Letters

RESEARCH LETTER

Industry Collaboration and Randomized Clinical Trial Design and Outcomes

Industry-funded clinical trials are more likely to have favorable, proindustry results compared with nonindustry funded trials,[1] but few studies have distinguished between industry funding in the context of industry collaboration in the design, analysis, or reporting of trials.[2,3] For a sample of clinical trials published in high-impact journals, our objective was to examine whether industry funding with collaboration was associated with certain trial design features and outcomes.

Related article

Methods | We identified randomized clinical trials of drugs and devices published between December 1, 2011, and November 31, 2012, in biomedical journals for which *Journal Citation Reports 2012* reported an impact factor greater than 11 and that published details on the "Role of the Funding Source/Sponsor." We excluded phase 1 or 2 trials and secondary trial analyses.

We categorized trials as having industry funding with collaboration when any for-profit organization funded the trial and had any role in its design, analysis, or reporting; as having industry funding without collaboration when any for-profit organization funded the trial but had no role in its design, analysis, or reporting; and as having neither industry funding nor collaboration.

Two authors (N.R. and N.Z.), blinded to industry funding and collaboration, independently assessed the following trial design features and outcomes: blinding (double, single, or none), intention-to-treat analysis, discussion of limitations (defined as using the word stems "weak" or "limit" when describing trial design in the Discussion section), superiority or noninferiority design, comparator drug (active vs placebo), primary outcome (positive [ie, statistically significant superiority or noninferiority favoring the product of the sponsor or sponsors], negative, or mixed), primary end point (clinical, surrogate [any radiology, pathology, or laboratory value], or mixed). Differences were resolved by consensus. Interrater agreement was high (κ = 0.9350). One investigator (N.R) subsequently recorded allocation concealment, funding (industry and/or government/nonprofit), and industry collaboration.

We conducted 2 sets of analyses comparing trial variables between trial groups (neither industry funding nor collaboration vs industry funding with collaboration and neither industry funding nor collaboration vs industry funding without collaboration) using relative risks (RRs) and Fisher exact tests. Statistical analyses were conducted using SAS version 9.3 (SAS Institute Inc). All *P* values were 2-tailed, with significance defined as $P < .05$.

Results | There were 219 articles from 10 high-impact journals describing the results of drug and device trials included in our analysis; 86 trials (39%) had industry funding with collaboration, 66 (30%) had industry funding without collaboration, and 67 (31%) had neither industry funding nor industry collaboration (**Table**). When compared with trials having neither industry funding nor collaboration, trials having industry funding with collaboration were significantly more likely to report a positive primary outcome (69.8% vs 52.2%; RR, 1.34; 95% CI, 1.03-1.75 [$P = .03$]) and use a surrogate primary end point (51.2% vs 16.4%; RR, 3.11; 95% CI, 1.75-5.56 [$P < .001$]) and less likely to discuss limitations (40.7% vs 58.2%; RR, 0.70; 95% CI, 0.50-0.97 [$P = .04$]). In contrast, there were no differences between trials having neither industry funding nor collaboration and trials having industry funding without collaboration.

Discussion | Among clinical trials published in high-impact journals, industry funding with collaboration in the design, analysis, or reporting was associated with increased likelihood of reporting a positive primary outcome and decreased likelihood of reporting of trial limitations. Collaborative trials' more com-

Table. Industry Funding and Collaboration Status and Trial Design and Outcome

	Neither Industry Funding Nor Collaboration (n = 67)		Industry Funding With Collaboration (n = 86)			Industry Funding Without Collaboration (n = 66)		
Trial Variable	No. (%)	RR (95% CI)	No. (%)	RR (95% CI)	*P* Value	No. (%)	RR (95% CI)	*P* Value
Trial used allocation concealment	65 (97.0)	1 [Ref]	80 (93.0)	0.96 (0.89-1.03)	.47	62 (93.9)	0.97 (0.90-1.04)	.44
Trial used double blinding	39 (58.2)	1 [Ref]	61 (70.9)	1.22 (0.95-1.56)	.12	34 (51.5)	0.89 (0.65-1.21)	.49
Trial used intention-to-treat analysis	40 (59.7)	1 [Ref]	46 (53.5)	0.90 (0.68-1.18)	.51	39 (59.1)	0.99 (0.75-1.31)	.99
Discussion of trial limitations in publication	39 (58.2)	1 [Ref]	35 (40.7)	0.70 (0.50-0.97)	.04	44 (66.7)	1.15 (0.88-1.49)	.37
Noninferiority trial design	11 (16.4)	1 [Ref]	17 (19.8)	1.20 (0.61-2.40)	.68	12 (18.2)	1.11 (0.53-2.33)	.82
Trial used placebo comparator	28 (41.8)	1 [Ref]	36 (41.9)	1.00 (0.69-1.46)	.99	26 (39.4)	0.94 (0.62-1.42)	.86
Trial with positive primary outcome	35 (52.2)	1 [Ref]	60 (69.8)	1.34 (1.03-1.75)	.03	31 (47.0)	0.90 (0.64-1.27)	.60
Trial used surrogate primary end point	11 (16.4)	1 [Ref]	44 (51.2)	3.11 (1.75-5.56)	<.001	13 (19.7)	1.20 (0.58-2.48)	.66

Abbreviations: Ref, reference; RR, relative risk.

mon use of a surrogate primary end point may, in part, explain why these trials were more likely to have a positive primary outcome. While publication bias may contribute to our findings, our study was also limited by our exclusion of high-impact journals that do not publish details on the "Role of the Funding Source/Sponsor," which was needed to assess trial collaboration.

Our results suggest that, in addition to disclosure of industry funding source, greater transparency of industry funders' role in trial design, analysis, and reporting might be valuable for assessing potential bias in trial findings.

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Study concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Roper.
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Statistical analysis: Roper.
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