290	276	0.0	-	Moderate	Serious	Not serious	Not serious	Not serious
***Bacillus coagulans* vs PLC**	-1.00 (-3.44, 1.44)	1	110	111	-	-	Low	Serious	Not serious	Not serious	Serious
***L. rhamnosus* vs PLC**	-0.54 (-2.48, 1.40)	2	122	131	0.0	-	Low	Serious	Not serious	Not serious	Serious
***L. reuteri* vs PLC**	-2.37 (-3.92, -0.83)	6	430	425	84.4	-	Low	Not serious	Not serious	Serious	Serious
***L. & B. & Strp.* vs PLC**	**5.75 (1.26, 10.24)**	1	75	75	-	-	Moderate	Serious	Not serious	Not serious	Not serious
***L. & B. & Sac* vs PLC**	-3.31 (-5.93, -0.68)	4	285	293	66.6	-	Low	Not serious	Not serious	Serious	Serious
***L. & B. & En.* vs PLC**	-2.47 (-4.63, -0.32)	2	71	71	0.0	-	Very low	Serious	Not serious	Not serious	Very serious
***L. & B.* vs PLC**	-2.08 (-4.03, -0.13)	8	657	644	92.0	-	Low	Not serious	Not serious	Serious	Serious
***B. animalis* subsp. *lactis* vs PLC**	-2.37 (-7.02, 2.27)	3	232	223	83.1	-	Low	Serious	Not serious	Serious	Serious
***B. breve* vs PLC**	-1.57 (-4.55, 1.40)	3	835	834	78.5	-	Moderate	Serious	Not serious	Serious	Serious
***B. bifidum* vs PLC**	-1.10 (-2.05, -0.15)	1	119	114	-	-	Moderate	Not serious	Not serious	Not serious	Serious
***B. & Strp.* vs PLC**	-0.96 (-2.80, 0.89)	2	620	624	37.5	-	Moderate	Serious	Not serious	Not serious	Serious
L. reuteri* vs *L. rhamnosus	**-4.50 (-6.21, -2.79)**	1	83	83	-	-	Low	Not serious	Not serious	Not serious	Very serious

*P-value of Eggers's test for small-study effects. Footnote: Results are mean difference (95% CIs) from DerSimonian and Laird random-effects meta-analysis. Numbers underlined in bold represent statistically significant results. "n" is number of infants randomized to each arm. RoB = overall risk of bias; PLC = Placebo. *Bac. coagulans: Bacillus coagulans; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. breve: Bifidobacterium breve; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Table 6: Results of direct pairwise comparisons with number trials and events for each trial arm and certainty of evidence (CoE) for duration of hospitalization

Comparison	MD (95% CI)	# trials	n comparison 1	n comparison 2	I^2	P-bias*	GRADE CoE	Imprecision	Indirectness	Inconsistency	Overall RoB
***S. boulardii* vs PLC**	-1.75 (-7.40, 3.89)	3	290	289	83.5	-	Low	Serious	Not serious	Serious	Serious
***Bacillus coagulans* vs PLC**	4.50 (-0.69, 9.69)	1	110	111	-	-	Low	Serious	Not serious	Not serious	Serious
***L. rhamnosus* vs PLC**	-4.00 (-8.12, 0.11)	4	173	174	0.0	-	Moderate	Serious	Not serious	Not serious	Not serious
***L. reuteri* vs PLC**	-8.08 (-13.46, -2.71)	5	709	711	96.1	-	Low	Not serious	Not serious	Serious	Serious
***L. acidophilus* vs PLC**	20.70 (-11.77, 53.17)	1	15	15	-	-	Low	Serious	Not serious	Not serious	Serious
***L. & B. & Strp* vs PLC**	7.25 (-3.71, 18.21)	1	75	75	-	-	Moderate	Serious	Not serious	Not serious	Not serious
***L. & B. & Sac* vs PLC**	-3.74 (-5.68, -1.81)	3	192	190	0.0	-	Moderate	Not serious	Not serious	Not serious	Serious
***L. & B. & En* vs PLC**	-6.00 (-17.49, 5.49)	1	40	40	-	-	Low	Serious	Not serious	Not serious	Serious
***L. & B.* vs PLC**	-3.03 (-5.86, -0.19)	7	672	677	81.9	-	Low	Not serious	Not serious	Serious	Serious
***B. animalis* subsp. *lactis* vs PLC**	**-13.00 (-19.57, -6.43)**	1	100	100	-	-	Moderate	Serious	Not serious	Not serious	Not serious
***B. breve* vs PLC**	1.67 (-2.12, 5.47)	3	766	765	0.0	-	High	Not serious	Not serious	Not serious	Not serious
***B. bifidum* vs PLC**	-0.60 (-11.48, 10.28)	1	119	114	-	-	Low	Serious	Not serious	Not serious	Serious
***B. & Strp.* vs PLC**	-2.75 (-4.00, -1.50)	1	548	551	-	-	High	Not serious	Not serious	Not serious	Not serious
L. reuteri* vs *L. rhamnosus	-9.10 (-12.88, -5.32)	1	83	83	-	-	Moderate	Not serious	Not serious	Not serious	Serious

*P-value of Eggers's test for small-study effects. Footnote: Results are Odds Ratio (95% CIs) from DerSimonian and Laird random-effects meta-analysis. Numbers underlined in bold represent statistically significant results. "n" is number of infants randomized to each arm. RoB = overall risk of bias; PLC = Placebo. *Bac. coagulans: Bacillus coagulans; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. animalis* subsp*. lactis: Bifidobacterium animalis* subsp*. lactis; B. breve: Bifidobacterium breve; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. acidophilus: Lactobacillus acidophilus; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

Appendix 8: Network meta-analysis results (league tables)

e-Table 7: Network meta-analysis results for all-cause mortality

Placebo																				
1.01 (0.46,2.23)	S. boulardii																			
0.91 (0.38,2.15)	0.90 (0.28,2.90)	L. sporogenes																		
0.80 (0.27,2.43)	0.79 (0.20,3.10)	0.88 (0.22,3.59)	L. rhamnosus																	
0.77 (0.51,1.17)	0.76 (0.31,1.87)	0.85 (0.33,2.21)	0.96 (0.29,3.14)	L. reuteri																
0.94 (0.18,5.01)	0.93 (0.15,5.93)	1.04 (0.16,6.79)	1.17 (0.16,8.71)	1.22 (0.22,6.83)	L. casei															
0.29 (0.03,3.12)	0.28 (0.02,3.51)	0.31 (0.02,3.99)	0.36 (0.03,4.97)	0.37 (0.03,4.19)	0.30 (0.02,5.61)	L. acidophilus														
0.40 (0.12,1.30)	0.39 (0.09,1.64)	0.44 (0.10,1.90)	0.49 (0.10,2.51)	0.51 (0.14,1.81)	0.42 (0.05,3.28)	1.38 (0.10,20.04)	Lactobacillus sp. & Bbifidobacterium sp. & S. thermophilus													
1.05 (0.51,2.17)	1.04 (0.35,3.05)	1.15 (0.37,3.56)	1.31 (0.35,4.92)	1.36 (0.59,3.14)	1.11 (0.18,6.90)	3.67 (0.30,44.67)	2.65 (0.65,10.73)	Lactobacillus sp. & Bbifidobacterium sp. & S. boulardii												
0.78 (0.23,2.62)	0.77 (0.18,3.29)	0.86 (0.19,3.80)	0.97 (0.19,5.03)	1.01 (0.28,3.64)	0.83 (0.11,6.54)	2.73 (0.19,39.89)	1.98 (0.36,10.82)	0.75 (0.18,3.07)	Lactobacillus sp. & Bbifidobacterium sp. & Enterococcus sp.											
0.56 (0.39,0.80)	0.55 (0.23,1.31)	0.61 (0.24,1.55)	0.69 (0.22,2.22)	0.72 (0.42,1.25)	0.59 (0.11,3.26)	1.94 (0.17,21.81)	1.40 (0.40,4.88)	0.53 (0.24,1.19)	0.71 (0.20,2.52)	Lactobacillus sp. & Bbifidobacterium sp.										
0.77 (0.11,5.35)	0.77 (0.09,6.20)	0.85 (0.10,7.07)	0.96 (0.10,8.96)	1.00 (0.14,7.25)	0.82 (0.06,10.59)	2.70 (0.12,58.61)	1.95 (0.20,18.98)	0.74 (0.09,5.83)	0.99 (0.10,9.70)	1.39 (0.19,9.96)	B. longum									
0.43 (0.16,1.15)	0.43 (0.12,1.51)	0.48 (0.13,1.75)	0.54 (0.12,2.36)	0.56 (0.19,1.62)	0.46 (0.07,3.18)	1.51 (0.11,20.01)	1.09 (0.23,5.11)	0.41 (0.12,1.40)	0.55 (0.12,2.62)	0.78 (0.27,2.20)	0.56 (0.09,3.57)	B. lactis								
0.83 (0.37,1.87)	0.82 (0.26,2.55)	0.91 (0.28,2.98)	1.03 (0.26,4.07)	1.07 (0.43,2.67)	0.88 (0.14,5.64)	2.89 (0.23,36.16)	2.09 (0.49,8.86)	0.79 (0.26,2.35)	1.06 (0.25,4.56)	1.49 (0.61,3.63)	1.07 (0.13,8.74)	1.91 (0.54,6.84)	B. clausii							
0.92 (0.63,1.34)	0.91 (0.38,2.19)	1.01 (0.39,2.59)	1.14 (0.35,3.69)	1.19 (0.68,2.09)	0.97 (0.18,5.41)	3.21 (0.28,36.13)	2.32 (0.66,8.12)	0.87 (0.38,1.99)	1.17 (0.33,4.18)	1.65 (0.98,2.79)	1.19 (0.16,8.54)	2.12 (0.74,6.07)	1.11 (0.45,2.73)	B. breve						
4.31 (0.20,90.52)	4.27 (0.18,99.26)	4.74 (0.20,112.26)	5.37 (0.21,137.17)	5.58 (0.26,120.68)	4.58 (0.14,147.64)	15.07 (0.31,723.99)	10.89 (0.41,286.73)	4.11 (0.18,94.15)	5.51 (0.21,146.14)	7.75 (0.36,166.44)	5.58 (0.15,205.85)	9.97 (0.41,244.32)	5.21 (0.22,121.97)	4.70 (0.22,101.12)	B. bifidum					
0.93 (0.02,47.20)	0.92 (0.02,50.61)	1.02 (0.02,57.03)	1.16 (0.02,68.58)	1.20 (0.02,62.53)	0.98 (0.01,70.51)	3.24 (0.03,322.88)	2.34 (0.04,142.46)	0.88 (0.02,48.17)	1.19 (0.02,72.51)	1.67 (0.03,86.38)	1.20 (0.02,95.93)	2.15 (0.04,123.22)	1.12 (0.02,62.12)	1.01 (0.02,52.45)	0.22 (0.00,31.06)	B. adolescentis				
0.95 (0.02,48.18)	0.94 (0.02,51.66)	1.05 (0.02,58.21)	1.19 (0.02,70.01)	1.23 (0.02,63.82)	1.01 (0.01,71.99)	3.33 (0.03,329.78)	2.40 (0.04,145.43)	0.91 (0.02,49.17)	1.22 (0.02,74.02)	1.71 (0.03,88.16)	1.23 (0.02,97.96)	2.20 (0.04,125.78)	1.15 (0.02,63.40)	1.04 (0.02,53.53)	0.22 (0.00,31.74)	1.03 (0.00,265.23)	Bacillus sp. & Enterococcus sp.			
0.84 (0.51,1.40)	0.84 (0.33,2.14)	0.93 (0.34,2.52)	1.05 (0.31,3.55)	1.09 (0.57,2.10)	0.90 (0.16,5.14)	2.96 (0.26,34.02)	2.13 (0.58,7.80)	0.81 (0.33,1.96)	1.08 (0.29,4.01)	1.52 (0.82,2.82)	1.09 (0.15,8.08)	1.96 (0.65,5.88)	1.02 (0.39,2.67)	0.92 (0.49,1.73)	0.20 (0.01,4.29)	0.91 (0.02,47.93)	0.89 (0.02,46.48)	Bbifidobacterium sp. & S. thermophilus	
0.39 (0.04,4.18)	0.38 (0.03,4.70)	0.43 (0.03,5.34)	0.48 (0.03,6.65)	0.50 (0.04,5.61)	0.41 (0.02,7.52)	1.35 (0.05,39.47)	0.98 (0.07,14.00)	0.37 (0.03,4.44)	0.49 (0.03,7.15)	0.70 (0.06,7.72)	0.50 (0.04,5.71)	0.89 (0.09,9.05)	0.47 (0.04,5.79)	0.42 (0.04,4.70)	0.09 (0.00,4.28)	0.42 (0.00,41.27)	0.41 (0.00,40.05)	0.46 (0.04,5.21)	B. lactis & longum

Footnote: Results are Odds Ratio (95% CIs) from the network meta-analysis. Odds ratios < 1 indicates the treatment in bottom right is better. Numbers in bold represent statistically significant results. Colors represent the certainty in evidence (CoE) for each pairwise comparison; Dark green = High CoE, light green = Moderate CoE, light yellow = Low CoE, and light red = Very Low CoE. *B. adolescentis: Bifidobacterium adolescentis; B. & B.: Bifidobacterium animalis* subsp*. lactis & Bifidobacterium longum* subsp*. longum; Bac. coagulans: Bacillus coagulans; Bac & En.: Bacillus* spp*. & Enterococcus* spp*.; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. animalis* subsp*. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; Bac. clausii: Bacillus clausii; L. acidophilus: Lactobacillus acidophilus; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Table 8: Network meta-analysis results for severe NEC

Placebo																			
0.81 (0.42,1.55)	S. boulardii																		
0.44 (0.21,0.90)	0.54 (0.20,1.43)	L. rhamnosus																	
0.55 (0.34,0.91)	0.69 (0.30,1.57)	1.27 (0.53,3.08)	L. reuteri																
1.00 (0.02,53.66)	1.24 (0.02,70.21)	2.30 (0.04,131.70)	1.81 (0.03,100.06)	L. acidophilus															
0.42 (0.16,1.13)	0.53 (0.16,1.72)	0.98 (0.29,3.31)	0.77 (0.25,2.31)	0.42 (0.01,25.68)	Lactobacillus sp. & Bbifidobacterium sp. & S. thermophilus														
0.73 (0.29,1.85)	0.90 (0.29,2.81)	1.67 (0.51,5.44)	1.31 (0.45,3.78)	0.73 (0.01,43.38)	1.71 (0.44,6.62)	Lactobacillus sp. & Bbifidobacterium sp. & S. boulardii													
0.28 (0.16,0.49)	**0.35 (0.15,0.82)**	0.65 (0.26,1.61)	0.51 (0.24,1.07)	0.28 (0.01,15.76)	0.67 (0.22,2.05)	0.39 (0.13,1.15)	Lactobacillus sp. & Bbifidobacterium sp. & Enterococcus sp.												
0.35 (0.20,0.59)	**0.43 (0.18,1.00)**	0.79 (0.32,1.96)	0.62 (0.30,1.30)	0.35 (0.01,19.21)	0.81 (0.27,2.49)	0.48 (0.16,1.40)	1.22 (0.57,2.62)	Lactobacillus sp. & Bbifidobacterium sp.											
0.25 (0.03,2.30)	0.32 (0.03,3.14)	0.58 (0.06,5.94)	0.46 (0.05,4.40)	0.25 (0.00,24.08)	0.60 (0.05,6.67)	0.35 (0.03,3.83)	0.90 (0.09,8.68)	0.74 (0.08,7.11)	B. longum										
0.31 (0.13,0.74)	0.39 (0.13,1.15)	0.72 (0.23,2.22)	0.57 (0.21,1.53)	0.31 (0.01,18.46)	0.74 (0.20,2.72)	0.43 (0.12,1.54)	1.11 (0.40,3.06)	0.91 (0.33,2.50)	1.24 (0.13,11.54)	B. lactis									
0.58 (0.20,1.65)	0.72 (0.21,2.47)	1.33 (0.37,4.75)	1.05 (0.33,3.34)	0.58 (0.01,83.88)	2.32 (0.25,21.04)	0.80 (0.20,3.24)	2.05 (0.63,6.65)	1.68 (0.52,5.44)	2.28 (0.20,26.09)	1.84 (0.48,7.12)	Bac. Coagulans								
0.98 (0.14,7.10)	1.22 (0.15,9.78)	2.26 (0.28,18.56)	1.78 (0.23,13.65)	0.98 (0.01,83.88)	2.32 (0.25,21.04)	1.36 (0.15,12.05)	3.47 (0.45,26.98)	2.85 (0.37,22.09)	3.87 (0.20,74.62)	3.13 (0.36,26.99)	1.70 (0.18,15.88)	B. clausii							
0.92 (0.64,1.32)	1.14 (0.54,2.41)	2.11 (0.94,4.75)	1.66 (0.90,3.08)	0.92 (0.02,50.13)	2.16 (0.76,6.16)	1.27 (0.47,3.44)	**3.25 (1.69,6.23)**	**2.66 (1.39,5.09)**	3.62 (0.39,33.70)	**2.93 (1.16,7.41)**	1.59 (0.53,4.80)	0.93 (0.13,6.97)	B. breve						
0.85 (0.02,43.14)	1.05 (0.02,56.50)	1.95 (0.04,105.99)	1.54 (0.03,80.48)	0.85 (0.00,228.31)	2.00 (0.03,114.62)	1.17 (0.02,66.31)	3.00 (0.06,158.24)	2.46 (0.05,129.66)	3.34 (0.04,301.84)	2.71 (0.05,150.66)	1.47 (0.03,85.41)	0.86 (0.01,70.14)	0.93 (0.02,47.73)	B. bifidum					
0.13 (0.01,2.51)	0.16 (0.01,3.35)	0.29 (0.01,6.30)	0.23 (0.01,4.73)	0.13 (0.00,18.47)	0.30 (0.01,6.92)	0.18 (0.01,3.99)	0.45 (0.02,9.32)	0.37 (0.02,7.64)	0.50 (0.01,20.43)	0.41 (0.02,9.02)	0.22 (0.01,5.18)	0.13 (0.00,4.64)	0.14 (0.01,2.79)	0.15 (0.00,20.78)	B. adolescentis				
0.23 (0.08,0.63)	**0.28 (0.09,0.95)**	0.53 (0.15,1.82)	0.41 (0.13,1.28)	0.23 (0.00,13.93)	0.54 (0.13,2.20)	0.32 (0.08,1.25)	0.81 (0.26,2.54)	0.66 (0.21,2.08)	0.90 (0.08,10.16)	0.73 (0.19,2.74)	0.40 (0.09,1.69)	0.23 (0.03,2.14)	**0.25 (0.09,0.73)**	0.27 (0.00,15.52)	1.79 (0.08,41.51)	Bacillus sp. & Enterococcus sp.		
0.38 (0.19,0.75)	0.47 (0.18,1.21)	0.87 (0.32,2.35)	0.68 (0.29,1.59)	0.38 (0.01,21.48)	0.89 (0.27,2.94)	0.52 (0.16,1.65)	1.33 (0.56,3.20)	1.09 (0.46,2.61)	1.49 (0.15,14.92)	1.20 (0.40,3.60)	0.65 (0.19,2.27)	0.38 (0.05,3.11)	**0.41 (0.19,0.89)**	0.44 (0.01,23.92)	2.95 (0.14,62.66)	1.65 (0.49,5.58)	Bbifidobacterium sp. & S. thermophilus	
1.42 (0.37,5.42)	1.76 (0.40,7.82)	3.27 (0.71,14.98)	2.57 (0.62,10.72)	1.42 (0.02,94.96)	3.35 (0.64,17.60)	1.96 (0.38,10.01)	**5.02 (1.19,21.29)**	4.12 (0.97,17.42)	5.60 (0.63,49.84)	**4.53 (1.13,18.16)**	2.46 (0.45,13.41)	1.45 (0.13,15.72)	1.55 (0.39,6.18)	1.67 (0.03,105.95)	11.12 (0.43,290.87)	**6.21 (1.16,33.17)**	3.77 (0.84,16.91)	B. lactis & longum

Footnote: Results are Odds Ratio (95% CIs) from the network meta-analysis. Odds ratios < 1 indicates the treatment in bottom right is better. Numbers in bold represent statistically significant results. Colors represent the certainty in evidence (CoE) for each pairwise comparison; Dark green = High CoE, light green = Moderate CoE, light yellow = Low CoE, and light red = Very Low CoE. *B. adolescentis: Bifidobacterium adolescentis; B. & B.: Bifidobacterium animalis* subsp*. lactis & Bifidobacterium longum* subsp*. longum; Bac. coagulans: Bacillus coagulans; Bac & En.: Bacillus* spp*. & Enterococcus* spp*.; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. animalis* subsp*. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; Bac. clausii: Bacillus clausii; L. acidophilus: Lactobacillus acidophilus; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Table 9: Network meta-analysis results for late-onset sepsis

Placebo																
0.77 (0.40,1.45)	S. boulardii															
1.15 (0.41,3.21)	1.51 (0.45,5.03)	Bac. Coagulans														
0.84 (0.45,1.57)	1.09 (0.45,2.67)	0.73 (0.22,2.41)	L. rhamnosus													
0.71 (0.41,1.26)	0.93 (0.40,2.18)	0.62 (0.19,2.00)	0.85 (0.37,1.96)	L. reuteri												
0.68 (0.35,1.30)	0.88 (0.36,2.19)	0.59 (0.17,1.97)	0.81 (0.33,1.99)	0.95 (0.40,2.22)	Lactobacillus sp. & Bifido sp. & S. thermophilus											
0.54 (0.28,1.04)	0.71 (0.28,1.75)	0.47 (0.14,1.58)	0.65 (0.26,1.59)	0.76 (0.32,1.77)	0.80 (0.32,2.00)	Lactobacillus sp. & Bifido sp. & S. boulardii										
0.43 (0.17,1.07)	0.56 (0.19,1.71)	0.37 (0.10,1.47)	0.51 (0.17,1.55)	0.60 (0.21,1.76)	0.64 (0.21,1.95)	0.80 (0.26,2.45)	Lactobacillus sp. & Bifido sp. & Entero sp.									
0.87 (0.60,1.27)	1.14 (0.54,2.39)	0.76 (0.25,2.26)	1.04 (0.50,2.17)	1.22 (0.62,2.42)	1.29 (0.61,2.75)	1.62 (0.76,3.45)	2.03 (0.76,5.42)	Lactobacillus sp. & Bifido sp.								
0.75 (0.23,2.50)	0.98 (0.25,3.83)	0.65 (0.13,3.17)	0.90 (0.23,3.48)	1.05 (0.28,3.96)	1.11 (0.28,4.37)	1.39 (0.36,5.45)	1.74 (0.39,7.88)	0.86 (0.24,3.04)	B. longum							
0.73 (0.38,1.43)	0.96 (0.38,2.41)	0.64 (0.19,2.16)	0.88 (0.35,2.18)	1.03 (0.43,2.45)	1.09 (0.43,2.75)	1.36 (0.54,3.43)	1.70 (0.55,5.26)	0.84 (0.39,1.81)	0.98 (0.29,3.27)	B. lactis						
0.70 (0.20,2.45)	0.91 (0.22,3.73)	0.60 (0.12,3.06)	0.83 (0.20,3.39)	0.97 (0.25,3.87)	1.03 (0.25,4.25)	1.29 (0.31,5.31)	1.61 (0.34,7.62)	0.80 (0.21,2.97)	0.92 (0.16,5.27)	0.95 (0.23,3.93)	B. clausii					
0.87 (0.48,1.55)	1.13 (0.48,2.68)	0.75 (0.23,2.44)	1.03 (0.44,2.43)	1.21 (0.54,2.73)	1.28 (0.53,3.07)	1.60 (0.67,3.84)	2.01 (0.68,5.91)	0.99 (0.49,1.99)	1.15 (0.30,4.38)	1.18 (0.49,2.85)	1.24 (0.31,4.98)	B. breve				
0.49 (0.13,1.85)	0.64 (0.15,2.80)	0.43 (0.08,2.28)	0.58 (0.13,2.54)	0.69 (0.16,2.91)	0.73 (0.16,3.19)	0.91 (0.21,3.99)	1.14 (0.23,5.69)	0.56 (0.14,2.24)	0.65 (0.11,3.91)	0.67 (0.15,2.95)	0.70 (0.11,4.39)	0.57 (0.13,2.42)	B. bifidum			
1.04 (0.52,2.06)	1.36 (0.53,3.46)	0.90 (0.26,3.09)	1.24 (0.49,3.14)	1.45 (0.59,3.55)	1.54 (0.59,3.97)	1.92 (0.74,4.98)	2.41 (0.77,7.51)	1.19 (0.54,2.60)	1.38 (0.34,5.51)	1.41 (0.54,3.68)	1.49 (0.36,6.25)	1.20 (0.49,2.95)	2.12 (0.47,9.46)	Bifido sp. & S. thermophilus		
0.77 (0.23,2.57)	1.01 (0.26,3.93)	0.67 (0.14,3.25)	0.92 (0.24,3.57)	1.08 (0.29,4.07)	1.14 (0.29,4.48)	1.43 (0.36,5.60)	1.79 (0.40,8.08)	0.88 (0.25,3.12)	1.03 (0.26,3.98)	1.05 (0.31,3.51)	1.11 (0.19,6.32)	0.89 (0.23,3.40)	1.58 (0.26,9.47)	0.74 (0.19,2.98)	B. lactis & longum	

Footnote: Results are Odds Ratio (95% CIs) from the network meta-analysis. Odds ratios < 1 indicates the treatment in bottom right is better. Numbers in bold represent statistically significant results. Colors represent the certainty in evidence (CoE) for each pairwise comparison; Dark green = High CoE, light green = Moderate CoE, light yellow = Low CoE, and light red = Very Low CoE. *B. & B.: Bifidobacterium animalis* subsp*. lactis & Bifidobacterium longum* subsp*. longum; Bac. coagulans: Bacillus coagulans; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. animalis* subsp*. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; B. clausii: Bacillus clausii; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Table 10: Network meta-analysis results for reduction in number of days to reach full enteral feeding

Placebo												
-1.02 (-3.64,1.61)	**S. boulardii**											
-1.00 (-5.78,3.78)	0.02 (-5.43,5.47)	**Bac. Coagulans**										
0.02 (-3.29,3.32)	1.03 (-3.19,5.25)	1.02 (-4.79,6.83)	**L. rhamnosus**									
-2.62 (-4.53,-0.71)	-1.60 (-4.85,1.64)	-1.62 (-6.77,3.53)	-2.64 (-6.08,0.81)	**L. reuteri**								
5.75 (-0.33,11.83)	6.77 (0.14,13.39)	6.75 (-0.98,14.48)	5.73 (-1.19,12.66)	8.37 (1.99,14.75)	**Lactobacillus sp. & Bifido sp. & S. thermophilus**							
-3.30 (-5.91,-0.69)	-2.29 (-5.99,1.42)	-2.30 (-7.75,3.14)	-3.32 (-7.52,0.89)	-0.68 (-3.91,2.55)	-9.05 (-15.67,-2.43)	**Lactobacillus sp. & Bifido sp. & S. boulardii**						
-2.57 (-6.55,1.41)	-1.56 (-6.32,3.21)	-1.57 (-7.79,4.65)	-2.59 (-7.76,2.58)	0.05 (-4.36,4.46)	-8.32 (-15.59,-1.05)	0.73 (-4.03,5.49)	**Lactobacillus sp. & Bifido sp. & Entero sp.**					
-2.15 (-3.78,-0.51)	-1.13 (-4.22,1.96)	-1.15 (-6.20,3.90)	-2.16 (-5.86,1.53)	0.47 (-2.05,3.00)	-7.90 (-14.20,-1.60)	1.15 (-1.94,4.24)	0.42 (-3.88,4.73)	**Lactobacillus sp. & Bifido sp.**				
-2.30 (-5.35,0.74)	-1.29 (-5.31,2.73)	-1.30 (-6.97,4.36)	-2.32 (-6.81,2.17)	0.31 (-3.28,3.91)	-8.05 (-14.86,-1.25)	1.00 (-3.02,5.01)	0.27 (-4.75,5.28)	-0.16 (-3.62,3.31)	**B. lactis**			
-1.53 (-4.30,1.24)	-0.51 (-4.33,3.30)	-0.53 (-6.05,4.99)	-1.54 (-5.85,2.76)	1.09 (-2.27,4.45)	-7.28 (-13.96,-0.59)	1.77 (-2.03,5.57)	1.04 (-3.81,5.89)	0.62 (-2.61,3.84)	0.78 (-3.34,4.89)	**B. breve**		
-1.10 (-5.31,3.11)	-0.08 (-5.05,4.88)	-0.10 (-6.47,6.27)	-1.12 (-6.47,4.24)	1.52 (-3.11,6.15)	-6.85 (-14.25,0.55)	2.20 (-2.76,7.16)	1.47 (-4.32,7.27)	1.05 (-3.47,5.57)	1.20 (-4.00,6.41)	0.43 (-4.61,5.47)	**B. bifidum**	
-1.35 (-4.66,1.95)	-0.34 (-4.56,3.88)	-0.35 (-6.16,5.46)	-1.37 (-6.04,3.30)	1.27 (-2.55,5.08)	-7.10 (-14.03,-0.18)	1.95 (-2.26,6.15)	1.22 (-3.95,6.39)	0.79 (-2.90,4.49)	0.95 (-3.54,5.45)	0.18 (-4.13,4.48)	-0.25 (-5.61,5.10)	**Bifido sp. & S. thermophilus**

Footnote: Results are mean change (95% CI) from the network meta-analysis. Mean difference values less than 0 indicates the treatment in bottom right is better. Numbers in bold represent statistically significant results. Colors represent the certainty in evidence (CoE) for each pairwise comparison; Dark green = High CoE, light green = Moderate CoE, light yellow = Low CoE, and light red = Very Low CoE. *Bac. coagulans: Bacillus coagulans; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. breve: Bifidobacterium breve; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

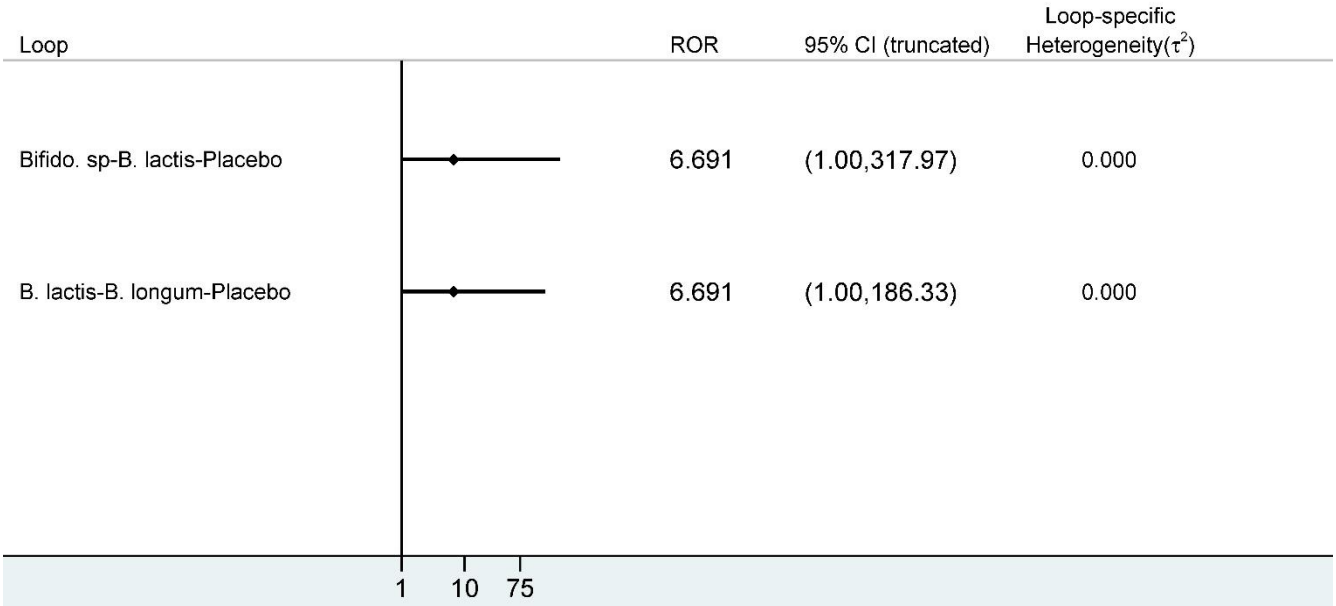
e-Table 11: Network meta-analysis results for duration of hospitalization (days)

Placebo													
-1.86 (-6.65,2.92)	**S. boulardii**												
4.50 (-4.33,13.33)	6.36 (-3.68,16.40)	**Bac. Coagulans**											
-1.85 (-7.62,3.91)	0.01 (-7.50,7.52)	-6.35 (-16.90,4.19)	**L. rhamnosus**										
-7.89 (-11.60,-4.17)	-6.03 (-12.10,0.05)	-12.39 (-21.97,-2.81)	-6.03 (-12.16,0.09)	**L. reuteri**									
20.70 (-12.55,53.95)	22.56 (-11.03,56.15)	16.20 (-18.20,50.60)	22.55 (-11.19,56.30)	28.59 (-4.87,62.04)	**L. acidophilus**								
7.25 (-5.83,20.33)	9.11 (-4.81,23.04)	2.75 (-13.03,18.53)	9.10 (-5.19,23.39)	15.14 (1.54,28.73)	-13.45 (-49.18,22.28)	**Lactobacillus sp. & Bifido sp. & S. thermophilus**							
-3.20 (-8.38,1.98)	-1.34 (-8.39,5.71)	-7.70 (-17.94,2.54)	-1.35 (-9.11,6.41)	4.69 (-1.70,11.07)	-23.90 (-57.55,9.75)	-10.45 (-24.52,3.61)	**Lactobacillus sp. & Bifido sp. & S. boulardii**						
-6.00 (-19.53,7.53)	-4.14 (-18.49,10.21)	-10.50 (-26.66,5.66)	-4.15 (-18.86,10.56)	1.89 (-12.14,15.92)	-26.70 (-62.60,9.20)	-13.25 (-32.07,5.57)	-2.80 (-17.29,11.69)	**Lactobacillus sp. & Bifido sp. & Entero sp.**					
-2.84 (-6.21,0.54)	-0.97 (-6.82,4.87)	-7.34 (-16.79,2.12)	-0.98 (-7.69,5.72)	5.05 (0.00,10.10)	-23.54 (-56.95,9.88)	-10.09 (-23.59,3.42)	0.37 (-5.81,6.55)	3.16 (-10.78,17.11)	**Lactobacillus sp. & Bifido sp.**				
-13.00 (-22.71,-3.29)	-11.14 (-21.96,-0.32)	-17.50 (-30.62,-4.38)	-11.15 (-22.44,0.14)	-5.11 (-15.51,5.28)	-33.70 (-68.34,0.94)	-20.25 (-36.54,-3.96)	-9.80 (-20.80,1.20)	-7.00 (-23.65,9.65)	-10.16 (-20.44,0.11)	**B. lactis**			
1.18 (-5.88,8.24)	3.04 (-5.50,11.58)	-3.32 (-14.63,7.98)	3.03 (-6.08,12.14)	9.07 (1.10,17.03)	-19.52 (-53.51,14.47)	-6.07 (-20.93,8.79)	4.38 (-4.38,13.14)	7.18 (-8.08,22.44)	4.01 (-3.82,11.85)	14.18 (2.18,26.18)	**B. breve**		
-0.60 (-13.61,12.41)	1.26 (-12.61,15.13)	-5.10 (-20.83,10.63)	1.25 (-12.98,15.49)	7.29 (-6.25,20.82)	-21.30 (-57.00,14.40)	-7.85 (-26.30,10.60)	2.60 (-11.41,16.61)	5.40 (-13.37,24.17)	2.24 (-11.21,15.68)	12.40 (-3.83,28.63)	-1.78 (-16.58,13.03)	**B. bifidum**	
-2.75 (-10.00,4.50)	-0.89 (-9.57,7.80)	-7.25 (-18.67,4.17)	-0.90 (-10.16,8.37)	5.14 (-3.01,13.28)	-23.45 (-57.48,10.58)	-10.00 (-24.95,4.95)	0.45 (-8.46,9.36)	3.25 (-12.10,18.60)	0.09 (-7.91,8.08)	10.25 (-1.86,22.36)	-3.93 (-14.05,6.19)	-2.15 (-17.05,12.75)	**Bifido sp. & S. thermophilus**

Footnote: Results are mean change (95% CI) from the network meta-analysis. Mean difference values less than 0 indicates the treatment in bottom right is better. Numbers in bold represent statistically significant results. Colors represent the certainty in evidence (CoE) for each pairwise comparison; Dark green = High CoE, light green = Moderate CoE, light yellow = Low CoE, and light red = Very Low CoE. *Bac. coagulans: Bacillus coagulans; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. animalis* subsp*. lactis: Bifidobacterium animalis* subsp*. lactis; B. breve: Bifidobacterium breve; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. acidophilus: Lactobacillus acidophilus; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

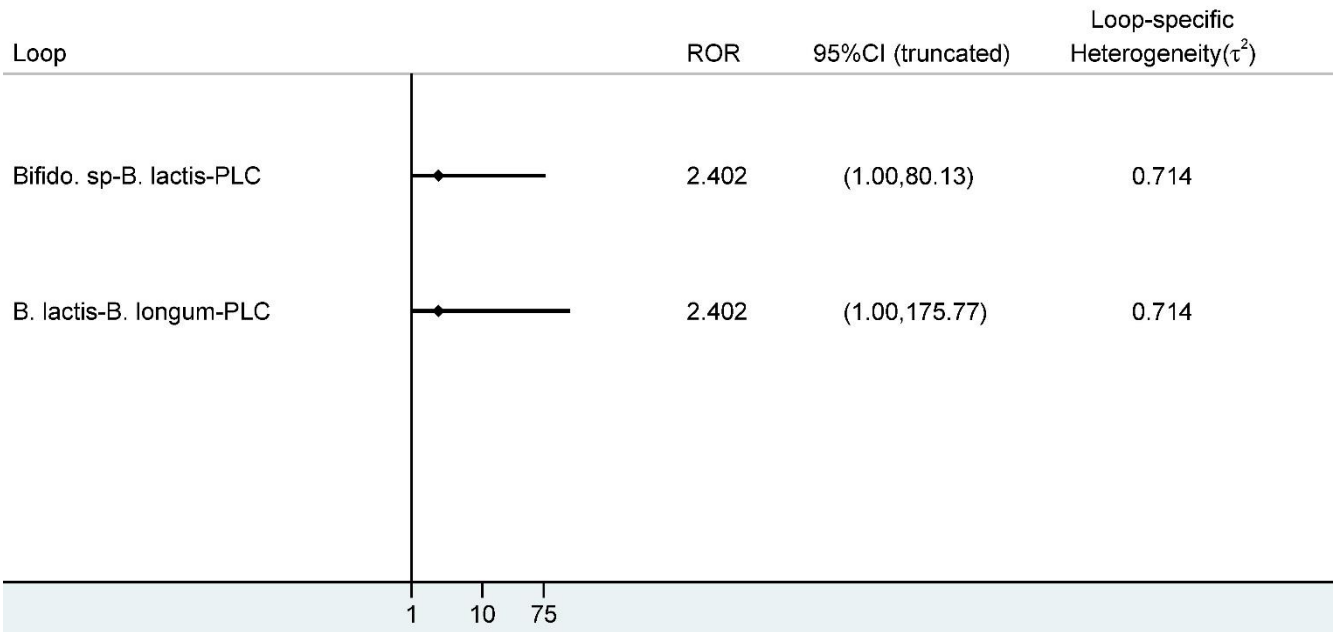
Appendix 9: Results from evaluating incoherence in loops of evidence

e-figure 6: Incoherence plot for all-cause mortality



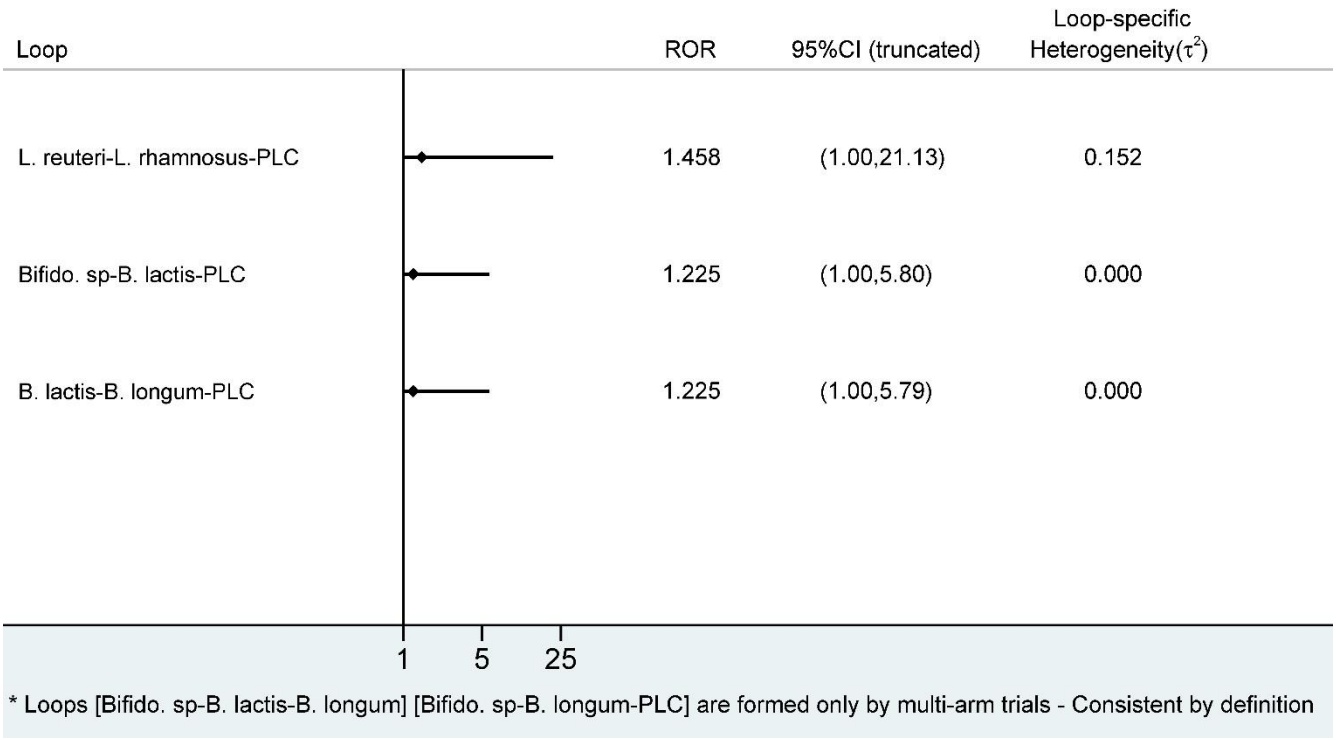
Incoherance factors (IF) along with 95% confidence intervals (CI) are displayed. IFs are calculated as the ratio of the ORs (ROR) from direct and indirect evidence in the loop. Comparisons that their lower CI limit does not reach the line of 1 are considered to present statistically significant incoherence. P value for the 'design-by-treatment' model (global test of incoherence) = 0.161. *Bifido* sp. = *Bifidobacterium* sp.

e-figure 7: Incoherence plot for severe NEC (Bell's stage II or more)



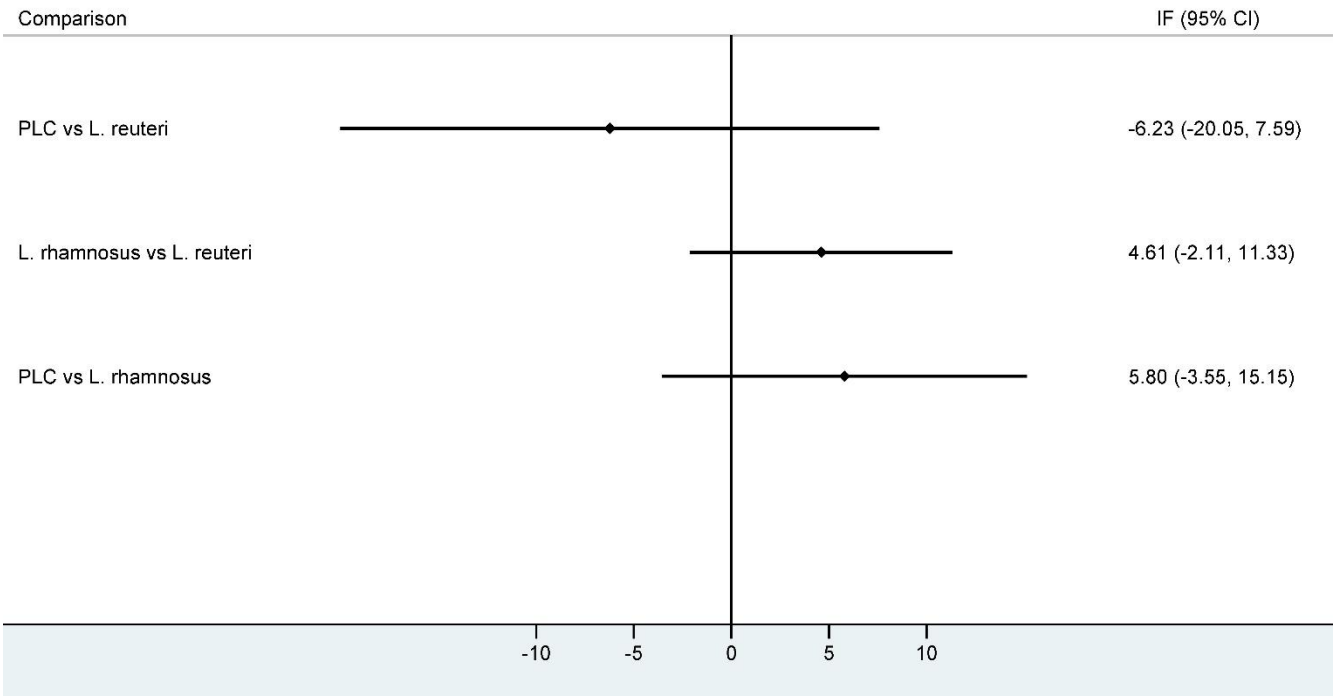
Incoherance factors (IF) along with 95% confidence intervals (CI) are displayed. IFs are calculated as the ratio of the ORs from direct and indirect evidence in the loop. Comparisons that their lower CI limit does not reach the line of 1 are considered to present statistically significant incoherence. P value for the 'design-by-treatment' model (global test of incoherence) = 0.349. PLC = placebo; *Bifido* sp. = *Bifidobacterium* sp.

e-figure 8: Incoherence plot for culture proven sepsis



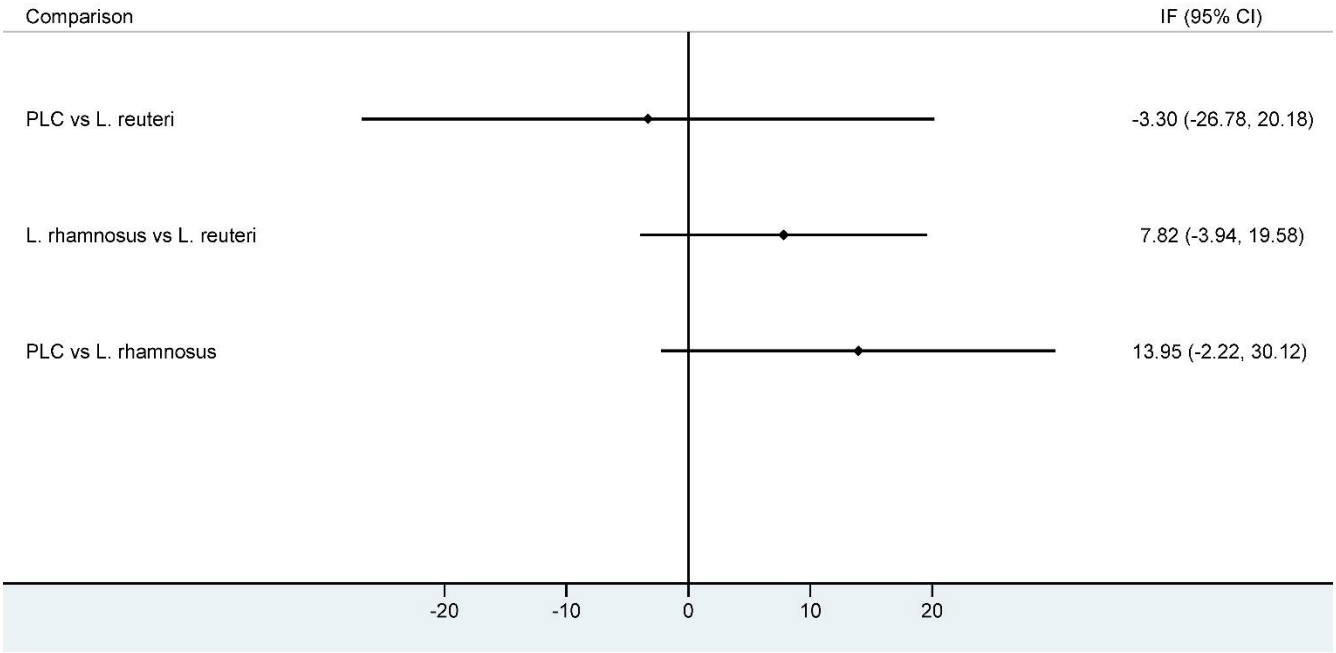
Incoherance factors (IF) along with 95% confidence intervals (CI) are displayed. IFs are calculated as the ratio of the ORs from direct and indirect evidence in the loop. Comparisons that their lower CI limit does not reach the line of 1 are considered to present statistically significant incoherence. P value for the 'design-by-treatment' model (global test of incoherence) = 0.166. PLC = placebo; Bifido sp. = Bifidobacterium sp.

e-figure 9: Incoherence plot for time to reach full enteral feed (days)



Incoherance factors (IF) along with 95% confidence intervals (CI) are displayed. IFs are calculated as the absolute difference between direct and indirect estimates. Comparisons that their lower CI limit does not reach the zero line are considered to present statistically significant inconsistency. P value for the 'design-by-treatment' model (global test of incoherence) = 0.179. PLC = placebo.

e-figure 10: Incoherence plot for duration of hospitalization (days)



Incoherance factors (IF) along with 95% confidence intervals (CI) are displayed. IFs are calculated as the absolute difference between direct and indirect estimates. Comparisons that their lower CI limit does not reach the zero line are considered to present statistically significant inconsistency. P value for the 'design-by-treatment' model (global test of incoherence) = 0.349. PLC = placebo.

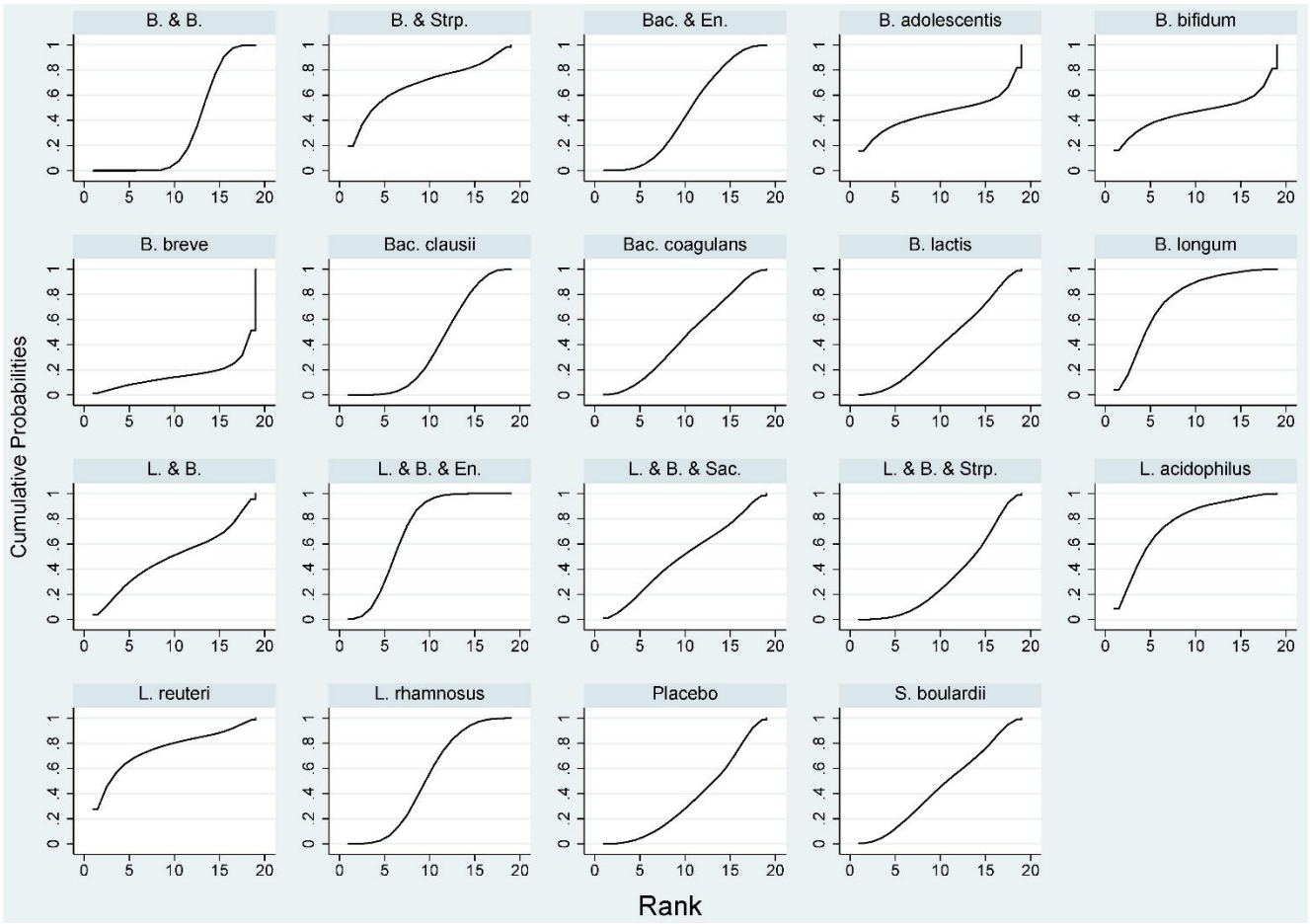
Appendix 10: SUCRA and cumulative probability plots

e-Table 12: The surface under the cumulative ranking (SUCRA) values and mean ranks for primary outcomes

Interventions	All-cause mortality		NEC (Bell's stage ≥ II)		Culture proven sepsis		Hospitalization		Time to reach full feed	
	SUCRA value	*Mean rank*	*SUCRA value*	*Mean rank*	*SUCRA value*	*Mean rank*	*SUCRA value*	*Mean rank*	*SUCRA value*	*Mean rank*
L. acidophilus	76.6	5.2	81.3	4.4	-	-	16.8	11.8	-	-
B. longum subsp. *longum*	75.8	5.4	70.9	6.2	53	8	-	-	-	-
L. reuteri	75.7	5.4	37.4	12.3	59.1	7.1	10.8	12.6	2.2	12.7
L. & B. & En.	71.1	6.2	68.5	6.7	39.3	10.1	59.9	6.2	64.5	5.3
B. & Strp.	69.1	6.6	15.7	16.2	48.9	8.7	36.5	9.2	23.9	10.1
L. rhamnosus	51.8	9.7	46.7	10.6	55.7	7.6	86.8	2.7	73.2	4.2
L. & B. & Sac.	49.9	10	76.8	5.2	81.9	3.7	69.5	5	68.1	4.8
L. & B.	49.5	10.1	69.7	6.5	50.4	8.4	95	1.7	65.6	5.1
B. bifidum	46.6	10.6	79.2	4.8	27.7	11.8	57.7	6.5	50.3	7
Bacillus coagulans	46.6	10.6	30.7	13.5	43	9.5	51.7	7.3	29.7	9.4
B. adolescentis	46.2	10.7	58.1	8.5	-	-	-	-	-	-
Bacillus & En.	45.7	10.8	64.3	7.4	-	-	-	-	-	-
S. boulardii	45.6	10.8	57.9	8.6	25.8	12.1	21	11.3	46.4	7.4
B. animalis subsp. *lactis*	41.9	11.5	45	10.9	54	7.9	34.2	9.6	53.2	6.6
Bacillus clausii	40	11.8	23.6	14.7	40.3	10				
L. & B. & Strp.	33.7	12.9	35.2	12.7	74.1	4.9	61.5	6	81.4	3.2
B. spp.	32.5	13.1	19.1	15.6	25.3	12.2				
B. breve	15.9	16.1	39.8	11.8	71.2	5.3	46.3	8	47.1	7.4

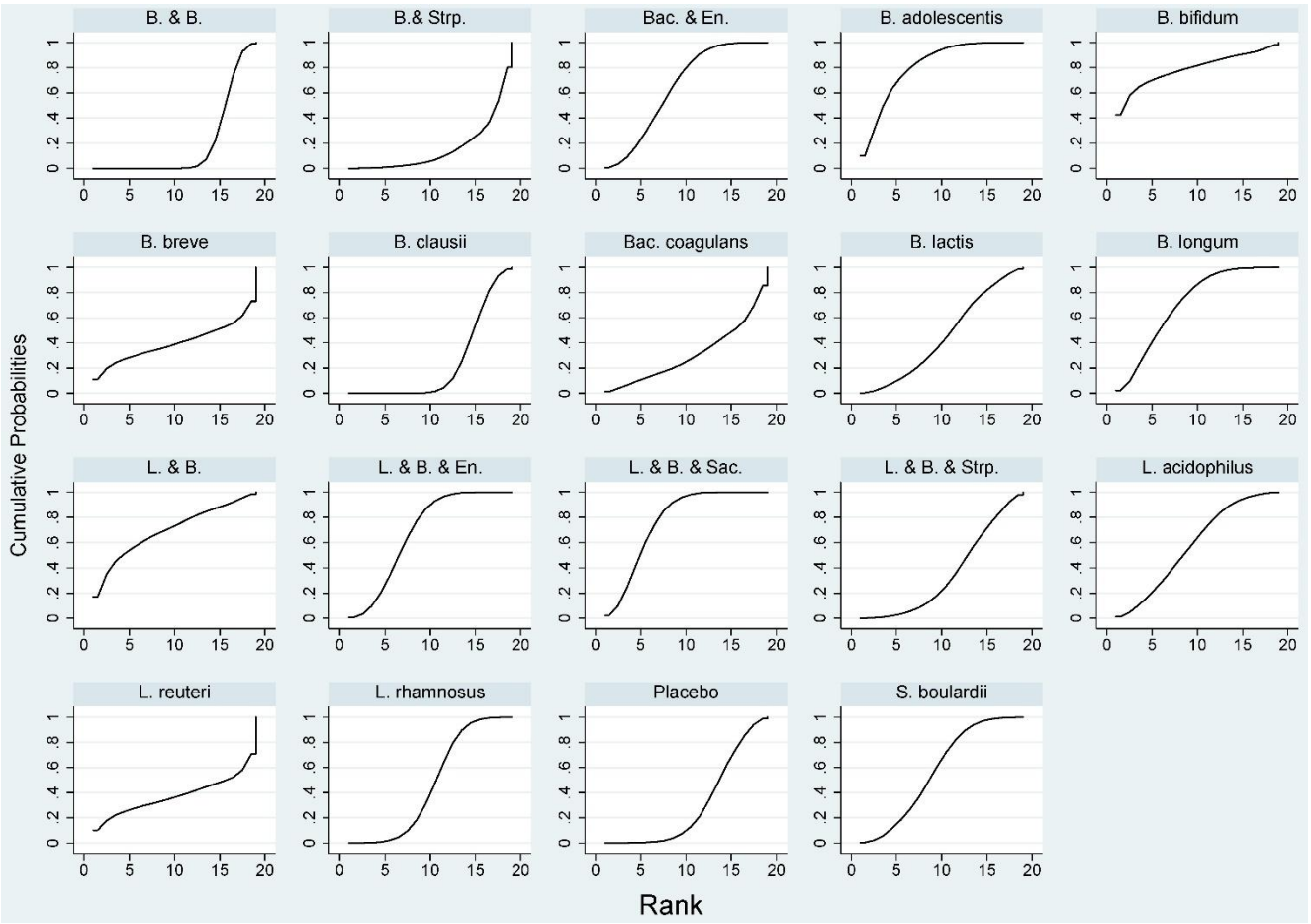
B. adolescentis: Bifidobacterium adolescentis; B. & B.: Bifidobacterium animalis subsp. *lactis & Bifidobacterium longum* subsp. *longum; Bac. coagulans: Bacillus coagulans; Bac & En.: Bacillus* spp. *& Enterococcus* spp.*; B. & Strp.: Bifidobacterium* spp. *& Streptococcus salivarius* subsp. *thermophilus; B. bifidum: Bifidobacterium bifidum; B. animalis* subsp. *lactis: Bifidobacterium animalis* subsp. *lactis; B. longum* subsp. *longum: Bifidobacterium longum* subsp. *longum; B. breve: Bifidobacterium breve; B. clausii: Bacillus clausii; L. acidophilus: Lactobacillus acidophilus; L. & B.: Lactobacillus* spp. *& Bifidobacterium* spp.*; L. & B. & En.: Lactobacillus* spp. *& Bifidobacterium* spp. *& Enterococcus* spp.*; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp. *& Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp. *& Bifidobacterium* spp. *& S. salivarius* subsp. *thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Figure 11: Plots of the surface under the cumulative ranking curves for all treatments for the 'all-cause mortality' outcome



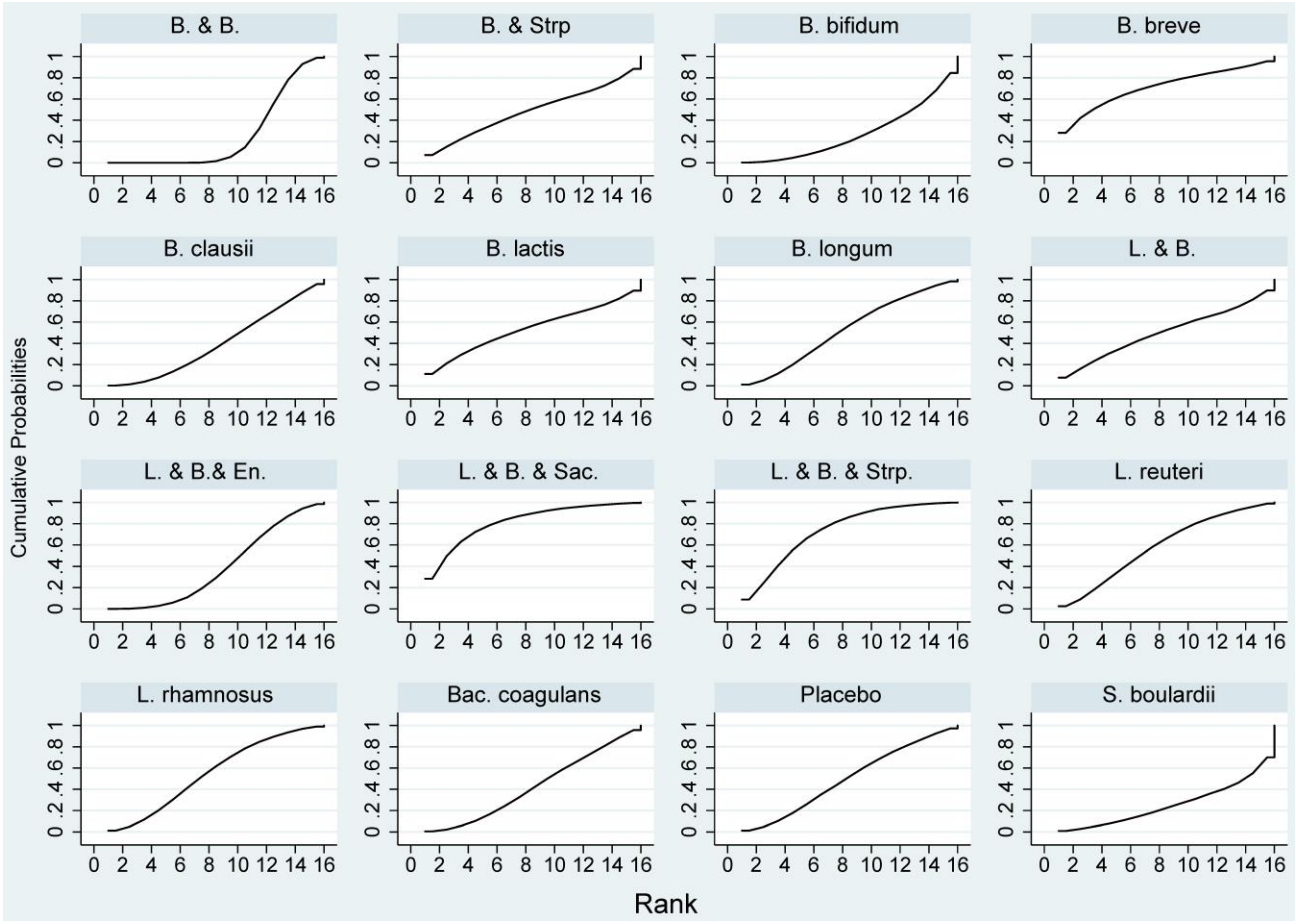
B. adolescentis: Bifidobacterium adolescentis; B. & B.: Bifidobacterium animalis subsp*. lactis & Bifidobacterium longum* subsp*. longum; Bac. coagulans: Bacillus coagulans; Bac & En.: Bacillus* spp*. & Enterococcus* spp*.; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; Bac. clausii: Bacillus clausii; L. acidophilus: Lactobacillus acidophilus; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Figure 12: Plots of the surface under the cumulative ranking curves for all treatments for the 'NEC stage II or more' outcome



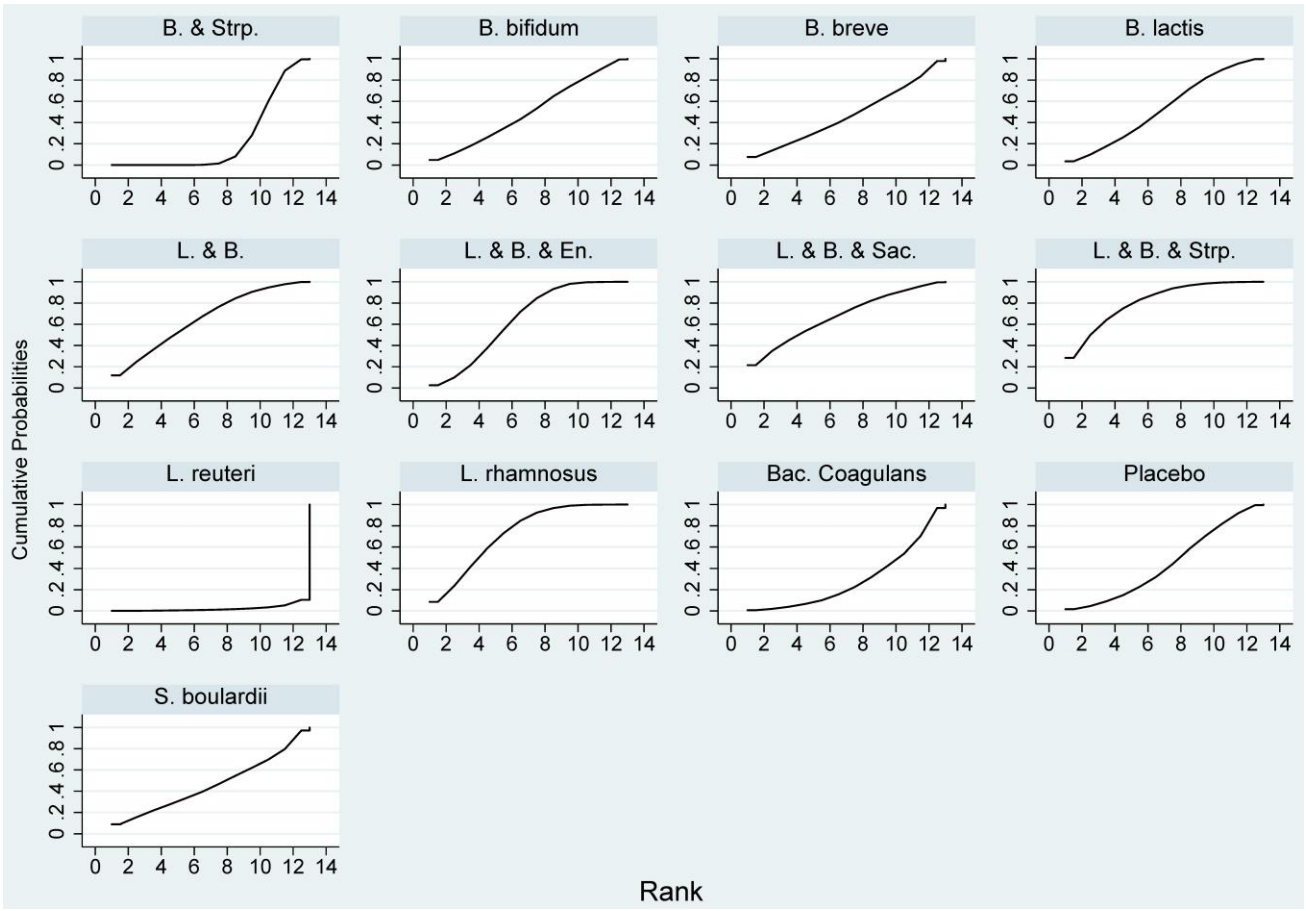
B. adolescentis: Bifidobacterium adolescentis; B. & B.: Bifidobacterium animalis subsp*. lactis & Bifidobacterium longum* subsp*. longum; Bac. coagulans: Bacillus coagulans; Bac & En.: Bacillus* spp*. & Enterococcus* spp*.; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; B. clausii: Bacillus clausii; L. acidophilus: Lactobacillus acidophilus; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Figure 13: Plots of the surface under the cumulative ranking curves for all treatments for the 'culture proven sepsis' outcome



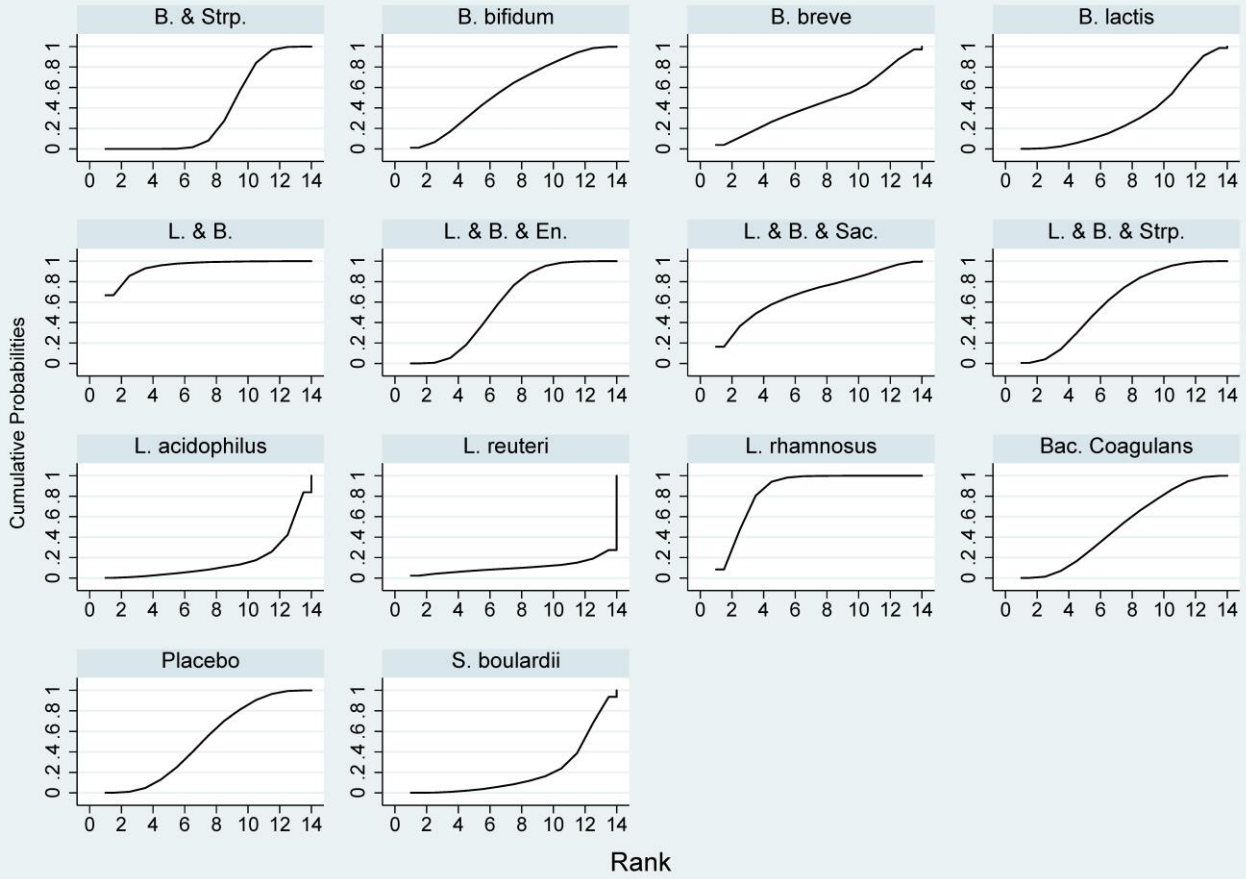
B. & B.: Bifidobacterium animalis subsp*. lactis & Bifidobacterium longum* subsp*. longum; Bac. coagulans: Bacillus coagulans; B. & Strp.: Bifidobacterium* spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. lactis: Bifidobacterium animalis* subsp*. lactis; B. longum: Bifidobacterium longum* subsp*. longum; B. breve: Bifidobacterium breve; B. clausii: Bacillus clausii; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Figure 14: Plots of the surface under the cumulative ranking curves for all treatments for the 'time to reach full enteral feed' outcome



Bac. coagulans: Bacillus coagulans; B. & Strp.: Bifidobacterium spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. breve: Bifidobacterium breve; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

e-Figure 15: Plots of the surface under the cumulative ranking curves for all treatments for the 'duration of hospitalization' outcome



Bac. coagulans: Bacillus coagulans; B. & Strp.: Bifidobacterium spp*. & Streptococcus salivarius* subsp*. thermophilus; B. bifidum: Bifidobacterium bifidum; B. lactis: Bifidobacterium animalis* subsp*. lactis; B. breve: Bifidobacterium breve; L. & B.: Lactobacillus* spp*. & Bifidobacterium* spp*.; L. & B. & En.: Lactobacillus* spp*. & Bifidobacterium* spp*. & Enterococcus* spp*.; L. acidophilus: Lactobacillus acidophilus; L. reuteri: Lactobacillus reuteri; L. & B. & Sac.: Lactobacillus spp. & Bifidobacterium* spp*. & Saccharomyces boulardii; L. & B. & Strp.: Lactobacillus* spp*. & Bifidobacterium* spp*. & S. salivarius* subsp*. thermophilus; L. rhamnosus: Lactobacillus rhamnosus; S. boulardii: Saccharomyces boulardii*

Appendix 11: GRADE presentation of continuous outcomes

Network meta-analysis results (mean difference [MD] and 95% CIs) sorted based on GRADE certainty of evidence (CoE) for the comparisons of active treatments vs. placebo (PLC) for time to reach full enteral feeding (days) and duration of hospitalization (days)

Outcome	CoE	Classification	Intervention	MD (95% CI) vs PLC
Time to Reach Full Enteral Feeding (days)	High (Moderate to High)	Among the most effective	*Lactobacillus* spp. & *Bifidobacterium* spp. & *S. boulardii*	**-3.30 (-5.91,-0.69)**
		Among the least effective	*S. boulardii*	-1.02 (-3.64,1.61)
			Lactobacillus spp. & *Bifidobacterium* spp. & *S. salivarius* subsp. *thermophilus*	5.75 (-0.33,11.83)
	Low (Low to very low)	May be among the most effective	*L. reuteri*	**-2.62 (-4.53,-0.71)**
			Lactobacillus spp. & *Bifidobacterium* spp.	**-2.15 (-3.78,-0.51)**
		May be among the least effective	*Lactobacillus* spp. & *Bifidobacterium* spp. & *Enterococcus* spp.	-2.57 (-6.55, 1.41)
			B. animalis subsp. *lactis*	-2.30 (-5.35, 0.74)
			B. breve	-1.53 (-4.30,1.24)
			Bifidobacterium spp. & *S. salivarius* subsp. *thermophilus*	-1.35 (-4.66,1.95)
			B. bifidum	-1.10 (-5.31,3.11)
			Bacillus coagulans	-1.00 (-5.78,3.78)
			L. rhamnosus	0.02 (-3.29,3.32)
Duration of Hospitalization (days)	High (Moderate to High)	Among the most effective	*B. animalis* subsp. *lactis*	**-13.00 (-22.71,-3.29)**
			L. reuteri	**-7.89 (-11.60,-4.17)**
		Among the least effective	*Bifidobacterium* spp. & *S. salivarius* subsp. *thermophilus*	-2.75 (-10.00,4.50)
			L. rhamnosus	-1.85 (-7.62,3.91)
			Lactobacillus spp. & *Bifidobacterium* spp. & *S. salivarius* subsp. *thermophilus*	7.25 (-5.83,20.33)
			B. breve	1.18 (-5.88,8.24)
	Low (Low to very low)	May be among the least effective	*Lactobacillus* spp. & *Bifidobacterium* spp. & *Enterococcus* spp.	-6.00 (-19.53,7.53)
			Lactobacillus spp. & *Bifidobacterium* spp. & *S. boulardii*	-3.20 (-8.38,1.98)
			Lactobacillus spp. & *Bifidobacterium* spp.	-2.84 (-6.21,0.54)
			S. boulardii	-1.86 (-6.65,2.92)
			B. bifidum	-0.60 (-13.61,12.41)
			Bacillus coagulans	4.50 (-4.33,13.33)
			L. acidophilus	20.70 (-12.55,53.95)