Influence of Author's Affiliation and Funding Sources on the Results of Cohort Studies on Occupational Cancer

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Background *Reliability and credibility of research conducted by industry have been questioned, including in the field of occupational health.*
Methods *Cohort studies on occupational cancer published between 2000 and 2010 were compared according to their results, their conclusions, their funding, and the affiliation of their authors.*
Results *Overall, 510 articles were included. Studies published by authors with public affiliation or funded by public grants concluded that their study showed an excess of cancer more frequently ($P = 0.01$) than studies published by authors with private affiliation or funded by private grants (88% [95%CI = 85–91] vs. 73% [95%CI = 56–88] and 92% [95%CI = 86–97] vs. 71% [95%CI = 57–84], respectively). Discrepancies between statistical results and conclusion occurred more frequently in articles written by authors from the private sector than from the public sector (42% [IC95% = 26–60] vs. 23% [IC95% = 18–26], $P = 0.02$).*
Conclusions *Industry affiliations of authors or industry support of studies are associated with the results of published studies on occupational cancer. The underlying mechanisms warrant further investigation.* Am. J. Ind. Med.

***KEY WORDS:* industry; conflict of interest; occupational exposures; neoplasms**

INTRODUCTION

The assessment of carcinogenicity in humans is based on mechanistic data, on cancer bioassays in experimental animals and, more importantly, on pertinent epidemiological studies. Although several types of epidemiological study may contribute to the assessment of carcinogenicity in humans, the most used in the field of occupational diseases are cohort studies and case-control studies.

Their results are, therefore, used to classify compounds for their carcinogenicity, to set occupational exposure limits, which occupational health widely rely on, and to compensate occupational cancers.

The validity and credibility of scientific data are central to all scientific endeavours, as well as to decision structures that use such data [McCarty et al., 2012]. Regulatory decisions or recommendations routinely made by national and international agencies such as the U.S. Environmental Protection Agency (EPA), the NIOSH or the European Commission have been challenged for relying on data generated by scientists or laboratories perceived to have a conflict of interest regarding the outcome of the decision [Sass et al., 2005; McCarty et al., 2012]. Yet, in recent years some have questioned the reliability and credibility of public

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health and environmental research conducted or funded by the chemical industry, suggesting that industry research is subject to conflict and hence may be unreliable [Devine, 2001; Sass et al., 2005], although other argued that a wide variety of mechanisms enabled policymakers and the public to assure themselves that studies performed by industry were identified as such, met high scientific standards, and were not suppressed when their findings are adverse to industry's interests [Barrow and Conrad, 2006].

Therefore, if studies performed, or funded, by industry are equally reliable or conflicted than those performed, or funded, by the public sector, their results should be comparable. To assess this, we performed a study to assess if the source of funding and the affiliation (private vs. public) of the authors of cohort studies on occupational cancers were associated with the statistical findings of the studies. We hypothesized that cohort studies performed by authors belonging to, or hired by, industries in which employees are exposed to carcinogenic compounds are more prone to reach conclusions that deny or understate a potential excess of cancer in their employees, as compared to studies performed by authors who are not directly affiliated with those industries.

MATERIALS AND METHODS

The first step aimed to identify a subset of cohort studies assessing the links between cancer and occupational exposure. We searched Medline for the cohort studies published over a 10 year-period; that is, between January 2000 and December 2009, using the search string ("Neoplasms"[Mesh] AND "Occupational Diseases"[Mesh] OR "Occupational exposure"[Mesh] AND "Cohort Studies"[Mesh]). We excluded the references without abstract, which left us with 903 abstracts. All of them were checked to include only cohort studies. The other types of studies were excluded (e.g., case reports, case-control studies, biological studies). We excluded case-control studies because they are very rarely conducted by authors from the private sector. We classified the remaining 510 studies, on the basis of the abstract, according to the following criteria: design (classified as cancer mortality study, cancer incidence study, or mortality and incidence study), results (classified as "excess of cancer, statistically significant," or "excess of cancer, non-statistically significant," or "no excess of cancer"), and conclusion (classified as "documented excess of cancer in the population studied," "impossible to conclude," or "no excess of cancer").

One of the authors (to ensure reproducibility) assessed if the conclusion of the abstract was supported by the data presented in the Result section of the abstract.

In cases where the result section mentioned no excess or a non significant excess of cancer and the conclusion mentioned a documented excess of cancer in the population study, the conclusion was classified as "discrepant, positive."

In cases where the result section mentioned a significant excess of cancer and the conclusion stated "impossible to conclude" or "no excess of cancer", the conclusion was classified as "discrepant, negative."

In other cases, the conclusion was considered as non discrepant.

The last step was to identify the affiliations of all the authors. They were obtained from the Pubmed record, for the first authors, and from the full text for co-authors. This step was always performed after classification of the different criteria we studied, in order to limit classification bias.

We obtained the full text of 237 articles, among the 510 articles included in our study (47%), using publisher websites (open access or journals accessible through our university library), and public or private deposits.

When the full text was not accessible, we searched Pubmed to identify other articles published by each of the co-authors, in the same period of time, and we repeated the above-mentioned method to identify their affiliation. We also searched Google and Google Scholar for information on the authors.

We then classified authors' affiliations into four categories: University, Agency (e.g., International Agency for Research on Cancer, NIOSH), Consultant or Industry. For the analysis, we gathered University and Agency into a "Public" category, and Consultant or Industry in a "Private" category, respectively. Articles with mixed authorships were excluded from the analysis of the impact of the affiliation of each author and co-author.

In the very rare cases of authors with multiple affiliations, we considered as "private" any author than displayed at least one private affiliation, even if he was also appointed by the public sector.

All the authors' affiliations that were uncertain (consultant or university, e.g.) were reviewed by two study authors (LR and JFG) to ensure agreement.

We searched for information in each of the articles for which we had the full text about the funders of the research, and classified it into public funding, private funding (industry grants), mixed funding, or no funding.

Statistical analysis included Pearson $\chi 2$ test with the α risk set at 5% and calculation of proportions with their confidence interval 95% (95%CI). All statistical analyses were conducted with the STATA software program, version 9.0 (Statacorp LP, College Station, TX).

RESULTS

Description of Included Studies

A total of 903 articles were identified by the original literature search, of which 393 were ineligible after abstract review because the article was not a cohort study, but a literature review (n = 83), a case-control study (n = 93), a case report (n = 68), a methodological article (n = 139), an article about cancer treatment (n = 5), or had no abstract in English (n = 5). Of the 510 articles finally included, the first author's and co-authors' affiliations were identified for 508 and 505 articles, respectively.

The articles were published in 97 different journals, with 50 journals which had published only 1 article and 5 journals which had published more than 20 articles. One journal (Occupational and Environmental Medicine) had published 80 of the 510 articles.

The cancer sites that were investigated were principally the lung (n = 153), digestive system (n = 63), urogenital tract (n = 55), head and neck (n = 28), or pleura (n = 23).

The compounds studied in the 510 studies were very diverse, but some were retrieved frequently such as pesticides (n = 50), asbestos (n = 44), solvents (n = 35).

The studies were completed on all continents; 46% originated from Europe and 38% from America.

Overall, the number of authors varied between 1 and 52 per article, with a mean of 5.7 (95%CI = 5.3–6.0]. The description of the studies included in the analysis is displayed in Table I.

According to the first author's affiliation, 10% (n = 53) of the studies came from the private sector and 90% (n = 455) from the public sector. The major contributors for the public sector were University departments of public or environmental health (n = 187), some of them being very productive (e.g., 16 studies from the Institute of Occupational Health of University of Birmingham), and national or international agencies, such as the National Cancer Institutes (n = 36), NIOSH (n = 23), IARC (n = 12), or the FIOH (n = 9). The 53 studies for which the first author belonged to the private sector came from external consultant organizations (n = 27), chemical manufacturing industries (n = 14), and oil and gas industries (n = 10).

Excess of Cancer Observed in the Studies According to Authors' Affiliations

The results of the studies were significantly different according to the first author's affiliation: they were more often positive (i.e., mentioned an excess of cancer) when the first authors had a public affiliation than a private affiliation (Table II). When considering the affiliation of all the authors, the results were also more often positive when all the authors worked in the public sector than when all authors had private affiliation. Nevertheless, this was only significant when comparing "significant or non significant excess of cancer" to "no excess of cancer," but not when comparing "significant excess" with "no significant or no excess of cancer" (Table III).

TABLE I. Description of Included Studies

	% (n)
Design of the studies (n = 510)	
Mortality study	59 (299)
Incidence study	33 (170)
Mortality and incidence study	8 (41)
Results of the studies (n = 510)	
Excess of cancer in the population studied, statistically significant	74 (380)
Excess of cancer in the population studied, not statistically significant	11 (54)
No excess of cancer	15 (76)
Conclusions of the studies (n = 510)	
Documented excess of cancer in the population study	53 (269)
Impossible to conclude	36 (182)
No excess of cancer	11 (59)
Affiliation of the first author (n = 508[a])	
"Public"[b]	90 (455)
"Private"[b]	10 (53)
Affiliation of all the authors (n = 505[a])	
Exclusively "Public"[b]	80 (405)
Exclusively "Private"[b]	7 (33)
Mixed of "Public" and "Private"[b]	13 (67)

[a]Among the 510 included studies, first author's affiliation and all authors' affiliation were identified for 508 and 505 articles, respectively.
[b]"Public" affiliation = University or public sector (e.g., NIOSH, IARC. . .); "Private" affiliation = Industry or consultant.

Discrepancies Between the Statistical Results and the Conclusion

To analyze the discrepancies between the statistical results and the conclusions of the articles, we only considered articles in which all authors belonged exclusively to the "public" sector or to the "private" sector (n = 438; 67 articles with a mixed of authors' affiliation being excluded).

In 76% (95%CI = 72–80) (332 out of 438) of the studies, the conclusions were supported by the data presented in the Result section of the abstract, for example, the conclusion stated that there was an excess of cancer and the results section mentioned a statistically significant excess, or vice versa. Nevertheless, discrepancies between the written conclusions of the abstract and the Result section of the abstract were observed in nearly one-quarter (n = 106) of the studies. The discrepancies were either positive or negative, but the majority of them consisted of a conclusion characterizing the excesses as less likely to be "true" than the results suggested, (99 of 106; 93%); the converse was considerably less common (7 of 106; 7%; $P < 0.001$). These discrepancies were significantly more prevalent in the studies published by authors from the private sector (14 out of 33, 42%) than in those published by authors from the

TABLE II. Comparison of the Statistical Significance of the Results of the Studies According to the Affiliation of the First Author

	Affiliation of the first author		
Result of the study	**"Public"[a] (n = 455)**	**"Private"[a] (n = 53)**	**Significance (χ2 test) *P***
Excess of cancer, statistically significant[b]	76% (CI95% = 73–81) (347/455)	58% (CI95% = 44–72) (31/53)	0.005
Excess of cancer, statistically significant or not[c]	87% (CI95% = 83–90) (395/455)	68% (CI95% = 54–81) (36/53)	0.001

[a]"Public" affiliation = University or public sector (e.g., NIOSH, IARC. . .); "Private" affiliation = Industry or consultant.
[b]Compared to no excess of cancer or excess not statistically significant.
[c]Compared to no excess of cancer.

TABLE III. Comparison of the Statistical Significances of the Results of the Studies According to Affiliation of All the Authors[b]

	Affiliation of all the authors		
Result of the study	**"Public"[a] (n = 405)**	**"Private"[a] (n = 33)**	**Significance (χ2 test) *P***
Excess of cancer, statistically significant[c]	77% (IC95% = 73–82) (315/405)	63% (IC95% = 48–85) (21/33)	0.16
Excess of cancer, statistically significant or not[d]	88% (IC95% = 85–91) (356/405)	73% (IC95% = 56–88) (24/33)	0.01

[a]"Public" affiliation = University or public sector (e.g., NIOSH, IARC. . .); "Private" affiliation = Industry or consultant.
[b]Studies which included a mixed of Public and Private sector (University, public sector, industry, and consultant) were not included in this analysis.
[c]Compared to no excess of cancer or excess not statistically significant.
[d]Compared to no excess of cancer.

public sector (92 out of 405, 23%) ($P = 0.02$), as shown in Table IV.

When a study observed a significant excess of cancer, the conclusion of the authors was more often "strong probability of link between cancer and exposure" among publicly affiliated authors (73% [95%CI = 68–78]) than among privately affiliated authors (33% [95%CI = 11–55])

Influence of Funding

Among the 237 articles for which we had the full text, information about funding was present in 162 of them (68%). From those, Public funding, Private funding (Industry grants), mixed funding, or no funding were found in 99 (61%), 48 (30%), 7 (4%), and 8 (5%), respectively. The influence of funding on the results of the studies is presented in Table V. Briefly, the results of the studies were significantly different according to their funders: they were significantly more often positive (i.e., mentioned an excess of cancer) when the study had a public funding than a private one.

The discrepancies between the results and the conclusion sections of the abstracts were not significantly different according to the source of funding.

DISCUSSION

Our study demonstrated that the cohort studies on occupational exposures and cancer published by authors belonging to the private sector (industry or consultant), or funded by the private sector, concluded significantly less often that an excess of risk of cancer was found than those published by authors affiliated to universities or public institutions. Furthermore, private authors more frequently downplayed the risk in the Conclusion section of the abstract, as compared to the Results section, than public authors did.

The main limitation of our study is that we had to rely on the official affiliations declared by authors at the time of the submission of the manuscript, and we had no possibility to

TABLE IV. Discrepancies Between the Result and Conclusion Sections of the Abstracts, According to the Affiliation of Authors (Number of Studies)

	Negative conclusion		Neutral conclusion/impossible to conclude		Positive conclusion	
Results	**Authors from public sector**	**Authors from private sector**	**Authors from public sector**	**Authors from private sector**	**Authors from public sector**	**Authors from private sector**
No excess of cancer	18	7	30	2	1[a]	0[a]
Excess (non-significant)	2	3	33	0	6[a]	0[a]
Excess (significant)	3[b]	8[b]	82[b]	6[b]	230	7

[a]Positive discrepancies: no statistical significant excess, but conclusion mentioning an excess of cancer.
[b]Negative discrepancies: statistically significant excess, but conclusion mentioning no excess of cancer.

TABLE V. Comparison of the Statistical Significances of the Results of the Studies According to Their Funders[a]

Result of the study	Funders: "Public"[b] (n = 405)	"Private"[b] (n = 33)	Significance (χ2 test) *P*
Excess of cancer, statistically significant[c]	79% (IC95% = 70–87) (78/99)	60% (IC95% = 46–75) (29/48)	0.02
Excess of cancer, statistically significant or not[d]	92% (IC95% = 86–97) (91/99)	71% (IC95% = 57–84) (34/48)	0.01

[a]Studies which included a mixed of Public and Private funders were not included in this analysis.
[b]"Public" funders = University or public sector funders; "Private" funders = Industry.
[c]Compared to no excess of cancer or excess not statistically significant.
[d]Compared to no excess of cancer.

investigate previous affiliations that could have influence the authors [Claxton, 2007].

We did not assess the potential influence of the conflicts of interest declared by the authors, because several studies have shown that authors do not always reveal conflicts of interest that may influence the significance of their studies [Ong and Glantz, 2000].

Another limitation concerns the involvement of authors in the articles to which their names are attached. Despite the recommendations of the International Committee of Medical Journals Editors, authors typically perform specific roles within a multi-authored paper, and it is usually not clear if all authors assume equal levels of credit and responsibility [Rennie et al., 1997]. In our study, we considered that it was impossible to assess separately the real input of each co-author. Since this could have bias the analysis for the multi-authored papers in which authors from the public and the private sector were mixed, we decided to exclude those studies from the analysis of the impact of the affiliation of each author and co-author. Nevertheless, this concerned, in fact, only a small proportion (13%) of the papers. Another limitation of our study could be the classification bias. However, as the results and conclusions were classified prior to searching for affiliation of the authors, we considered that there was no significant risk of classification bias.

We demonstrated that cohort studies of occupational exposures and cancer published by authors belonging to the private sector (industry or consultant) concluded that an excess of risk of cancer was found significantly less often than those published by authors affiliated with universities or public institutions. Several explanations can be considered.

The first one could be linked to the subject of study. Not all studies are positive, because some agents have no cancer impact. However, there is no reason why private authors would have investigated such instances more frequently that public authors. On the other hand, private authors may investigate smaller populations than those to which public authors have access, and this could be part of the explanation of the more frequent negative results among the former.

Another hypothesis is that negative results have less chance to be published [Scherer et al., 2007]. However, to explain our results, the publication bias should affect only articles submitted by public sector's authors, which seems unlikely.

Authors belonging to the private sector may be constrained by their employer or by the company that financed the study (for consultants) from publishing positive results [Sass et al., 2005]. The influence of industry on publication has been suggested in the asbestos crisis, and Castleman cited that some experimental studies that demonstrated a link between asbestos and cancer were completed in the 1940s but that authors were forbidden to publish. Their corporate sponsors precluded them from publishing anything about their findings without their approval resulting in publication a decade later [Castleman, 1991]. On the other hand, industry may promote negative studies to counter the conclusions of previously published positive studies [Dearfield et al., 1993], such as the response of the Tobacco industry to the influential Hirayama study on second-hand smoke [Hong and Bero, 2002].

Another important finding of our study was that, among a subset of 438 studies, conclusive statements in the abstract were not or only partially supported by the results in a quarter of them.

The discrepancies between the Conclusion and the Result section of the abstracts were significantly higher for the manuscripts published by authors from the private sector than among those from the public one. Furthermore, none of the studies with authors exclusively from the private sector exaggerated the conclusions ("positive discrepancies"). Yet, in those articles, all the observed discrepancies between the Conclusion and the Result section of the abstract led to a conclusion that appeared to diminish the importance of the statistical findings.

The fact that conclusive statements in the abstract sometimes differ from those in the full text has already been demonstrated [Altwairgi et al., 2012]. Space constraints, influence of the comments from the editor and reviewers and the fact that abstract conclusions taken out of the body of the article may distort the interpretation of the study results can explain this [Boutron et al., 2010]. The discrepancies among results and conclusion in an abstract may be the consequence of the complexity of summarizing complex data in one or two sentences. Yet, confidence in a study's findings (e.g., evidence for or against an association) involves considering the strength of the association, the potential for specific biases or confounding, the direction and distortion of those biases or confounding, and the sensitivity of the study to detect an effect. For example, if a study finds an association between exposure and disease despite concern about bias toward the null, the findings could be considered, nevertheless, as supporting evidence. On the other hand, if the direction of the bias is unknown or away from the null, the results could be considered as unreliable by the authors [National Toxicology Program, 2015].

Nevertheless, this phenomenon should not be more prevalent in the articles published by private than public author.

The source of funding was not mentioned in 32% of articles, which could be a problem since we demonstrated that the source of funding had a significant impact on the results of the studies. The studies funded by the private sector had also a lower probability to find significant excess of cancer than studies funded by public grants. The influence of industry support on the results on studies has already been demonstrated for drugs, but had not been evaluated yet, to our knowledge, in occupational health studies [Jørgensen et al., 2008; Sun et al., 2013].

Overall, this study suggests that the affiliation of authors and the source of funding are to be taken into consideration when interpreting the links between occupational exposures and cancer in cohort studies. Therefore, when considering changing regulations on occupational carcinogens, threshold values or compensation schemes for occupational diseases, it would be useful to factor in the affiliation of the authors and the financial support of the studies when examining the relevant scientific literature.

AUTHORS' CONTRIBUTIONS

LR and JFG made substantial contributions to the conception and design of the work and to the acquisition of data. All authors made substantial contributions to the analysis and interpretation of data for the work. All authors made substantial contributions to drafting the work or revising it critically for important intellectual content. All authors approved the final version to be published. All authors agree be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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