Supplemental file

Do probiotics help prevent ventilator-associated pneumonia in the critically ill patients?

A systematic review with meta-analysis

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Conflict of interest

The authors declare no conflict of interest.

Supplemental Table 1. PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	4	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	5	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4, 5
Information sources	4	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	4	Present full electronic search strategy for at least one database, including any limits used, such	4

		that it could be repeated.	
Study selection	5	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	5	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	6	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	6	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5, 6
Summary measures	7	State the principal summary measures (e.g., risk ratio, difference in means).	6,7
Synthesis of results	7	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7
Risk of bias across studies	7	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	7	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	7	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	8	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7,8

Risk of bias within studies	9,10 11,12	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8-13
Results of individual studies	9,10 11,12	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	8-13
Synthesis of results	9,10 11,12	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	8-13
Risk of bias across studies	9,10 11,12	Present results of any assessment of risk of bias across studies (see Item 15).	8-13
Additional analysis	9,10 11,12	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	8-13
DISCUSSION			
Summary of evidence	13,14 15,16	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-15
Limitations	16,17	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16
Conclusions	17	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16
FUNDING			
Funding	19	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	17

Reference: Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and

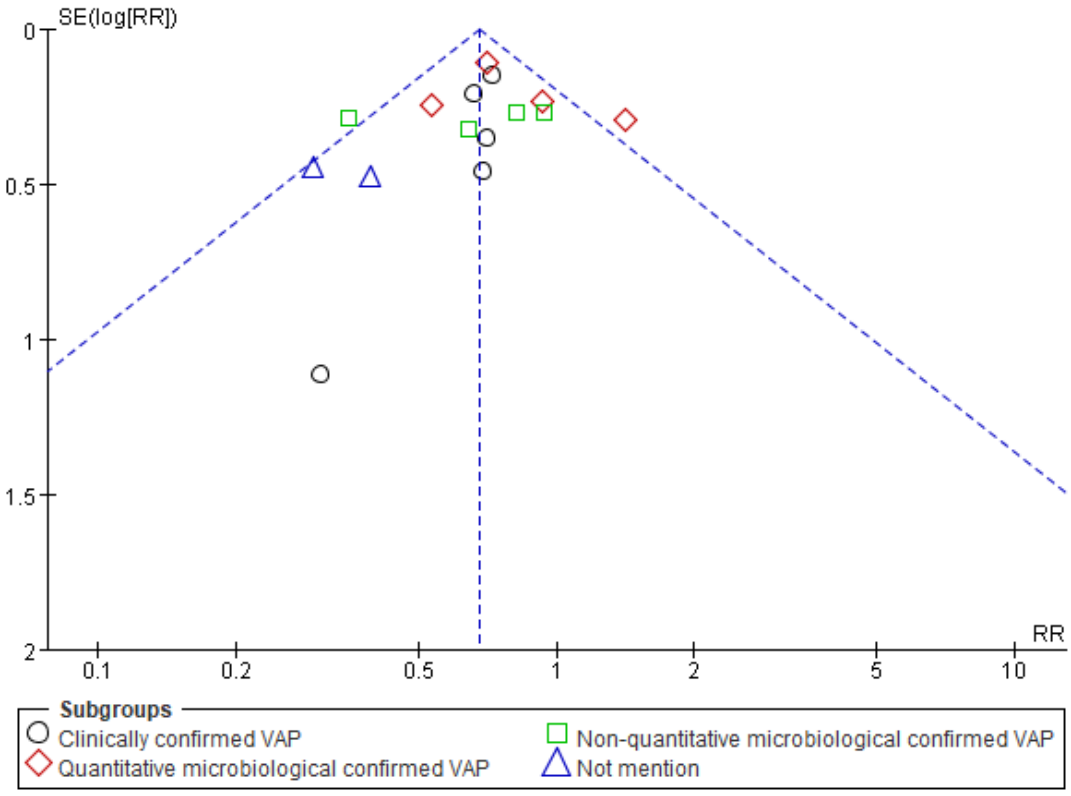
meta-analyses: the PRISMA statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi: 10.1371/journal.pmed.1000097. Epub 2009 Jul 21.

Supplemental Table 2. Clinical characteristics of the included articles

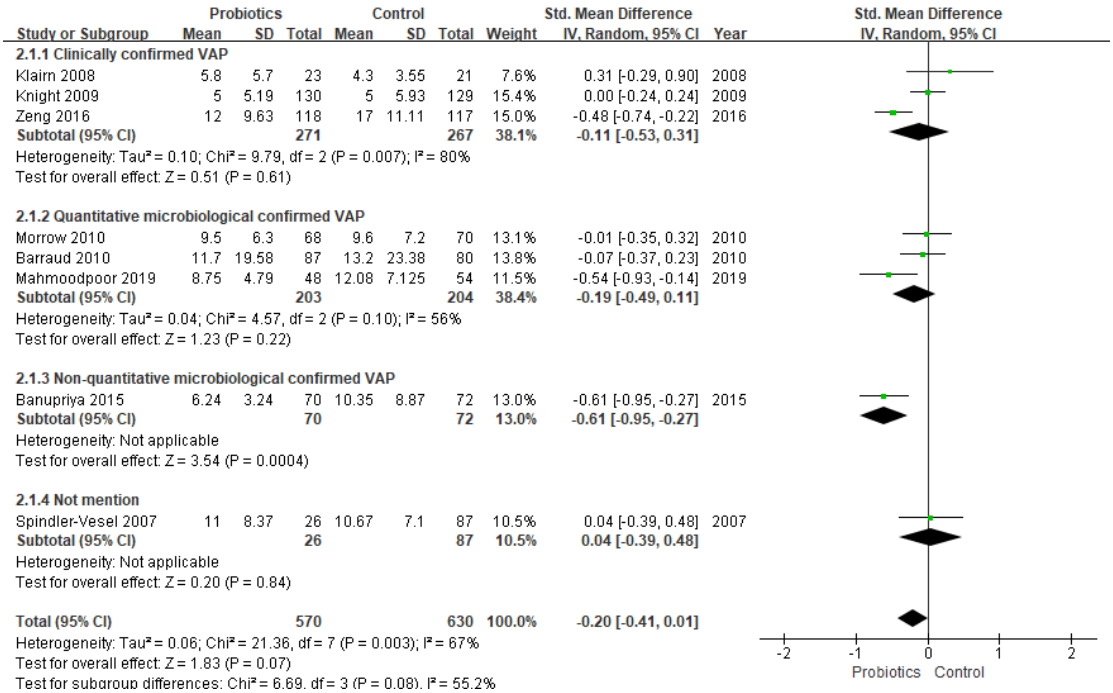
Study	Admission diagnosis, n (%)						APACHE II Score	
	Respiratory	Sepsis	Hemodynamic	Neurogenic	Trauma	Others	Probiotics group	Control group
Mahmoodpoor 2019	4 (3.9)	0 (0)	42 (41.2)	0 (0)	4 (3.9)	42 (41.2)	24.1±6.2	22.8 ± 4.7
Klarin 2018	17 (12.4)	34 (24.8)	40 (29.2)	0 (0)	7 (5)	39 (28.4)	22 (18 to 27)	24 (18.75 to 28)
Shimizu 2018	0 (0)	72 (100)	0 (0)	0 (0)	0 (0)	0 (0)	19 (14 to 24)	20 (14 to 26)
Zeng 2016	A mixed population of medical, surgical, trauma and neurologic patients						14.7 ± 3.9	16.6 ± 4.3
Rongrungruang 2015	Elderly females with co-morbidities and severe health problems leading to mechanical ventilation						19.4 ± 7.04	19.9 ± 6.89
Banupriya 2015	28 (18.6)	33 (22)	0 (0)	59 (39.3)	0 (0)	30 (20)	Not mentioned	
Li 2012	128 (77.6)	37 (22.4)					Not mentioned	
Tan 2011	Severe TBI						14.8 ± 3.6	14.3 ±3.6
Morrow 2010	36 (24.7)	0 (0)	14 (9.5)	25 (17.1)	54 (36.9)	17 (11.6)	22.7 ± 7.5	23.7 ± 8.0
Barraud 2010	58 (35)	Shock: 77 (46); Coma: 6 (3.5)				26 (15.5)	Not mentioned	
Knight 2009	41 (15.8)	Surgery :113 (43.6)			58 (22.3)	47 (18.1)	17 (12 to 23)	17(12 to 22)
Giamarellos-Bourboulis 2009	Severe multiple organ injury						Not mentioned	
Forestier 2008	24 (11.4)	Post-operation: 61 (29.4)			50 (24.2)	73 (35)	Not mentioned	
Klarin 2008	8 (18.2)	11 (25)	11 (25)	0 (0)	3 (6.8)	10 (22.7)	22 (11 to 39)	27 (9 to 37)
Spindler 2007	Multiple injured patients						13± 7	

TBI: Traumatic brain-injured patients; APACHE II: Acute Physiology and Chronic Health Evaluation; APACHE II Score are presented as median (range) or mean ± SD

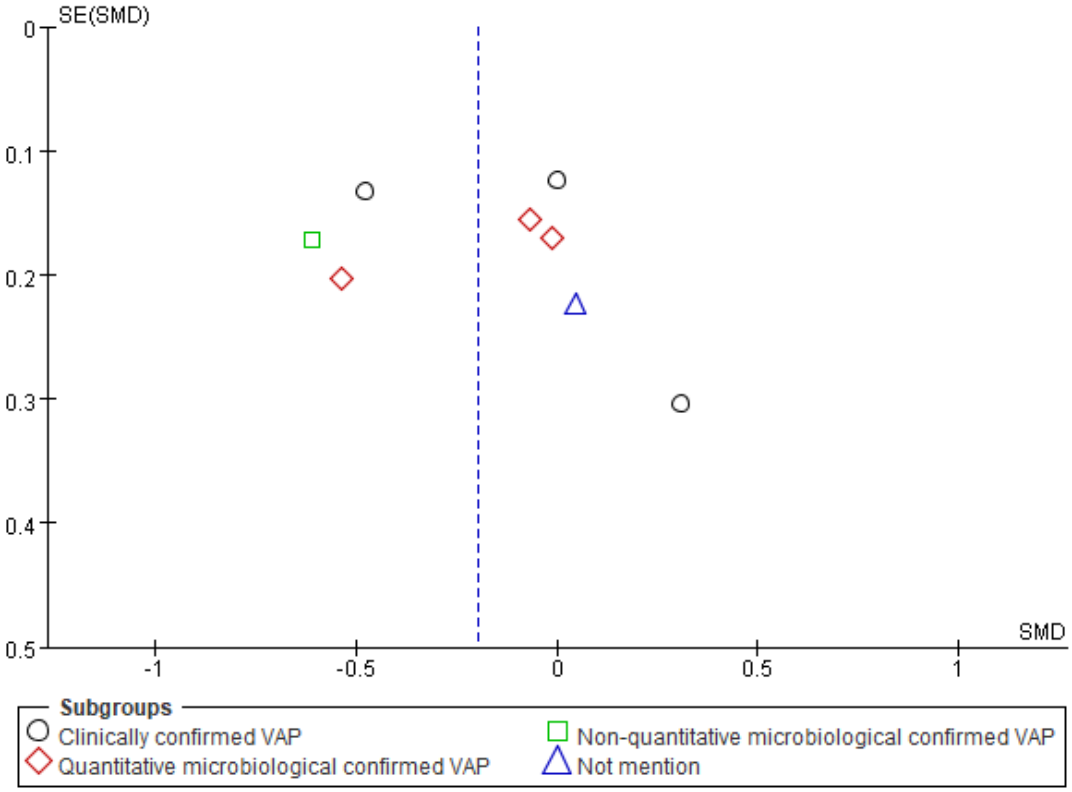
Supplemental Figure 1. Funnel plot for effect of probiotics on ventilator-associated pneumonia



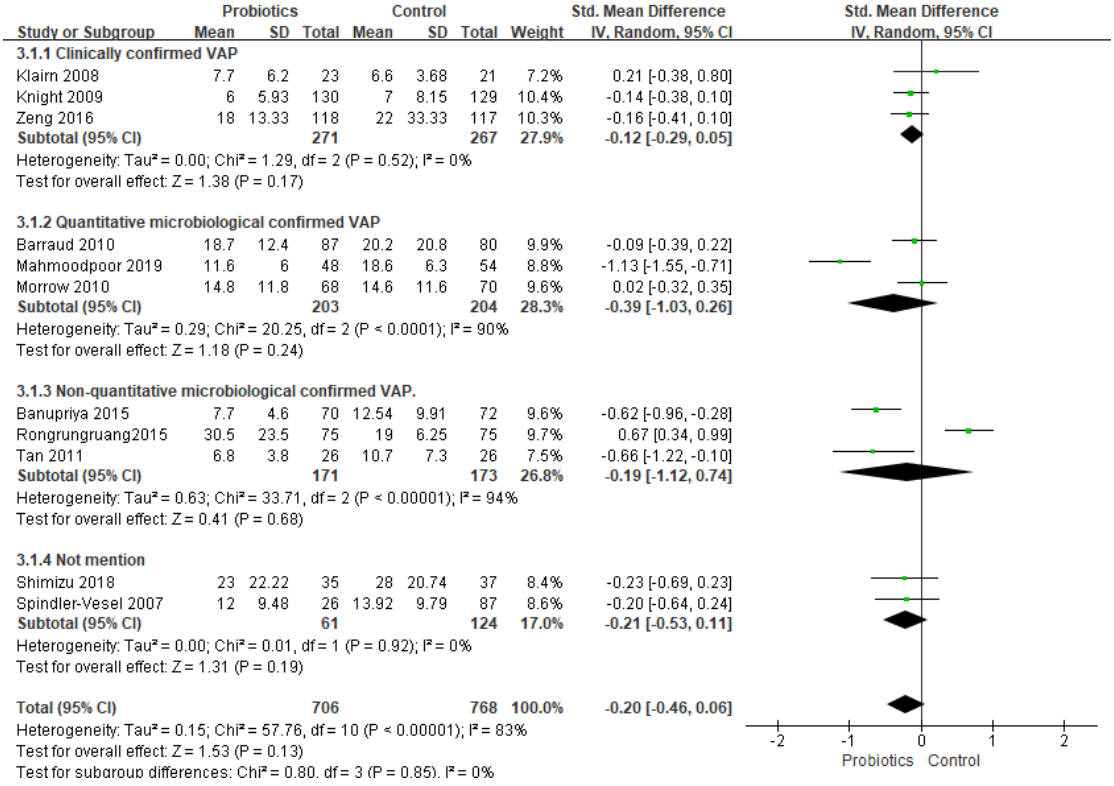
Supplemental Figure 2. The pooled and subgroup analysis for the effect of probiotics on duration of MV base on eight studies compared to control group using a random effect model.



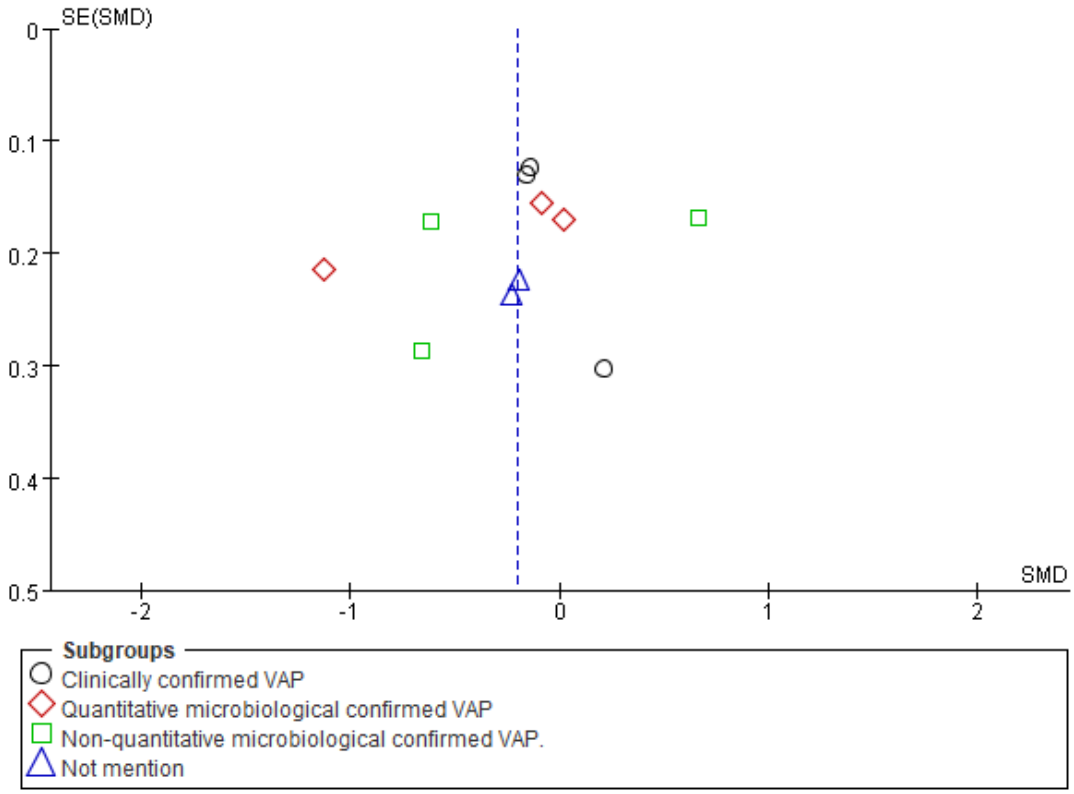
Supplemental Figure 3. Funnel plot for effect of probiotics on MV duration



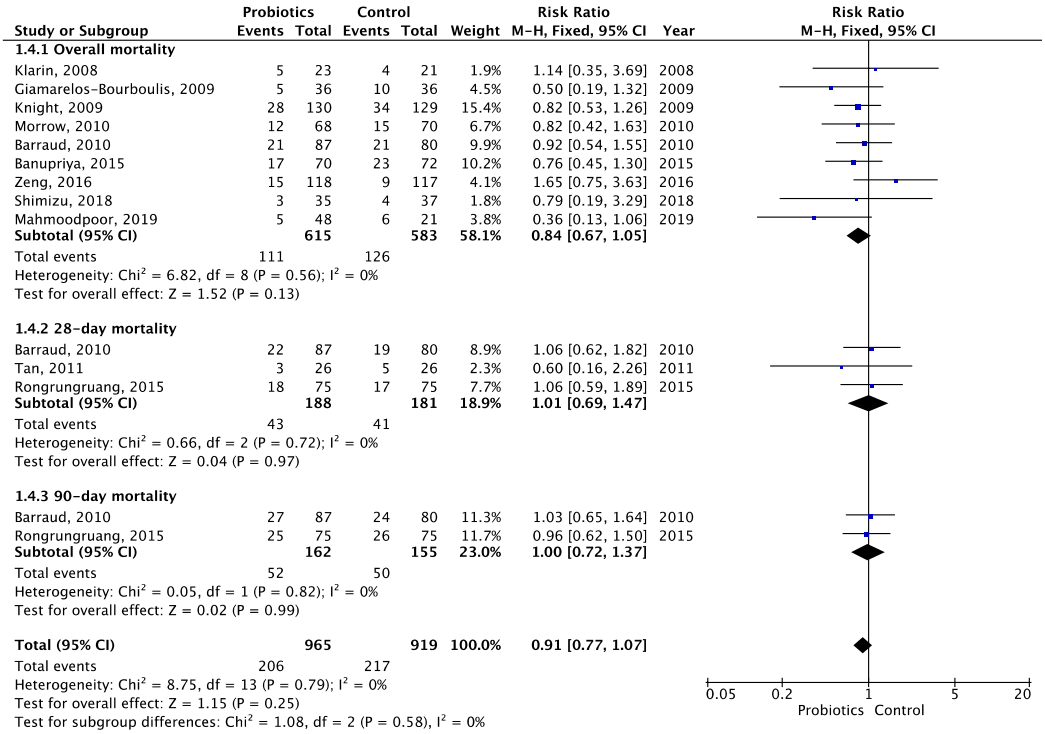
Supplemental Figure 4. The pooled and subgroup analysis for the effect of probiotics on length of ICU stay involving 11 studies compared to a control group.



Supplemental Figure 5. Funnel plot for effect of probiotics on length of ICU stay



Supplemental Figure 6. The pooled analysis for the effect of probiotics on mortality, including total mortality, 28-day mortality, 90-day mortality, and overall mortality, compared with a control group.



Supplemental Figure 7. Funnel plot for the effect of probiotics on the patient mortality