Supplementary Material 4: Efficacy results of probiotics for antibiotic-associated diarrhea and publication bias

Table S4.1. Network and traditional meta-analysis results for the incidence of diarrhea, and quality of evidence.

Interventions	Incidence of diarrhea			
	Network meta-analysis OR (95% CI)	Quality of evidence	Pairwise meta-analysis OR (95% CI)	Quality of evidence
Multi-genera II vs. Placebo	0.55 (0.41, 0.75)	Low*†	0.71 (0.60, 0.83)	Low*†
Multi-genera III vs. Placebo	0.94 (0.63, 1.43)	Moderate*	0.94 (0.68, 1.31)	Moderate†
LGG vs. Placebo	0.24 (0.14, 0.42)	Moderate*‡ψ	0.26 (0.17, 0.40)	Moderate*ψ
L. rhamnosus vs. Placebo	0.46 (0.19, 1.13)	Moderate*	0.46 (0.24, 0.92)	Moderate*ψ
L. casei vs. Placebo	0.24 (0.10, 0.57)	Moderate*ψ	0.27 (0.16, 0.46)	Moderate*ψ
L. acidophilus vs. Placebo	0.41 (0.26, 0.65)	Moderate*‡ψ	0.46 (0.34, 0.61)	Moderate*ψ
L. reuteri vs. Placebo	0.46 (0.14, 1.59)	Moderate*†ψ	0.45 (0.16, 1.26)	Low*†ψ
L. plantarum vs. Placebo	0.82 (0.18, 3.70)	Low*‡	0.82 (0.22, 3.14)	Moderate*
B. clausii vs. Placebo	0.26 (0.07, 0.94)	Moderate*ψ	0.29 (0.11, 0.77)	Moderate*ψ
S. boulardii vs. Placebo	0.35 (0.24, 0.51)	Moderate*†ψ	0.36 (0.28, 0.46)	Low*†
Multi-genera III vs. Multi-genera II	1.70 (1.03, 2.80)	Moderate*†ψ	1.68 (0.69, 4.08)	Moderate*†ψ

LGG vs. Multi-genera II	0.43 (0.23, 0.82)	Moderate*†ψ	0.53 (0.11, 2.59)	Low*†ψ
L. rhamnosus vs. Multi-genera II	0.84 (0.33, 2.14)	Low*†	NA	NA
L. casei vs. Multi-genera II	0.43 (0.17, 1.08)	Moderate*ψ	NA	NA
L. acidophilus vs. Multi-genera II	0.75 (0.44, 1.28)	Moderate*†ψ	NA	NA
L. reuteri vs. Multi-genera II	0.84 (0.24, 2.96)	Very low*†‡	NA	NA
L. plantarum vs. Multi-genera II	1.48 (0.32, 6.82)	Very low*†‡	NA	NA
B. clausii vs. Multi-genera II	0.47 (0.12, 1.75)	Low*†‡ψ	NA	NA
S. boulardii vs. Multi-genera II	0.63 (0.40, 1.01)	Moderate*†ψ	0.53 (0.11, 2.59)	Low*†ψ
LGG vs. Multi-genera III	0.26 (0.13, 0.67)	Moderate*†ψ	NA	NA
L. rhamnosus vs. Multi-genera III	0.49 (0.18, 1.31)	Moderate†	NA	NA
L. casei vs. Multi-genera III	0.26 (0.10, 0.67)	Moderate*†ψ	NA	NA
L. acidophilus vs. Multi-genera III	0.44 (0.24, 0.81)	Moderate*ψ	NA	NA
L. reuteri vs. Multi-genera III	0.49 (0.13, 1.81)	Low*†‡ψ	NA	NA
L. plantarum vs. Multi-genera III	0.87 (0.18, 4.16)	Very low*†‡	NA	NA
B. clausii vs. Multi-genera III	0.28 (0.07, 1.07)	Low*†‡ψ	NA	NA
S. boulardii vs. Multi-genera III	0.37 (0.21, 0.65)	Moderate*ψ	NA	NA
L. rhamnosus vs. LGG	1.93	High	NA	NA

	(0.50, 7.50)			
L. casei vs. LGG	1.00 (0.36, 2.81)	Moderate*	NA	NA
L. acidophilus vs. LGG	1.72 (0.83, 3.57)	Moderate*	NA	NA
L. reuteri vs. LGG	1.93 (0.50, 7.50)	Moderate*	NA	NA
L. plantarum vs. LGG	3.42 (0.68, 17.07)	Moderate*‡ψ	NA	NA
B. clausii vs. LGG	1.08 (0.26, 4.41)	Low*‡	NA	NA
S. boulardii vs. LGG	1.46 (0.75, 2.85)	Moderate*	1.00 (0.18, 5.63)	Moderate*
L. casei vs. *L. rhamnosus*	0.52 (0.15, 1.78)	Moderate‡	NA	NA
L. acidophilus vs. *L. rhamnosus*	0.89 (0.33, 2.42)	Moderate‡	NA	NA
L. reuteri vs. *L. rhamnosus*	1.00 (0.22, 4.57)	Moderate‡	NA	NA
L. plantarum vs. *L. rhamnosus*	1.77 (0.31, 10.16)	Moderate‡	NA	NA
B. clausii vs. *L. rhamnosus*	0.56 (0.12, 2.67)	Moderate‡	NA	NA
S. boulardii vs. *L. rhamnosus*	0.76 (0.29, 1.97)	Moderate‡	NA	NA
L. acidophilus vs. *L. casei*	1.72 (0.65, 4.56)	Very low*†‡	NA	NA
L. reuteri vs. *L. casei*	1.93 (0.43, 8.68)	Very low*†‡	NA	NA
L. plantarum vs. *L. casei*	3.41 (0.60, 19.31)	Moderate*‡ψ	NA	NA
B. clausii vs. *L. casei*	1.08 (0.23, 5.07)	Low*‡	NA	NA

S. boulardii vs. *L. casei*	1.46 (0.57, 3.71)	Low*‡	NA	NA
L. reuteri vs. *L. acidophilus*	1.12 (0.30, 4.16)	Moderate*	NA	NA
L. plantarum vs. *L. acidophilus*	1.98 (0.41, 9.55)	Moderate*	NA	NA
B. clausii vs. *L. acidophilus*	0.63 (0.16, 2.45)	Low*‡	NA	NA
S. boulardii vs. *L. acidophilus*	0.85 (0.47, 1.52)	Low*†	NA	NA
L. plantarum vs. *L. reuteri*	1.77 (0.25, 12.39)	Moderate*	NA	NA
B. clausii vs. *L. reuteri*	0.56 (0.09, 3.32)	Low*‡	NA	NA
S. boulardii vs. *L. reuteri*	0.76 (0.21, 2.73)	Moderate*	NA	NA
B. clausii vs. *L. plantarum*	0.32 (0.04, 2.29)	Moderate*‡ψ	NA	NA
S. boulardii vs. *L. plantarum*	0.43 (0.09, 2.01)	Moderate*‡ψ	NA	NA
S. boulardii vs. *B. clausii*	1.35 (0.35, 5.15)	Low*‡	NA	NA

Abbreviations: OR=odds ratio; CI=confidence interval; NA=not applicable.

*Limitations in study design or execution (risk of bias); †Inconsistency in results; ¶Indirectness of evidence; ‡Imprecision of results; §Publication bias; ψMagnitude of the effect.

Table S4.2. Traditional meta-analysis results for the incidence of diarrhea.

Interventions	Trails	Participants	Effect Estimate OR (95% CI)	Heterogeneity
Multi-genera II vs. Placebo	16	5234	0.71 (0.60, 0.83)	P=0.00, I^2=59.2% (29.3%, 76.5%), tau^2=0.23
Multi-genera III vs. Placebo	9	1287	0.94 (0.68, 1.31)	P=0.19, I^2=32.8% (0%, 72.9%), tau^2=0.09
LGG vs. Placebo	7	881	0.26 (0.17, 0.40)	P=0.99, I^2=0.0% (0.0%, 78.0%), tau^2=0.00
L. rhamnosus vs. Placebo	2	412	0.46 (0.24, 0.92)	P=0.68, I^2=0.0%, tau^2=0.00
L. casei vs. Placebo	3	414	0.27 (0.16, 0.46)	P=0.20, I^2=36.9% (0.0%, 79.9%), tau^2=0.16
L. acidophilus vs. Placebo	5	904	0.46 (0.34, 0.61)	P=0.51, I^2=13.8% (0.0%, 53.8%), tau^2=0.05
L. reuteri vs. Placebo	2	63	0.45 (0.16, 1.26)	P=0.51, I^2=0.0%, tau^2=0.00
L. plantarum vs. Placebo	1	163	0.82 (0.22, 3.14)	NA
B. clausii vs. Placebo	1	100	0.29 (0.11, 0.77)	NA
S. boulardii vs. Placebo	10	2078	0.36 (0.28, 0.46)	P=0.07, I^2=38.5% (0.0%, 70.7%), tau^2=0.18
Multi-genera III vs. Multi-genera II	1	39	1.68 (0.69, 4.08)	NA
LGG vs. Multi-genera II	1	42	0.53 (0.11, 2.59)	NA
S. boulardii vs. Multi-genera II	1	42	0.53 (0.11, 2.59)	NA
LGG vs. *S. boulardii*	1	42	1.00 (0.18, 5.63)	NA

Abbreviations: CI=confidence interval; OR=odds ratio; NA=not applicable.

Table S4.3. Traditional meta-analysis results for *C. difficile* infection rate.

Interventions	Trails	Participants	Effect Estimate OR (95% CI)	Heterogeneity
Multi-genera II vs. Placebo	6	3971	0.54 (0.35, 0.85)	P=0.27, I^2=21.0% (0.0%, 65.8%), tau^2=0.12
Multi-genera III vs. Placebo	2	104	0.30 (0.10, 0.89)	P=0.72, I^2=0.0%, tau^2=0.00
LGG vs. Placebo	2	257	0.36 (0.14, 0.92)	P=0.48, I^2=0.0%, tau^2=0.00
L. rhamnosus vs. Placebo	1	240	0.35 (0.11, 1.12)	NA
L. casei vs. Placebo	1	258	0.16 (0.06, 0.47)	NA
L. acidophilus vs. Placebo	5	904	0.22 (0.13, 0.38)	P=0.44, I^2=0.0% (0.0%, 79.2%), tau^2=0.00
L. plantarum vs. Placebo	1	150	1.03 (0.20, 5.24)	NA
S. boulardii vs. Placebo	3	839	0.35 (0.19, 0.63)	P=0.18, I^2=41.9% (0.0%, 82.2%), tau^2=0.30

Abbreviations: CI=confidence interval; OR=odds ratio; NA=not applicable.

Table S4.4. Summary table of meta-regression for the incidence of diarrhea.

Covariate	Coefficient (95% CI)	Standard Error	*P* value
Mean age	1.56 (1.13, 2.15)	0.25	0.17
Sex ratio	1.43 (0.79, 2.57)	0.41	0.76
Recruiting area	2.37 (0.56, 9.97)	1.68	0.45
Antibiotic in use	4.56 (2.09, 9.96)	1.77	0.07
Indication	1.86 (1.06, 3.25)	0.51	0.61
Dosage	1.70 (1.42, 2.03)	0.15	0.45
Duration	1.75 (1.41, 2.19)	0.19	0.97

Abbreviations: CI=confidence interval.

Figure S4.1. Forest plot of network meta-analysis for the efficacy outcomes compared with placebo arm.

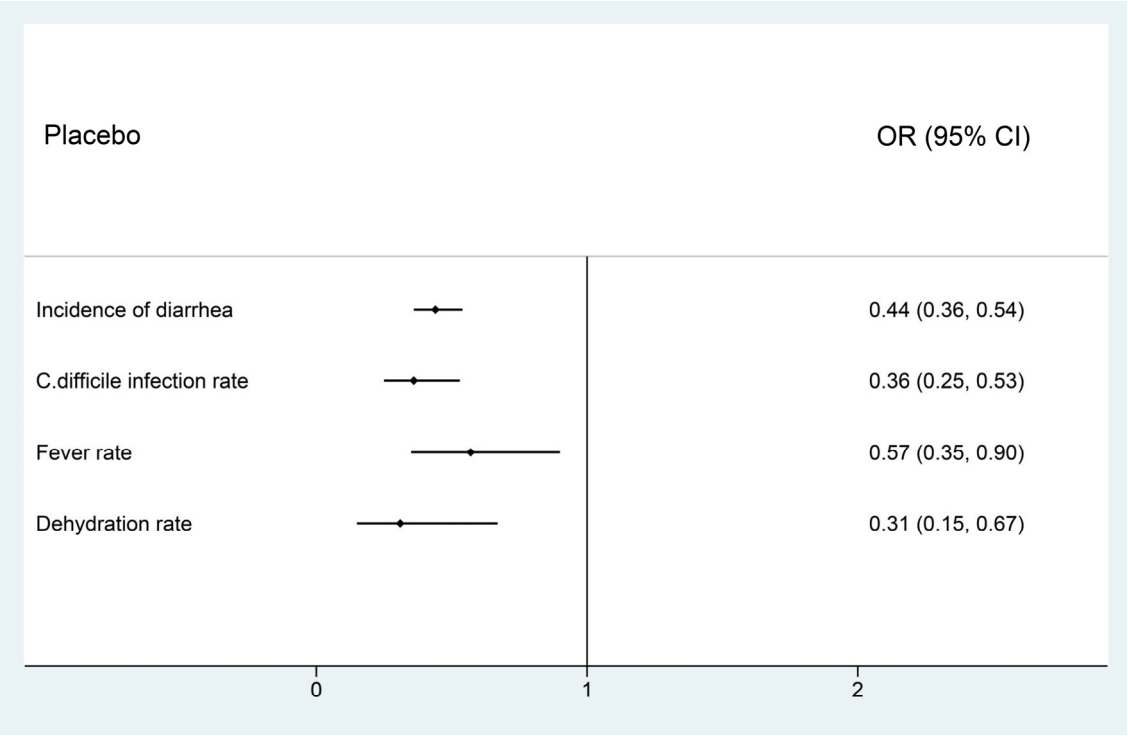

Figure S4.2. Comparison-adjusted funnel plot of network analysis for the incidence of diarrhea compared with placebo arm.