How prevalent are financial conflicts of interest in dermatology randomized controlled trials? A cross-sectional study

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Summary

Since the last assessment of conflicts of interest (COIs) in dermatology randomized controlled trials (RCTs) in 2004, several countries have introduced transparency databases. We assessed the prevalence of financial COIs in dermatology RCTs and quantified payments from study sponsors to academic/clinical authors using transparency databases, which are available in the USA, France, Australia, Belgium and the Netherlands, while the UK has a noncompulsory transparency database. We included RCTs from the top 10 dermatology journals and the top 7 general medical journals published in 2019. The study assessed 83 RCTs, and COIs were identified in 69%. The highest prevalence was in exclusively industry-funded trials (46/47, 98%), which consisted of personal payments to an academic/clinical author (96% of trials) and having authors who were employees/stockholders (96%). Payments were identified for 31/56 (55%) academic/clinical first/final authors (median payment US$28 746, maximum US$597 299, interquartile range US$17 061–146 253), and 24/31 payments (77%) payments were each > US$10 000.

A conflict of interest (COI) occurs when professional judgement concerning a primary interest (such as the validity of research) may be influenced by a secondary interest (such as financial gain).1 The topic of COIs has been hotly debated in both dermatology and medicine.2–4 A series in the New England Journal of Medicine argued that excessive focus on COIs may discourage productive collaboration between industry and academics/clinicians, which in dermatology has led to major therapeutic advances in psoriasis, eczema and advanced melanoma. However, the series drew strong criticism for falsifying a sentiment of anti-industry bias, failing to distinguish marketing-based prescribing from evidence-based medicine and for downplaying the potential issues of COIs.4 Recognition of the issues of COIs has contributed to the development of transparency databases.1 Although these have been used to report on COIs in dermatology, they have not yet been used to investigate COIs in dermatology randomized controlled trials (RCTs).

In the current study, we assessed the prevalence of potential COIs in phase 2–4 RCTs pertaining to dermatologists published between 1 January and 31 December 2019 in the top 10 dermatology journals and top 7 general medical journals (based on Clarivate impact factor), listed in Supplementary Appendix S1. A COI was defined as (i) an author having received personal fees from the manufacturer of the study intervention, or (ii) an employee/stockholder as an author. We also used transparency databases to quantify payments for first and final academic/clinical authors, which were available for the USA, France, Belgium, the Netherlands and Australia. A noncompulsory database is also available in the UK (search.disclosureuk.org.uk/). Data extraction was performed by two authors independently (LS, AH). Full methodology is listed in the appendix (Supplementary Data File S1).
Report

The study included 83 trials: the included journals, funding sources, topic and intervention assessed are shown in Table 1, and the funding source for each intervention is shown in Table 2. Exclusive industry funding was most common for drug trials (86%).

COIs were identified in 69% of all trials (57/83). By funder, COI prevalence was highest for trials with undisclosed funding (100%) and exclusively industry funding (98%), followed by trials with mixed funding (67%), no funding (14%) and non-industry funding (6%). COIs in exclusively industry-funded trials consisted of personal fees to an academic/clinical author from the manufacturer (96%) and having authors who were also employees/stockholders (96%).

By intervention, COI prevalence was highest for sunscreen/emollient and dressings (100%), followed by drugs (92%), photodynamic therapy/phototherapy/laser (40%), behavioural interventions (14%) and surgical/procedural interventions (0%).

Personal payments were identified for 31/56 (55%) academic/clinical first/final authors based in countries with transparency databases. The median payment was US$28 746 (interquartile range US$17 061–46 253). Most (24/31, 77%) of the payments were for sums > US$10 000, and the five highest value payments all totalled > US$300 000 (Fig. 1a). The combined total of the 31 payments was US$3.28 million.

For US-based authors, personal payments were most commonly (46%) consulting fees (Fig. 1b). Details regarding definitions of each type of personal payment for US-based authors is available in Supplementary Appendix S1. Research payments (i.e. payment for different types of research activities, including enrolling patients into studies of new drugs or devices) were identified for 11 US-based authors (median US$8009, interquartile range US$40 022–60 063).

The prevalence of potential financial COIs (69%) was higher in this study than that previously reported (43%) across four dermatology journals in 2000–2003. Our study was novel in quantifying payments to academic/clinical authors. Use of direct honoraria for conducting research was less common than use of associated payments, such as consulting or speaking fees. For 77% of the assessable COIs on transparency databases, the payments exceeded US$10 000 (a threshold previously considered ‘significant’), and each of the five highest value payments was > US $300 000.

Certain payments will reflect fair compensation for expert advice and facilitation of clinical research over several years, which can offer great societal benefit. However, such payments have the potential to influence authors, either consciously or subconsciously. This potential for bias is recognized by the Cochrane Collaboration, as well as by certain pharmaceutical companies, who have committed to developing policies and practices to address this. Bias does not appear to be only a theoretical concern. In addition to historical examples of harms from COIs, support has been

Table 1 Study results.

| Parameter                        | n (%) |
|----------------------------------|-------|
| Journal                          |       |
| JAAD                            | 26 (31) |
| BJD                             | 23 (28) |
| JEADV                           | 15 (18) |
| JAMA Dermatol                   | 5 (6)  |
| Lancet                          | 3 (4)  |
| NEJM                            | 3 (4)  |
| JID                             | 3 (4)  |
| Am J Clin Dermatol              | 3 (4)  |
| Contact Dermatitis              | 2 (2)  |
| Funding source                  |       |
| Exclusively industry funding     | 47 (57) |
| Non-industry funding            | 16 (19) |
| Mixed funding                   | 12 (14) |
| No funding/study sponsor        | 7 (8)  |
| Funding source not stated        | 1 (1)  |
| Topic investigated              |       |
| Psoriasis                       | 24 (29) |
| Actinic keratoses               | 13 (16) |
| Eczema                          | 11 (13) |
| Surgery                         | 4 (5)  |
| Melasma, naevus of Ota          | 3 (4)  |
| Acne                            | 2 (2)  |
| Alopecia areata                 | 2 (2)  |
| Contact dermatitis              | 2 (2)  |
| Urticaria                       | 2 (2)  |
| Hidradenitis suppurativa        | 2 (2)  |
| Melanoma                        | 2 (2)  |
| Nonmelanoma skin cancer         | 2 (2)  |
| Pruritus, prurigo nodularis     | 2 (2)  |
| Vitiligo                        | 2 (2)  |
| Other                           | 10 (12) |
| Intervention assessed           |       |
| Drug                            | 51 (61) |
| PDT/phototherapy/laser          | 15 (18) |
| Behavioural                     | 7 (8)  |
| Procedure/surgery               | 7 (86) |
| Sunscreen/emollient             | 2 (2)  |
| Dressings                       | 1 (1)  |

Am J Clin Dermatol, American Journal of Clinical Dermatology; BJD, British Journal of Dermatology; JAAD, Journal of the American Academy of Dermatology; JAMA Dermatol, Journal of the American Medical Association Dermatology; JEADV, Journal of the European Academy of Dermatology and Venereology; JID, Journal of Investigative Dermatology; NEJM, New England Journal of Medicine; PDT, photodynamic therapy.

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withdrawn for published guidelines by both the World Health Organization (WHO) and European Association for Cardio-Thoracic Surgery (EACTS) in the past year, with COIs implicated in both decisions.8,9 The consistent finding of more favourable efficacy results and conclusions in industry-funded research has also raised concern.10 Proposed explanations for this finding range from the benign (the considerable de-risking that precedes large trials and the frequent comparisons with placebo as part of regulatory approval) to the more sinister (suppression of negative findings, trial design choices and spin).

The potential for bias with COIs highlights the importance of ensuring adherence to initiatives to maintain high standards in RCTs, such as CONSORT (Consolidated Standards of Reporting Trials) and prospective trial registration. However, while industry-funded trials frequently out-perform non-industry funded trials on quality checklists,11 compliance is still imperfect, with examples of trials that are still incompletely reported,12,13 published without prospective registration12,14 their primary outcomes misrepresented,14,15 their study protocols and statistical analysis plans publicly inaccessible.

Practising evidence-based medicine is challenging when most trials have COIs.11 However, industry trials provide value by bringing new drugs to market, which is an expensive, challenging and risk-fraught process. It has been suggested that they should not additionally be expected to ‘practically perform the assessments of their own products’,11 which has led to calls for more funding of independent research, including of head-to-head trials, in order to answer the questions most pertinent to patients and clinicians and to better enact evidence-based medicine. The funding for such research remains a challenge. Some authors have called for more public funding,11 whereas others have highlighted attempts (unsuccessful to date) in the USA to use a model in which public regulators assign industry-funding to independent research teams.

This study had some limitations, including assessment of a subset of dermatology RCTs, assessing only financial COIs, and having a reliance on transparency databases for payments, which were available only for certain countries and may have inaccuracies. The most common countries for which payments could not be accessed were Germany (n = 22), Canada (n = 4) and Spain (n = 4). Although we assessed COIs for all authors, we quantified payments only for first/final authors, and thus payments made to authors of dermatology RCTs may be underestimated. Finally, payments were not linked to specific trials/interventions on databases, and payments may thus have related to older interventions.

Learning points

- The potential for COIs to cause bias is recognized by the Cochrane Collaboration.
- Compulsory transparency databases, introduced in response to concerns about COIs, can help investigate COIs, and are currently available in the USA, France, Belgium, the Netherlands and Australia, while the UK has a noncompulsory database (search.disclosureuk.org.uk/).
- COIs are present in 69% of contemporary dermatology trials, with the highest prevalence in exclusively industry-funded trials (98%) and drug trials (92% for interventions with > 2 studies).
- Most payments to first/final clinical authors (24/31, 77%) totalled > US$10 000, and the five highest value payments all totalled > US $300 000.

| Table 2 | Funding source of trials by intervention. |
|---------|-----------------------------------------|
| Intervention assessed | Exclusively industry, n (%) | Mixed, n (%) | Non-industry, n (%) | None, n (%) | Not clearly stated, n (%) |
| Drug | 44 (86) | 3 (6) | 3 (6) | 1 (2) | 0 (0) |
| Behavioural | 0 (0) | 2 (29) | 4 (57) | 1 (14) | 0 (0) |
| Procedure/surgery | 0 (0) | 1 (14) | 5 (71) | 1 (14) | 0 (0) |
| PDT/phototherapy/laser | 2 (13) | 5 (33) | 4 (27) | 4 (27) | 0 (0) |
| Sunscreen/emollient | 1 (50) | 0 (0) | 0 (0) | 0 (0) | 1 (50) |
| Dressings | 0 (0) | 1 (100) | 0 (0) | 0 (0) | 0 (0) |

PDT, photodynamic therapy. a% refers to percentage of studies of the intervention funded by the funding source.
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Figure 1  (a) Box plot of nonresearch payments to first or final academic/clinical authors in countries with transparency databases; (b) categorization of personal payments for US-based authors (further information on payment types is available from https://www.cms.gov/OpenPayments/About/Natures-of-Payment).
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Conflict of interest

LS and EE are current UK Dermatology Clinical Trials Network Fellows. LS is an National Institute for Health Research Academic Clinical Fellow and an associate editor of Clinical and Experimental Dermatology. AH declares that they have no conflicts of interest.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:
Appendix S1. Full methodology