e-Table 1: Summary of randomized controlled trials where prevention or treatment of Clostridium difficile-associated diarrhea (CDAD) was the primary or secondary outcome

Trial; primary outcome	Probiotic and duration (formulation, CFU/d)	Outcome measure (length of follow-up)	Results: Probiotic group, n/N (%)	Results: Placebo group, n/N (%)	Results: Risk difference (95% CI) (placebo–probiotic)	Compliance and adverse effects	Quality score*	Comments
Primary outcome								
Plummer et al, 2004;[15] prevention	Lactobacillus acidophilus and Bifidobacterium bifidum for 20 d (capsule, 20×10^9 CFU/d)	Presence of C. difficile (20 d)	11/69 (13.0)	9/69 (15.9)	–2.8 (–8.7 to 15.3)	Not assessed	3	No difference in toxin positivity between treatment arms among patients with positive culture; lower incidence of diarrhea reported among culture- and toxin-positive subjects in probiotic group; short follow-up
McFarland et al, 1994;[16] treatment	Saccharomyces boulardii for 4 wk (2×250 mg capsules, 30×10^9 CFU/d)	Diarrhea and at least 1 positive assay for C. difficile by culture, toxin A or toxin B (8 wk)	15/57 (26.3)	30/64(46.9)	20.5 (2.2 to 37.0)	11.3% noncompliant in probiotic group for an average of 2 d; more subjects in probiotic group experienced thirst and constipation	5	Concomitant use of different antibiotics for differing lengths of time; no difference in culture positivity between treatment arms but significantly fewer toxin B positive cases in probiotic group
			First-time CDAD:					
			6/31 (19.3)	8/33 (24.2)	4.9 (–17.6 to 26.4)			
			Recurrent CDAD:					
			9/26 (34.6)	22/34 (64.7)	30.0 (2.3 to 50.6)			
Surawicz et al, 2000;[17] treatment	S. boulardii for 28 d (2×250 mg capsules, CFU/d not reported)	Diarrhea and at least 1 positive assay for C. difficile by culture, toxin A or toxin B (8 wk)	39/89 (43.8)	37/69 (53.6)	9.8 (–6.7 to 25.6)	Compliance not reported; no significant difference in side effects between groups	3	Concomitant antibiotic assigned to patients after randomization; no difference in culture or toxin positivity in high-dose vancomycin group; results not reported for other groups
			High-dose vancomycin:					
			3/18 (16.7)	7/14 (50)	33.0 (–0.3 to 62.0)			
			Low-dose vancomycin:					
			23/45 (51.1)	17/38 (44.7)	–6.4 (–16.2 to 28.1)			
			Metronidazole:					
			13/26 (50.0)	13/27 (48.2)	–1.9 (–25.8 to 29.2)			
Wullt et al, 2003;[18] treatment	L. plantarum 299v for 38 d (fruit drink containing oats fermented with probiotic, 50×10^9 CFU/d)	Diarrhea (5–10 d)	1/12 (91.6)	0/9 (100)	–8.3 (–40.3 to 29.6)	80% harboured probiotic in fecal samples; no apparent side effects	4	Small sample; no difference in culture positivity after treatment among 20 patients who had no diarrhea after 5–10 d
		Positive assay for C. difficile toxins A or B (11–13 d)	5/12 (58.3)	2/9 (77.8)	–19.4 (–64.7 to 15.5)			
Secondary outcome								
Surawicz et al, 1989[19]	S. boulardii starting within 48 h of beginning antibiotic until 2 wk post-antibiotic ($2 \times$ 250 mg capsules, 1 g/d)	Acquired C. difficile after enrolment (duration of probiotic treatment, minimum of 8 d)	22/81 (27)	5/36 (14)	–13.3 (–25.7 to 4.7)*	Compliance not reported; no side effects	5	Probiotic resulted in a significant reduction in the risk of AAD; C. difficile tested only in those with ≥ 3 stool samples; short follow-up
McFarland et al, 1995[20]	S. boulardii starting from within 72 h of beginning anti-biotic until 3 d after last dose of anti-biotic (2×250 mg capsules, 30×10^9 CFU/d)	Diarrhea among C. difficile- or toxin-positive subjects (7 wk after probiotic was discontinued)	3/10 (30)	14/96 (28.6)	–1.4 (–3.5 to 4.1)	Compliance not reported; no significant adverse reactions due to probiotic	4	Probiotic resulted in a significant reduction in the risk of AAD; only available result for CDAD was not based on a comparison between randomized subjects
Lewis et al, 1998[21]	S. boulardii for duration of antibiotic treat-ment (2×113 mg capsules, CFU/d not reported)	Positive assay for C. difficile toxin (duration of antibiotic treatment)	5/33 (15.2)	3/36 (8.3)	–6.8 (–22.6 to 8.0)	Compliance not reported; no side effects	4	Probiotic had no effect on AAD; C. difficile tested regularly every 4 d and whenever subjects had diarrhea; small number of CDAD cases; short follow-up
Thomas et al, 2001[22]	L. GG starting within 24 h of beginning anti-biotic treatment for 14 d (capsule, 20×10^9 CFU/d)	Diarrhea and positive assay for C. difficile toxin (21 d)	2/133 (1.5)	3/134 (2.2)	0.7 (–3.0 to 4.5)	86.2% of probiotic subjects were compliant; same prevalence of side effects (e.g., nausea) in both groups	4	Probiotic had no effect on AAD; C. difficile toxin results obtained from medical chart; small number of CDAD cases; short follow-up

Note: CFU = colony-forming unit, CI = confidence interval, AAD = antibiotic-associated diarrhea.
*The quality of the studies was assessed using the scale described by Jadad et al.[14] A score of 5 indicates best quality.