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Timely Use of Probiotics in Hospitalized Adults Prevents *Clostridium difficile* Infection: A Systematic Review With Meta-Regression Analysis

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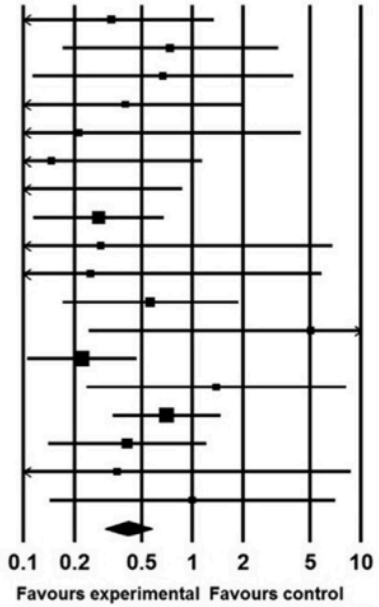
Meta-analysis parameters

- RCT reporting CDI (positive stool cytotoxin, culture or PCR)
- Inclusion criteria:
  - 18+ years old
  - Receiving antibiotics for any reason
- Probiotics VS control
  - Had to be a study testing CDI prevention rather than treatment
  - All doses considered
    - Range: 4 bn – 900 bn organisms per day
  - 4 genera studied:
    - *Lactobacillus*
    - *Saccharomyces*
    - *Bifidobacterium*
    - *Streptococcus*
- Primary outcome: incidence of CDI
- 19 studies passed all filters

“We attempted to contact the investigators of trials without published data, but we received no responses.”

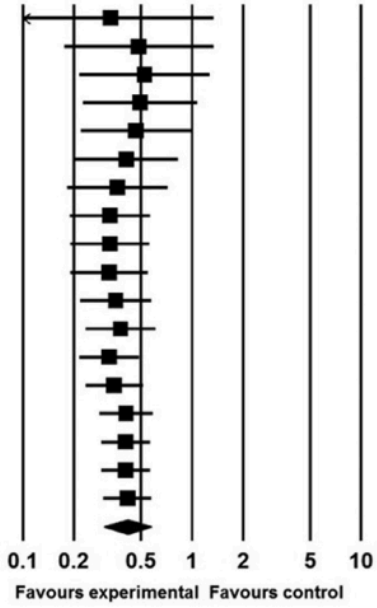
A

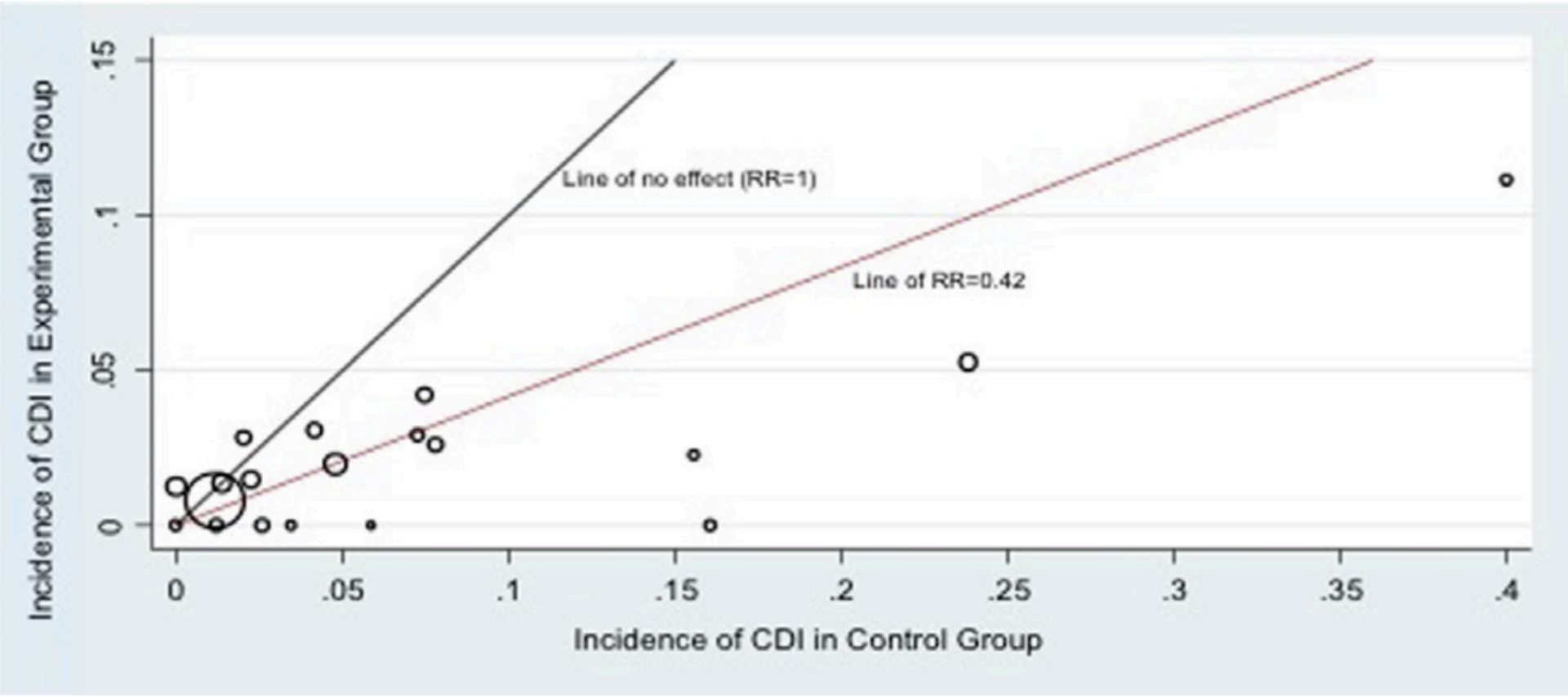
Study name	Events / total: Probiotics	Events / total: Control	Relative weight	Risk ratio
Surawicz 1989	3 / 116	5 / 64	5.30	0.33
McFarland 1995	3 / 97	4 / 96	4.80	0.74
Thomas 2001	2 / 133	3 / 134	3.30	0.67
Plummer 2004	2 / 69	5 / 69	4.02	0.40
Can 2006	0 / 73	2 / 78	1.14	0.21
Beausoleil 2007	1 / 44	7 / 45	2.46	0.15
Hickson 2007	0 / 57	9 / 56	1.30	0.05
Rafiq 2007	5 / 45	22 / 55	13.16	0.28
Wenus 2008	0 / 34	1 / 29	1.04	0.29
Safdar 2008	0 / 23	1 / 17	1.05	0.25
Miller 2008a	4 / 95	7 / 94	7.26	0.57
Miller 2008b	2 / 157	0 / 159	1.13	5.06
Gao 2010	9 / 171	20 / 84	18.82	0.22
Pozzoni 2012	3 / 106	2 / 98	3.32	1.39
Allen 2013	12 / 1470	17 / 1471	19.16	0.71
Ouwehand 2014	6 / 304	7 / 146	9.01	0.41
Wong 2014	0 / 76	1 / 82	1.02	0.36
Ehrhardt 2016	2 / 146	2 / 146	2.74	1.00
Summary estimate				0.42



B

Study name	Cumulative statistics: Point	Lower limit	Upper limit	*P*-value	Relative weight
Surawicz 1989	0.33	0.08	1.34	.12	5.30
McFarland 1995	0.49	0.18	1.34	.16	10.09
Thomas 2001	0.53	0.22	1.27	.15	13.39
Plummer 2004	0.49	0.23	1.07	.07	17.41
Can 2006	0.47	0.22	0.99	.05	18.55
Beausoleil 2007	0.41	0.20	0.83	.01	21.00
Hickson 2007	0.36	0.18	0.72	.00	22.31
Rafiq 2007	0.33	0.19	0.56	.00	35.46
Wenus 2008	0.33	0.19	0.56	.00	36.50
Safdar 2008	0.32	0.19	0.55	.00	37.55
Miller 2008a	0.36	0.22	0.57	.00	44.81
Miller 2008b	0.38	0.24	0.61	.00	45.94
Gao 2010	0.32	0.22	0.48	.00	64.76
Pozzoni 2012	0.35	0.24	0.51	.00	68.07
Allen 2013	0.41	0.28	0.59	.00	87.23
Ouwehand 2014	0.41	0.29	0.57	.00	96.24
Wong 2014	0.41	0.29	0.56	.00	97.26
Ehrhardt 2016	0.42	0.30	0.57	.00	100.00
Summary estimate	0.42	0.30	0.57	.00	

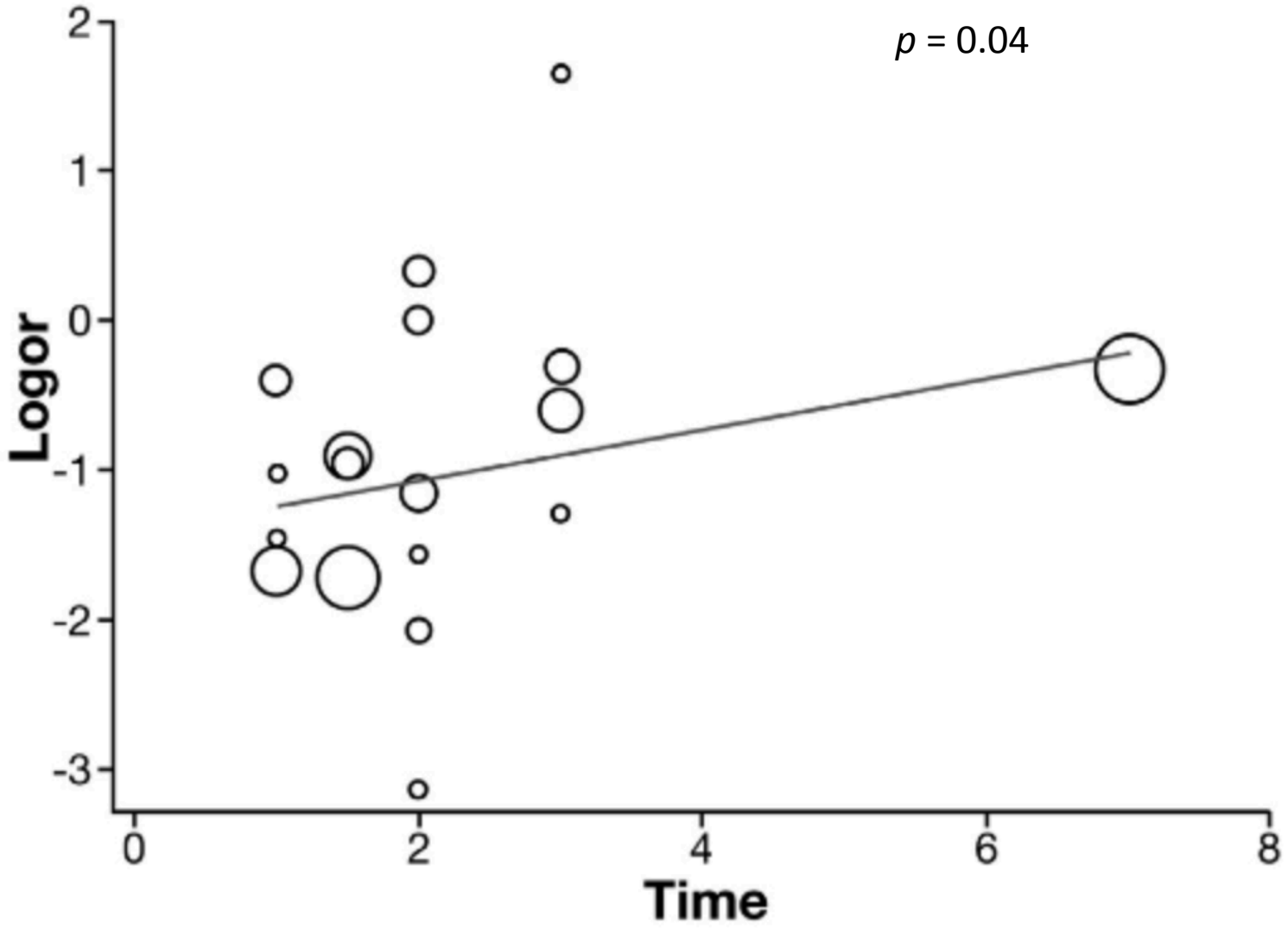



Incidence of CDI in Experimental Group
0
.05
.1
.15
Line of no effect (RR=1)
Line of RR=0.42
0
.05
.1
.15
.2
.25
.3
.35
.4
Incidence of CDI in Control Group

Sensitivity analysis

- Assumed missing data in experimental groups had 2x and 5x the incidence of CDI than the rest of the experimental group of the same study

- Aggregate risk ratio is preserved under these conditions


p = 0.04
Logor
2
1
0
-1
-2
-3
0
2
4
6
8
Time