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Original Research

Impact of industry collaboration on randomised controlled trials in oncology

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Abstract ***Background:*** Industry funders can simply provide money or collaborate in trial design, analysis or reporting of clinical trials. Our aim was to assess the impact of industry collaboration on trial methodology and results of randomised controlled trials (RCT).
Methods: We searched PubMed for oncology RCTs published May 2013 to December 2015 in peer-reviewed journals with impact factor > 5 requiring reporting of funder role. Two authors extracted methodologic (primary end-point; blinding of the patient, clinician and outcomes assessor; and analysis) and outcome data. We used descriptive statistics and two-sided Fisher exact tests to compare characteristics of trials with collaboration, with industry funding only, and without industry funding.
Results: We included 224 trials. Compared to those without industry funding, trials with collaboration used more placebo control (RR 3·59, 95% CI [1·88–6·83], p < 0001), intention-to-treat analysis (RR 1·32, 95% CI [1·04–1·67], p = 02), and blinding of patients (RR 3·05, 95% CI [1·71–5·44], p < 0001), clinicians (RR 3·36, 95% CI [1·83–6·16], p≤·001) and outcomes assessors (RR 3·03, 95% CI [1·57–5·83], p = 0002). They did not differ in use of overall survival as a primary end-point (RR 1·27 95% CI [0·72–2·24]) and were similarly likely to report positive results (RR 1·11 95% CI [0·85–1·46], p = 0.45). Studies with funding only did not differ from those without funding.

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Conclusions: Oncology RCTs with industry collaboration were more likely to use some high-quality methods than those without industry funding, with similar rates of positive results. Our findings suggest that collaboration is not associated with trial outcomes and that mandatory disclosure of funder roles may mitigate bias.

1. Introduction

Involvement of the pharmaceutical and device industries in clinical research may lead to bias in the evidence base [1]. Industry sponsorship has been associated with practices used to distort evidence [2] and with positive clinical trial outcomes [3–5], although methodological rigour has been shown to be similar in published funded and unfunded studies [6]. When industry sponsors trials, the nature of their involvement varies; companies can simply provide funding or may be involved in study design, data interpretation or manuscript preparation. These different degrees of involvement may have different effects. A recent study sought to differentiate the impacts of funding alone versus collaboration (defined as participation in study design, analysis or reporting) on randomised controlled trials (RCTs) across medical specialities and found that industry collaboration was associated with a higher likelihood of reporting a positive primary outcome (i.e. in favour of the study drug) compared with no industry involvement [7]. Industry funding alone without collaboration was not associated with a positive primary outcome.

Industry plays a particularly important role in funding and conducting clinical trials in oncology and is critical to the continued development of new therapeutics. The role of industry in oncology trials has expanded [8–10], and in 2011 industry funded over half of oncology clinical trials [11]. There has been concern about bias related to industry involvement in oncology trials from American Society of Clinical Oncology (ASCO) and others [12,13], and ASCO has called for clinical trials to focus on overall survival (OS) as the most clinically meaningful outcome [14,15]. In addition, there have been broad calls for increased transparency [16], and many journals now require authors of clinical trial reports to disclose the role of the funding source [17].

Several studies have examined the relationship of industry funding to positive clinical trial outcomes specifically in oncology, with mixed results [9,18]. Further, funded trials have similar quality of study design [6] and perhaps higher rates of appropriate blinding [18] compared with unfunded trials. However, studies have not differentiated trials with industry funding alone from funded trials in which industry collaborated in the design, analysis or reporting.

Given the importance of industry in the development of new cancer therapies and the potential different impact of industry collaboration in clinical trials versus simple funding, we set out to determine the specific impact of industry collaboration on the design and results of oncology RCTs. We hypothesised that collaboration would be associated with a higher rate of positive outcomes, similar quality of study methodology and similar use of the outcome of OS, compared with no industry involvement. We further hypothesised that industry funding alone would not be associated with positive trial outcomes compared with no industry involvement.

2. Methods

2.1. Journal and study selection

We searched Web of Science for journals that publish in oncology-relevant categories (e.g. immunology, haematology) and selected journals with 5-year impact factor greater than 5 and a requirement that authors report the role of the funder. We conducted a power calculation based on previous findings [5,7] and estimated that 250 studies were required to provide 80% power to detect differences at a significance level of 0·05 between studies with no industry funding and studies with industry collaboration. We searched PubMed for oncology RCTs published in the selected journals. The search strategy is shown in Appendix Fig. 1 in the Supplement.

We included all RCTs evaluating drugs or devices in patients diagnosed with cancer. We excluded studies with unclear industry collaboration, preventative trials, surgical trials, behaviour trials, trials comparing dosing regimens, post-hoc analyses, unplanned interim or follow-up analyses, follow-up studies evaluating secondary end-points of the original trial and single-arm studies. Beginning with the most recent articles (published December 3, 2015), we reviewed articles for inclusion in reverse chronological order by publication date until including an adequate number based on our power calculation. The oldest included articles were published in May 2013.

2.2. Data abstraction

All articles underwent primary review by one of two authors (A.L., A.Y.) and an independent secondary