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The pros, cons, and many unknowns of probiotics

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Trials not showing a significant effect							
Reference	**Type outcome**	**N probiotics**	**N probiotics Positive outcome**	**N placebo**	**N placebo Positive outcome**	**P-value / CI (range)**	**Probiotic intervention**
Bravo 2008[1]	CDAD	41	0	45	0	N/A	S. boulardii
Cindoruk 2007 [2]	CDAD	6	0	8	0	N/A	S. boulardii
Fominykh 2013 (Meeting abstract)	CDAD	80	0	40	0	N/A	L. lactis, Lactobacillus, Bifidobacterium and S. thermophilus
Georgieva 2015[3]	CDAD	49	0	48	0	N/A	L. reuteri DSM 17938
Koning 2008[4]	*C. difficile* culture	19	0	21	0	N/A	B. bifidum W23, B. lactis W18, B. longum W51, E. faecium W54, L. acidophilus W37 and W55, L. paracasei W72, L. plantarum W62, L. rhamnosus W71, and L. salivarius W24
Selinger 2013[5]	CDAD	117	0	112	0	N/A	VSL#3
Shimbo 2005[6]	*C. difficile* culture	18	0	17	0	N/A	C. butyricum MIYAIRI 588
Siitonen 1990[7]	Toxin detection	6	0	6	0	N/A	L. rhamnosus GG
Allen 2013[8]	CDAD	1470	12	1471	17	0.35	L. acidophilus (CUL60, NCIMB 30157, CUL21, NCIMB 30156), B. bifidum CUL20, NCIMB 30153; and B lactis CUL34, NCIMB 30172
Arvola 1999[9]	CDAD	61	1	58	1	N/A	L. rhamnosus GG
Barker 2017[10]	Recurrent CDAD	13	1	15	1	0.96	L. acidophilus NCFM, L. paracasei Lpc-37, B. lactis Bi-07 and B. lactis Bl-04
Beausoleil 2007[11]	CDAD	44	1	45	7	0.06	L. acidophilus CL1285 and L. casei
Can 2006[12]	CDAD	73	0	78	2	N/A	S. boulardii
Duman 2005[13]	CDAD	5	0	11	1	N/A	S. boulardii
Ehrhardt 2016[14]	CDAD	146	2	146	2	N/A	S. boulardii

Kotowska 2005[15]	CDAD	9	3	29	10	N/A	S. boulardii
Lawrence 2005[16]	Recurrent CDAD	8	3	7	1	2.6 (0.3-19.9)	L. rhamnosus GG
Lewis 1998[17]	Toxin detection	33	5	36	3	N/A	S. boulardii
Lönnermark 2010[18]	Toxin detection	69	3	76	3	Not calculated	L. plantarum 299v
McFarland 1995[19]	CDAD	10	3	14	4	not calculated	S. boulardii
Miller 2008 (Meeting abstract)	CDAD	95	4	94	7	0.26	2 x 10^{10} L. rhamnosus GG
Miller 2008 (Meeting abstract)	CDAD	157	2	159	0	0.25	6 x 10^{10} L. rhamnosus GG
Nord 1997[20]	*C. difficile* culture	11	2	12	5	N/A	L. acidophilus and B. bifidum
Ouwehand 2014[21]	CDAD	144	1.80%	146	4.80 %	0.25	Low dose: L. acidophilus NCFM, L. paracasei Lpc-37, B. lactis Bi-07, B. lactis Bl-04
Plummer 2004[22]	CDAD	69	2	69	6	0.4 (0.08 - 1.99)	L. acidophilus, B. bifidum
Pozzoni 2012[23]	CDAD	106	3	98	2	1	S. boulardii
Ruszczyński 2008 [24]	CDAD	120	3	120	7	0.2	L. rhamnosus (strains E/N, Oxy and Pen)
Safdar 2008[25]	CDAD	3	0	4	1	0.27	L. acidophilus
Sampalis 2010[26]	Toxin detection	16	1	30	4	0.645	L. acidophilus CL1285
Sullivan 2004[27]	*C. difficile* culture	18	2	18	2	N/A	L. paracasei F19
Surawicz 1989[28]	CDAD	32	3	16	5	0.07	S. boulardii
Thomas 2001[29]	CDAD	133	2	134	3	>0.99	L. rhamnosus GG
Wenus 2008[30]	*C. difficile* culture	34	1	29	1	N/A	L. rhamnosus GG, L. acidophilus La-5, B. lactis Bb-12
Wenus 2008[30]	Toxin detection	34	1	29	0	N/A	L. rhamnosus GG, L. acidophilus La-5, B. lactis Bb-12

Wong 2014[31]	CDAD	76	0	82	1	N/A	Lactobacillus casei Shirota
Wullt 2003[32]	Recurrent CDAD	11	4	9	6	0.37	L. plantarum 299v
Trials showing a significant effect							
Reference	**Type outcome**	**N probiotics**	**N probiotics Positive outcome**	**N placebo**	**N placebo Positive outcome**	**P-value / CI (range)**	**Probiotic intervention**
Gao 2010[33]	CDAD	86	1	84	20	0.002	Double dose: L. acidophilus CL1285 +Lactobacillus casei LBC80R
Gao 2010[33]	CDAD	85	8	84	20	0.03	Single dose: L. acidophilus CL1285 +Lactobacillus casei LBC80R
Hickson 2007[34]	CDAD	56	0	53	9	0.001	L casei, L bulgaricus, and S thermophilus
Klarin 2008[35]	*C. difficile* culture	71	0	80	4	0.0485	L. plantarum 299v
Morrow 2010[36]	CDAD	68	4	70	13	0.02	L. rhamnosus GG
Ouwehand 2014[21]	CDAD	160	1.80%	146	4.80 %	0.02	High dose: L. acidophilus NCFM, L. paracasei Lpc-37, B. lactis Bi-07, B. lactis Bl-04
Pancheva 2009 (Meeting abstract)	Toxin detection	78	6	78	17	0.35 (0.15 - 0.85)	L. acidophilus, L. delbruecki sbsp. bulgaricus, B. bifidum
Rafiq 2007Meeting abstract	CDAD	45	5	55	22	0.001	L. acidophilus, L. bulgaricus, B. bifidum, S. thermophilus
Shan 2013[37]	CDAD	139	1	144	8	0.13 (0.02 - 1.05)	S. boulardii

Supplemental Table 1. Individual trials included in meta-analyses addressing a role for probiotics in *C. difficile* diarrhea, infection or recurrence. Trials with more than one intervention arm appear as separate rows with the difference indicated in the "probiotics intervention" column. Eight trials had a significant effect, and 34 trials did not. P-values and confidence intervals (CI) are taken from the published works; NA indicates that these values were not calculated as part of the work; CDAD, *Clostridium difficile*-associated diarrhea; N, number of subjects.

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