**Appendix Table E5. Included studies for probiotic nonstandard treatments**

| **Author, Year, Country,****Funding Source** | **Population, Age** | **Sample Size, Intervention(s),****Control(s), Study Duration** | **Adverse Events\*** |
| --- | --- | --- | --- |
| ***Newly identified randomized trials*** |  |  |  |
| Ouwehand, 2014[70](#_ENREF_70)ChinaIndustry | 503 adult in-patients aged 30-70 on antibiotic therapy, mean age 50 | Four-strain preparation of *L. acidophilus*, *L. paracasei*, and *Bifidobacterium*High-dose, 1.70 x 1010 CFU (n = 168)Low-dose, 4.17 x 109 CFU (n = 168)Placebo (n = 167)Treatment duration: 10-21 days; antibiotic duration plus 7 days Followup: 4 weeks after antibiotic course | High-dose: 4.2%Low-dose: 4.2%Placebo: 7.2%allergy to seafood (2), arrhythmia (2), fever (10), headache (2), left upper arm fracture (1), runny nose (4), and vomiting (4) |
| Allen, 2013[71](#_ENREF_71)United KingdomGovernment | 2981 adult inpatients aged 65 years and older, mean age 77.2, exposed to one or more parenteral antibiotics  | Multistrain preparation of *lactobacilli* and *bifidobacteria*, 6 x 1010 organisms for 21 days (n=1493)Placebo (n=1488)Followup: 8 weeks after recruitment, chart review at 12 weeks | No serious adverse events attributed to participation in the trial |
| Selinger, 2013[72](#_ENREF_72)United KingdomIndustry, government | 229 adult hospital inpatients, mean age 58 exposed to systemic antibiotics | VSL#3 probiotic, 450 x 109 cfu/day (n=117)Placebo (n=112)Treatment duration: antibiotic duration plus 7 daysFollowup: 28 days | Treatment group: 14/117Placebo: 16/112 |
| Pozzoni, 2012[73](#_ENREF_73)ItalyHospital | 275 adult hospital inpatients exposed to antibiotics without ongoing diarrhea or recent use of probiotics, mean age 72 | *S. boulardii,* within 48 hours of starting antibiotic therapy (n=141)Placebo (n=134)Treatment duration: antibiotic duration plus 7 daysFollowup: 12 weeks | Treatment group: 52/141Placebo: 42/135 |
| Gao, 2010[74](#_ENREF_74)ChinaIndustry | 255 adult inpatients exposed to antibiotics, aged 50-70, without active diarrhea or CDI within 3 months, mean age 60 | *L. acidophilus* CL1285 and *L. casei* LBC80R, 100 x 109 CFU/day (n=86)*L. acidophilus* CL1285 and *L. casei*, LBC80R, 50 x 109 cfu/day (n=85) within 36 hours of starting antibiotic therapy until 5 days after discontinuation; antibiotic duration 3-14 daysPlacebo (n=85)Followup: 21 days after last study drug dose | Treatment group: 1/171Placebo: 2/84 |
| Lonnermark, 2010[75](#_ENREF_75)SwedenFunding NR | 239 adults (137 inpatients) treated for infections, mean age 45 | *L. plantarum* 299v, 10 x 109 cfu/day, within 48 hours of starting antibiotic therapy until 7 days after discontinuation (n=118)Placebo (n=121)Followup: ≥1 week after last study drug dose | Treatment group: 3/80Placebo: 3/83 |
| Psaradellis, 2010[76](#_ENREF_76)CanadaIndustry | 437 adults (248 inpatients) prescribed antibiotics, mean age 59 | *L. acidophilus* CL1285 and *L. casei*, 25 x 109 CFU/day ,for 2 days then 50 x 109 cfu/day until 5 days after discontinuation of antibiotic (n=233)Placebo (n=239)Followup: 21 days after last study drug dose | Treatment group: 87/216Placebo: 99/221 |
| Safdar, 2008[77](#_ENREF_77)United StatesIndustry NR | 40 adult inpatients, elderly U.S. veterans exposed to antibiotics, mean age 69 | *L. acidophilus*, 60 x 109 cfu/day during and 14 days after antibiotic course (n=23)Placebo (n=17)Followup: NR | Treatment group: 2/23Placebo: 5/17 |
| Beausoleil, 2007[78](#_ENREF_78)CanadaIndustry | 89 adult inpatients who were anticipated to take systemic antibiotics, mean age 71 | *L. acidophilus* CL1285 and *L. casei*, 25 x 109 cfu/day for 2 days, then 50 x 109 CFU/day for antibiotic duration (n=44)Placebo (n=45)Followup: 21 days after last study drug dose  | Treatment group: 21/44Placebo: 20/45 |
| Duman, 2005[79](#_ENREF_79)TurkeyFunding NR | 204 adults who received 14 days triple therapy for *Helicobacter pylori* eradication, mean age 45 | *S. boulardii*, 30 x 109 cfu/day for antibiotic duration (14 days) (n=204)No treatment (n=185)Followup: 4 weeks after last study drug dose | Treatment group: 3/196No treatment: 4/180 |
| ***Newly identified observational study*** |  |  |  |
| Maziade, 2013[80](#_ENREF_80)CanadaOpen prospectiveHospital | 31,832 hospitalized patients receiving antibiotics, mean age NR  | Standard care (n=1580)Standard care plus *L. acidophilus* CL1285and *L. casei* LBC80R 50-60 × 109 cfu/day (n= 4968)Treatment duration: minimum 30 days or antibiotic duration Study duration: 6 years | No serious adverse events |
| Bakken, 2014[81](#_ENREF_81)Unites StatesNone | 25 patients with recurrent CDI | Staggered and tapered antibiotic withdrawal regimen with orgal ingestion of 5 oz probiotic liquid kefir 3 times per day.Followup: up to 1 year | 4/25 relapsed within 9 months.No serious adverse events reported. |
| ***Previously identified trials*** |  |  |  |
| Hickson, 2007[82](#_ENREF_82)United KingdomFoundation | 135 adult inpatients, mean age 74 | *L. casei immunitas* DN-114 001, 19 x 109 CFU/day; *L. bulgaris*, 1.9 x 109 cfu/day; and *S.thermophiles*, 19 x 109 cfu/day within 48 hours of starting antibiotic therapy until 7 days afterdiscontinuation (n=69)Placebo (n=66)Followup: 4 weeks after last antibiotic or study drug dose | Treatment group: 0/56Placebo: 0/53 |
| Can, 2006[83](#_ENREF_83)TurkeyFunding NR | 151 adult inpatients aged 25-50, mean age NR | *S. boulardii*, lyophilized 20 x 109 cfu/day ≤48 hours of antibiotic start dose (duration of study drug course NR) (n=73)Placebo (n=78)Followup: 4 weeks after last antibiotic dose | No serious adverse events |
| Plummer, 2004[84](#_ENREF_84)United KingdomFunding NR | 150 older adult inpatients | *L. acidophilus* and *Bifidobacterium bifidum*, 20 x 109 cfu/day within 36 hours of starting antibiotic therapy, for 20 days (n=69)Placebo (n=69)Followup: Last day of study drug dose | NR |
| Thomas, 2001[85](#_ENREF_85)United StatesIndustry | 302 adult inpatients, mean age 56 | *L. rhamnosus* GG, 20 x 109 cfu/day within 24 hours of starting antibiotic therapy, for 14 days (n=152)Placebo (n=150)Followup: 7 days after last study drug dose | Treatment group: 37/133Placebo: 52/134 |
| Lewis, 1998[86](#_ENREF_86)United KingdomHealth organization | 72 older adult inpatients, mean age 74 (range 70-85) | *S. boulardii,* 113 mg (n=33)Placebo (n=36) | NR |
| McFarland, 1995[87](#_ENREF_87)United StatesFunding NR | 193 adult inpatients, mean age 41 | *S. boulardii* lyophilized, 30 x 109 cfu/day within 72 hours of starting antibiotic therapy until 3 days after discontinuation (n=97)Placebo (n=96)Followup: 7 weeks after last study drug dose | Treatment group: 0/93Placebo: 12/92 |
| Surawicz, 1989[88](#_ENREF_88)United StatesIndustry | 318 adults inpatients (n=138 had CDI tested), mean age 48 | *S. boulardii* lyophilized, 20 x 109 cfu/day within 48 hours of starting antibiotic therapy until 2 weeks after discontinuation (n=212)Placebo (n=106)Followup: mean 17 days | Treatment group: 0/116Placebo: 0/64 |

CDI=C. difficile infection; NR=not reported
\* No serious adverse events reported that were attributed to probiotic treatment.