Letter to the Editor

Industry Sponsorship and Outcomes of Nutrition Studies: is there an Association when looking at the Trial Level?

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Dear Editor,

Very recently, Nicholas Chartres and colleagues published a systematic review and meta-analysis regarding association of industry sponsorship with outcomes of nutrition studies.¹ The authors included 12 reports and found one which examined effect sizes and concluded that studies sponsored by the food industry reported significantly smaller harmful effects for the association of soft drink consumption with energy intake and body weight than those not sponsored by the food industry. Also, 8 reports, including 340 studies, assessed the association of industry sponsorship with authors' conclusions. Industry-sponsored studies tended to be more likely to have favorable conclusions than non-industry-sponsored studies with a difference not reaching statistical significance (risk ratio, 1.31 [95%CI, 0.99-1.72]). They concluded that these findings suggest but do not establish that industry sponsorship of nutrition studies is associated with conclusions that favor the sponsors, and further investigation of differences in study results and quality is needed.

While we agree with the authors about the need for further research into this subject is needed, it is – as always - important to distinguish between association and causality. There are several explanations for the finding that industry-sponsored studies are more likely to have conclusions favorable to industry than non-industry sponsored studies including a possible more rigorous proposal review process for industry funded studies, which may lead to higher quality reviews. Still, further investigation of differences in study results and quality is needed for research in general, but also particularly for nutritional research.

We have recently investigated the effects of nutritional support and outcomes in malnourished medical inpatients.² We included 22 randomized trials with a total of 3736 participants in this meta-analysis and found significant effects of nutritional therapy in regards to increase in weight, caloric intake and protein intake as well as a lowering in risk for unplanned hospital readmissions and shorter length of hospital stays in the subgroup of patients with established malnutrition. No effects were found with respect to mortality, hospital-acquired infections and functional outcome. In the initial report we conducted several subgroup analyses based on a previous protocol, which, however did not include stratification by industry-sponsoring.

Based on the report by Chartres et al. we have now compared the effects of nutritional therapy on outcomes in subgroups based on industry sponsorship using our 2016 meta-analysis dataset.¹ Based on the conflict of interest and funding statements included in the original publications, we found that out of 22 included trials 11 (50%) declared industry sponsoring or partial industry sponsoring, 8 (36%) declared non-industry sponsoring or no sponsoring and 3 (14%) did not disclose sponsorship (**Table 1**). Our subgroup results indicate that there is no evidence for better results in trials with industry sponsoring compared with no-industry sponsoring (**Table 2**). In fact, effects of nutritional therapy were stronger among trials with no-industry sponsoring compared with to industry sponsoring in regard to improvement in functional outcome as assessed by Barthel index (4.0 points vs -0.97 points, p for subgroup difference =0.001) and tended to be stronger in regard to reduction in length of hospital stay (-2.25 days vs 0.37 days, p for subgroup difference=0.08).

As discussed in our initial report², there are several limitations regarding our meta-analysis including low overall study quality, small number of trials and small samples sizes of many trials. Nevertheless, at least for the medical inpatient setting, there appears to be no evidence on a trial level that industry sponsoring would favorably be associated with (or favorably influence) trial results. Given the paucity of high quality trials in this domain, large-scale randomized trial are needed to provide more definite conclusions^{3,4}. Of note, we did not receive food industry sponsoring, neither for our initial meta-analysis, nor for this report.

Table 1. Overview of sponsorship in nutritional trials regarding medical inpatients

First author, year of publication	Funding source	Disclosed Author Conflicts of Interest
Trials reporting industry sponsoring or partial industry sponsoring		
Hogarth 1996	Industry (energy supplement (Lucozade) and placebo preparation were provided by SmithKline and Beecham)	None disclosed
Holyday 2011	Nonindustry (private) / Industry (The Gut Foundation (Randwick, Australia). Pharmatel Fresenius Kabi Pty Ltd.)	None
McWhirter	Industry (Clintec Nutrition Ltd)	McWhirter reported receiving support from Clintec Nutrition
Munk 2014	Nonindustry (public)/Industry (Herlev University Hospital Research Unit. Toft Care System, Copenhagen, Denmark for protein powder.)	None
Potter 2001	Nonindustry (public)/Industry (grant from the Chief Scientist's Office of Scottish Office. Frusenius UK Ltd provided the sip feed supplements free of charge)	None disclosed
Rüfenacht 2010	Nonindustry (public)/ Industry (Independent Research Fund of the Department of Internal Medicine of Kantonsspital Winterthur. Additional support by the Federation of the Swiss Medical Nutrition Industry)	None disclosed
Ryan 2004	Nonindustry (public/private) / Industry („Contrat de plan inter-regional Pays de Loire-Bretagne “. Nutricia in association with the Société française de Nutrition Entérale et Parentérale)	None disclosed
Saudny-Unterberger 1997	Nonindustry(public/private)/Industry (supported by a grant from Quebec Lung Association and the Research Centre of the Montreal Chest institute. Supplements are provided by Abbott Laboratories, Montreal, Canada)	None disclosed
Starke 2011	Nonindustry(public)/Industry (Exchange Organisation StudEx/Switzerland and the German Academic Exchange Service (DAAD)/Germany. Nestlé Nutrition/Switzerland for biochemical analyses.)	None
Vermeeren 2004	Industry (Numico Research BV, The Netherlands)	None disclosed
Vlaming 2001	Nonindustry (public)/Industry (Grant from Responsive Funding Group of the North Thames Regional Health Authority NHS R&D. Abbott Laboratories Ltd supplied sipfeeds and placebo drinks, provided supplementary financial support. Seton Heath Care provided the vitamin tablets and placebos)	None disclosed
Trials reporting no industry sponsoring		
Broqvist 1994	Nonindustry (public/private) ("Forenade liv" Mutual Group Life Insurance Company, Stockholm, Sweden. Lions Research Foundation, Sweden, Pharmacia AB, Sweden. The County Council of Östergötland, Sweden. The Research Foundation of	None disclosed
Bunout 1989	the University Hospital of Linköping, Sweden and The Swedish Society of Cardiology.)	None disclosed
Feldblum 2011	Nonindustry (public) (Israel National Institute for Health Policy and Health Services Research)	None
Hickson 2004	Nonindustry (public) (National Health Service)	None disclosed
McEvoy 1982	Nonindustry (private) (Mrs. B. Davison and Mr. A. Torrance of dietetic department for dietary assessments)	None disclosed
Neelemaat 2011	Nonindustry (public) (Netherlands Organisation for Health Research and Development (project number 94506203))	None
Somanchi 2011	Nonindustry (public) (Johns Hopkins Hospital)	None disclosed
Volkert 1996	Nonindustry (public/private)(Bundesministerium für Gesundheit, Bonn and from Fa. B.Braun, Meldungen, Germany.)	None disclosed
Trials not disclosing sponsorship		
Gariballa 2006	None disclosed	None disclosed
Gazzotti 2003	None disclosed	None disclosed
Ollenschläger 1992	None disclosed	None disclosed

Table 2. Overview of subgroup effects in regard to reported sponsorship

	Mortality	Adverse events (excl. death)	Function (Barthel index, points)	Infections	body weight	Non-elective readmissions	Length of stay (days)	Daily caloric intake (kcal)	Daily protein intake (g)	Weight change (kg)
	RR (95%CI)	OR (95%CI)	Mean difference (95%CI)	OR (95%CI)	Mean difference (95%CI)	RR (95%CI)	Mean difference (95%CI)	Mean difference (95%CI)	Mean difference (95%CI)	Mean difference (95%CI)
Stratification by Sponsorship										
Industry-sponsoring	0.91 (0.7, 1.3)	1.61 (0.2, 17.1)	-0.97 (-2.8, 0.9)	0.40 (0.1, 1.6)	-0.07 (-2.7, 2.6)	0.68 (0.5, 1.0)	0.37 (-1.1, 1.8)	356 (269, 444)	17.3 (8.8, 25.7)	0.76 (0.4, 1.1)
No industry-sponsoring	0.80 (0.6, 1.1)	0.92 (0.1, 6.0)	4.00 (1.7, 6.3)	0.77 (0.2, 3.5)	0.73 (-2.3, 3.8)	0.45 (0.2, 1.0)	-2.25 (-3.9, -0.5)	399 (111, 687)	16.2 (4.5, 27.9)	0.25 (-0.9, 1.4)
Sponsoring not declared	1.69 (1.0, 2.9)	1.31 (0.9, 1.9)	-0.30 (-0.9, 0.3)	0.79 (0.5, 1.2)	-0.78 (-3.7, 2.1)	0.75 (0.6, 1.0)	-0.73 (-2.1, 0.6)	850 (530, 1170)	32.2 (20, 44)	1.09 (0.4, 1.8)
<i>Test for subgroup difference as I² (p-value)</i>	62.5% (p=0.07)	0% (p=0.92)	85.1% (p=0.001)	0% (p=0.66)	0% (p=0.78)	0% (p=0.49)	61.1% (p=0.08)	76.5% (p=0.01)	57.5% (p=0.10)	0% (p=0.42)

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