**Lynne McFarland Probiotic Dataset**

**For randomized controlled trials published 1977-2017
Probiotic interventions for selected disease indications**

**Data extracted from published randomized controlled trials or meeting abstracts. Supplementary data indicated by colored font from author(s) of paper or from manufacturer website. Trials with multiple study arms in one study are indicated by grey rows. Data entered in chronological order and by mode (prevention or treatment) and by disease indication.**

**All errors are the responsibility of Dataset creator/administrator (Lynne McFarland).
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## Common abbreviations:

[other abbreviations may be found in table footnotes]

**AAD**: antibiotic associated diarrhea

**B. or Bif.:** Bifidobacterium

**CDI:** *Clostridium difficile* infections

**cfu:** colony-forming units (number of microbiologic colonies)

**F/up:** follow-up post-probiotic intervention

**IBS:** irritable bowel disease

**IBD:** inflammatory bowel disease

**L.:** Lactobacillus

**mon**: months

**nr:** not reported

**ns:** not significantly different from controls (P>0.05)

**S.:** Saccharomyces

**VSL#3**: 8-strain mixtures of:*3 Bifido (longum and infantis and breve) +4 Lacto. (acidophilus and casei and delbrueckii and plantarum) and Strept thermophilus.*

# Prevention

## Allergies: Prevention

Atopic dermatitis (atopic eczema) defined as a type of inflammation of the skin (itchy, red, swollen) and was diagnosed by physician by standard criteria.

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| **+/-** | **Probiotic**  | **Daily dose (cfu/day) and to whom**  | **Population studied, country and (attrition)** | **Duration (& follow-up)** | **Probiotic outcome:AD** | **ControlsAD** | **Reference** |
| + | *Lactobacillus rhamnosus* GG (ATCC 53103)  | 2 x 1010Capsules to mothers (2-4 wks before delivery), then 6 mon post-natally if breast feeding. If not-just powder in liquid to babies to 6 months | 159 mother infant pairs enrolled with family history of allergy; 132 done (17% attrition ) FINLAND | 6 monthsF/up: 1.5 yr [until 2 yrs old] | By aged 2 yrs:atopic dermatitis15/64 (23%) P<0.05 | placebo 31/68 (46%)  | **Kalliomaki** M 2001Lancet  |
| - | *Lactobacillus rhamnosus* GG (ATCC 53103)  | 2 x 1010/d | young adults with birch allergy and apple allergy 38 enrolled, 31 done (18% attrition)FINLAND | 5.5 months  during 1999 pollen seasonF/up: none | Change in allergic rhinitis symptoms scores: +7.8 (-0.8, +16.4) NS | Placebo +13.6(+3.2, +23.9) | **Helin** T 2002 Allergy |
| - | *Lactobacillus rhamnosus* GG (ATCC 53103)  | 1 x 1010/d to mothers(4-6 wks pre delivery, then 3 mon) and to babies 3 mon- 6 mon old | 105 pregnant women with family history of AD, 94 done (10% attrition)GERMANY | 7.5 wksF/up: until babies were 2 yrs old | At 2 yrs:14/50 (28%) babies developed Atopic dermatitis, NS | At 2 yrs:placebo 12/44 (27%) | **Kopp** MV 2008Pediatrics |

+/-, positive efficacy or negative (not significant) efficacy; AD: atopic dermatitis; cfu, colony-forming units; F/up, follow-up; NS, not significantly different; mon, months

## Antibiotic-associated diarrhea (AAD): Prevention

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AAD typically defined as: diarrhea (>3 loose/watery stools/d for >2 days) associated with antibiotic exposure or <8 weeks post-antibiotic discontinuation (delayed onset).

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| **+/-** | **Probiotic** | **Population** | **Daily dose** | **Duration** | **AAD in Probiotic** | **AAD** **in controls** | **Reference** |
| *+* | *S. boulardii*vs placebo | 388 hospitalized adultsFRANCE | 4 x 109**capsules** |  7 daysF/up: nr | **AAD**:4.5%\*9/199 | AAD17.5%33/189 | **Adam** J 1976Gaz Med Fra |
| *+* | *S. boulardii*vs placebo | 240 adults on oral antibioticsPORTUGAL | 4 caps/d, dose nr in full paper**capsules** | 6 days,F/up: 0 | **AAD** (>2 BM/d):19/121 (15.7%)\* | placebo:33/119 (27.7%) | **Monteiro** E 1981Acta Med Port |
| *+* | *Enterococcus faecium* SF68 | 200 adults with tuberculosis | nr | 60 daysF/up: nr | **AAD**:5/100 (5%)\* | 18/100(18%) | **Borgia** M 1982Curr Ther Res |
| *+* | *Entero. faecium* SF68vs placebo | 1323 adults on antibiotic  | 2 caps/dcfu nr**capsules** | 7 daysF/up: nr | **AAD**:57/661 (9%)P<0.001 | 107/662 (16%) | **Frigerio** G1986 Dig Dis Sci31(10 Suppl):496SMtg Abstract only |
| *+* | *S. boulardii*vs placebo | 180 hospitalized adults | 2 x 1010**capsules** | 28 daysF/up: mean of 17 days | **AAD**:9.5%\*11/116  | 21.8%14/64 | **Surawicz** CM 1989 Gastroenterol |
| *-* | *Enterococcusfaecium* SF68 | 45 adult patients | 1.5 x 107 | 7 daysF/up: nr | **AAD**:8.7% ns2/23 | 27.2%6/22 | **Wunderlich** PF1989 J Int Med Res |
| *+* | *S. boulardii*vs placebo | 193 hospitalized adults (1 or more beta-lactam antibiotics) | 2 x 1010**capsules** | duration antibiotic plus 3 days,F/up: 7 wks  | **AAD**: 7.2%\*7/97On abx 5/97(5.1%) ns post abx2/92 (2.3%) | AAD:14.6%14/96On abx 8/96 (8.3%) post abx6/84 (7.1%)p=0.15 | **McFarland** LV 1995Am J Gastro |

\*, P<0.05; AAD, antibiotic-associated diarrhea; abx, antibiotics; AE, adverse events; cfu, colony-forming units; F/up, follow-up; nr, not reported; NS, not significantly different; mon, months; txt, treatment; wks, weeks

**AAD page 2**

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| **+/-** | **Probiotic** | **Population** | **Daily****dose** | **Duration** | **AAD in Probiotic** | **AAD****in controls** | **Reference** |
| *-* | *S. boulardii*vs placebo | 72 enrolled, (4% attrition) done: 69 elderly (>65 yrs old) inpatients on abx(70-85 yrs old)U.K. | 4.5 X 109226 mg/d**capsules** | duration abx(mean 7 days)F/up: 0 | **AAD**:7/33 (21%) ns p=0.53 | AAD: 5/36 (13.9%) | **Lewis** SJ 1998J Infect |
| **-** | *L. rhamnosus GG “*Gefilus*”* whey drink vs milk control | 59 children (5 mon-11 yrs) outpatients, for otitis media, all on amoxicillinFINLAND | 8 x 1010200 ml/d**drink** |  7 daysF/up: 0 | **AAD**26% ns6/23 | milk control22%8/36 | **Vaisanen** ML 1998 AbstractMicro Ecol Health & Dis |
| **+** | *L. rhamnosus* GG vs placebo | 167 children (2 wks-13 yrs old) enrolled, 119 done (29% attrition due to long f/up)66% ampic.outpatients with URT Infections (26%) or otitis media (74%)FINLAND | 4 x 1010**capsules** | duration abx. (mean=7-10 days) follow-up: 3 months APP | **AAD** 3/61 (5%) \* | **AAD** 9/58 (16%) | **Arvola** T1999Pediatrics |
| **-** | *S boulardii versus control (diosmectitic-anti-spasmodic)*double blinded | 779 enrolled, 616 done, children (1-5 yrs) with resp infection, mix of antibiotics, outpatients**(21% attrition)**FRANCE | 4.5 x 109226 mg/d**capsules** | Abx durationmean=8 + 2 daysF/up: 0 | **AAD**:25/327 (7.6%), p=0.29 ns | anti-spasmodic control:16/289 (5.5%) | **Benhamou** PH 1999 Med Chir Dig |
| **+** | *L. rhamnosus* GG + inulinvs placebo | 202 children enrolled (6-120 mon old) outpatients on mix of abx, 188 done (**7% attrition)USA** | 1-2 x 1010**capsules** | 10 daysF/up: 0APP | **AAD**7.5%\*(7/93)p=0.001duration: 4.7 d | inulin & placebo:26%(25/95)duration:5.9 days | **Vanderhoof** JA1999J Ped |

**AAD- page 3**

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| **+/-** | **Probiotic** | **Population** | **Daily****dose** | **Duration** | **AAD in Probiotic** | **AAD****in controls** | **Reference** |
| *-* | *L. rhamnosus* GGvs placebo | 302 enrolled, 267 done (11.6% attrition)adult inpatients | 2 x 1010**capsules** | 14 daysF/up: nrAPP | **AAD** (29.3%) 39/133 ns | AAD (29.9%)40/134 | **Thomas** MR2001Mayo Clin Proceed |
| *+*  | *Lactobacillus rhamnosus GG "*GiFlorex*"* vs nothing. open study | 120 asymptom. Hp+ carriers Hospital staff, adults.May-July 1999, one site, 117 done (2.5% lost) All on triple therapy for 7 days: (claritho, pantoprazole, tinidazole)ITALY | 1.2 x 1010**Sachet** | 14 daysF/up: 6 wksITT | **AAD**: 8/60 (13.2%) P<0.001**Hp-:** 48/60 (80%), p=0.6**Any AE**: 26 (43%) p=0.04 | controlAAD: 29/60 (48.2)Hp-: 46/60 (76.6%)Any AE: 37 (62%) | **Armuzzi** A2001 **A** Digestion |
| *+* | *Lactobacillus rhamnosus GG "*GiFlorex*"* vs placeboblinded studyAll on triple therapy for 7 days(claritho, rabeprazole, tinidazole) | 60 asymptom. Hp+ carriers Hospital staff, adults.Sept 1999-Jan 20000% attritionITALY | 1.2 x 1010**Sachet** | 14 daysF/up: 6 wksITT | **AAD:** 1/30 (3.3%), p=0.01 10%\***Hp neg**:25/30 (83.3%) p=1.0**Any AE**: 12/30 (40%)\* p=0.04 | placebo:AAD: 8/30 (26.6%)Hp-: 24/30 (80%)Any AE:20/30 (67%) | **Armuzzi** A2001 **B**Alim Pharm & Therapeutics |

**AAD page 4**

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|  | **Probiotic** | **Population** | **Daily****dose** | **Duration** | **AAD in Probiotic** | **AAD****in controls** | **Reference** |
| *-* | *L. rhamnosus* GG vs placebo | 42 *H. pylori* + on triple therapy, adults | 6 x 109 | 7 daysF/up: 4 wks  | **AAD**:5% ns 1/21 p=0.09 | 30%6/21 | **Cremonini** F 2002B Amer J Gastroenterol |
| *+* | *S. boulardii*vs placebo | 43 *H. pylori* + on triple therapy, adults | 5 x 109 | 7 daysF/up: 4 wks  | **AAD**:5%1/22\*p=0.046 | 30%6/21 | **Cremonini** F 2002B Amer J Gastroenterol |
| *+* | *L. acidophilus* La5 + *Bifido animalis* subsp *lactis* Bb12 [*Strept thermo* *L. bulgaricus*yogurt “AB Yogurt” vs ‘no yogurt’ control- | 160 outpatient adults *H. pylori* + (mean age 48 yrs)all on triple therapy (2 abx + PPI)open design,not blinded,no placebo | 1 x 1010 | 4 wks F/up: 4 wks  | **AAD**:2/80 (2.5%)p=0.03 | no txt control: AAD10/80 (12.5%) | **Sheu** BS 2002Ali Pharm Ther |
| *+* | *Clostridium butyricum* MIYAIRIvs no txt controls | 110 children,[72 completed] (1-180 months), on mostly cephalosporins or penicillin for URT or gastro infection(34% attrition)JAPAN | 1-4 x 107 **capsules** |  6 daysF/up: 0  | **AAD**:6/86 (7%)\*Claim “normalizes GI flora disturbed by Abx” & more anaerobes | no txt control, not blinded59%16/27 | **Seki** H 2003Pediatr Intl |
| *+* | *S. boulardii*vs nothing for each abx group:No placeboOpen trials | 466 children (1-15 yrs old)on sulbactam-ampicillin (SAM) or on azthromycin (AZT), outpatients(TURKEY | 250 mg/d5 x 109**sachets** | during abxF/up: 2 wks post abx | **AAD**:7/117 (5.7%) on SAM\*but 7/127 AZT, ns | 30/117 (25.6%) SAM only.12/105 (11.4%) AZT only | **Erdeve** O 2005J Trop Ped |

**AAD page 5**

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| **+/-** | **Probiotic** | **Population** | **Daily dose** | **Duration**  | **AAD in Probiotic** | **AAD in controls** | **Reference** |
| + | *S. boulardii*vs placebo.with otitis media or resp infectionsonly 36% power | 269 children (6 mon-14 yrs) enrolled, 246 children finished(8.6% attrition), in and outpatientPOLAND | 1 x 1010500 mg/d**wafers** | Varied during abx. 7-9 d (Sb) & 5-13 d (placebo)F/up: 2 wks | **AAD**: 9/119 (8%)\*onset: 4.8 + 2.5 (2-8 days)excluding rotaviral:4/119 (3.4%) | **AAD**:29/127 (23%)onset: 4.9 + 3 (1-11 days)excluding rotaviral:22/127 (17.3%) | **Kotowska** M2005Ali Phar Ther |
| *-* | *C. butyricum* MIYAIRI 588 vs no probiotic control | 35 *H. pylori*+ adults all with 1 week triple therapyJAPAN | 120 mg tid, cfu/d nr | 2 wksF/up: 6 wk | **AAD** 5/18 (27.8%)p=0.09Hp neg: 13/17 (94%) ns | AAD 10/17 (58.8)Hp neg: 13/17 (73%) | **Shimbo** I 2005 World J Gastroenterol |
| *+* | *S. boulardii*“Reflor”, Sanofi-Sythelabo) vs ‘no Sb’ control (no placebo) | adults peptic ulcers on abx.389 enrolled, 376 completedall given Hp+ triple therapy (amox+clarithro+PPI)in 9 hospitalsTURKEY | 1 x 10101 gram/d | 2 wks &F/up: 4 wks | **AAD**:14/204 (6.9%\*)p=0.007AAD on Abx (86%) | AAD:28/185 (15.1%)AAD on Abx (75%) | **Duman** DG 2005 Eur J Gast Hepta |
| *+* | *S. boulardii*vs placebo | 151 adult inpatients | 1 x 1010 | duration abxF/up: ~10 days post-abx | **AAD**: 1.4%\* (1/73)1 case on abx (day 2 of abx)postabx 0% p=0.06 | 9.0%(7/78)On abx: 2/78 (2.6%) & post-abx (5/76, 6.6%) 5-10 days  | **Can** M 2006Med Sci Monit |
| *-* | *"*AB Yogurt"*L acidophilus La5 + Bif. animalis subsp lactis Bb12*[starters: *L. bulgaricus + Strept thermophilus*].vs no txt controlAll on **quadruple** therapy (AmoxMetroOmeBs) (7 days) | 138 adults who failed triple Hp therapy with ulcers or gastritis, 129 done (6% attrition)TAIWAN | 400 ml/d4 x 1011/d**Yogurt**single blinded (Hp assessor) | 4 wksF/up: 6 wks & 3 months if neg at 6 wks.ITT | **AAD:** 9/69 (8.7%) p=0.053 Chi2Hp-:59/69 (85%)\*P=0.04Any AE**:** patient level data nr | **AAD:** 18/69 (26%)Hp-:49/69 (71%)Any AE**:** nr | **Sheu** BS2006Am J Clin Nutri |

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|  | **Probiotic** | **Population** | **Daily****dose** | **Duration** | **AAD in Probiotic** | **AAD in controls** | **Reference** |
| *+* | *L. casei DN114001[L. bulgaricus)S. thermophilus]*Actimel drinkvs Yazoo (milkshake) | 135 adult inpatients (>50 yrs old) on abx, 112 completed (16% attrition)89/135 (66%) on high risk antibiotics (Table 1) | 1.9 x 1010per day**drink** | durationabx + 1 weekF/up: 0APP | **AAD** 7/57 (12.3%)\*p=0.006if on Abx: 4 (6.2%) nspost-Abx:3 (5.7%) P=0.003 | placeboAAD 19/56 (33.9%)if on Abx;5 (8.1%) ns, p=0.74post-abx: 14 **(**27.5**%)** p=0.003peak 8 d | **Hickson** M2007Brit Med J |
| *+* | “Lacidofil”*L. [acidophilus] helveticus R52 + L. rhamnosus* R11 vs open controls | n=34 children (10 mon-3 yrs old) with resp tract infections on abx.**UKRAINE** | 2-4 x 109/d [depends on age]**capsules** | 2-4 weeks varied on antibiotic durationF/up: nr | **AAD:** 2/16 (12.6%) p<0.05**duration diarrhea**: 2.6 + 1.1 p<0.05 | open controls AAD: 8/18 (44.8%)**duration**:5.9 + 1.2 d | **Marushko** YV2007Perinatol & Paediatrics |
| *-* | *L. rhamnosus GG* vs. placebo(maltodextrine)All given 7 d of 2 abx (amox and clarithr) and PPI | 83 kids (5-17 yrs old)., 64 done (23% attrition) inpatients*H. pylori +* eradication,.**POLAND** | 1 x 109 /d **capsules** | 7 daysF/up: 6 wks APP | **AAD**: 2/34 (6%) NS*H pylori* neg: 23/34 (69%) NS  | AAD:6/30 (20%)Hp- : 22/32 (68%)  | **Szajewska** H 2009 J Ped Gastroenterol & Nutrition |
| *+* | “Lacidofil”*L. helveticus* R0052 + *L. rhamnosis* R0011vs open controls | n=36 children with cystic fibrosis on abx (<1 yr old) | 1 capsule bid-tid varied by age range**capsule** | variedF/up: nr | **AAD**:1/18 (5.5%)p<0.05 | open**AAD**:5/18 (28.9%) | **Aryayev** M2009Odessa Med JMtg abstract |

**AAD page 7**

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|  | **Probiotic** | **Population** | **Daily****dose** | **Duration** | **AAD in Probiotic** | **AAD****in controls** | **Reference** |
| *+* | *“BioK+”(L. acido CL1285 + L. casei LBC80R + L. rhamnosus CLR2)* vs placebo milk | 89 hosp adults (mean >59 yrs old) on a variety of abx1 hospitalin Quebec **CANADA** | 5 x 1010 **milk**ITT | 8-10 d, duration of antibiotic,F/up: 21 d  | **AAD**: 7/44 (15.9%)\*p=0.03**AE**: 21(48%) | **AAD**16/45 (35.6%)**AE**: 20 (44%) | **Beausoleil** M 2007 Can J Gastroestopped early cuz she got her Masters and graduated |
| *+* | *S. boulardii* (“Reflor”) in Turkey BCX, vs nothing; both on triple therapy, open | 124 adults outpatients with *H. pylori* + dyspepsiaTURKEY | 2 x 1010(1g/d)**sachets** | 2 wks F/up: 6 wks  | **AAD**:9/62 (14.5%)\*Hp- (71%) nsCDI 6/62 (9.7%) p=0.8 | 19/62 (30.6%)Hp- 60%CDI 8/62 (12.8%) | **Cindoruk** M2007Helicobacterblue: data from author |
| *-* | *S. boulardii* vs placebo | 86 adult outpatients on amoxicillin (5-10 d) | 1 x 1010 /d | 12 daysF/up: 9 days 4% power | **AAD**: 3/41 (7.3%) p=0.72**duration diarrhea**: 11.4 +2.0 d | AAD: 5/45 (11.1%)duration: 11.5 + 2.2 d | **Bravo** MV 2008 RevMed Chiletranslated from Spanish |
| *-* | *C. butyricum* CBM588 (low dose) vs control | 19 adults with GI ulcers and H. pylori +unclear if outpatient or inpatientJAPAN | 6 **tablets** cfu/d not reported | 1 weekF/up: 0 | **AAD**:single dose 1/12 (8.3%)ns | No probiotic control:AAD3/7 (43%) | **Imase** K 2008 Microbiol Immunol |
| *-* | *“Lacidofil”(L helveticus R52+L. rhamnosus R11)* | not randomizedin 45 childrenUkraine | 4 x 109**capsules** | 3 wkF/up: 1 wk | **AAD** 2/25 (8%) p=0.06 | 7/20 (35%) | **Gnaytenko** O 2009Prac Med |

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| **+/-** | **Probiotic** | **Population** | **Daily dose** | **Duration** | **AAD in Probiotic** | **AAD****in controls** | **Reference** |
| *-* | *L rhamnosus GG* vs placebo | N=316 inpatient adults on antibioticsCANADA | 1.2 x 1011 /d | 14 daysF/up: 4 wks | **AAD**: 8/157 (5.1%), p=0.18**AE**:4/157 (2.5%) ns | **AAD**: 4/159 (2.5%)AE: 0/159 (0%) | **Miller** M 2008**B**Meeting Abstract ICAAC Washington DC  |
| *+* | “Lacidofil WM”*L. helveticus R52 + L. rhamnosus R11* | n=96 adult women with C-sections and cefotaxime pre-op abx. | 6 x 109/d (3 caps/d)**capsules** | 7 daysF/up: none | (n=56)**AAD**: 0/56 (0%) p<0.05 | (n=40)**AAD**: 4/40 (10%) | **Liskovich** VV2010Health |
| *-* | *S. boulardii* (Bioflor) vs S.b. + mucoprotective agent (DA9601) vs control. All on triple therapy | Adultoutpatients, N=991, *H. pylori*+outpatients**Korea** | 3 x 1010**capsules** | 4 wksF/up: 4 wks | Sb only: **AAD** 11/330 (3%) p=0.14Sb+mucop agent: 9/330 (3%), n=0.06 | AAD in control:20/331 (6%) | **Song** M2010Heliobacteria |
| *-* | *“Lacidofil” capL. rhamnosus (Rosell-11) + L. helveticus (Rosell-52)vs placebo caps* | 214 adults (>18 yrs old) on abx<48 hrs for resp infections in 10 hospitals KOREAITT analysis | 2 x 109/cap**capsules** | within 48 hrs for 14 days.No f/up | **AAD** 4/103 (3.9%), ns CDI data, NS | AAD:8/111 (7.2%) | **Song** HJ2010 Gastr & Heptaol |

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|  | **Probiotic** | **Population** | **Daily****dose** | **Duration** | **AAD in Probiotic** | **AAD****in controls** | **Reference** |
| *+* | *BioK+ (L. acido CL1285 + L. casei LBC80R +L. rhamnosus CLR2) low dose (1 capsule) vs placebo* | (Oct 2008-Mar 2009)255 eligible adults (50-70 yrs old) on pen, ceph, clindaat 1 hospital**Shanghai** | Low dose (1 cap/d) 5 x 1010**capsule** | duration abx’s (3-14 days plus 5 more daysFollowed 21 days more. | **Low** dose Bio-K AAD 24/85, (28.2%) p=0.02Duration AAD: 4.1+ 1.5\* d**Abd pain:** 24.7% ns | placebo (n=84)AAD 37/84 (44.1%)Duration= 6.4+ 1.8 daysAbd pain: 40.5% | **Gao** XW 2010 Amer J Gastroenterol |
| *+* | *BioK+ (L. acido CL1285 + L. casei LBC80R +L. rhamnosus CLR2) high dose: 2 capsules vs placebo* | High dose(2 caps/d)1 x 1011 **capsule** | **Higher** dose (2 caps)**AAD** 13/86, (15.5%) P<0.001)(duration=2.8 + 0.8\* d)**Abd pain**: 12.8% | **Gao** XW 2010 Amer J Gastroenterol |
| *trend* | *“BioK+”(L. acido CL1285 + L. casei LBC80R + L. rhamnosus CLR2)*  vs placebo, Screened 2151, 1679 excluded (recent abx, vanco or metro) | 472 randomized, 437 done (8% attrition)Adults (>18 yrs old) on 3-14 days antibiotics (77% b-lactams) In 8 Canadian hospitals 3/2006-10/07.CANADA | 5 x 1010/d fermented **milk** | within 48 hours of abx—to 5 days post-abx (mean 12 days, ranging 29-40 days)F/up: 21 dAPP | **AAD** (>2 days diarr)47/216 **(21.8%,)**p=0.067**Duration** AAD= 0.67 + 20 d p=0.04**AE**: 33.3% ns | **AAD**65/221**(29.4%)**Duration AAD= 1.2 + 3.2d**AE**: 34.4% | **Sampalis** J &Dylewski J 2010 Arch Med Sci |

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**AAD—page 10**

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|  | **Probiotic** | **Population** | **Daily dose** | **Duration** | **AAD in Probiotic** | **AAD in controls** | **Reference** |
| *+* | *S boulardii* + 14 day triple therapy (Amox+Clarthirtho+Lansoprazole)vsControls (triple therapy only) | N=223 Hp+ randomizedadultsKOREA | dose nrform nr | 2 weeksF/up: 4 weeks by 13C-urea testITT | **AAD**: 32/107 (29.9%)\*P=0.041**erad**: 73/107 (**68.2**%) p=0.905 NS | AAD: 50/116 (43.1%)erad: 80/116 (69.0%) | **Lee** JY2011J Gastro & HepatolMtg Abstract.2011; 26(S5):257Asian Pacific Digestive Week, 1-4 October 2011, SUNTEC Singapore |
| *-* | *L. acidophilus LA-5 + Bifido. lactis Bb-12* vs 2 control groups | 88 *H pylori*+ outpatient adults (18-65 yrs old), asymptomatic, given triple therapy at wk 5 GERMANY | 2 x 109/dfruity **yogurt** | 8 weeksF/up: 0  | **AAD**:5/30 (16.7%), ns against either controls | AAD heat killed yogurt 2/29 (7%) or milk control (8/29, 27%) | **de Vrese** M 2011 J Diary Res |
| *-* | *S. boulardii*CNCM I-745(Biocodex )vs placebo | Hospitalized adults (>50 yrs) at Lucco Hosp in Italy, 4/2009-7/2010. Of 562 eligible, only 275 (49% randomized),204 done , 71 (26**%** attrition), not ITTITALY | 1 x 1010/d lost 35 in SB group and 36 in placebo (~1/2 due to death, but ~1/2 due to lost to follow-up or stopped txt – | during antibiotics and 7 more daysF/up: 12 wks  | **AAD** 16/106 (15.1%, NS, mean onset 36 days.Chi=0.14, p=0.70mean diarrhea **duration**=2.5 dCDI3/106 (2.8%), p=0.84Died 12.7% ns | AAD13/98 (13.3%)mean onset= 16 dayspower=4%Duration:=3 daysCDI2/98 (2%)Power=3%Died 15.6% | **Pozzoni** P & Riva A2012Am J GastroNotes:no data on compliance26% attrition-no comparison with other AAD studies. |

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| *+/-* | **Probiotic** | **Population** | **Daily dose** | **Duration** | **AAD in Probiotic** | **AAD in controls** | **Reference** |
| *-* | *S. boulardii* (Lab Biocodex)All had triple therapy (Amox+clarithro + omeprazole) for 14 days | 100 Hp+ adults with peptic ulcers,One hospital0% attritionCHINA | ~5 x 109/dvs no txt control**Sachet** | 14 days F/up:  1 yrITT | **AAD** 3/50 (6%) NS **Hp-:** 42/50 (84.4%)\*p=0.04all AE : 8/50 (16%)\* p<0.001 | AAD: 8/50 (16%) p=0.2Hp-: 32/50 (64.4%)all AE: 34/50 (68%) | **Chu** Y 2012African J Pharmacy & Pharmacology |
| *-* | "PY" Probiotic yogurt. Strains not defined- emailed author. emailed author. He replied yogurt was: *Lactobacillus acidophilus* La5 + *Bifido. bifidum* Bb12. vs non-probiotic yogurt control (blinded) vs no yogurt control (open) | 102 Hp + adultssymptomatic,[18-85 yrs old]88 done (14% attrition) Both double blinded controls and open (no txt) controls All had triple therapy (Amox, Clarithro, Pantoprazaole for 7 days)IRAN | nr cfu/day in paperresponse in author email on dose: ~2 x106/d300 mg/d**yogurt** | 7 daysF/up: 4 weeksAPP analysis | **AAD**: 7/31 (22.6%) ns Hp erad:19/31 (61%)NS Any AE:20/31 (64%) ns | Non-probiotic yogurt:  AAD: 8/31 (25.8%) p=0.77Hp-: 20/31 (64.5%) p=0.79Any AE: 21 (68%) p=0.79No yogurt control:AAD: 8/26 (30.8%) p=0.48 Hp-: 19/26 (73.1%) p=0.35Any AE: 22 (85%)p=0.13 | **Mirzaee** V 2012Iranian Red Crescent Med Jdata from author in email |
| *+* | *S. boulardii* vs open control All got TT (AmoxClarithOmep)x 14 days. | n=82 Hp+childrenpeptic ulcers (n=33) or chronic gastritis (n=49)CHINA | 250 mg/dcfu/d nr | 2 wksF/up4 wks | **AAD**: 5/41 (12.2%)\*p<0.05**AE:** 5/41 12.2%\* less | AAD: 13/41 (31.7%)Open cntrl:AE: 13/41 (31.7%) | **Zhang** Y2012J Clin Pediat*[In Chinese]* |

 **AAD page 11**

**AAD page 12**

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| ***+-*** |  | **Population** | **Dose/day** | **Duration**  | **AAD in SB** | **Controls** | **Reference** |
| *+* | *S. boulardii* lyo vs 'no treatment' controls | 333 children (6 mon-14 yrs old) Resp infections, inpatients, 283 done,(50% attrition)CHINA | 1 x 1010/d**powder** | for 2 weeks F/up: 2 wks | **AAD** (11/139, 7.9%) p<0.001 | AAD (42/144, 29.2%) | **Shan** L2013Bene Micro |
| *-* | *S. boulardii* vs nothing as controlsJune-October 2012St Louis Hosp open design | 140 children (6 mon-18 yrs). 136 done (3% attrition),in or outpatients, IV or oral abxPHILLIPINES | 500 mg/d1 x 1010 /dform nr | duration of antibioticF/up: not specifically stated ~ within 2 weeks of abx | **AAD**:11/66 (16.7%) p=0.39duration= 2.45 + 0.7 days, p=0.03 | **AAD**:16/68 (23.5%) duration= 3.06 + 0.68 days | **Casem** RAO2013Phili Infect Dis Soc Proceed Journal 2013;14:70-76dose from author |
| *+* | “Yomogi”*S. boulardii*All had triple txt Amox-Clarythro-lam x 14 days vs nothing | 160 *H. pylori* + adults with gastritisat 1 hospitalIRAN | 1 x 1010/d**capsules** | 2 wksF/up: 8 wksITT | **AAD**: 27/80 (33.8%) p=0.04by end of week 10 | Open controls:58/80 (72.5%) | **Zojaji** H2013Gastro & Hepatol |
| *-* | *L. rhamnosus* GG vs placebo | 59 Hp+ symptomatic adults(>18 yrs old)0% attritionAll had triple therapy:Amox/Clarith/Omep (7 days)Single blinded (outcome assessor)VENEZUELA | 1.2 x 1010per day**"Vial"** | 2 weeksF/up: 0ITT | **AAD**: 4/29 13.8% nsp=0.73**Any AE**: 10/29 (34.4%) ns | AAD: 6/30 (20%)Any AE: 10/30 (33.3%) | **Padilla** Ruiz M2013Rev Gastroent Perutranslated[in Spanish]  |
| *+* | *S. boulardii* CNCM I-745"UltraLevure" vs no txt **controSingle blinded** (Patients unaware of other txt arm) | Adults with dyspepsia. Of 125 screened, 70 enrolled (aged 18-75 yrs old at one Greek hospital) 60 done (14% attrition)Both groups got triple therapy ( amoxicillin (2 g/d), clarithromycin (1g/d), & omeoprazole (40 mg/d) For 14 days. GREECE | 300 mg/d 6 x 106/d**Capsule**[50 mg with 106 cfu/cap] | 14 daysF/up:6 wksITT | **AAD**:1 (2.8%)\* p=0.026**Hp-:** 30/36 (83.4%)\*, p=0.034 | **AAD**: 7 (20.6%)**Hp-:** control 20/34 (58.8%) | **Kyriakos** N 2013 Hosp Chronicles |

**AAD- page 13**

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| **+/-** | **Probiotic** | **Population** | **Daily****dose** | **Duration** | **AAD in Probiotic** | **AAD****in controls** | **Reference** |
| *-* | Mix of *L. acid.* La5 + *Bifido. lactis* Bb12 vs placebo | N=396 adults (18-70 yrs old) given 7 days of abx for URTIoutpatients at 4 hospitalsINDIA | Dose nr in abstract | 14 daysF/up: nr in abstract | **AAD** (21/198)10.8% p=0.2  | AAD(31/198)15.6% | **Chatterjee** S2013J Asso Physician India |
| *-* | *S. boulardii* vs open control All got TT (AmoxClarithOmep)x 14 days. | n=60 Hp+childrenwith chronic gastritisCHINA | 500 mg/d | 2 wksF/up:4 wks | **AAD**: 0/30 (0%)p=0.11**Erad:**27/30 (90%)\*p<0.05**AE**: sign less but data in Chinese | Open cntrl: AAD: 4/30 (13.3%)**Erad**20/30 (66.7%)AE: raw data? | **Zhang** H 2013Med J Chinese People Health*[In Chinese]* |
| - | *L. acidophilus La-5 + Bifido. bifidum Bb-12* vs no txt control.All had triple:[Amox or Metro] + Clarith + Omeprazole(14 days) | 100 Hp+childrensymptomaticone site – a GI clinic88 done(12% attrition)Jan 2009-June 2010CHINA | if **<**5 yrs old: 1 x108/dif > 5 yrs old:2.1 x 108/d**Sachets** | 6 wksF/up:none!”APP | **AAD**: 3/43 (7%) p=0.7 ns**Hp-:** 36/43 (83.7%)\**X2*=4.3p=0.04**AE**: 5/43 (11.6%) p=0.07 | AAD: 5/45 (11.1%)Hp-:29/45 (64.4%) AE: 12/45 (26.7%) | **Wang** YH2014WJ Microbiol Biotech[data supplied by author email]not funded |
| + | *S. boulardii"*Bioflor"vs no txt controlAll had triple(Amox/Clarith/Omeproz) (14 days) | 240 children Hp+(5-11 yrs old) with gastritis, ulcers or inflammation0% attritionCHINA | 500 mg/d1 x 1010**Capsules** | 14 daysF/up: 4 wksITT | **AAD**: 27/120 (22.5%)\* p=0.008 **Hp**-: 102/120 (85%) ns p=0.07**AE**: nr | AAD: 47/120 (39.1%)Hp-:91/120 (75.8%) | **Zhao** HM2014Zhongguo Dang Dai Erke Za Zhi[in Chinese] |

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| **+/-** | **Probiotic** | **Population** | **Daily dose** | **Duration**  | **AAD in Probiotic** | **AAD in controls** | **Reference** |
| *+* | *L. casei* defensis DN114001 "Actimel" (Danone) vs *L. casei* Shirota "Yakult" (Yakult) | 60 inpatients, adults at 1 hospital, mostly (80%) resp and GU infections, mixed types of abx 60% ampicillin or cephalosp) No attrition reportedGERMANY | "Actimel":2 x 1010/d **drink**vs"Yakult"2 x 1010/d**drink** | duration abx(mean 6 days)F/up: 0ITT | L. casei DN114001**AAD**2/30 (6.7%)p=0.02 | *L. casei* ShirotaAAD10/30 (33.3%) | **Dietrich** CG2014World J Gastroenter  |
| *+* | *S. boulardii*CNCM I-745vs. no treatment controlsAll had triple erad therapy: AmoxClarrithOmeprazole or Metro ClarOmp if allergic to Amox x 14 days | N=205 enrolled, Hp+children(22 months-16 yrs)n=194 done (5.4% attrition)CHINA | 1 x 1010/d500 mg/d**sachets** | 14 daysF/up:4 wks 13C urea breath test in subgroup of 42 kids>12 yrs old | **AAD**: 12/102 (11.8%) p=0.004**Any AE**: nrCompliance to std ther 100%p=0.03 | AAD: 26/92 (28.3%)Complaince: 86/92 (93.4%) | **Bin** Z 2015Ped Gastroentero, Hepatol & Nutrition |
| *-* | *“Lacidofil”Lacto. helveticus R52 + Lact. rhamnosus R11*vs placebo | Phase 2 safetyn=160 healthly adultsAll received Amox-clavu for 1 weekCANADA | 8 x 109/day**capsule** | 2 weeksF/up:7 wks | **# AAD:**19/76 (**25%**) p=0.3ITT AAD on Abx: 8/77 (10%) nsPost-Abx: 12/77 (16%)ns p=-.32**duration of diarrhea=**2.7 + 0.4 days p=0.04AE 9(12%)  | #AAD:23/70 (33%) ITT AAD on Abx: 9/78 (11%) Post-Abx: 17/78 (22%)duration of diarrhea=3.7 + 0.4 daysAE 20 (28%) | **Evans** M2016Br J Nutr |

**AAD page 14**

**AAD-page 15**

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|  | **Probiotic** | **Population** | **Daily****dose** | **Duration** | **AAD in Probiotic** | **AAD****in controls** | **Reference** |
| *-* | **"SacBo Trial"***Saccharo. boulardii*[Perenterol Forte®]HANSEN CBS5926vs placebo[Manufactured by UCB Brussels, Belgium]due to low enrollment, RCT stopped prematurely at interim analysisLow rate of AAD explained by authors: 1) ‘young’ pop enrolled (mean 60 yrs), 2) any abx included, not just high risk patients3) high attrition | Adults (mean age: 60 Sb and 56 placebo yrs) inpatients at 15 hospitals in Germany (07/2010-10/2012) receiving systemtic antibiotics *(80% beta-lactams*)Screened 2444enrolled N=477 enrolled, **292** done (39% attrition)Phase 3 trialGERMANY | 1.8 x 1010/d**capsules**Attrition high (n=185 dropped due to incomplete diaries) | duration of antibiotic (mean 8 days)plus 7 daysMax. txt was set at 8 weeks.F/up: 6 weeksITT and PP | Sb **AAD** ITT: 21/246 (8.5%)P=0.6p=0.26 by episode [21 episodes]**3% power**Onset AAD=18.4 d**AE:** 18/245 (7.3%)Time in study same:44.1 + 22.5 days, p=0.26 | placebo**AAD** ITT:17/231 (7.4%) [19 episodes of AAD](2 had 2 episodes)Onset AAD=18.9 dAE:12/222 (5.4%)time in study: 44 + 22 days | **Ehrhardt** S2016Open Forum Infect Dis Poor study conduct due to: 1) high attrition rate due to incomplete diaries;2) 13 patients did not receive correct study drug assignment,3) #episodes used not #patients with AAD4) low power due to early termination of study5) survival curve not provided |
| *+* | *S. boulardii* CNCM I-745vs open, no intervention control.Randomized | n=163 older inpatient adults on broad-spectrum antibiotics Jan 2014-Dec 2015**CHINA** | 1 g/day(1 x 1010 cfu/d)**capsule** | for 21 daysF/up: not in abstract | **AAD**: 12/81 (14.8%) \* P<0.05**Duration**: 3.0 + 1.1 days\* | **AAD**: 23/82 (28.0%) **Duration**5**.**7 + 1.8 days | **Zhang** DM2017Zhonghua Nei Ke Za Zhi [in Chinese] |

##  Clostridium difficile infections (CDI)- Primary prevention

CDI are due to a spore-forming gram positive anaerobe (*C. difficile*) and diagnosis was based on detection of *C. difficile* toxins along with new onset of symptomatic diarrhea not due to medications or other chronic GI conditions.

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| ***+/-*** | **Probiotic** | **Population** | **Daily dose** | **Duration** | **CDI in Probiotic** | **CDI in Controls** | **Reference** |
| ***-*** | *S. boulardii* CNCM I-745 vs placebo1 hosp41% single abx., 36% cephalo | 318 enrolled, inpatientsadults 180 done (43% attrition) [64 ineligible, 74 dropped]USA | 2 x 1010within 48 hrs1 g**capsules** | duration + 14 daysF/up: Mean of 17 daysAPP | **CDI**:3/116 (2.6%)p=0.13*26.5% power**Of 48 CD toxin+, 3/32 (9.4%) CDI* | placebo:5/64 (7.8%)*Of 48 toxin +, 5/16 (31%) CDI p=0.07* | **Surawicz** C1989 GastroenteroPrevention of AAD study |
| ***-*** | *S. boulardii*CNCM I-745vs placebo4 hosp | 208 enrolled, 193 eligible all inpatientsadults on beta-lactam abx, 18% single antibiotics129 done (38% attrition)USA | 3 x 1010within 72 hrs1 g/d**capsules** | duration + 3 days7 wk f/upAPP | **CDI**3/97 (3.1%) ns p=0.72*2.6% power*but only 133 were tested for CDOf 10 toxin+, 3/10 (30%) CDI, 7 carriers | CDI:4/96 (4.2%)Of 14 toxin +, 4/14 were CDI and 10 were carriers, p=0.46 ns | **McFarland** L1995 AJGPrevention of b-lactam AAD study |
| ***-*** | *S. boulardii* CNCM I-745 vs placebo1 UK hosp | 72 enrolled, 69 done (4.2% attrition), **elderly** (>65 yrs old)inpatientson abx (most multiple abx, nr types)U.K. | 4.5 x 109within 24 hrs226 mg/d**capsules** | duration (mean 7 d),no f/upAPP | **CDI**: 5/33 (15%) p=0.47 ns*7.2% power* | CDI:3/36 (8.3%) | **Lewis** SJ 1998J InfectPrevention of AAD study |

**Primary CDI prevention-page 2**

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| ***+/-*** | **Probiotic** | **Population** | **Daily****dose** | **Duration** | **CDI in Probiotic** | **CDI in Controls** | **Reference** |
| ***-*** | *L. rhamnosus* GG vs placebo | 167 children(2 wks-13 yrs old) enrolled, 119 done (29% attrition due to long f/up)66% ampic.outpatients with URT Infections (26%) or otitis media (74%)FINLAND | 4 x 1010**capsules** | duration abx. (mean=7-10 days) F/up: 3 months APP | **CDI**1/61 (1.6%) NS p=1.0*10% power* | 1/58 (1.7%) | **Arvola** T 1999Pediatrics |
| ***-*** | *L. rhamnosus GG* vs placebo1 hosp | 302 enrolled, 267 done(11.6% attrition)Adult inpatients18-93 yrs old07/06-10/9969% b-lactamsUSA | 2 x 1010within 24 hrs**capsules** | 2 wksF/up: 1 wkAPP | **CDI**2/133 (1.5%) ns p=1.0*power 2.7%* | placebo3/134 (2.2%) | **Thomas** MR 2001 Mayo ClinicProcedures(Prevention of AAD) |
| ***-*** | *S. boulardii*CNCM I-745vs placebo wafers3 Polish Ped hosp and 2 outpatient clinics enrolled from 11/2002-05/200441% cephalo. | 269 enrolled children6 mon-14 yrs oldinpatient (27%) & outpatients on abx for resp (68%) or otitis media (29%)246 done (8.5% attrition)POLAND | 1 x 1010500 mgwithin 24 hrs**wafers** | duration (mean 7 days),no f/upAPP | **CDI**3/119 (2.5%)ns p=0.09*35.9% power* | placebo10/127 (7.9%) | **Kotowska** M 2005 APTPrevent AAD study |

**Primary prevention of CDI-page 3**

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| ***+/-*** | **Probiotic** | **Population** | **Daily****dose** | **Duration** | **CDI in Probiotic** | **CDI in Controls** | **Reference** |
| ***-*** | *S. boulardii* CNCM I-745 vsno txt controlsAll received triple therapy (Amox/Clarith/Omepr x 2wks)9 hospitals | 389 outpatient adults Hp+ with PUD.376 done (3.3% attrition)TURKEY | 1 x 1010/d1 g/d**capsules** | duration abx (mean=2 weeks)F/up: 4 weeksITT | **CDI**:0/204 (0%)p=0.48*3.3% poweronly those with diarrhea tested for Cdiff (n=5)* | open controls:1/185 (0.5%)*only 11 with diarrhea tested for Cdiff* | **Duman** DG2005Euro J Gastro Hepat |
| ***-*** | *S. boulardii* CNCM I-745vs placebo1 hosp | 151 inpatient adults(25-50 yrs old), 151 done, on abx (83% beta-lactams)TURKEY | 1 x 1010**capsules** | duration of abxF/up: 4 wksITT | **CDI**: 0/73 (0%) ns p=0.50, *9.1% power* | Placebo CDI:2/78 (2.6%) | **Can** M 2006Med Sci Monitor |
| ***-*** | "Bio-K+"*L. acido* CL1285 + *L. casei LBC80R + L rhamnosus CLR2* fermented milk vs placebo milk1 hosp Quebec | 89 enrolled, inpatient adultson varied Abx (59% quinolones) for 92% resp infections0% attrition09/03-05/04 CANADA | 5 x 1010 within 48 hrs**milk** | duration of abx (mean 7-8 days)F/up:21 daysITT | **CDI**1/44 (2.3%) P=0.06TREND*44.2% power*AE n=21 (48%) ns | placebo milk7/45 (15.6%)AE: n=20 (44%) | **Beausoleil** M 2007CJGPrevention of AAD study |
| ***-*** | *S. boulardii*  CNCM I-745 (Reflor) in Turkey BCX, vs nothing; both on triple therapy | 124 adults with *H. pylori* + dyspepsia | 2 x 1010(1g/d) | 2 wks with 6 wk f-up | **CD** toxin+:6/62(9.7%) | Control CD toxin +: 8/62 (12.9%) | **Cindoruk** M 2007not blinded |

**Primary prevention of CDI-page 4**

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| ***+/-*** | **Probiotic** | **Population** | **Daily****dose** | **Duration** | **CDI in Probiotic** | **CDI in Controls** | **Reference** |
| ***pos*** | *L. casei* DN 114001 ‘immunitass’ + [*L. bulgaricus + Strept. thermophilus]*(Actimel drink) vs placebo milkshake,3 London hospitals | 135 inpatient adults > 50 yrs old109 done (19% attrition) 11/02-01/0561% single abx, 66% on high risk antibiotics (amoxicillin or cephalosporins)for 49% respiratory infectionsU.K. | 2 x 1010within 48 hrs (200 g)**drink** | duration of abx + 1 weekF/up: 4 wkAPP | **CDI**:0/56 (0%) p=0.001 *80.8% power*1o outcome was 7/57 (12.3%) AAD | placebo9/53 (17%)1o outcome was19/56 (33.9%) AAD | **Hickson** M 2007 BMJ Prevention AAD studyEstimated cost of preventing one case of CDI with probiotic: $120.00.  |
| Letters to BMJ on the Hickson 2007 paper. Criticisms:(1) Of 1760 screened, only 112 completed (only 7% potential target population). [**Wilcox** MH 2007 BMJ Letters](2) No high risk Antibiotics given. [**Hillyard** T 2007 BMJ letters]Actually only recent prior use of high risk antibiotics were excluded in 4 weeks prior to enrollment. During the study 66% did receive high risk antibiotics.  | **see above** |
| ***-*** | *L rhamnosus* GG vs placeboPILOT study | 189 adults (>18 yrs old) inpatients receiving mixed types of antibiotics: b-lactams, pen, ceph (50%), single/multipleCANADA | 4 x 1010**capsules**(within 72 hrs of abx)Primary outcome: prevent CDIITT | duration abxx=14 days, 30 days of f/up | **CDI** 4/95 (4.2%) NS p=0.37*9.2% power*No difference in AE (2.1%)  | placebo (7/94, 7.4%)AE (4.2%) | **Miller** M 2008**A**48th ICAAC mtg abstract K-4200.Study #1*Same abstract, but 2 pilot studies reported* |
| ***-*** | *L rhamnosus* GG vs placebo[triple of the LGG dose of previous and larger study]stopped early | 316 adults (>18 yrs old) inpatients receiving mixed types of antibiotics: ceph (~50%), quinolones, IV vanco, metro 69% single abx.CANADA | 1.2 x 1011**capsules**Primary outcome: prevent CDIITT | duration abx: x=14 days, (within 72 hrs of abx. Start)30 days of f/up | **CDI**2/157 (1.3%) ns P=0.25*11.2% power*AE: 2.5%, ns | placebo (0/159, 0%)AE: 0% | **Miller** M 2008**B**48th ICAAC mtg abstract K-4200.Study #2 *Same abstract, but 2 pilot studies reported* |

**Primary prevention of CDI-page 5**

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| ***+/-*** | **Probiotic** | **Population** | **Daily dose** | **Duration** | **CDI in Probiotic** | **CDI in Controls** | **Reference** |
| ***-*** | *S. boulardi*  CNCM I-745 vs placebo1 hospital88% resp. infections | 86 adults on amoxicillin, outpatients, 82 done (4.6% attrition)CHILE | 1 x 1010(500 mg/d)**capsules** | 12 daysF/up: 9 days ITT | **CDI**n=0/41 (0%)p=1.0 | CDI in placebo:0/45 (0%) | **Bravo** MV 2008 Rev Med Chioriginal in Spanish-translated |
| ***low dose pos*** | BioK+ (L. *acidophilus* CL1285 + *L. casei* LBC80R *+ L. rhamnosus* CLR2) vs placebo1 Shanghai hosp  | 255 inpatients adults (50-70 yrs) Jan-March 2009. Randomized to low dose (9% attrition) or high dose (7% attrition) vs controls 47% resp infectionsMixed abx: cephl (37-41%), pen or clindaCHINA | **Low** dose (5 x 1010/day)within 36 hours**capsule** | During abx (3-14 days) plus 5 daysF/up: 21 days ITT | **CDI**:Low dose:8/85 (9.4%) p=0.03*power 64.0%* | Placebo20/84 (23.8%) | **Gao** XW2010AJG[also **Musher** D 2009 IDSA abstract] |
| ***high dose pos*** | **High** dose (1 x 1011/d)within 36 hours**capsule** | High dose1/86 (1.2%) p=0.002power *99.2%* |
| ***-*** | BioK+ (L. *acidophilus* CL1285 + *L. casei* LBC80R *+ L. rhamnosus* CLR2)vs placebo fermented milks*Screened 2151, 1679 excluded (recent abx, vanco or metro)* 8 hospitals | 472 adults randomized, 437 done (7.4% attrition) 57% inpatients[35 excluded cuz too short on abx or diarrh at enrollment] on 3-14 days antibiotics (78% b-lactams), 39% had resp infec, 3/2006-10/07CANADA | 5 x 1010/d within 48 hours**milk** | duration + 5 days post-abx (mean 12 days txt) , range of txt: 29-40 days.F/up: 21 dAPP | **CDI**1/216 (0.5%), p=0.40 ns*12.5% powerOnly total of 46 screened for C diff!*Sub-group of CD+: CDI  1/16 (6.2%) ns p=0.64 | n=2214/221 (1.8%)Sub-group of CD+ only:CDI: 4/30 (13.3%) | **Sampalis** J,Psaradellis E et al. 2010Arch Med Sci**incorrectly cited** Dylewski J 2010 Arch Med Sci 2010also as:Ki 2008 Mtg abstract Am Coll Gast Oct 2008 |
| *+* | *L rhamnosus GG* vs placebo*Not all on antibiotics-only 50 (34%) with VAP (author email)mixed abx(nr types)* | 146 adult inpatients in ICU on mechanical ventilation (high risk),138 done, 5% attritionUSA | 4 x 109**capsule** | duration of intubation (mean 15 days)F/up: noneAPP | **CDI**4/68 (5.8%)p=0.02*power 52.9%*# on abx: n=33 | CDI13/70 (18.6%)# on abx: n=17 | **Morrow** LE 2010Am J Resp Crit Care Med |

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| *+/-* | **Probiotic** | **Population** | **Daily****dose** | **Duration** | **CDI in Probiotic** | **CDI in Controls** | **Reference** |
| ***-*** | *S. boulardii*( CNCM I-745 Biocodex) vs placebo1 hospital69% single abx | 275 inpatient adults on variety of antibiotics, 204 done (26% attrition)ITALY  | 1 x 1010[within 2 days of antibiotic]**capsules** | while on abx +7 daysF/up: 12 wk APP | **CDI**3/106 (2.8%) nsp=1.0*power 3%* | CDI placebo2/98 (2%) | **Pozzoni** P2012Amer J Gastroprimary outcome AAD |
| ***+*** | *S. boulardii* lyo CNCM I-745 vs ‘no treatment’ controlswith acute lower resp infections, 52% on ceph1 hospital | 333 inpatient children (6 mon-14 yrs old) with resp infections, 283 done [50 dropped] (15% attrition)CHINA | 1 x 1010/d[500 mg/d]**powder** | duration of abx: mean=2 weeksF/up: 2 wksAPP | **CDI**(1/139, 0.72%) p=0.04*51.9% power* | open controls:CDI(8/144, 5.6%)  | **Shan** L2013 Beneficial Microbes  |
| ***-*** | *L. casei* defensis DN114001 "Actimel" (Danone)vs*L. casei* Shirota "Yakult" (Yakult) | 60 inpatients, adults at 1 hospitalmostly (80%) resp and GU infections, mixed types of abx 60% ampicillin or cephalosp) No attrition reportedGERMANY | "actimel":2 x 1010/d**drink**vs"yakult"2 x 1010/d**drink** | duration abx(mean 6 days)F/up: noneITT | *L. casei* DN114001**CDI**:0/30 (0%)p=0.24*power 21.3%*  | *L. casei* Shirotacontrol:**CDI**:3/30 (10%) | **Dietrich** CG2014World J Gastroenter |

**Primary prevention of CDI-page 6**

**Primary prevention of CDI-page 7**

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| *+/-* | **Probiotic** | **Population** | **Daily dose** | **Duration** | **CDI in Probiotic** | **CDI in Controls** | **Reference** |
| *-* | **"SacBo Trial"***Saccharo. boulardii*[Perenterol Forte®]HANSEN CBS5926 *(aka*  CNCM I-745) vs placebo[Manufactured by UCB Brussels, Belgium]due to low enrollment, RCT stopped prematurely at interim analysis | Adults (mean age: 60 Sb and 56 placebo yrs) inpatients at 15 hospitals in Germany (07/2010-10/2012) receiving systematic antibiotics *(80% beta-lactams*)Screened 2444enrolled N=477 enrolled, 292 done (39% attrition)Phase 3 trialGERMANY | 1.8 x 1010/d**capsules**[within 2 days of antibiotic]Attrition high (n=185 dropped due to incomplete diaries**)** | duration of antibiotic (mean 8 days)plus 7 daysMax. txt was set at 8 weeks.F/up: 6 weeksITT and PP | Sb **CDI**: 2/246 (0.8%) ns**AE:** 18/245 (7.3%) | Placebo:**CDI**: 2/231 (0.9%)low rate!AE:12/222 (5.4%) | **Ehrhardt** S2016Open Forum Infect Dis Poor study conduct due to: 1) high attrition rate due to incomplete diaries;2) 13 patients did not receive correct study drug assignment,3) low power due to early termination of study |
| *-* | *S. boulardii* CNCM I-745vs open, no intervention control.Randomized | n=163 older inpatient adults on broad-spectrum antibiotics Jan 2014-Dec 2015CHINA | 1 g/day(1 x 1010 cfu/d)**capsule** | 3 weeksF/up: 9 weeks | (N=81)**CDI**: 3/81 (3.7%) ns | (N=82)**CDI**: 4/82 (4.9%) | **Zhang** DM2017Zhonghua Nei Ke Za Zhi[in Chinese] |

## Enteral feeding: prevention of diarrhea

Definition of outcome=days of diarrhea (score-based on >3 nonformed stools/day) while on enteral nutrition.

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| **+/-** | **Probiotic** | **Population** | **No.**  | **Dose** | **Duration** | **Outcome****in Probiotic** | **Oucome****in controls** | **Reference** |
| + | *S. boulardii*I-745 | adults in ICU | 40ITT | 5 x 109/d | 11-21 days | 34/389 (8.7%)\* diarrhea days | 63/373 (16.9%) days | **Tempe** JD1983 Sem Hop Paris |
| + | *S. boulardii*I-745 | burnt adults 18-70 yrs | 20 enrolled, 18 done | 2 g/d2 x 1010/d | 8-28 days | 3/204 (1.5%\*) days | 19/208 (9.1%) days | **Schlotterer** M1987 Nutr Clin Metabol |
| + | *S. boulardii*I-745 | adults | 131 enrolled, 128done | 2g/d2 x 1010/d | 21 days | 91/650 (14%)\* days | 134/705 (19%) days | **Bleichner** G1997Intens Care |

**Abbreviations**ICU=Intenstive Care Unit; \*p<0.05

## Helicobacter pylori trials: prevention of adverse reactions

Outcome defined as any adverse reaction (nausea, diarrhea, abdominal pain, vomiting, etc.) associated with triple or quadruple treatments for the eradication of *H. pylori*.

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| **+/-** | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Dose/day** | **Duration**  | **Incidence of any adverse reaction in probiotic** | **Any adverse reaction in controls** | **Reference** |
| *+* | *Lactobacillus rhamnosus GG "*GiFlorex*"* vs nothing. All on triple therapy for 7 days: (claritho, **pantoprazole**, tinidazole) | Hp+ carriers Hospital staff, adults.May-July 1999, one site, 117 done (2.5% lost) ITALY | n=120 | 1.2 x 1010**Sachet** | 14 daysf/up: 6 wks | 26 (43%) p=0.04  | 37 (62%) | **Armuzzi** A2001 **A** Digestion |
| *+* | *Lactobacillus rhamnosus GG "*GiFlorex*"* vs placebo**blinded** studyAll on triple therapy for 7 days(claritho, **rabeprazole**, tinidazole) | asymptom. Hp+ carriers Hospital staff, adults.Sept 1999-Jan 20000% attritionITALY | n=60 | 1.2 x 1010**Sachet** | 14 daysf/up: 6 wks | 12/30 (40%)\* p=0.04 | 20/30 (67%) | **Armuzzi** A2001 **B**APT |
| *+* | **RCT with three txt arms:***L. rhamnosus GG"*Giflorex" vs placeboAll triple therapy(7 days) ClaRanTin | adultsasymptomatic41 done (5% attrition placebo, 0% LGG)ITALY | n=42 | 1.2 x 1010**sachets** | 14 daysf/up: 5-7 wks | 3/21 (14%)p=0.004 | 12/20 (60%) | **Cremonini** F 2002 AJG |
| *+* | *S boulardii"*Codex"vs placeboAll triple therapy(7 days) ClaRanTin  | adults40 done(5% attrition in placebo, 9% Sb)ITALY | n=42 | 1 x 1010 **sachets** | 14 daysf/up: 5-7 wks | 3/21 (14%)p=0.004 | 12/20 (60%) |

**Prevention of AE due to *H. pylori* treatments-page 2**

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| **+/-** | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Dose/day** | **Duration**  | **Incidence of any adverse reaction in probiotic** | **Any adverse reaction in controls** | **Reference** |
| *-* | *SB "*Reflor*"*Randomized, OPEN trial(SB vs nothing)Triple txt (amox, clarithro, omeprazole)for 14 days | adults with peptic ulcers (3% attrition)TURKEY | 384 enrolled, 376 done | 1 x 1010/d **Capsules** | 2 wks, Follow-up: 4 wks | 3 (1.5%) ns | 3 (1.7%) | **Duman** DG 2005Euro J Gastro & Hept |
| *+* | *L. acido +L. rhamnosus* vs controls (triple therapy only)“Lacidofil”All got 10 days of triple therapyAmoxClarith +PPI | children(7-18 yrs old) with H. pylori dyspepsia or ulcers POLAND | n=60 | 6 x 109/d**Capsules** | 20 daysF/up: 7 wks | 1/30 (3%) p=0.002\* | ]11/30 (38%) | **Plewinska** E 2006Gastroenterol Poltranslated in Polish notes from author |
| *+* | *S. boulardii("*Reflor", Biocodex)vs placebo.All got triple therapy (ACL)(14 days) | outpatientsTURKEY | n=1240% attrition | 2 x 1010/d**Sachets** | 2 weeksF/up: 6 wks | 14/62 (23%)\* P<0.001 | 37/62 (60%) | **Cindoruk** M 2007Helicobacter |

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|  | P**revention of AE due to *H. pylori* treatments-page 3** |
|  | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Dose/day** | **Duration**  | **Incidence of any adverse reaction in probiotic** | **Any adverse reaction in controls** | **Reference** |
| *+* | *"*Lacidofil*"L. helveticus R0052 + L. rhamnosus* R0011 vs no txt controlAll got triple therapy (OmeAmoxClarith)for 7 days | adultsgastritis or ulcersUKRAINE | n=490% attrition | 8 x 109/d**capsules** | 10 daysF/up:4-6 wks | 1(4%)\*p=0.049 | 6/24 (25%) | **Vdovychenko** V2008[Current Gastroenterol] translated[In Ukrainian][data from company] |
| *+* | *S boulardii* (Enterol, Biocodex)vs no txt controlAll had triple therapy (Omer or Eso [3 wks] & Amox/Clar)(7-10 days) **Single blinded** (outcome assessor) | symptomatic children 3-18 yrsROMANIA | n=90 | 1 x 1010**Capsule** | 4 wksfup: 4-6 wks | 4/48 (8%)\*p=0.047 | 13/42 (31%) | **Hurduc** B 2009 Act Paed |
| *-* | *L. rhamnosus GG* vs placeboall had triple therapy (amox and clarithr and Omeprazole) for 7 days | childrenasymptomatic *Hp +* inpatientsPOLAND | n=8366 done (20% attrition | 2x 109 **Capsule** | 7 daysF/up:6 wks | 18/35 (51%) ns p=0.8 | 13/32 (41%) | **Szajewska** H 2009 JPGN |
| *-* | **2 txt arms:***S. boulardii vs*vs no txt control.All got triple therapy OAC(7 days) **Single blinded** (UBT outcome assessor) | 991 adultsHp+ symptomatic (ulcer, gastritis)SOUTH KOREA | n=991932 done | 2.2 x 1010**Capsule** | 4 wksF/up:4 weeks | 48/330 (14.5%) p=0.12 | 63/331 (19%) | **Song** MJ 2010Helicobacter |
| *+* | *S. boulardii +* **mucoprotective agent** (extract of *Aartemisia asiatica*)  |  | 30/330 (9.1%) \* p<0.001 |

**Prevention of AE due to *H. pylori* treatments-page 4**

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| **+/-** | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Dose/day** | **Duration**  | **Incidence of any adverse reaction in probiotic** | **Any adverse reaction in controls** | **Reference** |
| *+* | ***Concomitant****S. boulardii* and triple therapy x 7 days, *controls*: triple therapy only x 7 daysopen (no placebo)TT: Amox + Clarith + rabeprazolefor 7 days | 135 Hp+adults >18 yrs oldactive gastritis9/2010-02/2012CHINA | n=85 | 1.5 x 1010/d**capsule** | 7 daysF/up:4 wks | 16/41 (39%) p=0.02 | 28/44 (63.6%) | **Gao** C, Xie R Ma T, Wu S.2012Chin J Gastroentero.I**n Chinese** |
| *+* | *S. boulardii* (Lab Biocodex)All had triple therapy (Amox+clarithro + omeprazole) for 14 days | Hp+ adults with peptic ulcers CHINA | n=100 | ~5 x 109/d **Sachet** | 14 days F/up:  1 yr | 8/50 (16%)\* p<0.001No SAE | 34/50 (68%) | **Chu** Y 2012African J Pharmacy & Pharmacology |
| *+* | All got TT (AmoxClarithOmep)x 14 days.randomized to:*S. boulardii* vs open control | Hp+childrenpeptic ulcers (n=33) or chronic gastritis (n=49)CHINA | n=82  | 250 mg/d | 2 wksF/up4 wks | 5/41 12.2%\*  | 13/41 (31.7%) | **Zhang** Y2012J Clin Pediat*[In Chinese]* |
| *-* | *L. rhamnosus* GGvs placeboAll had triple therapy:Amxo/Clarith/Omep (7 days)**Single blinded** (outcome assessor) | adults(>18 yrs old)symptomaticVENEZUELA | n=59 | 1.2 x 1010per day**"Vial"** | 2 weeksF/up: none | 10/29 (34.4%) ns |  10/30 (33.3%) | **Padilla** Ruiz M2013Rev Gastroent Perutranslated[in Spanish]  |

## Necrotizing enterocolitis (NEC)- prevention

NEC outcome was new onset of Bell’s stage 2 or 3, but stage not reported in all studies.

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| **+/-** | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Dose/day** | **Duration**  | **Incidence of NEC (Bell’s stage) in probiotic** | **NEC (stage) in controls** | **Reference** |
| *-* | *L. rhamnosus GG* | preterm neonates(<33 wks or <1500 g) | 585 | 6 x 109 | 48 d(until discharge) | NEC (nr)4/295 (1.4%) nsp=0.26 | NEC (nr)8/290 (2.7%) | **Dani** C 2002Biol Neonate |
| *-* | *S boulardii* CNCM I-745 in formula vs control (maltodextrin) | pretermneonates(28-32 wks old)GREECE | 87 | 2 x 109/d | 30 d | NEC (nr)5/51 (9.8%)p=0.51 | NEC (nr)6/36 (16.7%) | **Costalos** C 2003Early Human Devel |
| *+* | *Bifid. infantis, Strept. therm, Bifid bifidus “*ABC Dophilus” formula vs control formula | <1500 gISRAEL | 145 | 1 x 109 | 36 wks | NEC(> 2):1/72 (4%)p=0.01died: 3/72 (4.2%) ns | NEC(> 2):10/73 (16.4%)died:8/73 (11%) | **Bin-Nun** A2005J Pediat |
| *-* | *L. rhamnosus GG“Dicloflor”* | neonates (<1500g) in NICU | 80 | 6 x 109 | from day 3 of life to 6 wks | NEC (> 2)1/39 (2.5%)p=0.62 | NEC (> 2)3/41 (7.3%) | **Manzoni** P 2006Clin Infect Dis |
| *-* | *Bifido. lactis* Bb12 | Pre-term neonates (<37 wks)  | 69 | 4.8 x 109 | 21 d | NEC (> 2)2/21 (9.5%)p=1.0 | NEC (> 2)1/17 (5.9%) | **Mohan** R 2006J Clin Microbiol |
| *+* | *Bifido. bifidum NCDO1453+ L. acidophilus NCDO1748“Infloran”* | low BW(<1500 g) neonates o<34 wks oldTAIWAN | 434  | 2 x 109/d | 6 wks | NEC(> 2): 4/217 (1.8%)\*p=0.03 | Control formulaNEC(> 2): 14/217 (6.5%) | **Lin** HC2008Pediatrics |
| *+* | *L. casei subsp rhamnosus* GGvs placeboBoth with bovine lactoferrin too | infants <1500 gITALY | n=319 | 6 x 109/d**formula** | 4 wks | NEC2:0/151 (0%)\* | NEC210/168 (6%) | **Manzoni** P2009JAMA |

Abbreviations: NEC, necrotizing enterocolitis; NICU, neonatal intensive care unit; NS, not significant; VLBW, very low birth weight

**NEC- page 2**

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| *+/-* | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Daily dose** | **Duration** | **Incidence of NEC**  | **NEC in Controls** | **Reference** |
|  | *Bifido lactis* Bb12 vs placebo | Neonates (<30 wks or <1500g)VLBW | 183 | 1.2 x 1010/d | 6 weeks | NEC (nr)2/93 (2.1%) ns | NEC (nr)4/90 (4.4%) | **Mihatsch** WA2010 Neonat |
|  | *L. reuteri* DSN 17938 “BioGaia AB” vs placebo | Neonates (<2000 g) in NICU | 750 | 1 x 108drops | until discharge | NEC (2)9/372 (2.4%) p=0.23 NS | Placebo:NEC (2)15/378 (4%) | **Rojas** MA2012Pediatrics |
| *-* | *S. boulardii*  CNCM I-745 in formula ("Reflor" France)vs control formula (no SB)Oct 2010-Nov 2011 Turkey | Prematureinfants (<1500 g & age <32 wks old) | n=208 | 1 x 109cfu/kg/d | duration hosp stay | NEC (> 2)7/104 (6.7%) NSsepsis: 28.8% nsNo AE | NEC (> 2)7/104 (6.7%)sepsis:23% | **Serce** O 2013Early Human Develop |
| *+* | ‘ProPerms trial’“ABC Dophilus”*:Bifido. infantis, B. lactis, Strept. thermos* vs placebo powder | < 32 wks & <1500 g | 1,099ITT | 1 x 109(1.5 g)powder | 40 wks of life or until discharge | NEC(> 2): 11/548 (2%), p=0.03Died 4.9% NS | NEC(> 2):24/551 (4.4%)Died 5.1% | **Jacobs** SE2013Pediatrics |
| *-* | *S. boulardii*  CNCM I-745 in formula ("Reflor" France)vs control formula (no SB)March-Nov 2011 Turkey | Prematureinfants <1500 g & age <32 wks old | n=278 randomized n=271 done (3% attrition) | 5 x 109/diven in breast milk or formula | duration hosp stayF/up: none | NEC (nr): 4.4% of 135, NSSepsis: 35%, p=0.03died: 3.7% nssepsis significant!: 34.8%, p=0.03 | NEC (nr): 5.1% of 136.Sepsis: 48% Died: 3.6%sepsis 47.8% | **Demirel** G 2013Acta Paediatr |

**NEC page 3**

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|  | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Daily dose** | **Duration** | **Incidence of NEC**  | **NEC in Controls** | **Reference** |
| *+* | **3 txt arms:***(1) L. rhamnosus* GG + bovine lactoferrin (LGG-BL) (2) control: just lactoferrin (BL) vs (3) placebo | VLBW infants in ICUmultisite Italy and New Zealand | 743 | 6 x 109 | Until discharge or day 30 | **NEC**(LGG-BL): 0/238 (0%), p<0.001 | **NEC** (bovine lactoferrin control): 5/247 (2%), p=0.06**Placebo**:NEC 14/258 (5.4%) | **Manzoni** P2014Early Hum Dev |
| *-* | “Infloran”*L. acidophilus* nr + *Bifido. bifidum* nr | neonates <34 weeks & BW <1500 gThailand | 60 | 2 x 109capsule in liquid | 6 wks | NEC(> 2):1/31 (3.2%) nsAE: none | NEC(> 2):1/29 (3.4%) | **Saengtawesin**V 2014J Med Asso Thai |
| *-* | *L. reuteri* DSN17938“BioGaia AB”vs placebo | neonates | n=400 | 1 x 108per dayformula | duration hosp stay | NEC(> 2):8/200 (4%) NS | NEC (> 2):10/200 (5%) | **Oncel** MY2014Arch Dis Child Fetal Neona Edu |
| *-* | *L. reuteri* DSN17938“BioGaia AB”vs nystatin | neonates | n=300 | 1 x 108per dayformula | duration hosp stayF/up: none | NEC(> 2)7/150 (4.7%) nsSepsis: 7.3% p=0.03 | NEC:(> 2)9/150 (6%) Sepsis: 14.7%  | **Oncel** MY2015J Mat Fet Neona Med |
| *+* | *L. reuteri protectis* DSM17938 “BioGaia”vs control | preterm infants28-32 wks or 1400-1800 g BWIRAN | N=60 | 4 x 107/d | until first enteral feed | **NEC** (nr):2/30 (6.7%)\***Sepsis:**4 (13.3%)\***Died:**1 (3.3%) ns | **NEC** (nr):11/30 (36.7%)**Sepsis:**10 (33.4%)**Died:**2 (6.7%) | **Nouri** Shadkam M2015Iran J Neonat |

## Nosocomial Infections-prevention

Nosocomial infections defined as new onset of disease>48 hours after admission

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| **+/-** | **Probiotic** | **Given to** | **Dose and Duration** | **Outcome and Effect in Probiotic group\*** | **Effect in Control group** | **Reference** |
| - | *L rhamnosus GG* | 61 pediatric patients admitted to pediatric ICUUSA | 1 x 1010**capsule**duration of stayF/up: none | **Any nosocomial infection:**6/31 (19.3%) ns(developed at least one nosocomial infection) Types:bacteremia (2, 6%)pneumonia (2, 6%)bronchitis (5, 16%)UTI (2, 6%)No AE | Any noso infection:3/30 (10%)Types:bacteremia (n=3, 13%)No AE | **Honeycutt** TCB 2007 Ped Crit Care Med |
| *+* | *L. rhamnosus* GGvs fermented milk control**(\*did not count AAD cases [diarrhea+abx and neg stool pathogens] no data on AAD freq.** | 742 hospitalized children (>1 yr old, mean 10 yrs old)CROATIA | 109/d in 100ml milkduration of stay,followed for 7 days post-discharge | **Nosocomial GI disease**:19/376 (5.1%\*) [excluded cases of AAD] Noso Resp infections 8/376 (2.1%\*)LOS=5 days NS | Noso GI: 44/366 (12%)& Noso Resp tract infections (mostly Upper)-20/366 (5.5%)LOS=4 days | **Hojsak** I 2010 Pediatricsdata from author |

AAD, antibiotic-associated diarrhea; GI, gastrointestinal; LOS, length of stay, UTI, urinary tract infections

## Respiratory Infections – prevention

Respiratory infections defined as any of a variety of new onset upper respiratory infections, variety of outcomes reported by different trials.

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|  | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Dose/day** | **Duration**  | **Incidence of respiratory tract infection in:** | **Reference** |
|  | **Probiotic** | **Control** |  |
| *-* | *L. rhamnosus* GG in **milk** vs control milk | Healthy children (1-6 yrs old) in 18 day cares | 571 | 1-2 x 108 /d | 7 months | 21 days of resp infections in group, NS | normal milk22 days | **Hatakka** K 2001Brit Med J |
| + | *L. casei* DN114001milk"Dan Active" | Elderly volunteers(>60 yrs old)ITALY | 360 | cfu/d nr2 bottlesper day | 3 wks | n=180 20% reduction in all "winter infections”duration lower (7.0 + 3.2 d, p=0.02) | n=180longer duration 8.7 + 3.7 days | **Turchet** P 2003J Nutri Health Aging |
| *-* | *L rhamnosus* GG | pediatric patients admitted to ped ICU; followed for different types of nosocomial infections | 61 | 1 x 1010 | duration of stay | total **respiratory infections:**7/31 (22.6% NSalso:pneumonia (2, 6%), bronchitis (5, 16%) | Resp infections:0/30 (0%) | **Honeycutt** TCB 2007Ped Crit Care Med |
| *-* | *Actimel (L. casei DN114-001[L. bulgaricus, Strept thermo]* | Children (2-5 yr old) | 187 | 1 x 1010/d | 12 months | Time free from rhinitis: mean 6.2 mon NSMean # episodes=3.2\* | Placebo drink.Time free:5.1 monMean #: 4.8 | **Giovannini** M 2007Ped Res |
| *-* | Actimel(*L. casei* DN114001) vs control dairy product | elderly (>70 yrs old), healthy volunteers | pilot of 86, then confirm with n=222 | 2 bottles of 100 g/d,7 wks (pilot) or 13 wks (confirm) | got Influ B vaccine 4 wks post-txt | Significantly higher antibody titers to Influ B (~90 GMT); H1N1 NS; H3N2 ns | ~60 GMT for Influ B | **Boge** T 2009 Vaccine |

**Resp Infections-page 2**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Dose/day** | **Duration**  | **Incidence of disease**  | **controls** | **Reference** |
| *+* | *L. rhamnosus* GGvsfermented milk control | hospitalized children (>1 yr old, mean 10 yrs old) CROATIA | 742 | 109/d in 100ml**milk** | duration of stay,followed for 7 days post-discharge | **Noso Resp infections** 8/376 (2.1%\*)Noso GI disease 19/376 (5.1%\*) (excluded cases of AAD) | Noso Resp tract infections (mostly Upper)-20/366 (5.5%)Noso GI: 44/366 (12%) | **Hojsak** I 2010 Pediatrics |
| + | *L. casei* DN114001 (Actimel) drink with *L. delbrueckii* and *Strept thermo* | Elderly volunteers over 3 months of winter, >70 yrs old | 1072 | 2 x 1010/dvs non-fermented dairy product | 3 months with 1 mon f-up | Duration of all resp infections=6.5 d.cumulative incidence all resp infection=7 days, p=0.009 | Duration resp infections=8 d, p=0.008.Cumulative incidence=8 d | **Guillemard** E 2010Br J Nutrition |
| + | *L. rhamnosus* GG vs inert inulin-based placebo  | ventilator dependent hosp patients in ICU Not all on abx, from author email: | 146 enrolled, 138 done,5% attrition | 4 x 109/d | mean = 15 days | **Pneumon**:9%, p=0.007CDI (5.8%, p=0.02) | Pnemon 40%CDI 18.6% | **Morrow** LE 2010 Am J Resp Crit Care Med |
| + | *L. rhamnosus* GG (ATCC 53103) vs vs placebo | preterm neonates at Turku U Hosp, FINLAND | n=94,n=68 completed 1 yr f/up:.(28% attrition) | 1 x 109/d for Days 1-30 then 2 x 109/d day 31-60 | betweendays 3-60 of life.F/up: 1 yr | Mean # resp infections:1.2 + 1.6, p<0.001 | Mean # Resp in placebo:2.5 + 2.0 | **Luoto** R2014 J Aller Clin Immunol |
| - | *L. rhamnosus* GG (living) vs placebo | Prevent rhinovirus in healthyadults(18-65 yrs old)USA | 60 enrolled, 59 done(1.7%attrition) | 1 x 109/ d(~100 ml)Fruit **JUICE** | 6 wksF/up:none | Got colds14/19 (74%) NS, P=0.20**AE**: 9/19 (47.4%)\* | colds: 18/20 (90%)**AE**: 7/20 (35%) | **Kumpu** M2015Bene Microbes |

## Surgical Infections-preventive

Defined as any type of new onset infection occurring after day of surgery within follow-up period.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Daily dose** | **Duation** | **Incidence of post-surgery infections**  | **Reference** |
| *-* | *L. plantarum 299 (*living*)* + oat fibervs control (standard decontam treatment) | **Adults** having varied types of major abdominal surgery (liver, gastric, colon, pancreas) | 105 enroll,90 done(14% attrition) 10/1997-03/1999 | 2 x 109**Formula** | 4 days post-surgeryF/up: 6 days | Living:# infections3/30 (10%) NSAE: 7/30 (23%) NS*only sign if both living and dead pooled: 6/60(10%) p=0.02* | Std control: 9/30 (30%) AE 10(33%) | **Rayes** N2002 **A**Nutrition |
| *+* | *L. plantarum 299 (*living*)* + oat fibervs control (standard decontamin treatment) | Adults post-liver transplantationOutcome #post-op infections | 105 enroll, 95 done (9.5% attrition)10/1997-10/1999 | 2 x 109**Formula** | 12 days post surgeryF/up: none | **Living**Synbiotic: 4/31 (13% )\* infectionvs std txt P<0.05 AE: 19% | Control-std bowel prep:15/32 (48%) AE 25% | **Rayes** N2002 **B**Transplantation |
| *-* | *L. plantarum 299v*(“Proviva”), open trial no placebo, just untreated controls | adultspatients undergoing major abd surgery | 129 enrolled | ~2.5 x 109 cfu/d | Md 9 d pre-op and Md 5 days post-op | In 64, bacterial translocation 12%, p=0.82,**sepsis** (13%, ns) or gastric colonization with enterics (11%) ns | In 65 non-probiotic group, BT (12%), **sepsis** (15%) or gastric colonization (17%) | **McNaught** CE 2002 Gut |

**Surgical infections- page 2**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Daily dose** | **Duration** | **Incidence of post-surgery infections in probiotic** | **Infections in control** | **Reference** |
| **+** | *“Synbiotic 2000” ®(Pediacoccus pentosaceus 5-33:3 + Leuconostoc mesenteroides 77:1 +Lacto. paracasei ssp. Paracasei F19 +L. plantarum 2362)*and 4 fibers | adults scheduled for liver transplant | 66 enrolled n=66done | 2 x 1010 /dand 20g/d fibersachet | Started on day of surgery and then for 2 weeksF/up: 2 weeks | 1/33 (3%),P<0.05 | Placebo + 4 fibers only16/33 (48%) | **Rayes** N 2005Am J Transplant-ation |
| **+** | *“Synbiotic 2000” ®(Pediacoccus pentosaceus 5-33:3 + Leuconostoc mesenteroides 77:1 +Lacto. paracasei ssp. Paracasei F19 +L. plantarum 2362)*and 4 fibers | Multiple trauma patients at 5 ICUsGREECE | 65 | 4 x 1011per day(12 g/d of 4 fibers:inulin, oat bran, pectin, starch) | 15 daysF/up: until ICU discharge | 22/35 (63%), p=0.01 | 27/30 (90%) | **Kotzampassi** H2006Langenbecks Arch Surg |
| **+** | *“Synbiotic 2000” ®(Pediacoccus pentosaceus 5-33:3 + Leuconostoc mesenteroides 77:1 +Lacto. paracasei ssp. Paracasei F19 +L. plantarum 2362)*and 4 fibers | adults with pancreatic resection | 89 enrolled 80 done | 10 10 and 10g fiber | 9 days | 5/40 (12.5%)\* | 16/40 (40%) | **Rayes** N 2007 Annals of Surgery |
| **+** | *“Synbiotic 2000” ®(Pediacoccus pentosaceus 5-33:3 + Leuconostoc mesenteroides 77:1 +Lacto. paracasei ssp. Paracasei F19 +L. plantarum 2362)*and 4 fibers | multiple injured adults in surgical ICU. All had enteral feedSLOVENIA | 132 enrolledn=113 done | 4 x 1010/dand10 g fibers/d | nr | 5/26 (19%)p=0.03 | 46/87 (53%) | **Spindler**-Vesel A2007J Parent Enter Nutri |

**Post-surgical infections- page 3**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Daily dose** | **Duration** | **Incidence of post-surgery infections in probiotic** | **Infections in control** | **Reference** |
| **-** | *“Synbiotic 2000” ®(Pediacoccus pentosaceus 5-33:3 + Leuconostoc mesenteroides 77:1 +Lacto. paracasei ssp. Paracasei F19 +L. plantarum 2362)*and 4 fibers | Adults with hepatecomy surgeryAll had enteral feedingGERMANY | 19 | 2 x 1010sachet | 10 days | 3/9 (33%) ns | 4 fiber only controls:2/10 (20%) | **Rayes** N2012Benef Microbes |

## Travellers’ diarrhea- Prevention

Travellers’ Diarrhea defined as: diarrhea (>3 loose stools/day for 2 days or > 5 loose stools/48 hours) occurring during travel, not present at trip origin and not due to pre-existing chronic intestinal conditions.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  | **Frequency of traveler’s diarrhea** |  |
| **+/-** | **Probiotic** | **Numberin study** | **Population and destination** | **Dose/day** | **Duration** | **Probiotic** | **Placebo** | **Reference** |
| ***+*** | *S. boulardii*Hansen CBS5926 [now CNCM I-745] vs placebo | 832 | Austrian tourists to hot climatesmean age=42 yrs oldTURKEY | Low dose2 x 109250 mg**capsules** | 21 dF/up: none | 143/426 (34%)\* | 173/406 (43%) | **Kollaritsch** HH 1989Travel Med Intrl |
| ***+*** | *S. boulardii*Hansen CBS5926 [now CNCM I-745] vs placebo | 805 | Austrian tourists to hot climatesmean age=42 yrs oldTURKEY | High dose5 x 109500 mg**capsules** | 21 dF/up: none | 127/399 (31.8%) \**best in North Africa* | 173/406 (43%) | **Kollaritsch** HH 1989Travel Med Intrl |
| ***-*** | *Lactobacillus rhamnosus GG*vs placebo | 820 enrolled (402 in probiotic and 418 control), 756 done (8% attrition) | Finnish tourists to Turkey (10-80 yrs old), mean age=44 yrsFINLAND. | 2 x 109 **sachets** | 7-14 dduration of trip**92% compliance** | 153/373 (41%) ns p=0.06*but p=0.04 for Alanya destination* | 178/383 (46.5%) | **Oksanen** PJ 1990Ann Med |

**Prevention of TD continued-page 2**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  | **Frequency of traveler’s diarrhea** |  |
|  | **Probiotic** | **Numberin study** | **Population and destination** | **Dose/day** | **Duration** | **Probiotic** | **Placebo** | **Reference** |
| ***+*** | *S. boulardiiCNCM I-745*vs placeboHigh dose arm | 695 [used common placebo](392 dropped, 56% attrition) | Austrian tourists to hot climates mean age=44-45 yrTURKEY | High dose:2 x 10101 g/day **capsules** | 21 d**61% compliance** | **TD**: 87/303 (29%) \*p=0.005**AE**: 62/695 (8.5%) | TD: 141/361 (39%)**AE**: 69/727 (9.5%) | **Kollaritsch** HH 1993Fort. der Med [in German} |
| ***+*** | *S. boulardii* CNCM I-745“Perenterol”vs anti-diarrheal med (ethacridine-lactate | 60 enrolled, 43 done,(28% attrition) | Tourists adults with TD,Tunisia | 1 x 1010**capsules** | 5 days | 2.1 days mean diarrhea\* | 1.4 days diarrhea | **Bruns** R 1995[in German] |
| ***+*** | *Lactobacillus rhamnosus GG*vs placebo | 400 enrolled, 245 done(39% attrition) | NYC American tourists (17-80 yrs old, mean 50 yrs old) to various locationsUSA | 2 x 109**capsules** | 7-21 dduration of trip**64% compliance** | 5/126 (3.9%)p=0.05 \*n=2 abd cramps | 9/119 (7.4%) | **Hilton** E 1997J Travel Med |

## Urinary Tract Infections- prevention

UTI outcome defined as new onset of urinary tract infection or recurrence of new UTI.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  | **Frequency of rUTI** |  |
|  | **Probiotic** | **Number****in study** | **Population and destination** | **Dose/****day** | **Duration** | **Probiotic** | **Placebo** | **Reference** |
| **-** | *L. rhamnosus* GG “Gefilus”vs. no juice control | 150137 done(8.7% attrition) | outpatient women *E. coli* UTI mean age ~30 yrs old**Finland** | 4 x 1010 in 100 ml5d/wk**drink** | 1 yearF/up:1 yrs | UTI:19/49 (39%)NS | control 18/27 (36%) | **Kontiokari** T2001BMJ |
| **-** | *L. rhamnosus* GG vs milk control | 585 | preterm infants**ITALY** | 6 x 109milk | 7 daysF/up: none | n=2903.4% ns | n=2955.8% | **Dani** C 2002Biol Neon |
| **-** | *L. rhamnosus GG*- vs placebooutcome was any nosocomial infection, reported types sub-groups | 61 | children in PICU (1-216 mon old)**USA** | 1 x 1010 /d**capsule** | until dischargeF/up: none | (n=30)UTI:2/30 (6%) NS | (n=31)UTI0/31 (0%) | **Honeycutt** TCB2007;8:452-8Ped Crit Care Med |

# Treatment

## Adult Acute Diarrhea-treatment

Adult acute diarrhea defined as acute onset of diarrhea (>3 loose/watery stools/day for >2 days). Outcomes included percent reporting ‘cure’ (diarrhea resolved) or mean days of diarrhea.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| +/- | **Probiotic** | **Study population** | **Probiotic treatment** | **Probiotic group(cure or duration diarrhea)** | **Control group (cure or duration diarrhea)** | **Reference** |
| *+* | *Enterococcus faecium* SF68 | 78 Swiss adults with acute diarrhea | 2.2 x 108/d for 7 days | 37/40 (92.5%)\* cured | 33/38 (86.8%) | **Wunderlich** PF 1989J Int Med Res |
| *-* | *Enterococcus faecium* SF68 | 183 adults in Bangladesh with either cholera or *E. coli* diarrhea | 4 x 109/dfor 3 days | 3d (cholera)and1 d (*E. coli*) ns | 3 d (cholera) and1 d (*E. coli*) | **Mitra** AK 1990Gastroenterol  |
| *+* | *S. boulardii* CNCM I-745  | 92 German outpatient adults with acute diarrhea | 1 x 1010300-600 mg/d for 8 days | -17.2\* diarrhea score reduction | -13.6 | **Hochter** W 1990Munch Med Wschr |
| *+*  | *S. boulardii* CNCM I-745 | 35 French AIDS patients with chronic diarrhea | 6 x 10103 g/d for 7 days | 11/18 (61%)\* cured  | 2/17 (12%) | **Saint-Marc** T 1992Sem Hop Paris |
| *+* | *Enterococcus faecium* SF68 | 185 adults with diarrhea in Belgium | 4.5 x 10 8 /dfor 5 days | 1.7 + 0.6d \*duration of diarrhea | 2.8 + 0.9 | **Buydens** P 1996Scan J Gastroenterol |
| *-* | *S. boulardii* CNCM I-745 | 10 adults mixed etiologies, cross-over study | 2 x 10107 days | 3.8 stools/d by end, ns | 3.9 stools/d | **Attar** A 1999Gastroenterol |
| *+* | *S. boulardii* CNCM I-745 + Metro vs Metro only controlalso see amboebiasis | 57 enrolled, n=54 done,adults with *E. histolytic* amoebic dysentery | 1.5 x 1010 [750 mg/d]for 10 days4 week f/up | 100% cure\*duration diarrhea: 12 + 3.7 d, p<0.001 | Metro only:5/27 (19%) cured, duration 48 + 18.5 d | **Mansour-ghanaei** F 2003World J Gast |

**Treatment of acute adult diarrhea –page 2**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **+/-** | **Probiotic** | **Study population** | **Probiotic treatment** | **Probiotic group(cure or duration diarrhea)** | **Control group(cure or duration diarrhea)** | **Reference** |
| *+* | *S. boulardii* CNCM I-745 + metro vs metro only control | 65 adults with giardiasis | 1 x 1010for 10 days | 100% cure\* | 6/35 (17%) | **Besirbellioglu** BA 2006J Infect Dis |
| *-* | *“Zhengchangsheng”Bacillus licheniformis* [Korea] *vs “Bioflor”(S. boulardii* [Biocodex]2 probiotics compared, no control/placebo used | n=158 adults (20-75 yrs old) with diarrhea, n=151 done (4.4% attrition)**KOREA** | Bacillus: 6 caps/d (250 mg/cap) or 1.6 g/d no cfu/dSboulardii: 1 g/d, 4 caps/dFor 5 days,F/up: none**capsules** | (n=80) Sb**cured** by day 3: 756/80 (95%) p=0.33**Duration diarrhea**: 3.2 + 1.0 d, p=0.70 | (n=78) B. lich.cured: 71/78 (91%)Duration:3.15 + 1.1 d | **Heo** J2014Intestinal Research |

\*P<0.05

## Clostridium difficile infections (CDI): Treatment

Outcome was a new recurrence of CDI episode with 2 months of prior resolution of CDI.

**Treatment trials with primary outcomes for CDI**:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Population** | **Probiotic** | **Dose and duration of treatments** | **CDI recurred in Probiotic Group**  | **CDI recurredin ControlGroup** | **Reference** |
| + | adults with CDI. Outcome is CDI recurrenceAll got either vanco or metro | *S. boulardii* CNCM I-745 vs placebocapsules | 2 x 1010/d for 4 wksfollow-up 4 wks | overall: 15/57 (26.3%) p=0.05Recurrent CDI patients: 9/26 (34.6%) p=0.04but initial CDI: 19.3% ns p=0.86 | overall: 30/67 (44.8%)Recurrent:22/34 (65%)Initial: 24.2% | **McFarland** LV 1994JAMA |
| + | n=170 adults, all got vanco (2 g/d or 500 g/d) or metro (1 g/d) for 10 daysadults with recurrent CDI | *S. boulardii* CNCM I-745vs placebocapsules | 2 x 1010/d for 4 wksfollow-up 4 wks | **Recurred**:only in high dose vanco: 3/18 (16.7%) p=0.05ns for low dose vanc and metroNo AE | high dose vanco & placebo: 7/14 (50%) | **Surawicz** CM2000Clin Infect Dis |
| - | 25 inpatient & outpatient adults on vancomycin or metronidazole (7-10 days), **recurrent** (n=9) and **initial** (n=16) CDIattrition nrUSA | *Lactobacillus rhamnosus* GG in yogurtvs placebo | cfu/d nr **yogurt**3 weeks F/up: 4 weeksITT | **Recurred**4/11 (36.4%) nsp=1.05.7% power**Initial** CDI: 0/6 recurred, p=0.25**RCDI**: 4/5 (80%) recurredp=0.52 | 5/14 (35.7%)Initial CDI: 3/10 (30%) recurredRCDI: 2/4 (50%) recurred | **Pochapin** MB2000;95(1):S11-S13.Amer J Gastro Meeting abstract onlydata from authorterminated early due to poor enrollment |
| - | 15 adults on vanco or metro (80% on metro) doses Abx nr but mean duration Vanco or Metro (18 days), **Recurrent CDI only**,enrolled over 9 months0% attritionMissouri USA | *L. rhamnosus GG* and inulin | 5.6 x 1011*(2.8 x 1011 per 40 mg capsule bid)***capsule**duration of antibiotics (median 18 days) + 21 days=total 39 daysF/up: 21 days | **Recurred**: 3/8 (37.5%)p=0.57, ns5.3% powerMore bloating (25%) & gas (37.5%) | Placebo + inulinrecurred:1/7 (14.3%) | **Lawrence** SJ 2005J Med Microbiolpoor enrollment stopped early, low power |

## Pediatric Colic-Treatment

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Probiotic** | **Age of subjects (months)** | **No. in study** | **Dose givenper day** | **Duration of treatment(days)** | **Percent cured or duration of diarrhea (days) in probiotic | controls**  | **Reference** |
| *+* | *L. reuteri strain 55730 vs simethicone*outcome is "crying" | infantile colic, breast-fed 21-90 days old | n=90 colicky infants, 83 done | 1 x 108 live /d | 28 days | 39/41 (95%) responded (less crying), p<0.001Crying time: 51 min/d, p<0.001 | 3/42 (7%)Crying time: 145 min/d | **Savino** F 2007 Pediatrics |
| *+* | *L. reuteri* DSM 17938 vs placeboResponders=50% reduction in crying | 2-16 weeks old | 50 infants with colic, 46 done, no AE | 1 x 108/d | 21 days | Crying times: Median=35 min/d NSResponders: 24 (96%), p=0.04 | crying time: 90 min/dResponder: 15 (71%) | **Savino** F2010Pediatrics |
| *+* | *L. reuteri* DSM 17938 vs placeboOutcome: responders had >50% less crying | <5 months old with colic | N=80, mostly breast-fed | 1 x 108/d | 21 daysF/up: 1 wk | Med crying 52 min/day P<0.001Responders 40/40 (100%) | Med crying 120 min/day Responders 25/40 (62.5%) | **Szajewska** H2013J Pediatri |
| *+* | *L. reuteri* DSM 17938 vs placeboItaly | 1-3 months old with colic | N=589 randomized |  | 90 days | Mean duration of crying= 38 min/d, p<0.01 | Crying: 71 min/d | **Indrio** F2014JAMA Pediat |

Outcome was mean or median time of infant crying/day

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **+/-** | **Probiotic** | **Number in study** | **Daily dose**  | **Duration** | **Outcome in Probiotic** | **Controls****placebo** | **Reference** |
| *+*  | *Activia yogurt (Bifido animalis* DN173010) + FOS vs control dessert | 266 adult women with functional constipation and 112 with normal stool function | 2 x 1010 (2 units of 108 cfu/g) | 14 daysF/up: 0 | BM/week:in constipated:x=6.1 + 2.7/wk p<0.001Sign better on straining on defection and pain symptomsin normal: NS | Control yogurtx=5 + 2.6/wk | **DePaula** JA 2008Acta Gastroenterol Latinoam |
| *+* | *Activia yogurt (Bifido animalis* DN173010)vs acidified control milk with DEAD bacteria | 135 constipated women (25-65 yrs old), 126 done(7% attrition)CHINA | 1 x 1010100 g**Milk/yogurt** | 14 daysF/up: 0 | Living:BM/week: 4.1 + 1.7, p<0.05 | Dead:2.6 + 1.0 | **Yang** YX 2008 World J Gastroenterol |
| *-* | *Activia yogurt (Bifido animalis* DN173010)vs control milk (non-fermented milk) | 159 children (3-16 yrs old) with mean of 3 yrs Rome III constipation. 148 done (7% lost).In Netherlands and Poland.  | 8 x 109**yogurt** or **milk** | 3 wksF/up: 0 | Living: cured27/71 (38%) p=0.06 trend. What happened to 3 subjects? Not reported in paper.Increase by 2.9 +3.2 BM/wk, p=0.5 NS | Cured in placebo:17/72 (24%).[Missing 2 subjects]Increase by 2.6 + 2.6 bm/wkNo SAEs | **Tabbers** MM 2011**A** Pediatrics.Neg cuz?Low dose?Severe disease?Too short?No efficacy? |

## Constipation- treatment

Outcome of constipation trials was mean stools/week

## H. pylori treatment

**-page 1**

*H. pylori* clearance based on DOB <5 at 30 minutes is negative for *H. pylori* (excess labeled CO2)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **+/-** | **Probiotic** | **Population** | **Dose** | **Duration** | **Probiotic** | **Controls** | **Reference** |
| *+ erad-AEAAD nr* | *L. acidophilus Lb*"Lacteol Fort" vs no txt control All on **triple** txt (ACR x 7 days). | 120 Hp+ adults, dyspepsia117 done (2% attrition)ITALY | 1.5 x 1010**Capsules** | 10 daysF/up: 6 wksITT | **Hp erad** 52/60 (87%) p=0.02**AE**: 6 (10%)p=1.0 | **Hp-:**42/60 (70%)AE: 6 (10%), ns | **Canducci** F 2000Alim Pharm & Therapeuticsorigin of *L acido* LB strain (p1628) |
| *-eradAE nrAAD nr* | *L. acidophilus LB* culture supernatant vs no txt controlAll had **double** txt: Amox (14 days) + Omeprazole (30d) | 84 consecutive adults dyspepsia or ulcers, 0% attritionITALY | 2 x 1010/day**Capsules** | 14 daysF/up:4-6 wksITT | **Hp erad:**30/47 (63.8%) nsAE: nrAAD: nr | Hp -:26/37 (70.3%) | **De Francesco** V 2000Dig Liver Dis[letter] |
| *- erad- + AE+ AAD*  | *Lactobacillus rhamnosus GG "*GiFlorex*"* vs nothing. **open** studyAll on triple therapy for 7 days: ( claritho, **pantoprazole**, tinidazole) | 120 asymptom. Hp+ carriers Hospital staff, adults.May-July 1999, one site, 117 done (2.5% attrition) ITALY | 1.2 x 1010**Sachet** | 14 daysF/up: 6 wksITT | **Hp-:** 48/60 (80%), p=0.6**Any AE**: 26 (43%) p=0.04**AAD**: 8/60 (13.2%) P<0.001  | controlHp-: 46/60 (76.6%)Any AE: 37 (62%)AAD: 29/60 (48.2) | **Armuzzi** A2001 **A** Digestion |
| *- erad+ AE+ AAD* | *Lactobacillus rhamnosus GG "*GiFlorex*"* vs placebo**blinded** studyAll on triple therapy for 7 days(claritho, **rabeprazole**, tinidazole) | 60 asymptom. Hp+ carriers Hospital staff, adults.Sept 1999-Jan 20000% attritionITALY | 1.2 x 1010**Sachet** | 14 daysf/up: 6 wksITT | **Hp neg**:25/30 (83.3%) p=1.0**Any AE**: 12/30 (40%)\* p=0.04**AAD:** 1/30 (3.3%), p=0.01**Nausea** 10%\* | placebo:Hp-: 24/30 (80%)Any AE:20/30 (67%)AAD: 8/30 (26.6%)Nausea 37% | **Armuzzi** A2001 **B**Alim Pharm & Ther |

Abbreviations: AAD: antibiotic-associated diarrhea; AE, adverse events; Hp+, *H. pylori* positive; Hp-, *H. pylori* negative (eradicated); ITT, intent-to-treat analysis; nr, not reported; ns, not significant

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Probiotic** | **Population** | **Dose** | **Duration** | **Probiotic** | **Controls** | **Ref** |
| *-*erad/*-AAD+any AE* | **RCT with three txt arms:***L. rhamnosus GG"*Giflorex" vs placeboAll triple therapy(7 days) ClaRanTin | 21 LGG21 placebon=42adultsasymptomatic41 done (5% attrition placebo, 0% LGG)ITALY+ | 1.2 x 1010**sachetsdouble blinded** | 14 daysF/up: 5-7 wksAPP | **Hp eradicated:**16/21 (76%) nsp=1.0**Any AE:**3/21 (14%)p=0.004**AAD:** 1/21 (5%), ns | **Hp eradicated:**16/20 (80%) ns**Any AE:**12/20 (60%)**AAD:** 6/20 (30%) | **Cremonini** F2002 Amer J Gastro |
| *-*erad/***+****AAD+any AE*  | *S boulardii**"*Codex"vs placebo All triple therapy(7 days) ClaRanTin  | 22 Sb21 placeboasymptomaticn=42adults40 done(5% attrition in placebo, 9% Sb)ITALY | 1 x 1010 **sachets double blinded** | 14 daysF/up: 5-7 wksAPP | **Hp eradicated:**17/20 (81%) nsp=1.0**Any AE:**3/21 (14%)p=0.004**AAD:** 1/21 (5%)p=0.045 | **Hp eradicated:**16/20 (80%) ns**Any AE:**12/20 (60%)**AAD:** 6/20 (30%) | **Cremonini** F2002 Amer J Gastro |
| + erad+ AE+AAD | "AB Yogurt"*L. acidophilus La5 + Bifido. animalis subsp lactis Bb12* & 2 starters *(Strept therm + L. bulgaricus)* vs. controls no txtAll triple therapy (7 days) ACL | 160 Hp+ adultssymptomatic149 done, (7% attrition)Jan-Dec 2001 TAIWAN | 1 x 1010/d**yogurt** | 4 wksf/up:4-8 wksITT | **Hp-**: 73/80 (91%)\*p=0.045**Any AE:**15/80 (18.8%)\*p<0.001**AAD**: 2/80 (2%)\*p=0.03More Bifido in stool | **Hp-**: 63/80 (78%)**Any AE:**53/80 (66%)**AAD**:10/80 (12.5%) | **Sheu** BS2002APTcompliance to triple ther:sign: 67.5% probiotic\* vs 43.8% controls |

**H pylori. page 2**

**Hp—page 3**

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|  | **Probiotic** | **Population** | **Dose** | **Duration** | **Probiotic** | **Controls** | **Ref** |
| *- erad+ AE AAD nr* | *C. butyricum MIYAIRI 588* vs no txt controlsAll got triple therapy AFO (7 days)f=furazolidone | 97 Hp+ symptomatic adults0% attritionCHINA | 120 mg/d, 1 x 107 cfu/d **Tablet** | 7 daysF/up: 4 wksITT | **Hp-:** 44/47 (94%) p=0.49**Any AE:** 6/47 (12.8%)p=0.04By chi2**AAD**: nr | **Hp-:** 44/50 (88%)Any AE: 15/50 (30%)**AAD**: nr | **Guo** JB2004Chin J Celiopathy[In Chinese, but English abstract] |
| *-erad-AADAE: nr* | *Clost. butyricum MIYAIRI 588* vs no txt controlsAll on triple therapy ACL (7 days)L=lansoprazole | 35 adults(41-64 yrs)Hp+ ulcers0% attritionoutpatientclinicJAPAN | 3 x 107 /d3 tablets of 120 mg/tab**Tablets** | 2 wksF/up:6 wksITT | **Hp-:**17/18 (94%) ns**AAD**: 1/18 (6%) p=0.60 no change in normal flora | **Hp-:**13/17 (76%)**Any AE**: nr**AAD**: 2/17 (11.8%) | **Shimbo** I2005WJG good summary of MIYAIRI strain (p. 7520) |

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|  | **Probiotic** | **Population** | **Dose** | **Duration** | **Probiotic** | **Controls** | **Ref** |
| *-*eradAE nrAAD nr | **Two treatment arms:**Open study*1)Lact acidophilus LB "*Lactol Forte" only(**no triple therapy**) vs control triple therapy(AmoxClaritLanz x 8 days) | 120 children 5-12 yrs old, 91 completed(24% attrition)asymptomatic CHILE | 2 x 109**Capsules** | 8 wksf/up: noneAPP | (n=46)DEAD Eradication of Hp 3/46 (6.5%)worse in probiotics DOB\*\*\* post txt=33.4No AAD or AE data | (n=45)triple therapy:66% (30/45) eradication  p<0.001DOB post triple=8.4No AAD or AE data | **Gotteland** M 2005 Acta Paedia*shows probiotic by itself not effective for Hp eradication*! |
| -eradAE nd | *2) S. boulardii lyo and inulin* (5 g inulin) only(**no triple therapy**)"Perenteryl"vs 8 days of triple therapy(AmoxClaritLanz) | 119 children 5-12 yrs old, 95 completed(20% attrition)  asymptomaticCHILE | 1 x 1010500 mg**Sachet** | 8 wksf/up: noneAPP | Living Sb (n=50)eradication of Hp was 6/51 (12%)worse in probiotics DOB post txt =31.2No AAD or AE data |  (n=45)triple therapy:66% (30/45) eradication  p<0.05DOB post triple=8.4 | **Gotteland** M 2005Acta Paedia *shows probiotic by itself not effective for Hp eradication* |
| +erad+AEAAD nr | *L. acidophilus (helveticus) +L. rhamnosus* vs controls (triple therapy only)“Lacidofil”All got 10 days of triple therapyAmoxClarith +PPInotes from author | 60 children(7-18 yrs old) with H. pylori dyspepsia or ulcers POLAND | 6 x 109/d**Capsules** | 20 daysF/up: 7 wksITT | **Hp-:** 30/30 (100%)\*P=0.011**AE**: 1/30 (3%) p=0.002\***AAD**: nr | **Hp-:** 23/30 (76.6%)**AE**: 11/30 (38%) **AAD**: nr | **Plewinska** E 2006Gastroenterol Poltranslated[Abstract in Polish] |

**Hp---page 4**

**Hp—page 5**

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|  | **Probiotic** | **No.** | **Dose** | **Duration** | **Probiotic** | **Controls** | **Reference** |
| + eradAE ndAAD neg(trend) | *"*AB Yogurt"*L acidophilus La5 + Bif. animalis subsp lactis Bb12*[starters: *L. bulgaricus + Strept thermophilus*].vs no txt controlAll on quadruple therapy (AmoxMetroOmeBs) (7 days) | 138 failed triple Hp therapy with ulcers or gastritis, 129 done (6% attrition)adultsTAIWAN | 400 ml/d4 x 1011/d**Yogurt**single blinded (Hp assessor) | 4 wksF/up: 6 wks & 3 months if neg at 6 wks.ITT | **Hp-:**59/69 (85%)\*P=0.04**Any AE:** patient level data nr**AAD:** 9/69 (8.7%) p=0.053 Chi243% Metro resistant62% Clarithro resistance | **Hp-:**49/69 (71%)**Any AE:** nr**AAD:** 18/69 (26%) | **Sheu** BS2006Am J Clin Nutri |
| + eradAE nrAAD nr | "Lacidofil"*Lactobacillus ~~acidophilus~~ helveticus R0052 + L. rhamnosus R0011)* 10 days triple therapyAmox + Clarith + Pantoprazole, PPI)  vs 4 triple therapy control groups:**Control IA (Triple)**: 10 days of Amox + Clarith + pantoprazole (PPI)**Control IB (Quadruple)**:10 days of Tetracycline + Tinidazole +Bismuth salts +pantoprazole (PPI)Two other control groups txt by antibiogram for their Hp strain (n=155) | 641 adults with peptic ulcers or gastritis and Hp+(18-81 yrs old)1999-2002but 4 different control groups!0% attritionPOLAND | 8 x 109/d4 capsulesper daycfu/d not reported in paperbut 2 x 109/cap**Capsules** | 20 daysF/up:10 daysITT | **Hp-:**51/53 (96%)\*p=0.04 *X*2=4.2 BUT NOT CORRECT should be Fisher's exact test p=0.052power 40%vs IA (same triple therapy)vs. Quad p<0.001\*No data on AE or AAD49% resistance to Clarith & 59% to Metro found | did not use the other 2 control groups here.**Hp-:****Control IA (triple):** 165/192 (85.9%)**Control IB**: (**Quad)** 172/241 (71.4%)p<0.001 IB vs control IA.Quad less effective than triple therapy! | **Ziemniak** W2006J Physiol & Pharmacolpoor quality study: 1. poorly done randomization as group sizes not near equal2. No adverse effects datacompany emailed dose data |

**H pylori continues-- page 6**

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| **+/-** | **Probiotic** | **No Hp+.** | **Dose** | **Duration** | **Probiotic** | **Controls** | **Reference** |
| *-*erad/+distress*+ AAD+ AE* | *S. boulardii("*Reflor", Biocodex)vs placebo. All got triple therapy (ACL)(14 days)GDQ=Glasglow dyspepsia questionnaire | 124 adults with dyspepsia0% attritionoutpatientsTURKEY | 2 x 1010/d**Sachets** | 2 weeksF/up: 6 wksITT | **Hp-** (44/62, 71%) p=0.3**GDQ**=1.38 + 1.2\***Any AE**: 14/62 (23%)\* P<0.001**Epigastric distress**9 (14.5%)\***AAD:** 9/62 (14.5%)p=0.03 *X2***CDI**: 2/62 (9.7%) ns | **Hp-** (37/62, 59.7%) NSGDQ=2.2 + 1.4Any AE: 37/62 (60%)Distress:27 (43.5%)**AAD:** 19/62 (30.6%)**CDI**: 8/62 (12.9%)ITT | **Cindoruk** M 2007Helicobacter |
| -erad AE nrAAD nr | "Lacidofil*" L. helveticus* R0052 + *L. rhamnosus* R0011 vs no txt controlAll had Amox+Clari+Rabeprazole for 7 daysrandomized | 35 Hp+ adults duodenal ulcers18-70 yrs old0% lostUKRAINE | 1.2 x 1010per day6 caps/d**capsules** | 20 daysF/up:4 wksITT | **Hp-:** 18/20 (90%) ns4.5% powerRestored **normal flora** n=15 (75%), p=0.08 **Dyspepsia** better in (x=6 + 0.6 days) p<0.01 | Hp-: 13/15 (86.7%)Restored NF: 6 (40%)Dyspepsia better in (x=10 + 1 days)No **AE** or **AAD** data | **Babak** O2007News of Pharmacy & Medicine[translated:In Ukrainian]translateddata from company email  |
| *+erad+ Any AE AAD nr* | *"*Lacidofil*"L. helveticus R0052 + L. rhamnosus* R0011 vs no txt control.All got triple therapy (OmeAmoxClarith)for 7 days | 49 Hp+ adultsgastritis or ulcers0% attritionUKRAINE | 8 x 109/d4 caps/day**capsules** | 10 daysF/up:4-6 wksITT | **Hp-:** 24/25 (96%)\*p=0.049Healed peptic ulcer: 22 (88%) nsAny **AE** 1(4%)\*p=0.049**AAD**: nr | Hp-:18/24 (75%)Healed peptic ulcer17 (70.8%)Any AE:6/24 (25%) | **Vdovychenko** V2008[Current Gastroenterol] translated[In Ukrainian][data from company] |

**H pylori-page 7**

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| **+/-** | **Probiotic** | **No Hp+.** | **Dose** | **Duration** | **Probiotic** | **Controls\*** | **Reference** |
| *- eradAE nr* | *Clostridium butyricum* CBM588 vs no txt controlAll got triple therapyACL for 7 days | 19 peptic ulcer adults(32-71 yrs old)0% attritionJAPAN | 6 x 107/d to 1.2 x 108/d **tablets** | 7 daysF/up:noneITT | (n=12)**Hp-:**11/12 (92%) ns | (n=7)**Hp-:**6/7 (87%)**Any AE:** no data | **Imase** K2008Microb Immuno |
| *-*erad/*+all AEAAD nr* | *S boulardii* (Enterol, Biocodex)vs no txt control All had triple therapy (Omer or Eso [3 wks] & Amox/Clar)(7-10 days) **Single blinded** (outcome assessor) | 90 symptomatic children 3-18 yrsdyspepsia0% attrition ROMANIA | 500 mg/d1 x 1010**Capsule** | 4 wksfup: 4-6 wksITT | **Hp-:** 45/48(93.3%) p=0.75**all AE:** 4/48 (8%)\*p=0.047**AAD:** nr | Hp-: 34/42(80.9%)All AE: 13/42 (31%) **AAD:** nr | **Hurduc** B 2009 Act Paed |
| *-*erad/*-all AE- AAD* | *L. rhamnosus GG* vs placeboall had triple therapy (amox and clarithr and Omeprazole) for 7 days | 83 children, 66 done (20% attrition)asymptomatic *Hp +* inpatientsPOLAND | 2x 109 per day**Capsule** | 7 daysF/up:6 wksAPP | **Hp-:**23/34 (69%) , ns**Any AE:** 18/35 (51%)ns p=0.8**AAD:** 2 (6%) ns p=0.8 | Hp-:22/32 (68%)Any AE:13/32 (41%)AAD:6/30 (20%) | **Szajewska** H 2009 JPGN |

**Hp---page 8**

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|  | **Probiotic** | **Pop** | **Dose** | **Dura-tion** | **Probiotic** | **Controls** | **Reference** |
| *+*erad/-anyAE*+AAD* | *S. boulardii*  CNCM I-745 vs no txt control.All got triple therapy OAC(7 days) **Single blinded** (UBT outcome assessor)[excluded study arm with S. boulardii and muco-protective agent as no comparative control group (n=330) | 991 adultsHp+ symptomatic (ulcer, gastritis)932 done*Attrition:*control: n=33 (10%)Sb: n=18 (5.5%)Sb+MPA:n=8 (2%)SOUTH KOREA | 2.2 x 1010**Capsule** | 4 wksF/up:4 weeksITT | **SB only:** (n=330): **Hp-**: 264/330 (80.0%) \* p=0.01**any AE**: 48 (14.5%) p=0.12**AAD** 9/330 (3.3%) p=0.04*X2*=4 | No txt control: (n=331)**Hp-:** 237/331 (71.6%)**Any AE**:63 (19%)**AAD:** (20/331) 6% | **Song** MJ 2010Helicobacter |
| *- eradAE: nr+AAD* | *S boulardii* CNCM I-745 + 14 day triple therapy(Amox+Clarthirtho+Lansoprazole)vsControls (triple therapy only) | N=223 Hp+ randomizedadultsKOREA | dosenrform nr | 2 weeksF/up: 4 weeks by 13C-urea testITT | n=107**erad**: 73/107 (**68.2**%) p=0.905 NS**AAD**: 32/107 (29.9%)\*P=0.041 | n=116erad: 80/116 (69.0%)AAD: 50/116 (43.1%) | **Lee** JY2011Asian Pacific Digestive Week, 1-4 October 2011, SUNTEC SingaporeMtg Ab.J Gastro & Hep201126(S5):257 |

**Hp---page 9**

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|  | **Probiotic** | **Pop** | **Dose** | **Dura-tion** | **Probiotic** | **Controls** | **Reference** |
| *-eradAE nrAAD nr* | **2 control groups***:S boulardii*  CNCM I-745 + triple (LanClarAmox) vs **1.** **Triple** therapy (ACL for 14 days) vs**2.** **Sequential** ther (AmoEso x 5 days) then (EsoLevoMetro x 7days) for a total of 12 days | 285 adults Hp+ ulcer or gastritis273 done(4% attrition)TURKEY  | 5 x 109 per dayonly 250 mg/d **Capsules** | 14 daysF/up:5 wksITT | (n=98)**Hp-:**71/98 (72.4%)**WORSE!**No AE dataAAD nr | **Triple therapy controls:**Hp-: 82/95 (86.3%)p=0.02**Sequential**:85/92 (92.3%)p<0.05**Triple Txt vs Seq**=ns | **Ozdil** K2011Hepata-Gastro-enterology |
| *-erad+AEAAD nr* | Probiotic milk (*L. acidophilus* La5 + *Bifido. lactis* Bb12) [starter: Strept thermo] (n=30) **vs 2 controls**:**C1:** heat-killed fruit milk (n=29)**C2:** acidified milk control (n=29)All had triple: AmoClarOmer(7 days) during week 5 | 88 Hp+ adults[18-65 yrs old]asymptomatic 0% attritionGERMANY | 7.5 x 108/d**Fermented fruit milkDouble blinded** | for: 5 wksF/up: 3 weeksITT | **Hp-**: 30/30 (100%) ns**Any AE**: nrAt week5:Change in GI/Hp symptom **scores**: -1.4 +1.1 \*vs milk | **heat-killed milk control:Hp-**: 29/29 (100%)Sym scores: -1.2 +1.1 ns **Acidified milk control**: **Hp-**: 29/29 (100%)Sym scores:+2.6 + 1.1 | **de Vrese** M2011 J Dairy Research |
| *- erad+ AEAAD: nr* | ***Concomitant****S. boulardii* CNCM I-745 and triple therapy x 7 days, vs *controls*: triple therapy only x 7 daysopen (no placebo)TT: Amox + Clarith + rabeprazolefor 7 daysexcluded group (n=45) with sequential S. boulardii | 135 Hp+adults >18 yrs oldactive gastritis128 done(5% attrit)9/2010-02/2012CHINA | 500 mg/d1.5 x 1010/d**capsule** | 7 daysF/up:4 wksITT | **Erad**: 34/45 (75.6%) p=0.17 ns**AE:** 16/41 (39%) p=0.02 | controls:erad: 28/45 (62.2%)AE: 28/44 (63.6%) | **Gao** C, Xie R Ma T, Wu S.2012Chin J Gastroentero. 17:555-7.**In Chinese** |

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| **+/-** | **Probiotic** | **No Hp+.** | **Dose** | **Duration** | **Probiotic** | **Controls\*** | **Reference** |
| *+*erad/*+ AE-AAD* | *S. boulardii*  CNCM I-745 (Lab Biocodex)All had triple therapy (Amox+clarithro + omeprazole) for 14 daysenrolled 9/09-01/2011 | 100 Hp+ adults with peptic ulcers One hospital0% attritionCHINA | SB 500 mg/d ~5 x 109/dvs no txt control**Sachet** | 14 days F/up:  1 yrITT | **Hp-:** 42/50 (84.4%)\*p=0.04Improved symptoms: 48 (96%)\*Recurred: 5 (10%)\*all AE : 8/50 (16%)\* p<0.001No SAEAAD 3/50 (6%) NS | Hp-: 32/50 (64.4%)Improved symptoms: 31 (62%)Recurred: 13 (26%)all AE: 34/50 (68%)AAD: 8/50 (16%) p=0.2  | **Chu** Y 2012African J Pharmacy & Pharmacology |
| *- eradAE -AAE -* | "PY" Probiotic yogurt. Strains not defined in paper emailed author. He replied yogurt was: *Lactobacillus acidophilus* La5 + *Bifido. bifidum* Bb12. vs non-probiotic yogurt control (blinded) vs no yogurt control(open)All had triple therapy (Amox, Clarithro, Pantoprazaole for 7 days) | 102 Hp + adultssymptomatic[18-85 yrs old]88 done (14% attrition) **Both double blinded controls and open (no txt) controls**IRAN | nr cfu/day in paperresponse in author email on dose: ~2 x106/d300 mg/d**yogurt** | for 7 daysF/up: 4 weeks**APP analysis** | **Hp erad**:19/31 (61%)NS 2.6% power**Any AE**:20/31 (64%) ns**AAD:** 7 (22.6%) ns | **Non-probiotic yogurt:** Hp-: 20/31 (64.5%) p=0.79**Any AE**: 21 (68%) p=0.79**AAD**: 8 (25.8%) p=0.77**No yogurt control:**Hp-: 19/26 (73.1%) p=0.35Any AE: 22 (85%)p=0.13AAD: 8/26 (30.8%) p=0.48 | **Mirzaee** V 2012Iranian Red Crescent Med Jdata from author in email |

**H. pylori page 10**

**Hp continued- page 11**

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|  | **Probiotic** | **Pop** | **Dose** | **Duration** | **Probiotic** | **Controls\*** | **Reference** |
| *- eradAE +AAD +* | All got TT (AmoxClarithOmep)x 14 days.randomized to:*S. boulardii*  CNCM I-745 vs open control | n=82 Hp+childrenpeptic ulcers (n=33) or chronic gastritis (n=49)CHINA | 250 mg/d | 2 wksF/up4 wks | **Erad: ITT**37/41 (90.2%)ns**APP**: 37/38 (97.4%)\* p<0.05**AE:** 5/41 12.2%\* less**AAD**: 5/41 (12.2%)\* | Open cntrl:**Erad ITT**33/41 (80.5%)**APP**33/40 (82.5%)AE: 13/41 (31.7%)AAD: 13/41 (31.7%) | **Zhang** Y2012J Clin Pediat*[In Chinese]* |
| *erad +AE nrAAD neg* | All got TT (AmoxClarithOmep)x 14 days.randomized to:*S. boulardii*  CNCM I-745 vs open control | n=60 Hp+childrenwith chronic gastritisCHINA | 500 mg/d | 2 wksF/up4 weeks | **Erad:**27/30 (90%)\*p<0.05**AE**: sign less but data in Chinese**AAD**: 0/30 (0%)p=0.11 | Open cntrl:**Erad**20/30 (66.7%)AE: raw data?AAD: 4/30 (13.3%) | **Zhang** H 2013Med J Chinese People Health*[In Chinese]* |
| *+*erad/*+AADAE nr* | *S. boulardii* CNCM I-745 "UltraLevure" vs no txt controlBoth groups got triple therapy ( amoxicillin (2 g/d), clarithromycin (1g/d), & omeoprazole (40 mg/d)For 14 days. Single blinded (Patients unaware of other txt arm) | Adults with dyspepsia. Of 125 screened, 70 enrolled (aged 18-75 yrs old at one Greek hospital) Randomized 36 to Sb and 34 to nothing.60 done (14% attrition)GREECE | 300 mg/d 6 x 106/dOne **Capsule**was 50 mg with 106 cfu/cap | 14 daysF/up:6 wksITT | **Hp-:** 30/36 (83.4%)\*, p=0.034completed 33/36 (91.7%)**AAD**:1 (2.8%)\* p=0.026**Any AE:** nr | **Hp-:** control 20/34 (58.8%)completed:27/34 (79.4%) p=0.2AAD: 7 (20.6%)  | **Kyriakos** N 2013 Hosp Chronicles |

**H. pylori-page 12**

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|  | **Probiotic** | **# Hp+.** | **Dose** | **Duration** | **Probiotic** | **Controls\*** | **Reference** |
| *- erad+AADAE nr* | "Yomogi"*S. boulardii* CNCM I-745 vs no txt controlAll had triple:Amox/Clarith/Omeprazole (14 days) | 160 Hp+ adults gastritis or ulcersIRAN | 1 x 1010/day500 mg/d**Capsules** | 2 weeksF/up:8 wksITT | **Hp-:** 70/80 (87.5%) p=0.35 ns**Any AE**: nr**AAD:** 10/80 (12.5%)\* p=0.04 | Hp-: 65/80 (81.2%)Any AE: nrAAD: 21/80 (26%) | **Zojaji** H2013Gastro & Hepatol |
| *erad: +AE: nrAAD nr* | All got triple ther:AmoxClarOmeprax 14 daysrandomized to:open control or“Lacidofil”*L. rhamnosus* R11 + *L. helveticus* R52 | n=45 Hp+childrenUkrain xe | 6 x 109**capsules** | 3 wksF/up:1 wk | **Erad**:24/25 (96%)\*p<0.05AE: not in abstractAAD: | Open cntrls:Erad:14/20 (70%)AE:AAD: | **Abuturov** OE2014Contemp Pediatri [Ukrainaine] |
| *+ eradAE - (trend)AAD neg* | *L. acidophilus La-5 + Bifido. bifidum Bb-12* vs no txt control.All had triple:[Amox or Metro] + Clarith + Omeprazole(14 days) | 100 Hp+childrenpeptic ulcersone site – a GI clinic88 done(12% attrition)Jan 2009-June 2010CHINA | **<5 yrs old:** 1 x108/d**> 5 yrs old**:2.1 x 108/d**Sachets** | 6 wksF/up:none!APP data:  | **Hp- erad:** APP: 36/43 (83.7%)\**X2*=4.3, p=0.04ITT¨36/49 (73%) ns**AE**: 5/43 (11.6%) p=0.07 TrendITT-AE: 5/49 (10.2%) p=0.2**AAD**: 3/43 (7%) p=0.7 nsITT-AAD: 3/49 (6.1%) p=0.4Less E coli | Hp-:APP: 29/45 (64.4%) ITT: 29/51 (56.9%)AE: 12/45 (26.7%)ITT AE: 12/51 (23.5%)AAD: 5/45 (11.1%)ITT-AAD:5/51 (9.8%)No change in *E. coli* flora. | **Wang** YH2014WJ Microbiol Biotech[data supplied by author email]not funded |

**H pylori-- page 13**

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|  | **Probiotic** | **# Hp+.** | **Dose** | **Duration** | **Probiotic** | **Controls\*** | **Reference** |
| *-eradAE nr+AAD* | *S. boulardii* CNCM I-745 *"*Bioflor"vs no txt controlAll had triple(Amox/Clarith/Omeproz) (14 days) | 240 children Hp+(5-11 yrs old) with gastritis, ulcers or inflammation0% attritionCHINA | 500 mg/d1 x 1010**Capsules** | 14 daysF/up: 4 wksITT | **Hp**-: 102/120 (85%) ns p=0.07**AAD**: 27/120 (22.5%)\* p=0.008 **Any AE:** nr | Hp-:91/120 (75.8%)AAD: 47/120 (39.1%)AE: nr | **Zhao** HM2014Zhongguo Dang Dai Erke Za Zhi[in Chinese] |
| *- eradAny AE nrAAD +* | *S. boulardii*CNCM I-745vs. no treatment controlsAll had triple erad therapy: AmoxClarrithOmeprazole or Metro ClarOmp if allergic to Amox x 14 days | N=205 enrolled, Hp+children(22 months-16 yrs)n=194 done (5.4% attrition)CHINA | 500 mg/d**sachets** | 14 daysF/up:4 weeks 13C urea breath test in subgroup of 42 kids>12 yrs old | **Erad**: 15/21(71.4%) p=0.5 ns**Any AE**: nr**AAD**: 12/102 (11.8%) p=0.004Compliance to std ther 100%p=0.03 | Erad: 13/21 (61.9%)AAD: 26/92 (28.3%)Complaince: 86/92 (93.4%) | **Bin** Zhang 2015Ped Gastroentero, Hepatol & Nutrition |

## Inflammatory Bowel Disease (IBD)- treatment

 **Page 1**

Inflammatory bowel disease may include ulcerative colitis, pouchitis or Crohn’s disease

Outcomes included: number of stools/day, or frequency of IBD relapse or time to relapse

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|  | **Probiotic** | **No.****in study** | **Dose** | **Duration** | **Relapse (or noted) in Probiotic** | **Relapse(or noted) in Controls** | **Reference** |
| *+* | *Saccharomyces boulardii* CNCM I-745 vs placebo | 20 enrolled, 17 done | 1.5 x 1010 | 7 wks | 3.3\*stools/day at week 9  | 4.6 stools/day at week 9 | **Plein** K 1993Z Gastro |
| *-* | *E. coli* Nissle 1917 “Mutaflor” + prednisone vs prednisone and placebo DB, R | 24 doneone center in Germany | 5 x 1011 | 1 year | 4/12 (33%), ns | 7/12 (58%) relapse | **Malchow** HA1997J Clin Gast |
| *+* | *Saccharomyces boulardii* CNCM I-745 *+* mesalamine (1g/d) vs mesalamine alone (3g/d)R, open | 32in remission in Italy | 1 x 1010 | 6 months | 1/16 (6% ) relapse\*p=0.04No AE | 6/16 (38%) relapse | **Guslandi** M2000Dig Dis & Sciences |
| *-* | *VSL#3 +* rifaximin (1.8 g/d) vs mesalazine (4 g/d) R, open | 40post-op in Italy | 3 x 1011(4g/d) | 9 months | 4/20 (20%)ns p=0.3 | 8/20 (40%) | **Campieri** M2000abstract A4179Gastroenterol |
| *-* | *VSL#3 +*rifaximin | 40 in remission | 1.8 x 1012 | 9 mon | 4/20 (20%) ns relapsed | 8/20 (40%) | **Rizzello** F 2000 Dig Liv Dis |
| *-* | *Lactobacillus rhamnosus* GG vs placeboDB, R | 45post-op in remission | 1.2 x 1010 | 1 yr | 3/23 (10.5%), ns | 2/22 (16.6%) | **Prantera** C2002Gut |
| *-* | *L. rhamnosus* GG + mesalazine (2.4 g/d)  | 35 adults | 1.8 x 1010 | 1 yr | 2/12 (17%)relapsed, ns | 3/12 (25%)relapsed | **Zocco** MA 2003 (abstract)Gastro |

**IBD- page 2**

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| +/- | **Probiotic** | **No.****in study** | **Dose** | **Duration** | **Relapse(or noted) in Probiotic** | **Relapse (or noted) in Controls** | **Reference** |
| *-* | *Lactobacillus rhamnosus* GG vs placebo | 11 with active disease | 2 x 109 | 6 months | 2/4 (50%) ns | 3/5 (60%) | **Schultz** M2004BMC Gastro |
| *-* | *L. rhamnosus* GG + inulin (295 mg) + std. therapy vsplacebo+std txt DB, R+ inulin | 75 children (5-21 yrs) in remission in 11 US centers | 2 x 1010 | 2 yrs | 12/39 (31%) ns, p=0.18time to relapse=9.8 months | 6/36 (17%) time to relapse=11 months | **Bousvaros** A2005Infl Bowel Dis |
| - | *S. boulardii* CNCM I-745 vs placeboAll had steroids or salicylates. 32 centers (09/04-01/10)FRANCE | 165 adults with Crohn's disease at remission for >4 wks,159 done (4% attrition).  | 2 x 1010/d1 g/d **Capsules** | 52 weeks with 3 month f/up | Remission:38/80 (47.5%) nstime to relapse: 40.7 wksBut sign better in non-smokers (34.6%, p=0.02). Smoking causes intestinal cell surface damage, more inflamm)AE: 57%SAE: 11% | Remission:42/79 (53.2%) time to relapse: 38 wks, nsAE: 58%SAE: 9.9%Relapse in non-smoking controls (72%) | **Bourreille** A 2013Clin Gastro & Help |

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| +/- | **Probiotic** | **No.****in study** | **Dose** | **Duration** | **Relapse in Probiotic** | **Relapse in Controls** | **Reference** |
| *\_* | *E. coli* (Nissle 1917) vsmesalamine (1.5 g/d) | 120 UC patients enrolled, 103 done | 2 x 1010 | 12 wks | 8/50 (16%) relapsens | 6/53 (11%) relapse | **Kruis** W 1997AP&T |
| *\_* | *E. coli* (Nissle 1917 vs 1-2.4 g/d low dose mesalamineBoth on gentamicinDB, R | 116UC patients | 1 x 1011 | 1 yr | 39/57 (68%) ITT relapse, nsAPP:26/39 (67%), ns | 44/59 (73%) relapse ITTAPP:32/44 (73%) | **Rembacken** BJ 1999Lancet |
| + | VSL#3(mix)  | 40 withpouchitis | 1.8 x 1012(6 g) | 9 months | **Recurred**:3/20 (15%)\* | **Recurred:**20/20 (100%)placebo  | **Gionchetti** P2000Gastroenterol |
| - | *L. rhamnosus GG* | 20 withpouchitis | 4 x 1010 | 3 mon | PDAI=8.0, ns\*\*n=10 | PDAI=8.4placebon=10 | **Kuisma** J 2003Alim Pharm & Ther |
| + | VSL#3(mix) DB, R | 40 withpouchitis | 9 x 1011 | 1 yr | New episode: 2/20 (10%)\* | New episode8/20 (40%)placebo  | **Gionchetti** P 2003Gastroenterol |
| *+* | *L. rhamnosus* GG  | 117 with surgery after UC | 1.4 x 1010 | 3 yrs | 3/39 (7.7%)\* | 20/78 (26%)no txt\*\*\*historic controls  | **Gosselink** MP2004 Dis Col Rectum |
| + | VSL#3(mix) DB, R | 36 with pouchitis | 3 x 1012(6 g) | 1 yr | 3/20 (15%)\*relapsed | 15/16 (94%)placebo | **Mimura** T2004Gut |
| *-* | *E. coli* (Nissle 1917) vs mesalamine (1.5 g/d)DB, R | 327 UC enrolled, 222 done | 2.8 x 1010 | 1 yr | 73/162 (45%), ns (ITT) relapseAPP: 40/110 (36%) ns | 61/165 (37%)APP: 38/112 (34%) | **Kruis** W2004Gut |
| *+* | *VSL#3 +* balsalazide vsbalsalazide | 90 UC patients | 9 x 108 | 8 wks | 86%\* cured | 73% | **Tursi** A2004Med Mon Sci |

**IBD- page 3**

UC, ulcerative colitis; ; \*\*PDAI mean symptom score

**IBD page 4**

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|  | **Probiotic** | **No.****in study** | **Dose** | **Duration** | **Relapse or noted in Probiotic** | **Relapse or noted in Controls** | **Reference** |
| *-* | *L. rhamnosus GG* vs mesalazine (2.4 g/d) vs LGG + mesalazine | 187 UC patients | 1.8 x 1010 | 1 yr | LGG only:10/65 (15%), ns versusLGG+mes:10/62 (16%) | Open controls:12/60 (20%) | **Zocco** MA2006Ali Phar & Th |
| + | VSL#3vs placebo | 15 adults pouchitis patients in remission,on antibiotics | 1.8 x 1012 (6g/d) | 12 months, followed:no | 0/10 (0%)\*also more diversity in normal flora foundMore E coli | 5/5 (100%) | **Kuhbacher** T 2006 Gut  |
| *+* | VSL#3 vs placebo. All got steroid and mesalamine txt. | 29 children (2-16 yrs old) with new UC | varied by weight (4.5 x 102-1.8 x 103/d) | 1 year | 13 (92.8%) cured P<0.001 | Placebo:4 (36.4%) cured | **Miele** E 2009Am J Gastro |
| *+* | VSL#3vs placebo | adults with mild to moderate active UC | 7.2 x 1012/d | 12 weeks | 33/77 (42.9%) remission, p<0.001 | 11/70 (15.7%) | **Sood** A 2009Clin Gastro & Hepat |
| *-* | *E coli* Nissle 1917 (EcN) vs placebo | 90 with moderate UC | 108 via enemas (10, 20 or 40 ml) | 2 weeksfollowed for 6 wks | Remission:10/23 (43.5%) 40 ml dose11/23 (47.8%) 20 ml dose8/22 (36.4%) 10 ml dose NS p=0.44 | placebo7/20 (35.0%)ITT analysis was ns, but PP was (don't count) | **Matthes** H 2010BMC Comple & Altern Med |
| *+* | VSL#3 vs placebo | 144 patients with relapsing UC | 3.6 x 1012/d | 8 weeks | Decrease in UCDAI of 50% or more: 63.1%\* P-.01 | placebo: 40.8% had 50% decrease in UCDAI | **Tursi** A 2010 Am J Gastro |

UC, ulcerative colitis; UCDAI, ulcerative colitis daily activity index

## Irritable Bowel Syndrome (IBS)-treatment

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|  | **Probiotic** | **No. randomized vs done** | **Dose** | **Duration** | **Probiotic** | **Controls** | **Reference** |
| *+* | *S. boulardiiI-745*vs placebo | 34ITT | 9 x 109**capsules** | 4 wks | decrease #stoolsmean -2.2/d \*13/16 (81%) improved | mean decrease -0.5/d, no raw # given13/18 (72%) | **Maupas** JL 1983Med Chirug Dig |
| - | *Lactobacillus rhamnosus* GG (LGG)vs placebo armCROSSOVER | 24, 19 doneRome IAPP | 1 x 1010**tablets** | 8 wks | 9/24 (37%) less pain, ns10/24 (42%) bloating, ns | 3/24 (13%) less pain7/24 (29%) bloating on cross-over | **O'Sullivan** MA 2000Dig Liver Dis |
| *+* | *Lactobacillus plantarum* DSM9843 (299v)in rose hip drink vs placebo | 60Rome II52 done, APP, 13% lost | 2 x 1010per day(400 ml/d)**drink** | 4 wks, 12 mon f-up | 11/25 (44%)\*less gas | 5/27 (18%) less gas | **Nobaek** S 2000Am J Gastro |
| *+* | *Lactobacillus plantarum* 299v“ProViva” drink~50% IBS-C and ~49% IBS-A | 40Manning criteriaITT, 0% lost | 2 x 1010**drink** | 4 weeks, 12 mon f-up | 9/20 (45%)\* IBS resolvedno pain (0/20)\* | 3/20 (15%) placebono pain 11/20 (55%) | **Niedzielin** K2001Eur J Gast Hepatol |
| - | VSL#3(8 strains) vs placebo | 25IBS-D,Rome IIUSA | 9 x 1011**powder** packet | 8 weeks | ITT:bloating score-13.7\*4/12 (34%) cured ns | placebo bloating score-1.75/13 (38%) cured | **Kim** HJ 2003Al Pharm & Therapy |

IBS outcome diagnosed by Rome II or III criteria. Outcomes may include: individual IBS symptoms, or change in IBS-SSS (symptom scores from baseline) or decrease in number of stools/day, or number reporting more or fewer IBS symptoms

**IBS page 2**

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| **+/-** | **Probiotic** | **No.** | **Dose** | **Duration** | **Probiotic** | **Controls** | **Reference** |
| *+* | *Bifido. infantis 35624**vs placebo* | 53, 49 doneRome IIAPP | 1 x 1010**drink** | 8 wks | VAS=9.4 \* painVAS=11.7\*bloating | VAS=14.9 painVAS=17bloating | **O’Mahony** L2005Gastroentero |
| *-* | *L. rhamnosus GG vs placebo**underpowered for diarrhea outcome* | 58 kids Rome IIAPP50 done | 2 x 1010**capsules** | 6 wks | 40% less abs pain, ns2/17 (12%) less diarrhea, ns0/17 (0%) bloating\* | 44% less pain0/18 (0%) less diarrhea6/25 (24%) bloating | **Bausserman** M 2005J Pediatrunder-powered |
| *+* | *VSL#3**yogurt**vs placebo* | 48Rome IIITTUSA | 8 x 109**yogurt** | 4 wks | VAS=29.7\* gasVAS=31.3 bloat, nsVAS=23 pain, ns 11/24 (46%) no bloating , ns | VAS=39.5VAS=38.5VAS=278/24 (33%) no bloating | **Kim** HJ 2005Ali Pharm & Ther |
| *-* | *L. plantarum 299v* rose hip drinkvs placebo | 66, APP 58 done (12% lost) | 2 x 109drink | 6 wks | Symptom score= 279 nsImproved: 10/29 (35%) NS | placebomean score 245Improved:11/29 (38%) | **Simren** M 2006GastroenterolMtg abstract |

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| **+/-** | **Probiotic** | **No.** | **Dose** | **Duration** | **Probiotic** | **Controls** | **Reference** |
| *+* | *3 dose arms:Bifido. infantis 35624 (low dose)*vs placebo | 362 womenAPPn=90 | **capsules**1 x 106 | 4 wks | Symptom score (SS):SS=2.15, nsCured 40/90 (44%) ns | placebo (n=92)SS=2.09cured 38/90 (42%) | **Whorwell** PJ 2006Amer J Gastro |
| *+* | *Bifido. infantis 35624 (medium dose)* | n=90 | 1 x 108 |  | SS=1.76\* (also gas/bloat)**cured 56/90 (62%) \*****less pain score 108 only** | **Whorwell** PJ 2006Amer J Gastro |
| *-* | *Bifido. infantis 35624 (high dose)*  | n=90 | 1 x 1010 |  | SS=2.13, ns (high dose clumped) cured 33/90 (37%) ns | **Whorwell** PJ 2006Amer J Gastro |
| *+* | *L. rhamnosus* GG vsplacebo*Large study of n=104 children with FAPD (function abd disorders: dyspepsia or IBS or abd pain). This is only IBS sub-set* | n=37kids with IBSPOLAND | 6 x 109**capsules** | 4 wksF/up:none | ITTIBS symptoms no abd pain:6/18 (33%)\*AE: none | IBS sub-set:placebo:No abd pain:1/19 (5%) | **Gawronska**A2007Arch Iran Med |
| *-* | **“**Activia**”** *Bifido animalis DN173-010[starters: Strept thermo + L. bulgaricus]* yogurt vs dead yogurt | 274 IBS-C, 267 done(2% attrition) | 2.4 x 1010/day**yogurt** | 6 wksF/up:none | Living *Responders* (>10% improved): 63% ns*Bloating score*: -0.5 ns*HRQoL* score change: +12.2 + 16.2 | **DEAD** heat-treated yogurt:*Responders* 56.8%*Bloating*: -0.31*HRQoL* score change: +13.5 + 19.3 ns | **Guyonnet** D 2007 Alimen Pharmacol Ther |

**IBS –page 3**

**IBS page 4**

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|  | **Probiotic** | **No.** | **Dose** | **Duration** | **Probiotic** | **Controls** | **Reference** |
| *+* | “Activia” *L. casei* DN 173-010 now called *Bifido. lactis* [+ 2 starters: *Strept* *thermophilus & L. bulgaricus]*vs control milk | 41 females (20-69 yrs old) IBS-C. If 41 enrolled, 38 randomized (3 dropped early). n=34 completed, but ITT. 2 had missing data | (2 x 1010cfu/day**milk** | 4 wks,F/up: 0 | (n=17) Significant reduction in bloating & abd distension Figures show sign reductionsOverall IBS score at 24 wks:3.3 + 0.15, p=0.03\*. | Fermented milk control: (n=17)Overall IBS-SSS:3.8 + 0.4 | **Agrawal** A 2009 AAlim Pharacol Therap |
| *+* | *L. plantarum* 299v vs placebo | 214 with Rome III IBS (63 female, 151 men, adults (19-70 yrs old) in 3 centers in India | 1 x1010 cfu/d | 4 wksF/up:nr | Global improved: 80.6%\*Less Abd pain score: 53%\*Less bloating score:68%\* | Global improved:8.8%Less abd pain score:15%Less bloating score:20%\* | **Sawant** PD & Ducrotte P2010DDW Mtg abstract, Chicago |
| *+* | *VSL#3* vs placebo  | 59 kids (4-18 yrs old) in 5 Ped care in Italy & India | 1 sachet/day (kids 4-11 yrs) or 2 sachets (kids 12-18 yrs old)no cfu/d data | 6 wks then 2 wk washout then 6 wks other txt | Global improvement of symptoms:2.1 (P<0.05) | Global improvement: 2.9 | **Guandalini** S 2010J Ped Gastroenterol Nutr |

**IBS continues page 5**

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|  | **Probiotic** | **No.** | **Dose** | **Duration** | **Probiotic** | **Controls** | **Reference** |
| *+* | *L. rhamnosus* GGvs placebo | n=141 childrenIBS or functional pain in 9 sites and a referral centerITALY | 6 x 108/d | 8 wks,F/up: least 4 wks | Success at week 12:48/71 67.6%) p=0.03AE: nr | Success in placebo at 12 wks:37/70 (52.9%) | **Francavilla** R 2010 Pediatr |
| *-* | *“Bioflor”S. boulardii I-745* [Biocodex]vs placebo | 67 IBS-D or IBS-A patients in Seoul **KOREA** | 4 x 10 11  | 4 wks | (n=34) Overall IBS symptoms-NS((1.2 at 4 wks)but sign improved QOL 15.4% p<0.05Score =70.9 day 1 and 80.8 at 4 wk) No AEQOL: -9.9 + 0.5 | (n=33)IBS score=1.3 at 4 wks)QOL improved in 7%Score: 74.8 Day 0 and 79 at 4 wks.n=1 pain/gasQOL: +4.2 + 0.4 | **Choi** CH 2011J Clin Gastro |
| *-* | *S. boulardii* I-745 vs controlsBangladesh June 2004-July 2005 | n=70 adults with diarrhea predominant IBS | 500 mg/d1 x 1010/d | 1 month&f/up: 1 month | (n=35)#BM/d: 2.9 + 1.4, p=0.6Change in abd. pain score: 0.47 + 0.7, P=0.6 | (n=35)#BM/d: 2.7 + 1.3Change in abd. pain score:0.4 + 0.74 | **Kabir** MA2011Mymenshingh Med |
| - | VSL#3Mix of:*3 Bifido (longum and infantis and breve) +4 Lacto. (acidop and casei and delbrueckii and plantarum) and Strept thermophilus.*vs placebo | n=24 adultsIBS-DUSA | 9 x 1011/d**capsule** | 8 wks | (n=15)Global score change:-1.3+ 0.6 nsBetter “satiety”No change in flora | placebo (n=9)Global score change: -0.7+ 0.7AEs: none, ns | **Michail** S2011ProbioticsAntimicrob Proteins |

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|  | **Probiotic** | **No.** | **Dose** | **Duration** | **Probiotic** | **Controls** | **Reference** |
| *+* | *L. plantarum* 299v (aka DSM 9843)vs placebo | IBS adultsn=214n=204 done(5% attrit)FRANCE | 1 x 1010/d**capsules** | 4 weeksF/up: 0 | (n=105)Less abd pain: 51.9%\* (p<0.05)BM/d sign lower78.1%\*improved | Placebo (n=106)Less abd pain:13.6%8.1% improved no AEs, ns | **Ducrotte** P2012World J Gastro |
| *+* | *S. boulardii* I-745(Biocodex) vs placebo. All given ispaghula husk (fiber) as std txt*.* | n=72 adults with IBS-D in PakistanPilot to study serum cytokines. | 750 mg/d | 6 wksF/up: 0 | (n=37)only 1/8 diarrheal symptoms improved (abd pain score -0.04 +0.9, p=0.005).Sign increase in anti-inflam IL-10 +1.6 +1.7\*Sign reduced pro-inflam IL-8 -3.3 +4.7\* and TNF -4.0 +4.3\*Better QOL (no data given) | (n=35) placeboabd pain score change since baseline=+0.3+0.5.IL-10: +0.4 +1.4IL-8: -0.6+2.2 TNF:-0.7 + 3.4  | **Abbas** Z2014Euro J Gastro & Hepatol *Confirms Choi 2011Pilot and underpoweredstudy, strong placebo effect-all better over time-due to fiber?* |

**IBS continues—page 6**

## Pediatric acute diarrhea-treatment

Pediatric diarrhea defined as new onset of acute infectious gastroenteritis symptoms (< 7 days duration) due to viral or bacterial etiologies but may be idiopathic. Outcomes defined as ‘cured’: resolution of diarrhea symptoms (typically >3 loose/watery stools/day) in subjects aged 1-18 years old, or change in Bristol stool scores, or mean duration of diarrhea

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| **+/-** | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Dose perday** | **Duration of treatment(days)** | **Percent cured or duration of diarrhea (days)** **Probiotic | Controls**  | **Reference** |
| *+* | *S. boulardii* CNCM I-745*+* ORT vs ORT control. Not randomized | 0.5-30 |  38 | 500 mg1 x 1010**sachet** | 5 | 18/19 (95%\*) cureddura nr | ORT only 15/19 (79%) | **Chapoy** P1985Ann de Ped |
| *+* | *S. boulardii* CNCM I-745vs placebo*(SAME AS Cetina-Sauri 1994!!!!* | 3-36kids (3 mon-3 yrs) acute diarrMEXICO | 130 | 2 x 1010[800 mg/d] | 4F/up: none | 55/65 (85%\*)curedmean=2 dno Std dev | 26/65 (40%)RR cure on Day 4 yes=1.9 (1.4-2.8)mean=3 d | **Cetina-Sauri** G1989 Trib Med [in Spanish] |
| + | *L. rhamnosus GG* | 4-45 |  71 | 2 x 1010-1011 | 5 | 1.4 d\*  | 2.4 d | **Isolauri** E1991Pediatrics |
| + | *L. rhamnosus GG* | 7-37 |  39 | 2 x 1010-1011 | 5 | 1.1 d\*  | 2.5 d | **Kaila** M 1992Pediatr Res |
| *+* | *L. rhamnosus GG* | 5-28 |  n=42 | 2 x 1010 | 5 | 1.5 d\*  | 2.3 | **Isolauri** E 1994Dig Dis Sci |
| *+* | *Lactobacillus acidophilus* LB(killed strain)vs placebovs active control (loperamide)All had either ORT or IV rehydration | 1-54 months, inpatientskids with acute diarrheaFRANCE | 103 in, 103 done (0% attrition) | varied3 x 1010 Day 1, then 2 x 1010 for 3 days**sachets** | Mean 4 daysF/up: none | **Dead** Time to recovery: 49.7 + 30 hours (2 days)\*n=38no AE | **Placebo**64.7 + 30 hours (2.7 days), n=33**Loperamide**60.9 hrs (n=32) | **Boulloche** J1994Ann Pediatr(in French) |
| - | *L. rhamnosus GG (alive) vs L. rhamnosus GG (dead)* | <4 yrs old txt rotaviral diarr, inpatient | 41, 26 rotov+ | 2 x 1010-11**liquid** | 5 daysF/up: none | Live LGG:10/12 (83% had rotoviral IgA)\* duration diarr=1.5 d NS | Dead LGG:2/13 (15%) roto IgA+duration diarr= 1.6 days | **Kaila** M 1995Arch Dis in Childhood |

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|  | **Probiotic** | **Age of subjects (months)** | **No.****in study** | **Dose givenper day** | **Duration of treatment (days)** | **Probiotic** | **Controls** | **Reference** |
| *+* | *Saccharomyces boulardii*  CNCM I-745vs placebo | 11-35 |  18 | varied | 30 | 4/7 (57%) cured\* | 2/8 (25%)dura: nr | **Chouraqui** JP1995J Ped Gastro Nutri |
| *+* | *S. boulardii* CNCM I-745vs placebo(Biocodex)Cuba | 6-36 monchronic diarr90% Giardiasis |  40 | 1 x 1010**sachets** | 30 | 14/20 (70%) \* improvedNo AEs | 2/20 (10%)placebo  | **Guillot** C1995Rev Mex de Pueric Y Ped |
| *+* | “Lacidofil”*L. acid [helveticus* R52]+ *L. rham* R11)vs control (clay, smectite) | kids with acute diarrhea**Czech** | 75 | 2 x 109/d | varied by duration of diarrhea | (n=33)4.8 + 2.1 days, p<0.05 | (n=42)8.7 + 4.2 days | **Tlaskal** P 1995 Cesko-Solven Ped [In Czech] |
| + | *L rhamnosus* GG vs*L. casei ST vsL. casei* LD- all active controls | 6-35txt acute rotavir diarrhea |  49 | 1 x 10105.5 x 1086 x 109 | 5 vs5 vs5 | 1.8 d\* Lr GG | vs. 2.8 d L. caseino placebo controls | **Majamaa** H 1995J Ped Gastroenterol Nutri |
| + | *L. rhamnosus GG* | 1-24 |  32 | 2 x 1010-1011 | 2 | 69%\*  | vs. 25% | **Raza** S1995Ped Infect Dis J |
| + | *L. rhamnosus GG* | <24 |  39 | not given | 2 | 1.9 d\* but reported subgroup only | vs. 3.3 | **Pant** AR 1996J Trop Ped |
| + | *L. rhamnosus GG* | 3-36 | 100 | 3 x 109 | 5 | 3.3 d\*  | vs 5.9 | **Guarino** A1997J Pedia Gastroent Nutr |

**Ped diarrhea-page 2**

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|  | **Probiotic** | **Age of subjects (months)** | **No.****in study** | **Dose givenper day** | **Duration of treatment (days)** | **Probiotic Percent cured or duration of diarrhea (days)**  | **Controls** | **Reference** |
| *+* | *S. boulardii*  CNCM I-745vs placebo All got ORTDBPCJan 1-Aug 30, 1996 | Hospitaized kids (mean 21 mon Sb or 22 mons old-plac)with mild dehyration & diarrhea, 1 siteMexico | 50 | 600 mg/d | 5 daysF/up:none | Sb:Cured by Day 4: 24/25 (96%)\* p=0.01no data on duration No AE | placebocured18/25 (28%) | **Hernandez** CL1998Revist Enferm Infecc Ped[in Spanish] |
| *+* | *L. casei* DN114001 [CNCM I-1518]Actimel yogurttxt of acute diarr | 7-32Kids in 12 day cares | 287 | Aged 6-18 mon (3 x 1010), over =6 x 1010) | 30 day60 days follow-up | 4.3 + 2.7d\* | Jellied milk: 8.0 + 5 daysStd yogurt: 5.3 + 2.5 | **Pedone** CA1999Ind J C P |
| + | *L. rhamnosus GG* + ORTvs placebo + ORT, multi-siteITALY | 1-36 months old with acute diarrh | 287 | 4 x 1010 | varied | 2.4+ 1.1 d\* LOS sign. shorter | vs. 3.0 + 1.5 days | **Guandalini** S2000J Pediatr Gastro Nuti |

**Txt Ped Acute Diarr---page 3**

Abbreviations: d, day; LOS, Length of stay; ORT=oral rehydration therapy

**Txt Ped Acute Diarr---page 4**

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| **+/-** | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Dose per day** | **Duration (days)** | **Percent cured or duration of diarrhea (days)** **Probiotic | Controls**  | **Reference** |
| *+* | *Lactobacillus acidophilus* LB (heat-killed strain) vs placeboAll had ORT Thailand  | 3-24 months, inpatients kids with acute diarr | 73(0% attrition) ITT | 2 x 1010(5 doses over 48 hours) | 2.5 daysF/up: 2 days AE: nr | Dead:1.8 d p=.03(43.4 + 25.9 hrs)Cured: 7/37 (19%) p=0.03 | Placebo:duration:2.4 days(57 + 36.3 hrs)Cured Day 2: 1/36 (2.8%) | **Simakachorn** N2000J Ped Gastroent Nutri |
| *+* | *L. casei DN114001*[aka CNCM I-1518][starters: L. bulgaricus + Strept thermophiles](Actimel) vs Indian Dahi yogurt vs heat-treated yogurt | 6 mon-5 yrs with diarrhea either inpatients or community | Pilot. n=110 | 3 x 1010/d**yogurt** | not given in paper | duration=1.5d inpatients P<0.05, but not community 2.0d. | duration inpatient yogurt (2d) vs heated yogurt (2 d) | **Agarwal** KN 2001 Indian Ped |
| + | *S. boulardii* CNCM I-745vs placebo  | 2-29 monthTURKEY | 100 | 5 x 109 | 3 df/up: none | 42/50 (84%)\*curedno duration data | 32/50 (64%) | **Urganci** N2001Arch Gastro |
| *+* | *S boulardii* CNCM I-745*+ ORS*vs ORS open control | 6 mon-5 yrsPAKISTAN | 101 | 500 mg/d | 6 days | On Day 6, % with diarrhea: 9/51 (17%)\* Also -1.1d diarrhea:x=3.6 +1.6 days(n=51) | ORS given only % diarrhea: 18/50 (37%)x=4.5 + 1.6(n=50) | **Hafeez** A2002 J Coll Phy Sur Pak |
| + | *L. casei DN114001[CNCM I-1518] & starters: [L. bulgaricus + Strept thermophiles] (*Actimel) vs Indian Dahi yogurt vs heat-treated yogurt | 6 mon-5 yrs in India | 150 (75 hosp and 75 comm) | 300 mg/d~ 3 x 1010/d | not stated in paper | hosp kids duration 1.5 + 0.5 d\*comm.-unity:1.9 + 0.8 days\*no normal flora done | heat-killed yogurt:hosp 2.1 + 0.7 comm2.4 + 0.9 | **Agarwal** KN 2002 Eur J Clin Nutr |

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| *+/-* | **Probiotic** | **Age of subjects (months)** | **No.in study** | **Dose per day** | **Duration (days)** | **Percent cured or duration of diarrhea (days)** **Probiotic | Controls**  | **Reference** |
| - | *L. rhamnosus GG* | <24 | 124 | 1 x 106 | 7 | 1.6 d  | vs. 1.6 ns | **Costa-Ribeiro** H2003J Ped Gastroenterol Nutr |
| - | *S. boulardii* CNCM I-745 *(n=30)* vs controls (n=29)also see belowArgentina | 6-24 monpersistentdiarrhea(>14 days) | 59 | 2 x 1012per day**powder in milk** | 5 days | #stools/d: 2 + 2 Duration diarr:25+3 d NS n=30 | n=29Milk control5+3 stools/day22+2 days duration | **Gaon** D2003Medicina |
| + | *Saccharomyces boulardii* CNCM I-745 vs placebo. All had ORTTurkey | 3-84 mon41% rotavirus or Shigella | 200 kids acute diarr | 250 mg5 x 109powderdiluted in liquid | 5 daysand 14 days f-up | (n=100)**duration**: all diarrhea4.7 +2.5d\*, p=0.03watery diarr2.8 + 1.0 d**LOS**: 2.9 + 1.2\* | (n=100)duration:all diarrhea 5.5 + 3.2watery diarr3.8 + 1.4 d**LOS**: 3.9 + 1.5 dno serious AEs | **Kurugol** Z2005Acta Paediatri |
| + | 3 arms:*1. Lacidofil (L. acido[helveticus R52] + L. rhamn R11)* vs 2. placebo vs 3. 'Hylac"*-prebiotic* | kids acute gastritis (12-72 mon old)**CZECH** | 113  | 2 x 109/d**capsules** | 10 daysF/up: none | 1. probiotic:(n=42)duration= 4.0 +2.0 d\* p<0.052. “Hylac" (n=29) ns6.1 + 3.2 d | (n=39) placebo: duration=5.4 + 2.3 d | **Tlaskal** P 2005 Nut Aliments Fonction Alimen Sante |

**Txt Ped Acute Diarr---page 5**

**Txt Ped Acute Diarr---page 6**

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|  | **Probiotic** | **Age**  | **No. in study** | **Dose given per day** | **Duration**  | **Probiotic [**  | **Control** | **Reference** |
| **+** | *S. boulardii*CNCM I-745 *+* ORT vs controls (ORT only) Pakistan | 2-12 yrs oldmild-moderateacute diar | 100 | 500 mg1 x 1010**powder**(diluted in water or food) | 5 days, followed 2 mon | (n=50)3.6 + 1.0 days diarr\*p=0.001no AE | (n=50)4.8 + 1.4 d (ORT only control) | **Billoo** AG 2006 World J Gastro |
| **+** | *S boulardii* CNCM I-745 + ORTvs placebo + ORTArgentinaAll also got ORT | 3-24 mon old, outpatswith mild-moderate diarrhea | 10088 done txt, 72 done f/upnot ITT | 5 x 109 if < 1yr old1 x 1010 if > 1 yr old**capsules** | 6 dF/up: 1 month | (n=44 ITT) or [n=35 APP]duration: 4.7 +1.9d\*(2-13 days range) | (n=44 ITT) or [n=37 APP]mean duration: 6.2 + 3.2 d(range 2-10 d) | **Villarruel** G2007**A**Acta Ped[also in Villarruel 2007**B** meeting abstract in J Ped Gastro & Nutr] |
| + | *L. acidophilus LB (heat killed)* + ORT "Lacteol Forte" vsplaceboAll had ORTECUADOR | Txt ped diarrhea in kids:mean age=10 monthseligible if <2 yrs, inpatients  | 800 lost, 0% attrition | 2 x 1010 per day**sachets** | 3 daysF/up: 1 dayITT | Dead cured 36/42 (86%)\* duration diarrhea: 39.5 + 10.5 hrs, p<0.05 | placebo + ORTcured 20/38 (53%)duration= 63.4 + 30 hrs | **Lievin-Le Moal** V 2007Pediatrics |

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|  | **Probiotic** | **Age of subjects (months)** | **No.****in study** | **Dose****givenper****day** | **Duration of treatment****(days)** | **Percent cured or duration of diarrhea (days) in****probiotic | ORT+ ORT | controls**  | **Reference** |
| + | *L. rhamnosus GG* + ORT “Dicoflor” vs ORT control | 3-36 | 192 | 6 x 109**in water** | 5 | 3.3 + 1.5 d \* n=100 | (n=92)4.8 + 1.0 dMedian=115.5 hrs | **Canani** RB 2007 BMJ |
| - | *S. boulardiiI-745*+ ORT “Codex” vs ORT control | 3-36 | 183 | 5 x 109 **in water** | 5 | 4.4 + 0.93 days nsMd=105 hrsn=91 | **Canani** RB 2007 BMJ |
| - | 4 strains of *Bacillus clausii*(O/C84, N/R84, T84,SIN84)+ ORT “Enterogermnia” vs ORT control | 3-36 | 192 | 1 x 109 **in water** | 5 | 4.9 + 1.03d nsMd=118 hrsn=100 | **Canani** RB 2007 BMJ |
| - | *E. faecium SF68*+ ORT “Bioflorin” vs ORT control | 3-36 | 183 | 7.5 x 107 **in water** | 5 | 4.7 + 1.7 d(n=91) ns | **Canani** RB 2007 BMJ |
| \*FROM CANINI 2007: Strains Daily dose Brand name Lactobacillus casei rhamnosus GG 6×109 CFU/dose Dicoflor Saccharomyces boulardii S boulardii It 5×109 CodexBacillus clausii O/C84, N/R84, T84, SIN8 4x 109 CFU/dose EnterogerminaEnterococcus faecium SF 68 7.5×107 CFU/dose Bioflorin† 109 CFU, 109 CFU, 109 CFU, 5×108 CFU/dose Lactogermina |

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| **+/-** | **Probiotic** | **Age of subjects (months)** | **No.****in study** | **Dose****givenper****day** | **Duration of treatment****(days)** | **Percent cured or duration of diarrhea (days) in****probiotic | controls**  | **Reference** |
| *+* | *S. boulardii* CNCM I-745with ORTvs control placebo | Children 6 mon-10 yrs with acute diarrheaOct 2004-March 2005TURKEY | 27 | 0.5 g /d  | 7 daysF/up: noneno duration diarrhea data | (n=16)By day 4, sign less stools/d:0.4 + 0.2\*also more IgA | (n=11)ORT only, day 4: 1.8 + 0.4, p<0.001No AEs | **Ozkan** TB 2007 J Int Med Res |
| *-* | *"*Lacteol*" L. acidophilus LB (heat-killed)* + ORS vs placebo + ORS | Txt of kids with acute ped diarrhea (3 months-4 years old) outpatientsPERU | n=80 3 lost, 77 done, (4% attrition), but ITT done | 3 x 1010 Day 2, then 2 x 1010 max 4.5 days**sachet** | 4.5 daysF/up: none | **DEAD**:36/40 (90%) cured, p=0.33 NSMedian duration diarrhea= 10 hrs, p=0.3 NSAE: 30% | Placebo:cured: 35/40 (87%)Median duration= 16.6 hrsAE: 15%  | **Salazar-Lindo** E 2007J Ped Gastroenterol & Nutri |
| + | *L rhamnosus GG* vs ORS only control | kids with persistent diarrhea1 hosp, inpatients INDIA | 253 random.(7.1% attrition), 235 done | 1.2 x 108/d | minimum of 7 days or until no more diarrhea. No f/up | Mean duration all diarrhea:5.3 + 2.1 d, p<0.05Duration CDI: 3.2 + 2.4 d p<0.05 | Mean duration all diarrhea:9.2 + 2.8 dDuration CDI: 8.0 + 2.8 d p<0.05 | **Basu** S 2007J Clin Gastroenterol |
| + | *S. boulardii*CNCM I-745vs placeboAll had ORT | India and Indonesiakids (3-33 months old) acute diarrhea | 202 kids, 188 done (7% attrition) | ORT+ 500 mg/d**formulation not reported** | 5 daysF/up: none | (n=93)Duration: 2.2 + 1.6 d\* Cured day 5: 97% p=0.13 ns | (n=95)Duration: 2.8 + 2.2 d Cured day 5: 90% | **Vandenplas** Y2007J Ped Gastro Nut[Euro Soc Ped Gastro Hep & Nut Mtg abstract] |

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|  | **Probiotic** | **Age of subjects (months)** | **No. in study** | **Dose per day** | **Duration (days)** | **Percent cured or duration of diarrhea (days) in****probiotic | controls**  | **Reference** |
| **+** | *S. boulardii*  CNCM I-745 *+ ORT* vsplacebo + ORTMyanmar | 3 mon-10 yrs21% E. coliacute diarrhea.May not be randomized “groups assigned alternatively” | 100(n=50 each group) | 500mg/d**formulation not reported** | 5 days | duration 3.08 + 0.95 d\*n=50 | 4.7 + 1.2 dn=50 | **Htwe** K 2008 Am J Prop Med Hyg |
| *+* | *S. boulardii*  CNCM I-745 *+* metro vs control (metro only)open RCT | mean 11.7 + 2.1 yrs oldacute bloody diarrhea by *Entamoeba histolytica*TURKEY | n=50 | 500 mg/d1 x 1010metro (60 mg/kg/d)**capsules** | 7 days,1 month follow-up | (n=25)duration diarr:46.1 + 18.2 hr \*1.8 + 0.7d\*all cysts cleared by day 5 | (n=25)73.9 + 32.4 hrs or 3.0 + 1.2 dOn day 5: 6/25 still cyst positive | **Dinleyici** EC 2009 Am J Trop Med |
| *+* | *VSL#3* vs placeboItaly | 1-16 yrs old, kids with ulcerative colitis, all given steroids and mesalamine | n=29 | 4.5-18 x 1011/d | 1 year | cured 13/14 (92.8%)p<0.05\*no AE | placebo4/15 (36.4%) cured | **Miele** E 2009Am J Gast |
| *-* | *S. boulardii*  CNCM I-745 (Reflor) + metro vs metro only controlOpen trialTurkey | 1-15 yrs old with *E. histolytica* diarr | n=90n=5 lost in Sb (non-compliant) 6% attrition | 250 mg/d (5 x 106/d)Metro:30-50 mg/kg/d | 10 daysF/up:10 dno std dev data | (n=40)duration diarr:median 4.5 days , p=0.96no mean sd data | (n=45) metro onlymedian= 5 daysNo AEs  | **Savas-Erdeve** S & Gokay S 2009 Turk J Ped |

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|  | **Probiotic** | **Age of subjects (months)** | **No. in study** | **Dose per day** | **Duration (days)** | **Percent cured or duration of diarrhea (days) in probiotic** | **Controls** | **Reference** |
| *+* | *S. boulardii*( CNCM I-745 Reflor®, Sanofi-Aventis, Turkey) vs fluid-extract from Pinar (*L. bulgaricus and S. thermophilus)* 107/100 ml yogurt not blinded, open trialORT & Zinc as needed | children with acute non-bloody diarrhea;x= 21 + 28mon old[5-168 mon]61-81% de hydratedTURKEY | 67 enrolled, 55 done(18% attrition) | SB: 500 mg (kids >2 yrs) or 250 mg if <2 yrs.in **fluid**30-60 ml/d dependent on age | 5 days | APP:Diarrhea resolved by Day 3:SB 13/28 (46.4%) ITT was Sb 48.5%\* ITTDuration diarrhea: 4.45 + 2.5d nseffect not sustained by Day 5 | Cured yogurt (6/27, 22.2%) p=0.06ITT 25.5%, p=0.03 denominator not givenITT duration: 5.4 + 3.1 day NS | **Eren** M 2010Am J Trop Med Hyg |
| *+* | *S. boulardii + ORT* vs placebo + ORT | n=76Children (1-23 mon)with rotaviral diarrhean=64 done(16% attrition)BOLIVIA  | n=41 | 8 x 1010/d**powder in water** | 5 daysno follow-up | (n=21)ORT+ SB: medianduration diarr= 58 (IQR 41) or 2.42 + 1.27d (p=0.04) | (n=20)ORT + placebo:median(IQR) duration diarr= 84.5 hrs (94 IQR)or est. 3.5 +2.9**d** | **Grandy** G 2010 BMC Infect Disstd dev from DinleyiciEC 2012] |

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|  | **Probiotic** | **Age of subjects (months)** | **No. in study** | **Dose per day** | **Duration (days)** | **Percent cured or duration of diarrhea (days) in probiotic** | **Controls** | **Reference** |
| *+* | *VSL#3* vs placebo | 4-18 yrs old with IBD, cross-over trial with 2 wk wash-out | 59 | 1 sachet (4-11 yrs old)or2 sachets (12-18 yrs old) | 6 weeks | 44/59 (74.6%) respond on VSL3.Mean Global symptom score=2.2 (p<0.01) | 17 did not respond while on placeboMean Global symptom score=3.0 | **Guandalini** S 2010 J Ped Gastroent Nutr |
| *+* | *S. boulardii* CNCM I-745in specific formulavs std formula controls (not the same formula as Sb patients)France | infants (1-9 mon old)(5.4 + 0.4 mon old) with acute diarrhea4-5% de hydrated | n=70 | 200 mg/d**formula** | 6 daysF/up: none | (n=34)duration diarrhea: 35.4 + 3.7 hrs or1.5 + 0.1 d, p<0.001 | (n=36)duration: 67.1 + 5 hrs or 2.8 + 0.2 days | **Le Luyer** B2010Archives de Pediatrie (in French) |
| *+* | *S. boulardii*  CNCM I-745(Reflor)vs metro vs control (no txt) Turkey | kids with *Blastocystis hominis* (leading GI pathogen in Turkey) | 48 | SB (500 mg/d)ORmetro (60 mg/kg)  | 10 daysF:up: 5 days | cured **SB**: 14/18 (77.7%)\*vs **metro**10/15 (66.6%)ns | control:6/15 (40%)  | **Dinleyici** EC 2011Parasito Res |
| *+* | *S. boulardii +*  CNCM I-745Zinc vs Zinc only vs 6 other control groups (+ formula, + Zinc) vs ORS only controlTurkey | 1-28 monpeds with rotavirus diarrhea | 480 | 250 mg/d**not reported formulation** | minimum of 5 days | (n=60)SB+Zn only: less diarrheaduration= 3.1 + 1.8 days, P<0.05if SB only(n=60) (4.8 + 1.5 days, NS) | (n=60)ORT controlduration: 5.3 + 1.8 days | **Dalgic** N2011Ped Int |
| *+* | *S boulardii*  CNCM I-745(Floratil-Merck) vs placebo, Brazil | 6-48 mon57% rotaviral, acute | 176 | 8 x 109/d | 5 days ITTno duration data | On day 3, 66/95 (69.5%) cured\* | placebo 40/91 (44%) cured | **Correa** NB 2011 J Ped Gastroent Nutri |

**Txt Ped Acute Diarr---page 11**

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|  | **Probiotic** | **pop** | **N** | **dose** | **duration** | **probiotic** | **controls** | **reference** |
| + | *Bacillus clausii*+ ORT versus open control ORT onlyPhase 3 RCT*See full publications Lahiri 2015A and 2015B of other site #2* | kids6 mon-5 yrs old with acute diarrhea <48 hrs1 of 6 sitesMumbai, India | n=56 site #1:Seth GS Med College KEM Hospital(from author) | 4 x 109 per d **spores** | 5 daysF/up:5 days | (n=28)duration diarrhea= 44.8 hrs \* p<0.01no std dev dataMd=41.3Cured Day 3 40.7%\* | (n=28)duration in ORT only:74.5 hrs no std dev Md=67.5 hrsCured Day 3 9.1% | **Lahiri** KR2011Abstract from 48th Annual National Conference of Indian Acad of PedJan 20-23 2011Jaipur INDIA**see other sites full papersLahiri KR2015 A-C** |
| *+* | *S. boulardii* + CNCM I-745ORTvs placebo + ORT in puffed rice powder | Children 3-59 mon with acute diarrhea, hospitalized, 58% dehydrated India | 108 | 500 mg**sachet**  | 5 days | (n=54)duration= 2.2 + 1.0 daysp<0.05or [52.1 +24.6 hrs] | (n=54)duration 2.7 + 1.3 days r [64.0 + 30.4 hrs] | **Riaz** M2012Indian J Pediatr |
| *-* | *S. boulardii*  CNCM I-745Biocodex ORT versus controls (ORT) | 5 mon-5 yrs old,all rotaviral diarrhea Turkey | n=50:Sb (n=25)and n= 25control | 6 x 109/d282.5 mg/d “Reflor” **sachet**note, low dose!! | variedf/up: none | durationSB=6.6 + 1.7 days, ns p=0.4n=25 | 7.0 + 1.6 daysn=25 | **Erdogan** O 2012 J Trop Med |

**Txt ed Acute Diarr---page 12**

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|  | **Probiotic** | **pop** | **N** | **dose** | **duration** | **probiotic** | **controls** | **reference** |
| *+* | *L. reuteri* DSM 17938 vsplacebo*Italy*all given ORT | 74 children (6-38 months), inpatients 3 hosp in Italy with acute diar.  | Of 74 enrolled, 69 done (7% attrition) | 4 x 108/d | given 7 daysno AE | **duration**= 2.1 + 1.7 days, p<0.03**Cured** day 3 (52%), p<0.02 | duration3.3 +2.1.Cured by day 3: 24% | **Francavilla** R2012APT vol 36 |
| *+* | *S. boulardii* CNCM I-745 *+*ORT vs std ORT (open study)  | inpatient kids (2 mon-5 yr) with watery diarrhea0% attrit **Pakistan** | N=420 | 500 mg/d**sachet** | 5 daysnote: sd nr in paper, calculated | (n=210)Duration: 3.43 + 1.69 days, p<0.05WMD duration: less by -25.7 hrs, p<0.05 | (n=210)Duration: 4.5 + 1.69 days. RR day 3= 0.09 (0.05-0.16) | **Khan** A2012Pakistan Paed J |
| *+* | *S. boulardii*  CNCM I-745 *+ ORT vs control (ORT) All had Zinc* | outpatient kids**India** | N=72n=70 done (3% attrition)07/09-07/11 | 500 mg/d**sachet** | 5 days | (n=35)duration:3.4 + 1.4 daysp<0.01 | (n=35)duration5.5 + 2.1 days | **Burande** MA2013J Pharm & Pharm |
| *+* | *S. boulardii*  CNCM I-745 *+* ORT vs ORT only control (open, randomized)*as part of a larger AAD trial* | Inpatient children(6 mon-14 yrs old) with acute AAD**CHINA** | n=42on placebo who developed diarrhea | 500 mg/d**powder** | 5 daysF/up: none | (n=23)91% **cured** p<0.05 &**duration** 2.3 + 0.95 d, P<0.01,No AE | (n=19)21% curedduration8.97 + 1.07 days | **Shan** LS2013BeneficialMicrobes |
| *-* | *L. rhamnosus GG*(ATCC 53103)vs placebo | Children (6 mon-5 yrs) with either rotavirus (n=82) or Crypto.(n=42) diarrhea**INDIA** | N=124enrol, n=123 done(0.8% attrition) | 1 x 1010 /d **capsules** | 4 weeksF/up: none*72% were 100% compliant, all 123 done had >80%*  | Duration diarr Med= 4 (IQR 3-6) NSRepeated diarrhea episode: 25%\*More IgG to rotavirus | Duration:Md=4 d(IQR 3-6)Repeat episode:46% | **Sindhu** KN2014Clin Infect Dis |

**Treatment ped diarrhea-page 13**

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|  | **Probiotic** | **pop** | **N** | **dose** | **duration** | **probiotic** | **controls** | **reference** |
| *+* | *L. reuteri* DSM 17938 vs. open control group (Just ORS). All had ORS *single blinded* | Inpatient children with diarr(3-60 mon old)**Turkey** | n=140n=127 done (9% attri) | 1 x 108/d**drops** | 5 daysF/up: none | diarr **duration**:70.7 + 26 hrs P<0.001**Cure** by Day 3 69%\*Less **LOS**: 4.3 + 1.3 d\*No AE | control:103.8 + 28.4 hrCured by Day 3: 12%LOS: 5.5 + 1.8 dNo AE | **Dinleyici** EC 2014Acta Paediatrica |
| *-* | Mix of 2 strains: *L. helveticus* Rosell-52 + *L. rhamnosus* Rosell-11“Lacidofil” vs. placebo | kids 4-48 mon old with gastro-enteritis3 sitesDBPC**Canada** | n=132n=123 done (7% attrition) | Low dose: 4 x 109/d vs high dose 8 x 109/d**sachets** | 5 daysF/up:none | missed >1 day daycare (37/61, 61% ns)**Duration** diarr: 71.1 + 78.3 hrs, p=0.39 NS | missed >1 day: 39/62, 63%)**Duration** diarr: 63.5 + 64.3 hrs | **Freedman**SB2015Clinical Pediat |
| *+* | *S. boulardii* CNCM I-745+ ORT/IV“Reflor”vscontrol (ORT/IV only) open trial RCT | 400 children in 8 hospitals(3-60 months old)363 done (9% attrition)TURKEY | n=363 all watery diarrheaInpatients (n=220), ER (n=51) or outpatient(n=92) | 500 mg/d1 x 1010/d**sachet** | 5 daysF/up: none | (n=220)**Duration:**75.4 + 33.1 h\*P<0.001[3.1 + 1.4 days]**LOS**: 4.6+ 1.7 days\*P<0.001  | (n=143)Duration diarr: 99.8 + 32.5 hrs[4.2 + 1.3 dys]LOS: 6.1 + 1.7No AE | **Dinleyici** EC 2015**A**Beneficial Microbes |
| *+* | *L. reuteri* DSM 17938 vscontrol, open All had ORS *single blinded* | Outpatient kids (3-60 mon old) with acute infectious diarr**Turkey** | n=64,60 done(6% attrit) | 1 x 108/d **drops** | 5 daysF/up: none | (n=29)diarr **duration**:2.5 + 1.0d p=0.01No AEs | (n=31)diarr **dura**:3.1 + 0.6 days | **Dinleyici** EC 2015**B**J Pediatrics |

**Treatment ped diarrhea-page 13**

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|  | **Probiotic** | **pop** | **N** | **dose** | **duration** | **probiotic** | **controls** | **reference** |
| *+* | *Bacillus clausii*  O/C, SIN/N/R, T strains) + ORT + Zinc vs ORT+Zinc controlRCTopen label | 131 hospitalized children (6 mon-12 yrs old) with acute diarrhea admitted to ped ward at one hospitalMumbiaIndia | 131inpatientkidsenrolled at site #2:Dr DY Patil Hosp in Mumbia India | 2 x 109/day**spores in vials** | 5 daysdata only collected until Day 3 | (n=69) duration diarr: **22.6** + nr hours, p<0.01#bm/day=1 p<0.05LOS=2.8 days p<0.05, less Cost too | (n=62) duration diarr: **47.05** + nr hours# bm/day= 2.5/dLOS=4.3 d | **Lahiri** K2015**A**IOSR J Dental & Med Sciencesemail from Keya Lahiri: 2015A and 2015B enrolled different periods from 2011-2014 |
| *+* | *Bacillus clausii (*O/C, SIN/N/R, T strains)+ ORT + Zinc vs ORT+Zinc controlRCTopen label | hospitalized children (6 mon-6 yrs) at one ped ward at a tertiary hospitalwith acute diarrheaMumbiaIndia | 160 enrolled at site #2:Dr DY Patil Hosp in Mumbia India | 2 x 109/day**spores in vials** | 5 daysdata only collected until 72 hrsF/up: none | (n=80)Duration diarrhea= **22.26** hrs no std dev datap<0.05No data on AEs | (n=80)durat diarr=**34.16** hrsno std dev data | **Lahiri** K2015**B**J Harmonized Research email from Keya Lahiri: 2015A and 2015B enrolled different periods from 2011-2014 |

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