

Letter to the Editor

Quoting a landmark paper on the beneficial effects of probiotics

To the Editor:

Probiotics are defined as “live microorganisms that when administered in adequate amounts should confer a health benefit on the host.”¹ Intriguingly, the rapid expansion of commercially available products that contain probiotics is in sharp contrast with the lack of scientific evidence for their efficacy and working mechanism. Few well conducted trials have appeared in high-impact journals. Amongst these is an article by Kalliomaki et al,² “Probiotics in primary prevention of atopic disease: a randomized control trial.” To date, this is the most quoted clinical trial on probiotics and atopic disease in peer-reviewed journals. Kalliomaki et al² reported a double-blind, placebo-controlled trial on supplementation of *Lactobacillus rhamnosus* GG to pregnant women with a family history of atopic disease starting 2 to 4 weeks before delivery. After delivery, breast-feeding mothers ingested the probiotics, and bottle-fed children received the supplementation mixed with water by spoon for 6 months. The intervention resulted in a reduced incidence of atopic eczema at the age of 2 years but had no effect on allergic sensitization or respiratory allergic disease. We speculate that the high quotation numbers may reflect an apparent urge to establish probiotics as a useful prevention measure. We therefore determined the quality of scientific quotations of this landmark publication.

By November 1, 2008, this article had been quoted in 663 separate publications. We were able to retrieve and examine 458 articles in English (supplemental text of this article’s Online Repository at www.jacionline.org). All quotations were randomly collected in a database, blinding the assessors to authors, year of publication, and specific journal. Each quotation was assigned to a specific section of the article by Kalliomaki et al² and assessed for accuracy by 2 researchers separately. Incorrect quotations were further subcategorized based on 4 model types of errors (misquotation of result or overinterpretation of data, secondary citing, no evidence for cited result, and specific misquotations of the materials and methods section). To establish a possible relation between the quality of a quotation and potential interfering factors, we separately obtained the year of publication, journal, 2006 journal impact factor, the number of quotations per publication, and type of publication. Of the 603 total quotations, 175 (29.0%) were incorrect (Fig 1). Thirty-four percent of the articles had at least 1 inaccurate quotation. The median impact factor between correct and incorrect quotations did not differ (correct, 3.4 [IQR, 3.1] vs incorrect, 2.7 [IQR, 3.1]; $P = .74$). The annual number of publications citing the article was stable, and we did not find a change of error frequency in time (Table I). We anticipated lower error rates in certain paragraphs that would be less subject to interpretation. Surprisingly, quotations concerning the materials and methods section showed the highest number of misquotations, 47.5% of cases. We found lower error rates for the other sections, 28.2% for results and 18.9% for conclusion/hypotheses. We found significantly more misquotations in basic research manuscripts (37%), followed by reviews (30.9%), clinical trials (23.0%), and miscellaneous (21.1%; Table I).

A common error was the generalization that *L rhamnosus* GG exerts a preventive effect on allergic diseases other than atopic

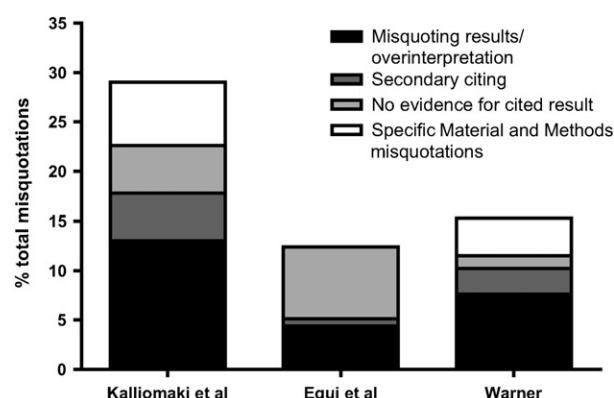


FIG 1. Total percentage of incorrect quotations of the landmark paper by Kalliomaki et al,² Equi et al⁴ (antibiotic treatment in cystic fibrosis), and Warner³ (asthma prevention) further subcategorized into the different model types of error.

eczema. Notably, the study reports an effect only on eczema, whereas allergic disease or IgE levels remained unaffected. Also, statements that *L rhamnosus* GG supplementation affected fecal flora composition in this trial were incorrect. This specific error suggests a causative relationship between changes in the intestinal microbial composition and prevention of eczema. For comparison, we performed similar analyses on 2 additional articles, 1 on cetirizine treatment as asthma prevention,³ and the study by Equi et al⁴ on azithromycin (antibiotic) treatment in children with cystic fibrosis that was published in the same journal in the same period as the study by Kalliomaki et al.² These articles were quoted 78 (60 articles)³ and 136 (86 articles)⁴ times, respectively, in articles written in English that we were able to retrieve. In these 2 studies, we established that 15% and 12.5% of the quotations were incorrect, compared with 29% for the article by Kalliomaki et al.² Respectively, 20% and 16% of the articles had at least 1 inaccurate quotation, compared with the 34% of the article by Kalliomaki et al.² When divided into the different subcategories of predefined errors, no significant differences were detected in the 2 comparator articles. We did not find any misquotations in the materials and methods of the article by Equi et al⁴ (Fig 1). These findings may indicate that the reason for the high rate of quotation errors concerning the study by Kalliomaki et al² is related to the subject: probiotics.

Studies on the percentage of quotation errors in issues of a journal have been published before. de Lacey et al⁵ found a quotation error rate of 15%, with 12% being major (the potential of dramatically changing the reader’s understanding of the original article). More recent work in the field of anatomy⁶ and head and neck surgery⁷ established similar figures of 19% and 17% for all inaccuracies and 18% and 11% for major errors. These number are similar to our results on the articles by Warner³ and Equi et al,⁴ but much lower than the misquotations of the article by Kalliomaki et al.²

Papers describing misquotations of a single article are rare. Recently, Porrino et al⁸ found an error rate of 41% in articles citing a commonly referenced hand surgery study, with 34% classified as major. These findings are comparable to our results

TABLE I. Quotation accuracy categorized by year and type of publication

Year	Clinical trial		Review		Basic research		Miscellaneous		Total percentage	
	Correct	Incorrect	Correct	Incorrect	Correct	Incorrect	Correct	Incorrect	Correct	Incorrect
2001	4	1	2	2	0	0	0	1	60	40
2002	12	4	43	17	4	1	12	2	75	25
2003	13	2	25	12	8	6	3	0	71	29
2004	9	4	30	10	15	9	3	1	70	30
2005	19	8	30	12	12	3	3	1	73	27
2006	29	9	27	15	13	5	4	2	70	30
2007	30	11	7	8	12	7	5	1	67	33
2008	28	4	15	4	11	13	0	0	72	28
Total	144	43	179	80	75	44	30	8	71	29

on the article by Kalliomaki et al.² They also reported more errors in review articles, which we were unable to detect. A study analyzing quotations of the results of a survey on HIV and primary care found 11% errors in quotations on the primary outcome.⁹ Porrino et al.⁸ suggested that the original article is widely misunderstood, without knowing whether this is the by-product of authors referencing from articles other than the original.⁸ We cannot exclude that this is also the case for the article by Kalliomaki et al.²

We conclude that misquotation is a common problem in biomedical literature and that the high percentage of errors on the most quoted probiotic trial calls for more awareness of editors, referees and, above all, authors.

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