EW14: Management of infections in the elderly

Probiotics in the elderly

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Definitions

- Probiotics: viable, defined microorganisms in sufficient numbers, which alter the microflora and exert beneficial health effects in the host
- Prebiotics: non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon
- Synbiotics: contains both probiotics and prebiotics, where the prebiotic compound selectively favors the probiotic compound

Improved vaccine response

Influenza prevention

H. pylori

Treatment of collagenous colitis

Rheumatoid arthritis

VAP prevention

IBD treatment

AAD prevention

Cholesterol

Irritable bowel syndrome

VAP prevention

Radiation colitis prevention

Aging wine

CDAD prevention

VRE

UTI prevention

Radiation colitis

SSI prevention

MDR colonization

Constipation

Celiac disease

Immune enhancement

Respiratory infections

Pancreatitis

Cirrhosis

Treatment of CDAD

Bacterial vaginosis

Post-operative infection

Treatment of diarrhea

Colorectal cancer prevention

Red anusitis

Prevention of *Pseudomonas aeruginosa* infections

Bias to look for

Observational studies

- Selection bias
- Selective reporting
- Analysis tricks

Randomized controlled trials

- Publication bias
- Selective reporting
- Multiple reporting

Effects of an intervention with no biological plausibility

Effects of remote, retroactive intercessory prayer on outcomes in patients with bloodstream infection: randomised controlled trial

Leonard Leibovici

What this study adds

Remote intercessory prayer said for a group of patients is associated with a shorter hospital stay and shorter duration of fever in patients with a bloodstream infection, even when the intervention is performed 4-10 years after the infection

Leibovici L. BMJ VOLUME 323 22–29 DECEMBER 2001

Outcomes commonly reported in RCTs on probiotics

Duration of all pathologies was significantly lower in the treatment group (7.0 3.2 days, n=180) than in the control group (8.7 3.7 days; n=180) (p=0.024), as was maximal temperature (38.3 0.5 °C treatment group vs. 38.5 0.6 °C control; p=0.01).

Serum albumin, prealbumin and protein increased significantly more in the treatment group compared with the control group among participants age≥80y (P=0.047, p=0.07, p=0.03 respectively)

In addition, the quality of life score for the 'eye/nose/throat' system after intake was significantly higher in the yoghurt group than in the milk group and the improvement of the score was correlated with the promotion of natural killer cell activity.

Also, plasma TGF-β1 concentration significantly decreased after treatment with both probiotic doses.

Considerations in the elderly

- Immunosenescence
  - Higher risk for infection
    - Higher risk for CDAD
  - Poorer vaccine response
- Constipation/ bowel disorders
- Malnutrition

Review of the evidence

- Randomized controlled trials or observational studies
- Clinical outcomes
  - Influenza vaccine immunogenicity
- Elderly, mean cohort age >65 years
- PubMed search, references, previous systematic reviews

Considerations in the elderly

- Immunosenescence
  - Higher risk for infection
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    - Influenza, common winter infections
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CDAD: incidence

	OR (95% CI)	P-value
Age 50-80 >80	 1.5 (1.1-2.1) 2.5 (1.7-3.7)	 0.0116 <0.0001
Haemodialysis	1.5 (1.1-2.0)	0.0227
Non-surgical admission	2.2 (1.9-2.2)	<0.0001
ICU stay (weeks)	2.1 (1.7-2.9)	<0.001

Independent risk factors for CDAD in hospitalised patients given broad-spectrum antibiotics

Risk group CDAD/ pt	Validation 288/ 41,224	Derivation 104/ 13,002
1	1.9	2.3
2	6.7	8.2
3	22.9	27.3
4	81.3	76.9

Rate/ 1000 admissions of CDAD per risk group

Garey et al. 2008 J Hosp Infect

CDAD: recurrence

Factor	OR (95% CI)
Age	6.1 (1-6.6)
Horn index severe or fulminant	9.6 (1.2-76.7)
Additional antibiotic use	10 (1.5-68.3)
Antitoxin A IgG <1.29	52.5 (1.5-1000)

Independent risk factors for recurrent CDAD

Risk group CDAD/ pt	Validation N=44 1998	Derivation N=64 2004-2006
0	0	0
1	33%	17%
2	71%	31%
3	87%	67%

Rates of recurrent CDAD

Hu et al. Gastroenterology 2009

CDAD: Higher mortality

Factor	<65	>65
N	130	148
LOS before CDAD	11.0±19.5	6.4±9.6
Prior antibiotic days	11.4±19.9	5.4±7.3
Fever, Tmax 38.5°C	41 (32%)	27 (18%)

All patients with CDAD in any ICU at the Barnes-Jewish Hospital during a 2-year period

Factor	OR (95% CI)	P
Age >75 yrs	3.95 (1.84–8.48)	<0.001
No chronic lung disease	3.55 (1.53–8.21)	<0.01
No leukocytosis	3.07 (1.17–8.13)	0.02
septic shock	2.34 (1.05–5.22)	0.04
APACHE II >20	2.07 (0.95–4.53)	0.07

Subgroup analysis: age>65 years, multivariable analysis of 30-day mortality

Zilberberg et al. Crit Care Med 2009

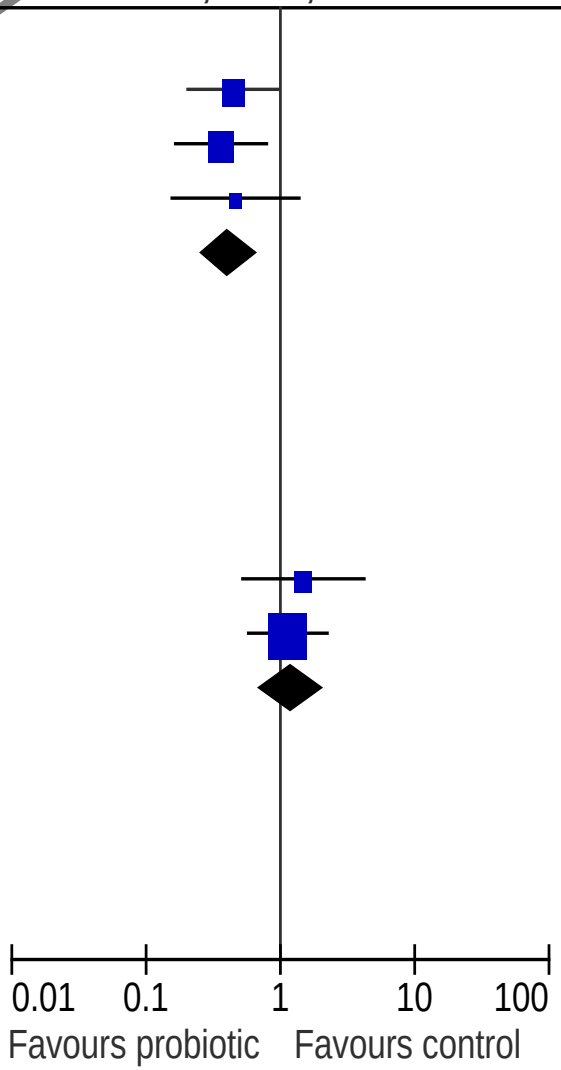
AAD/ CDAD

Study	Population	N	Design	Probiotic	Dose	Outcome
Beausoleil 2007	Hospital, mean age 71, Canada	89	RCT, DB	*Lactobacillus acidophilus; Lactobacillus casei*	$50X10^9$	AAD, CDAD, hosp duration, deaths
Lewis 1998	Medical wards, mean age 76 , UK	69	RCT, DB	*Saccharomyces boulardii*	113 mg	AAD, hosp duration
Pozzoni 2012	Medical wards, mean age 79, Italy	275	RCT, DB	*Saccharomyces boulardii*	$5X10^9$	AAD, CDAD, deaths
Safdar 2008	Hospital, mean age 69, US	40	RCT, DB	*Lactobacillus acidophilus*	$20X10^9$	AAD, CDAD
Zaharoni 2011	Geriatric orthopedic rehabilitation, mean age 76, Israel	215	RCT, DB	*Lactobacilli; Bifidobacteria; S. thermophilus*	$45X10^{10}$	Days with diarrhea ↓
Hickson 2007	Hospital, mean age 74, UK	135	RCT, DB	*Lactobacilli; S. thermophilus*	$2X10^8$	AAD, CDAD
Plummer 2004	Medical and geriatric wards, elderly, UK	138	RCT, DB	*Lactobacillus acidophilus; Bifidobacterium bifidum*	$20X10^9$	CDAD

AAD – antibiotic associated diarrhea, CDAD – Clostridium difficile associated diarrhea

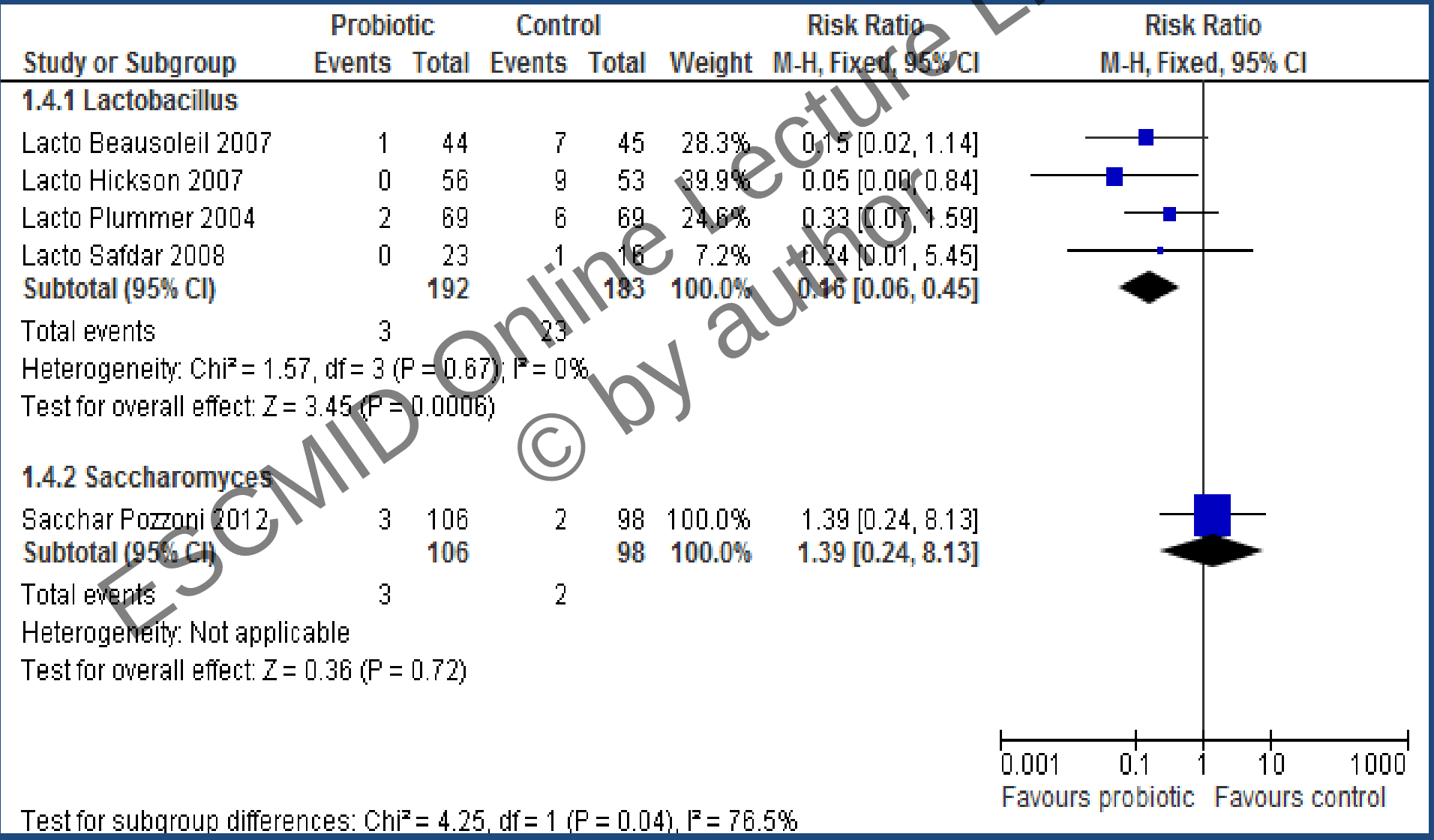
AAD

Study or Subgroup	Probiotic Events	Probiotic Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.3.1 Lactobacillus						
Lacto Beausoleil 2007	7	44	16	45	37.6%	0.45 [0.20, 0.98]
Lacto Hickson 2007	7	57	19	56	45.6%	0.36 [0.17, 0.79]
Lacto Safdar 2008	4	23	6	16	16.8%	0.46 [0.16, 1.38]
Subtotal (95% CI)		**124**		**117**	**100.0%**	**0.41 [0.25, 0.67]**
Total events	18		41			
Heterogeneity: Chi² = 0.19, df = 2 (P = 0.91); I² = 0%						
Test for overall effect: Z = 3.52 (P = 0.0004)						
1.3.2 Saccharomyces						
Sacchar Lewis 1998	7	33	5	35	26.4%	1.48 [0.52, 4.22]
Sacchar Pozzoni 2012	16	106	13	98	73.6%	1.14 [0.58, 2.24]
Subtotal (95% CI)		**139**		**133**	**100.0%**	**1.23 [0.70, 2.17]**
Total events	23		18			
Heterogeneity: Chi² = 0.18, df = 1 (P = 0.68); I² = 0%						
Test for overall effect: Z = 0.71 (P = 0.48)						



Test for subgroup differences: Chi² = 8.12, df = 1 (P = 0.004), I² = 87.7%

CDAD



Limitations

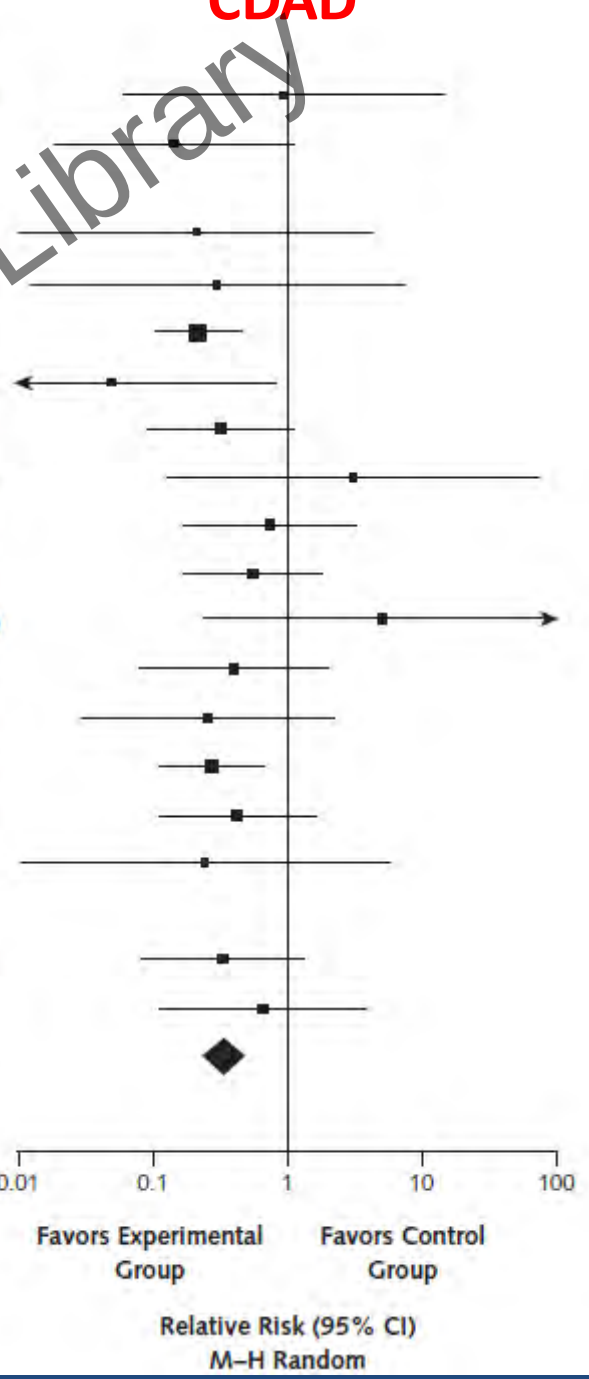
- Different probiotics/ doses of probiotic
  - Limited evidence per probiotic
- Variable probiotic treatment regimens
  - Usually started with antibiotic treatment and continued for 1-3 weeks post-treatment
- Different antibiotic treatments
- Not all patients with diarrhea tested for C. diff
- *Clostridium difficle* testing using ELISA essay for toxin A/B

CDAD

Study, Year (Reference)	Experimental Group, *n*		Control Group, *n*		Weight, %	Relative Risk (95% CI) M–H Random
	Events	Total	Events	Total		
Arvola et al, 1999 (32)	1	61	1	58	1.7	0.95 (0.06–14.85)
Beausoleil et al, 2007 (33)	1	44	7	45	3.0	0.15 (0.02–1.14)
Bravo et al, 2008 (34)	0	41	0	45	–	Not estimable
Can et al, 2006 (35)	0	73	2	78	1.4	0.21 (0.01–4.37)
Duman et al, 2005 (36)	0	196	1	180	1.2	0.31 (0.01–7.47)
Gao et al, 2010 (37)	9	171	20	84	23.0	0.22 (0.11–0.46)
Hickson et al, 2007 (38)	0	56	9	53	1.6	0.05 (0.00–0.84)
Kotowska et al, 2005 (39)	3	119	10	127	7.9	0.32 (0.09–1.14)
Lönnermark et al, 2010 (40)	1	80	0	83	1.3	3.11 (0.13–75.26)
McFarland et al, 1995 (41)	3	97	4	96	5.9	0.74 (0.17–3.23)
Miller et al, 2008 (47)	4	95	7	94	8.9	0.57 (0.17–1.87)
Miller et al, 2008 (47)*	2	157	0	159	1.4	5.06 (0.25–104.63)
Plummer et al, 2004 (42)	2	69	5	69	4.9	0.40 (0.08–1.99)
Psaradellis et al, 2010 (48)	1	216	4	221	2.7	0.26 (0.03–2.27)
Rafiq et al, 2007 (49)	5	45	22	55	16.1	0.28 (0.11–0.67)
Ruszczyński et al, 2008 (43)	3	120	7	120	7.2	0.43 (0.11–1.62)
Safdar et al, 2008 (44)	0	23	1	17	1.3	0.25 (0.01–5.79)
Selinger et al, 2011 (50)	0	62	0	62	–	Not estimable
Surawicz et al, 1989 (45)	3	116	5	64	6.5	0.33 (0.08–1.34)
Thomas et al, 2001 (46)	2	133	3	134	4.0	0.67 (0.11–3.96)
Total (95% CI)		1974		1844	100.0	0.34 (0.24–0.49)
Total events, *n*	40		108			

Heterogeneity: $\tau^2 = 0.00$; chi-square = 12.09; $P = 0.79$; $I^2 = 0\%$

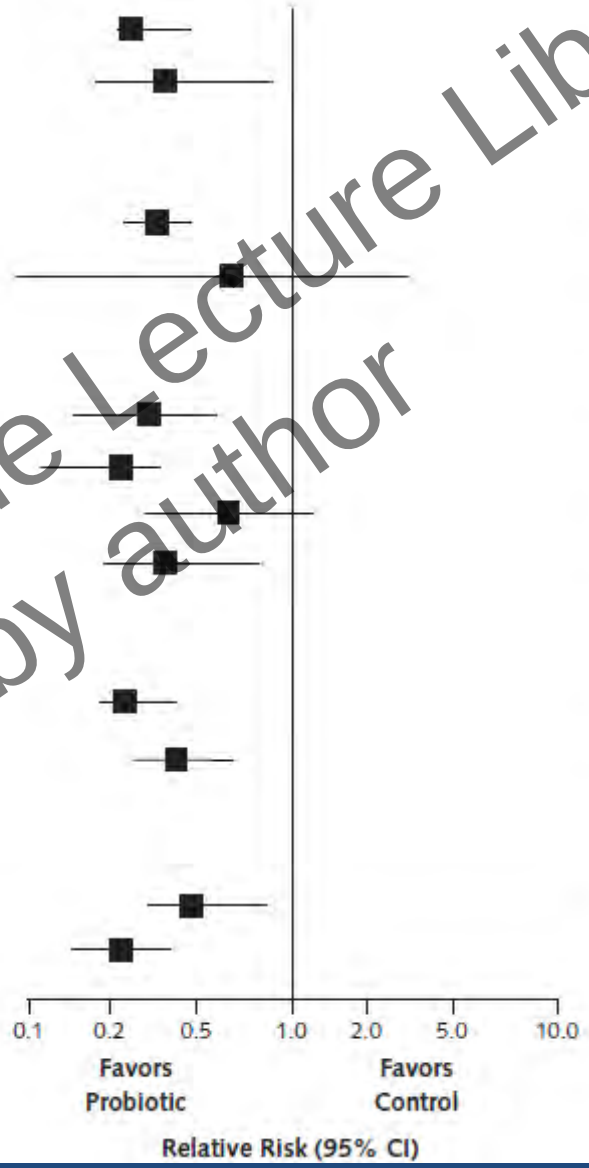
Test for overall effect: $Z = 5.87$; $P < 0.001$



Johnston et al. Ann Intern Med 2012. Twenty RCTs included

CDAD

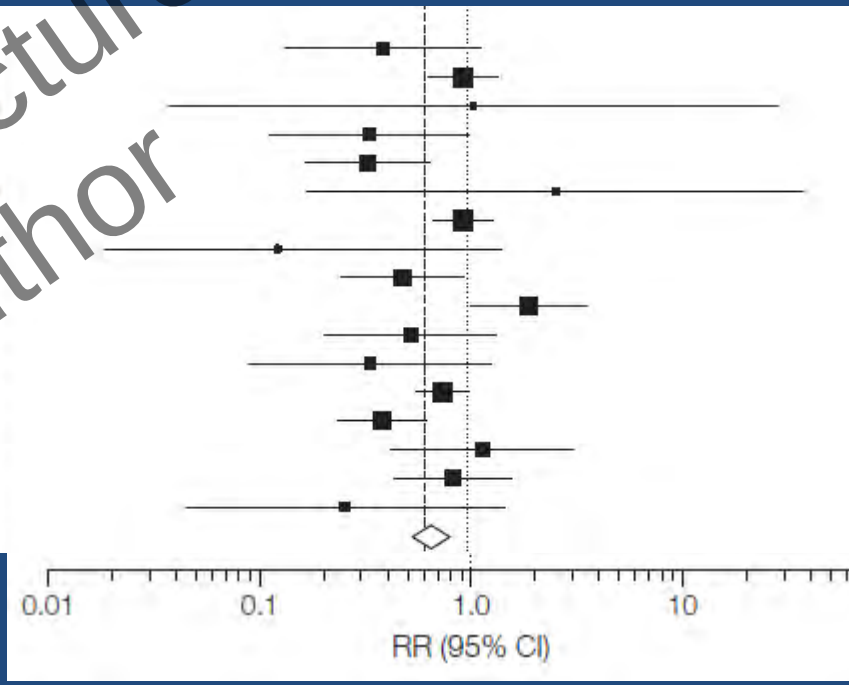
Subgroup	Events/Patients, *n/n*		Relative Risk (95% CI)	*P* Value for Test of Interaction
	Probiotic Group (*n* = 1974)	Control Group (*n* = 1844)		
Age				
Adults	33/1674	90/1539	0.22 (0.23–0.49)	
Children	7/300	18/305	0.40 (0.17–0.96)	0.69
Probiotic dosage				
>10 billion CFU/d	36/1775	98/1634	0.34 (0.23–0.49)	
≤10 billion CFU/d	4/199	10/210	0.61 (0.08–4.60)	0.57
Species				
Other (mixed) species	8/335	37/339	0.30 (0.15–0.61)	
L. acidophilus + *L. casei*	11/431	31/350	0.21 (0.11–0.42)	0.34
L. rhamnosus	12/566	18/565	0.63 (0.30–1.33)	0.15
S. boulardii	9/642	22/590	0.39 (0.19–0.82)	0.84
Risk of bias				
Low	17/695	52/613	0.27 (0.16–0.46)	
High or unclear	23/1279	56/1231	0.42 (0.26–0.68)	0.24
Species				
Single	21/1208	40/1155	0.50 (0.29–0.84)	
Multiple	19/766	68/689	0.25 (0.15–0.41)	0.06



Johnston et al. Ann Intern Med 2012

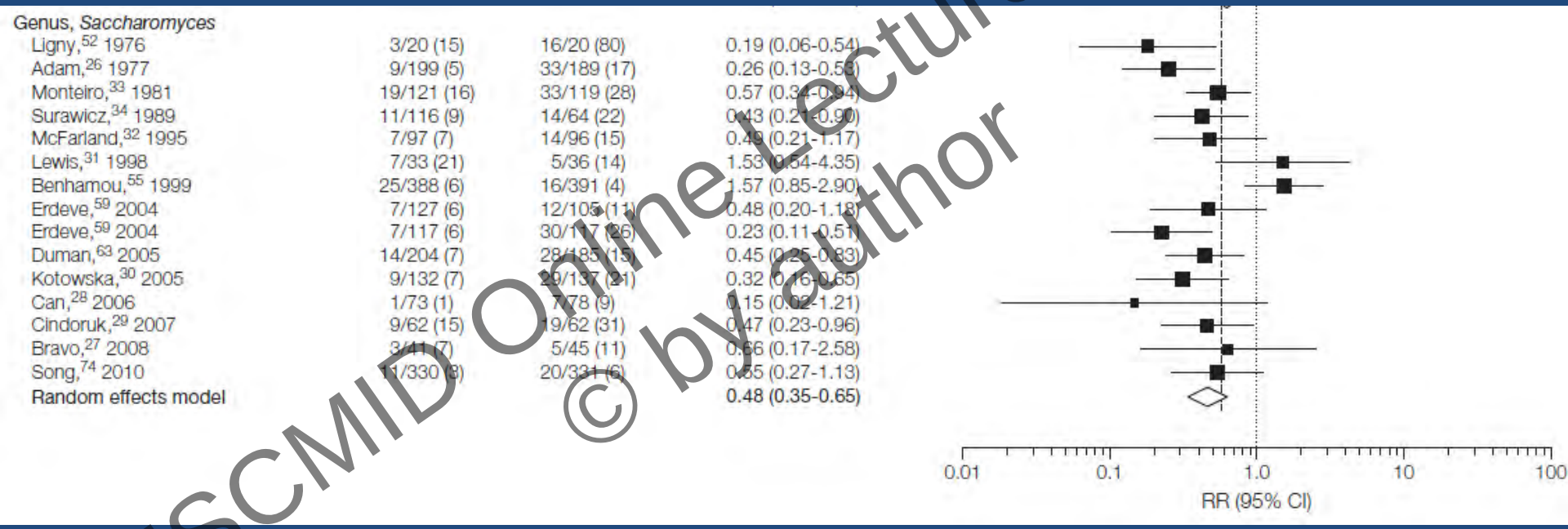
AAD
Lactobacillus

Genus, *Lactobacillus*			
Gotz,[33] 1979	3/48 (6)	9/50 (18)	0.35 (0.10-1.21)
Tankanow,[49] 1990	10/15 (67)	16/23 (70)	0.96 (0.61-1.50)
Reid,[54] 1992	0/19 (0)	0/21 (0)	1.10 (0.02-58.35)
Arvola,[37] 1999	3/89 (3)	9/78 (12)	0.29 (0.08-1.04)
Vanderhoof,[57] 1999	7/93 (8)	25/95 (26)	0.29 (0.13-0.63)
Felley,[56] 2001	1/26 (4)	0/27 (0)	3.11 (0.13-73.07)
Thomas,[50] 2001	39/152 (26)	40/150 (27)	0.96 (0.66-1.41)
Tursi,[62] 2004	0/35 (0)	5/35 (14)	0.09 (0.01-1.58)
Beausoleil,[17] 2007	7/44 (16)	16/45 (36)	0.45 (0.20-0.98)
Ruszczynski,[45] 2008	20/120 (17)	9/120 (8)	2.22 (1.06-4.68)
Safdar,[46] 2008	4/23 (17)	6/17 (35)	0.49 (0.16-1.48)
Szajewska,[48] 2009	2/44 (5)	6/39 (15)	0.30 (0.06-1.38)
Sampalis,[40] 2010	47/233 (20)	65/239 (27)	0.74 (0.53-1.03)
Gao,[41] 2010	13/86 (15)	37/84 (44)	0.34 (0.20-0.60)
Lönnermark,[44] 2010	6/118 (5)	5/121 (4)	1.23 (0.39-3.92)
Song,[47] 2010	11/103 (11)	14/111 (13)	0.85 (0.40-1.78)
Cimperman,[39] 2011	1/16 (7)	5/16 (3%)	0.21 (0.03-1.62)
Random effects model			0.64 (0.47-0.86)



Hempel et al. JAMA 2012. Total 82 RCTs included

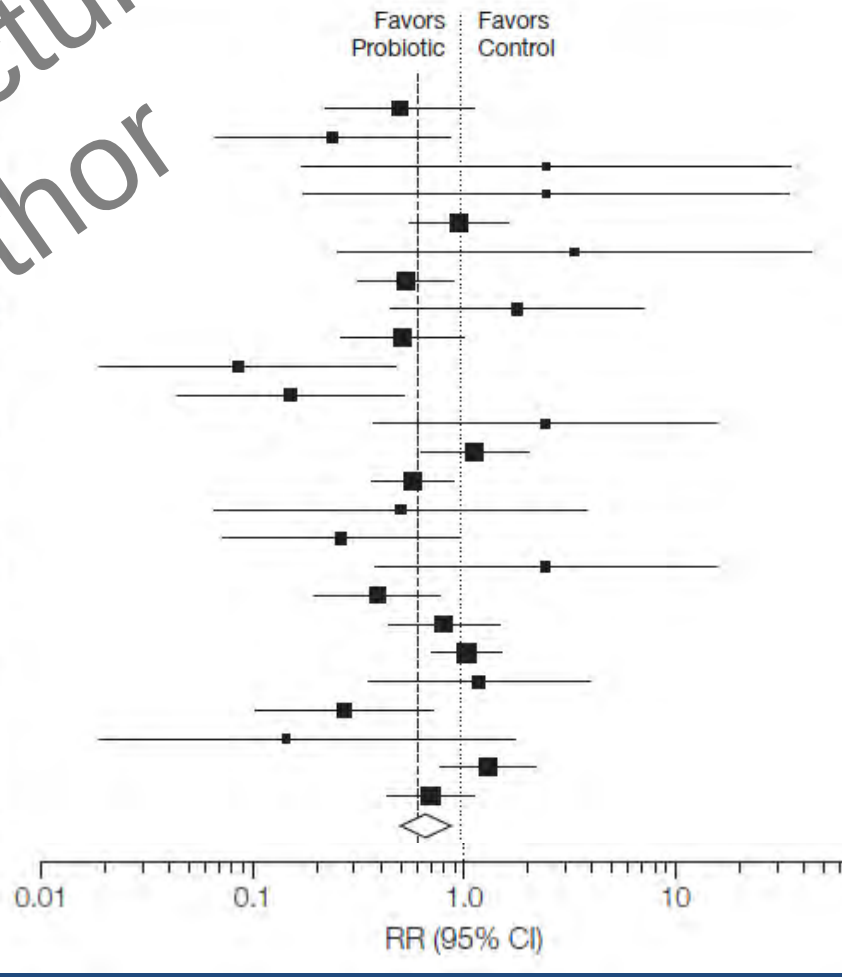
AAD
Saccharomyces



Hempel et al. JAMA 2012

AAD
mixed probiotics

Study	No. With Antibiotic-Associated Diarrhea/No. in Group (%) Intervention	Control	RR (95% CI)
Genus, Blend			
Jirapinyo,[20] 2002	3/8 (38)	8/10 (80)	0.47 (0.18-1.21)
Sheu,[57] 2002	2/80 (2)	10/80 (12)	0.20 (0.05-0.88)
Sullivan,[57] 2003	1/12 (8)	0/12 (0)	3.00 (0.13-66.80)
Lighthouse,[60] 2004	1/10 (10)	0/10 (0)	3.00 (0.14-65.55)
Plummer,[22] 2004	15/69 (22)	15/69 (22)	1.00 (0.53-1.88)
Schrezenmeir,[61] 2004	2/50 (4)	0/48 (0)	4.31 (0.21-87.30)
Corrêa,[18] 2005	13/87 (15)	24/82 (29)	0.51 (0.28-0.93)
Myllyluoma,[21] 2005	4/23 (17)	2/24 (8)	2.09 (0.42-10.32)
Conway,[64] 2007	9/149 (6)	17/137 (12)	0.49 (0.22-1.06)
de Bortoli,[65] 2007	1/105 (1)	16/101 (16)	0.06 (0.01-0.44)
Park,[66] 2007	2/176 (1)	17/176 (10)	0.12 (0.03-0.50)
Stein,[24] 2007	3/21 (14)	1/21 (5)	3.00 (0.34-26.56)
Kim,[67] 2008	16/168 (10)	14/178 (8)	1.22 (0.61-2.42)
Koning,[68] 2008	9/20 (45)	17/21 (81)	0.56 (0.33-0.94)
Szymański,[25] 2008	1/40 (2)	2/38 (5)	0.48 (0.04-5.03)
Wenus,[69] 2008	2/46 (4)	8/41 (20)	0.22 (0.05-0.99)
Engelbrektson,[70] 2009	3/20 (15)	1/20 (5)	3.00 (0.34-26.45)
Hickson,[19] 2007	7/69 (10)	19/66 (29)	0.35 (0.16-0.78)
Merenstein,[71] 2009	11/61 (18)	14/64 (22)	0.82 (0.41-1.67)
Koning,[72] 2010	13/17 (76)	9/13 (69)	1.10 (0.71-1.73)
de Vrese,[75] 2011	4/30 (13)	3/29 (10)	1.29 (0.32-5.26)
Saneeyan,[77] 2011	3/25 (12)	13/25 (52)	0.23 (0.07-0.71)
Selinger,[23] 2011	0/62 (0)	4/62 (6)	0.11 (0.01-2.02)
Yoon,[78] 2011	20/151 (13)	17/186 (9)	1.45 (0.79-2.67)
Bhalla,[38] 2011	19/176 (11)	26/167 (16)	0.69 (0.40-1.20)
Random effects model			0.66 (0.49-0.88)



Hempel et al. JAMA 2012

Limitations

- Different probiotics/ doses of probiotic
  - Limited evidence per probiotic
- Variable probiotic treatment regimens
  - Usually started with antibiotic treatment and continued for 1-3 weeks post-treatment
- Different antibiotic treatments
- Not all patients with diarrhea tested for C. diff
- *Clostridium difficile* testing using ELISA essay for toxin A/B
- Data on *Clostridium difficile*-associated diarrhea available only from 20/82 RCTs of probiotic treatment with antibiotics

Considerations in the elderly

- Immunosenescence
  - Higher risk for infection
    - Higher risk for CDAD
    - Influenza, common winter infections
  - Poorer vaccine response
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- Malnutrition

Influenza vaccine immunogenicity

Study	Population	N	Design	Probiotic	Results
Akatsu 2012	Hospitalized enterally fed	45	RCT, DB	*Bifidobacterium longum*	No effect
Bosch 2012	Nursing home residents	60	RCT, DB	*Lactobacillus plantarum*	Positive
Van Puyenbroeck 2012	Nursing home residents	737	RCT, DB	*Lactobacillus casei*	No effect
Namba 2010	Nursing home residents, Japan	37	RCT, DB	*Bifidobacterium longum*	No effect
Boge 2009	Nursing home residents	86	RCT, DB	*Lactobacillus paracasei*	Non-significantly positive
Boge 2009	Nursing home residents	222	RCT, DB	*Lactobacillus paracasei*	Positive
Bunout 2004	Community, dwelling	60	Clinic 1 vs. clinic 2	*Lactobacillus paracasei*	No difference

RCT – randomized controlled trial, DB – double blind

Limitations

- Heterogeneity in intervention type and timing
- Micronutrients/ prebiotics in addition to probiotic
- Multiple immunological response measures assessed
- Multiple time points for assessment

Considerations in the elderly

- Immunosenescence
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Influenza-like illness/ common infections

Randomized controlled trials

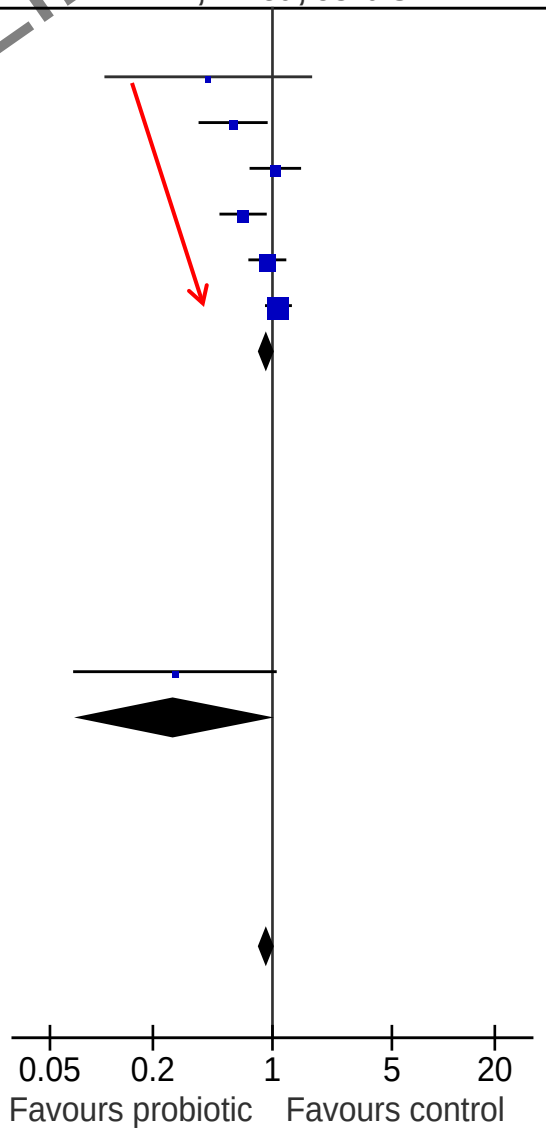
Study	Population	N	Design	Probiotic	Outcome
Akatsu 2012	Hospitalized enterally fed, Japan	45	RCT, DB	*Bifidobacterium longum*	Fever Influenza
Van Puyenbroeck 2012	Nursing home residents, Belgium	737	RCT, DB	*Lactobacillus Casei Shirota*	RTI RTI days
Shinkai 2012	Community dwelling, Japan	300	RCT, DB	*Lactobacillus pentosus*	Common cold
Mane 2011	Nursing home residents, Spain	50	RCT, DB	*Lactobacillus plantarum*	Febrile episodes
Namba 2010	Nursing home residents, Japan	37	RCT, DB	*Bifidobacterium longum*	Fever Influenza
Guillemard 2010	Community dwelling, Europe	1072	RCT, DB	*Lactobacillus casei*	Common infections
Makino 2010	Community dwelling, Japan	60 95	RCT	*Lactobacillus bulgaricus*	Common cold Influenza
Fukushima 2007	hospitalized, enterally fed, Japan	24	RCT, DB	*Lactobacillus johnsonii*	*Days with infection* ↓
Turchet 2003	Community dwelling, Italy	360	RCT	Lactobacillus casei	ILI Winter infections

RCT – randomized controlled trial, DB – double blind, RTI – respiratory tract infection, ILI – influenza-like illness

Influenza-like illness/ common infections

Randomized controlled trials

Study or Subgroup	Probiotic Events	Probiotic Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Lactobacillus						
Lacto Mane 2011	3	32	4	18	1.2%	0.42 [0.11, 1.68]
Lacto Makino 2010	20	72	33	70	7.9%	0.59 [0.38, 0.92]
Lacto Turchet 2003	52	180	50	180	11.8%	1.04 [0.75, 1.44]
Lacto Shinkai 2012	59	185	44	93	13.9%	0.67 [0.50, 0.91]
Lacto Guillemard 2010	105	537	112	535	26.5%	0.93 [0.74, 1.18]
Lacto Puyenbroeck 2012	172	375	153	362	36.8%	1.09 [0.92, 1.28]
Subtotal (95% CI)		**1381**		**1258**	**98.2%**	**0.93 [0.83, 1.04]**
Total events	411		396			
Heterogeneity: Chi² = 13.53, df = 5 (P = 0.02); I² = 63%						
Test for overall effect: Z = 1.22 (P = 0.22)						
1.1.2 Bifidobacterium						
Bifido Akatsu 2012	0	23	0	22		Not estimable
Bifido Namba 2010	2	13	8	14	1.8%	0.27 [0.07, 1.04]
Subtotal (95% CI)		**36**		**36**	**1.8%**	**0.27 [0.07, 1.04]**
Total events	2		8			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.90 (P = 0.06)						
Total (95% CI)		**1417**		**1294**	**100.0%**	**0.92 [0.82, 1.03]**
Total events	413		404			
Heterogeneity: Chi² = 16.80, df = 6 (P = 0.01); I² = 64%						
Test for overall effect: Z = 1.46 (P = 0.15)						
Test for subgroup differences: Chi² = 3.22, df = 1 (P = 0.07), I² = 68.9%						



Influenza-like illness/ common cold

Non-randomized studies

Study	Population	N	Design	Probiotic	Outcome	Result
Nagata 2011	Nursing home residents, Japan	77	CCT	Lactobacillus Casei Shirota	Norovirus gastroenteritis	No difference
Del Piano 2004	Hospitalized enterally fed, Italy	13	CCT	Bifidobacterium longum	Fever episodes Diarrhea	No difference
Bunout 2004	Community dwelling, Chile	60	Clinic 1 vs. clinic 2	Lactobacillus paracasei	Any infection	Less with probiotic

CCT – controlled clinical trial, DB – double blind, RTI – respiratory tract infection

Limitations

- Different populations
  - Community dwelling
  - Nursing home residents
  - Hospitalized
- Different interventions
- Different and multiple outcomes examined
- Small studies effect

Considerations in the elderly

- Immunosenescence
  - Higher risk for infection
    - Higher risk for CDAD
    - Influenza, common winter infections
  - Poorer vaccine response
- Constipation/ bowel disorders
- Malnutrition

Study	Population	N	Design	Probiotic	Results rates with probiotics
Granata 2013	Nursing home residents, chronic constipation, Italy	12	RCT	*Lactobacillus Rhamnosus + FOS*	Less constipation
Gallego 2011	Community dwelling, Spain	60	RCT, DB	*Lactobacillus plantarum*	Less constipation
Pitkala 2007	Nursing home residents, Finland	209	RCT, DB	*Bifidobacterium longum*	Less constipation
Zaharoni 2011	Hospitalized in rehabilitation, Israel	215	RCT, DB	*Lactobacilli and Bifidobacteria*	Less diarrhea and less constipation
An 2010	Nursing home residents, chronic constipation, Korea	19	Before-after	*Lactobacillus Pediococcus Bifidobacterium*	Less constipation
Carlsson 2009	Nursing home residents with dementia, Sweden	15	Before-after	*Lactobacillus Lactococcus*	No change in bowel function
Cassani 2011	Parkinson's disease, Italy	40	Before-after	*Lactobacillus casei Shirota*	Less constipation
Motta 1991	Bowel disorders , Italy	60	Before-after	*Lactobacillus acidophilus*	Bowel function improved
Ouwehand 2002	Chronic constipation, Finland	28	CCT	*Lactobacilli*	Improved constipation
Tanaka 1982	Bedridden, Japan	57	Before-after	*Bifidobacterium*	Less constipation

FOS – Fructooligosaccharide; CCT – controlled clinical trial

Considerations in the elderly

- Immunosenescence
  - Higher risk for infection
    - Higher risk for [illegible]
    - Influenza [illegible] winter infections
  - Poor [illegible] response
- Constipation/ bowel disorders
- Malnutrition

Quality of life

Quality of life

Study	Population	N	Design	Probiotic	Results rates with probiotics
Guillemard 2010	Community dwelling, Europe	1072	RCT, DB	*Lactobacillus casei*	No significant difference in SF-36
Makino 2010	Community dwelling, Japan	60 95	RCT	*Lactobacillus bulgaricus*	No significant difference in quality of life score
Mane 2011	Nursing home residents, Spain	50	RCT, DB	*Lactobacillus plantarum*	No significant difference in functional capacity (Barthel index)
Shinkai 2012	Community dwelling, Japan	300	RCT, DB	*Lactobacillus pentosus*	SF-26 significant improved p=0.016
Yamamura 2009	Community dwelling, Japan	29	RCT, DB	*Lactobacillus helveticus*	No significant difference in SF-36

In summary

- Probiotics, specifically *L. acidophilus* or *L. casei* in doses of ~10X10^9/day might prevent AAD/ CDAD when administered concomitantly and post-antibiotic treatment
- No convincing evidence on effect of probiotics on improved immunological response or decrease in common winter/ viral infections
- Reduction in bowel disorders/ constipation, relying mostly on observational data
- No evidence for effect on quality of life

Thank you