

LETTER

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Probiotics do not significantly reduce nosocomial pneumonia

Luciano Silvestri^{1*}, Hendrick KF van Saene² and Dario Gregori³

See related research by Liu et al., <http://ccforum.com/content/16/3/R109>

Liu and colleagues, in their recent meta-analysis, concluded that probiotics were associated with a statistically significant reduction in the incidence of nosocomial pneumonia (NP) (odds ratio = 0.75; 95% confidence interval = 0.57 to 0.97, $P = 0.03$) [1]. These results were obtained using the fixed-effect model, ignoring a moderate level of heterogeneity ($I^2 = 46\%$) [2]. However, we believe that the inclusion criteria, subjects, and interventions were different among the included studies, and might have impacted the results. Good practice would therefore be to choose a more conservative analysis; that is, the random-effects model. Using this model, the claimed reduction in NP would have been not significant (odds ratio = 0.70, 95% confidence interval = 0.46 to 1.05, $P = 0.085$) (Figure 1). We have already addressed this issue with reference to a previous meta-analysis on probiotics [3,4].

Remarkably, the authors used the random-effects model only when the I^2 test for heterogeneity was higher than 50%. However, the strategy of starting with a fixed-effect model and subsequently moving to a random-effects model if the heterogeneity test is significant is discouraged by some authors [5]. The selection of a model should be based solely on the issue of which model fits the distribution of the effect sizes and takes into account the relevant sources of error.

In conclusion, this meta-analysis showed that probiotics did not significantly reduce NP. Additionally, ventilator-associated pneumonia and mortality were not impacted. The use of probiotics to reduce these important outcomes is therefore not justified given the low level of evidence.

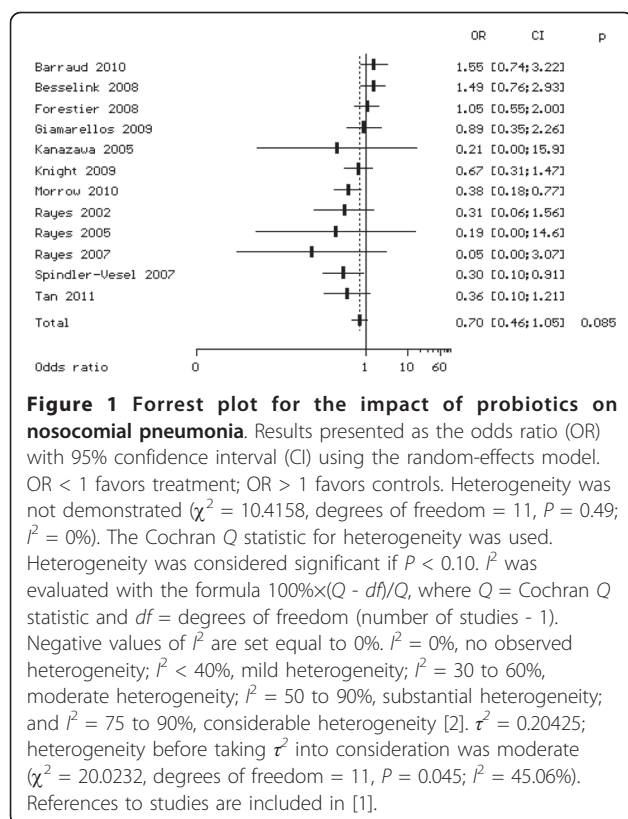
Silvestri and colleagues noted that a more conservative random-effects model should be used to analyze the pooled incidence of NP. The reason why we used a fixed-effect model in our analysis can be explained by the lack of statistical power. The confidence intervals tend to be wider especially when implementing a random-effects model, and the statistical significance is more likely to be lost. Regarding the potential misinterpretation among the special patient population in our review that is different from other studies [4,6], we pre-defined heterogeneity as low, moderate or high with I^2 values above 25%, 50%, and 75%, respectively, as recommended by some authors [7]. We calculated all pooled odds ratios based on this criterion to increase the consistency of our meta-analysis.

Silvestri and colleagues are also concerned about the switch between different models. However, our population of critically ill patients, as we mentioned above, is from a heterogenous group. Heterogeneity is an inevitable issue in studies on critical care. Using different models depending on heterogeneity [7] is supposed to be a more conservative way to interpret the results.

Despite the potential limitations of our work [1], we believe the available evidence suggests that probiotics have a marginal effect on the prevention of NP, and relevant research should not be discouraged to identify populations that benefit most from probiotics. We fully agree with Dr Silvestri and colleagues that further large-scale, randomized controlled trials are warranted. This was also clearly stated in the conclusions of our meta-analysis.

* Correspondence: lucianosilvestri@yahoo.it

¹Department of Emergency, Unit of Anesthesia and Intensive Care, Presidio Ospedaliero, Via Fatebenefratelli 34, 34170 Gorizia, Italy
Full list of author information is available at the end of the article



- Silvestri L, van Saene HKF, Gregori D, Agostini S, Francescon M, Taylor N: Probiotics to prevent ventilator-associated pneumonia: no robust evidence from randomized controlled trials. *Crit Care Med* 2010, **38**:1616-1617.
- Siempos II, Ntaidou TK, Falagas ME: Impact of the administration of probiotics on the incidence of ventilator-associated pneumonia: a meta-analysis of randomized controlled trials. *Crit Care Med* 2010, **38**:954-962.
- Borenstein M, Hedges LV, Higgins JPT, Rothstein HR: *Introduction to Meta-analysis* Padstow: TJ International, John Wiley & Sons Ltd; 2009.
- Gu WJ, Wei CY, Yin RX: Lack of efficacy of probiotics in preventing ventilator-associated pneumonia: a systematic review and meta-analysis of randomized controlled trials. *Chest* 2012, doi: 10.1378/chest.12-0679.
- Higgins JP, Thompson SG, Deeks JJ, Altman DG: Measuring inconsistency in meta-analyses. *BMJ* 2003, **327**:557-560.

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Authors' response

Kai-xiong Liu, Ying-gang Zhu, Jing Zhang, Li-li Tao, Jae-Woo Lee, Xiao-dan Wang and Jie-ming Qu

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Abbreviations

NP: nosocomial pneumonia.

Author details

¹Department of Emergency, Unit of Anesthesia and Intensive Care, Presidio Ospedaliero, Via Fatebenefratelli 34, 34170 Gorizia, Italy. ²Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool L69 3GA, UK.

³Department of Cardiological, Thoracic and Vascular Sciences, Unit of Biostatistics, Epidemiology and Public Health, University of Padova, 35133 Padova, Italy.

Competing interests

The authors declare that they have no competing interests.

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References

- Liu K, Zhu Y, Zhang J, Tao L, Lee J, Wang X, Qu J: Probiotics' effects on the incidence of nosocomial pneumonia in critically ill patients: a systematic review and meta-analysis. *Crit Care* 2012, **16**:R109.
- Higgins JPT, Green S: *Cochrane Handbook for Systematic Reviews of Interventions* 2011 [<http://www.cochrane-handbook.org>], Version 5.1.0 [updated March 2011]. The Cochrane Collaboration;

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