# Time trends in the reporting of conflicts of interest, funding and affiliation with industry in intensive care research: a systematic review

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# Time trends in the reporting of conflicts of interest, funding and affiliation with industry in intensive care research: a systematic review

Michael Darmon[1,2,3*], Julie Helms[4,5], Audrey De Jong[1,6], Peter Buhl Hjortrup[7,8], Emmanuel Weiss[9,2], Anders Granholm[7], Riccardo Pinciroli[10], Charlotte Poussardin[4], Marie Warrer Petersen[7], Stéphanie Sigaut[8], Bruna Brandao Barreto[1,11], Morten Hylander Moller[7] and Elie Azoulay[1,2,3]

## Abstract

**Purpose:** Conflict of interest (COI) may compromise, or have the appearance of compromising, a researcher's judgment or integrity in conducting or reporting research. We sought to assess time trends of COI and funding statement reporting in the critical care literature.

**Methods:** PubMed was searched by using Medical Subject Headings and the appropriate corresponding keywords: "INTENSIVE CARE UNIT" or "ICU" as a major topic. Four years in a 15-year time period (2001–2016) were arbitrarily chosen and one study month was randomly selected for each study period. Studies published during the selected months were included in the analysis.

**Results:** Three hundred and seventy-four studies were evaluated, including five reviews (1.3%) and ten randomized clinical trials (RCTs) (2.7%). COI statements were available in 65% of the studies and 8% had declared COI. COI statement rate, declared COI and funding statements increased over time, while the number of authors affiliated with industry and the discordance between the lack of COI statement and affiliation with industry decreased. Declared COI were more frequent in 2011–2016 as compared to 2001–2010 (OR 4.06; 95% CI 1.15–25.79) and in the higher quartile of a journal's impact factor (OR of 16.73; 95% CI 3.28–306.20). Surprisingly, focus of the study, country of the first author and/or endorsement of the study by a trial group were not associated with COI statements.

**Conclusion:** Our study suggests COI reporting to have been unintuitive to most investigators and unreliable before ICMJE statements, and that strong incentives are needed to implement adequate reporting of COI.

**Keywords:** Bibliometrics, Conflicts of interest, Disclosure/statistics and numerical data, Editorial policies, Journal impact factor, Periodicals as topic/standards, Bias

## Introduction

Conflict of interest (COI) involves a situation in which faculty or staff has financial or other personal considerations that may compromise, or have the appearance of compromising, their professional judgment or integrity in teaching, clinical care, conducting or reporting research. Patients trust their doctor and rightly expect them to act in their best interest. Similarly, as medical publishing intends to transfer knowledge that ultimately translates into improved quality of care, patients should be confident that decisions regarding their care are not influenced by the self-interest of their health care providers. Concerns that COI can bias interpretation and reporting of scientific research and care strategies have increased

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over the past decade [1]. The involvement of the pharmaceutical industry in medical research has considerably increased, leading to financial ties of this industry, either directly to researchers or through research grants to their institutions [1–5]. Whether these financial ties might affect scientific findings is established. For instance, COI is associated with change in study design, conduct, and reporting of studies that may influence findings [6]. Also, COI might affect research priorities, publication, teaching and medical education, and clinical decision making [7]. COI play a role in the assessment of peer-reviewers and editors of journals. Thus, COI being a potential bias, its disclosure may allow adequate interpretation of study results [7, 8].

Nearly 10 years ago, the Institute of Medicine (IOM) defined COI as "a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest (integrity of research, welfare of patients, quality of medical education) will be unduly influenced by a secondary interest (financial gain, professional advancement, personal achievement, different favors)" [9]. The need to protect the integrity of clinical research has, therefore, arisen [10] and led to an attempt to control such [10–12].

For researchers, transparent and thorough reporting of COI has been advocated [10, 13–15]. In this context, the World Association of Medical Editors (WAME) and the International Committee of Medical Journal Editors (ICMJE) have developed a disclosure form, which has been adopted by all ICMJE journals [1, 16].

We aimed to systematically assess time trends of COI reporting in the critical care literature since the millennium, and furthermore identify factors associated with the reporting of COI. We hypothesized that COI reporting has increased over the years, and that journal and study related factors would be associated with disclosure of COI.

## Methods

This systematic review was performed according to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [17]. We did not register the review at PROSPERO, as it was unrelated to health outcomes (https://www.crd.york.ac.uk/prospero/#aboutpage).

An internal protocol and statistical analysis plan was prepared prior to beginning the study.

### Definitions

COI statements: An explicit statement about the presence or absence of COI in the manuscript.

Declared COI: An explicit statement confirming presence of financial or non-financial COI.

Authors' affiliation to industry: A self-reported affiliation to any private company.

Discordance between a declared COI and affiliation to industry: The presence of any affiliation to industry without an explicit statement of this as a COI.

### Search strategy and eligibility criteria

PubMed was searched by using Medical Subject Headings (MESH) and the appropriate corresponding keywords: "INTENSIVE CARE UNIT" OR "ICU" as major topic. Four periods of 1 month in 15 years were decided a priori. Years were chosen arbitrarily (2001, 2006, 2011, 2016) and study month was randomly selected for each study period (November 2011, April 2006, August 2011 and September 2016). Studies published during the selected months were included in this analysis.

References were then downloaded for consolidation, elimination of duplicates, and further analysis. All study designs were included. Articles were evaluated by 11 authors (AD, EW, JH, MH, PH, MD, BB, CP, MP, SS, AG). Studies with explicit redundancies were only included once and studies in languages other than English were excluded.

### Data extraction and quality control

Eleven authors (AD, EW, JH, MH, PH, MD, BB, CP, MP, SS, AG) carried out data extraction. Disagreements were resolved with discussion among authors. Also, a 10% random selection of the included manuscripts was rechecked and the correlation between the extracted data was assessed.

For each included study, we extracted the following information:

Journal characteristics: Publisher, continent, focus, open access journal, and IF.

Study characteristics: Design, focus, sample size, a statistically significant effect in the primary outcome analysis, number of authors, and a trial group as co-author.

COI and affiliation to industry: COI statement, declared COI, affiliation to industry, study funding, type of COI, type of funding, discordance between COI and affiliation.

### Statistical analysis

The statistical analyses were conducted according to a pre-defined analysis plan. Any modifications to the planned analysis are called post hoc analyses. Results are reported as medians with interquartile ranges (IQRs) or numbers (percentages) as appropriate. Comparisons were performed using Chi-squared test or Fisher's exact

test for categorical variables or Wilcoxon rank-sum test for continuous variables.

For quality control, 10% of the dataset was randomly recoded and correlation (continuous variables) or concordance (Cohen's kappa coefficient—binary variables) reported.

We used binary logistic regression analyses to assess the independent association between journal and study characteristics and the presence of a COI statement (primary analysis 1) and with the presence of declared COI (secondary analysis). Variables of interest were selected a priori according to their relevance and statistical significance in univariate analysis. We used conditional stepwise regression with 0.2 as the critical *P* value for entry into the model, and 0.1 as the *P* value for removal. Interactions and correlations between the explanatory variables were carefully checked. Continuous variables for which log-linearity was not confirmed were transformed into categorical variables according to median or IQR. The final models were assessed by calibration, discrimination and relevancy. Residuals were plotted and the distributions inspected.

All tests were two-sided, and *P* values less than 0.05 were considered statistically significant. Analyses were done using R software version 3.4.4 (https://cran.r-project.org/).

## Results

The search yielded 427 citations, of which 25 were excluded, as no full-text could be obtained, and 28 were excluded as they were not in English. Accordingly, 374 studies were included and evaluated (Fig. 1).

### Quality control

We re-checked 10% of the dataset (Table S1). Overall, the concordance was above 80% for categorical discrete variables and 90% for continuous variables. Four variables however, had lower concordance rates: focus of the study (74%; 95% CI 58–87%), study sample size ($r=0.41$, $P=0.01$), type of funding (concordance of 34.2%; 95% CI 20–51%) and number of declared grants (concordance of 55.3%; 95% CI 38–71%).

### Characteristics of the included studies

Twenty-seven studies were published in 2001, 77 in 2006, 113 in 2011, and 161 in 2016.

Characteristics of the studies are reported in Table 1. The number of studies published in open-access journals increased steadily over the years from 4.3 to 32.9%, as well as the median IF. The design of the studies did not change over time, with the minority of studies being systematic reviews ($n=5$, 1.3%) and randomized clinical trials (RCTs) ($n=10$, 2.7%). Study sample size increased steadily over the years from median ten subjects (0–494) in 2001–134 (27–739) in 2016.

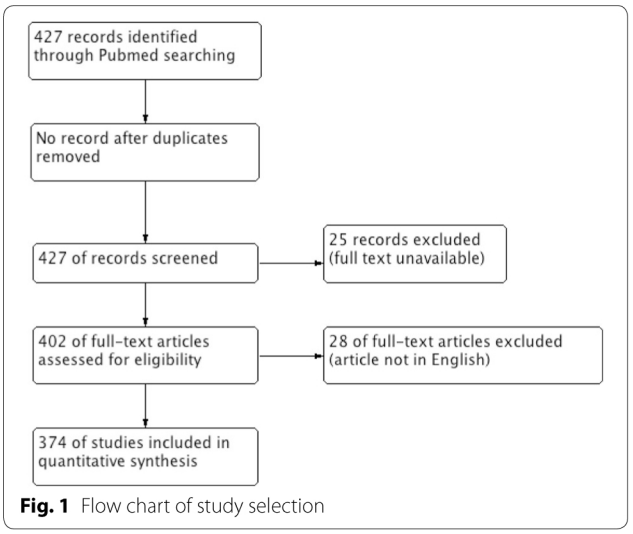


**Fig. 1** Flow chart of study selection

### Statement of COI, funding and affiliation with industry

Overall, COI statements were available in 65% of the studies and 29/374 studies (7.7%) reported COI (Table 1).

The rate of COI statements, declared COI and funding statements increased progressively over time (Table 1, Fig. 2, Fig. S1, Fig. S2). The vast majority of COI statements were financial COI or ties with industry (26/30, 86.7%).

Factors associated with a COI statement by univariate analyses are reported in Table 2. Overall, the COI rate varied according to journal characteristics (focus of the journal, year of publication, journal impact factor), but also with study characteristics (namely design of the study, and number of authors) (Fig. 3). The number of authors affiliated to industry, as well as discordance between the COI statement and affiliation with industry decreased over time (Table 1, Fig. S3).

After adjusting for potential confounders (Fig. 4), COI statements were more frequent in 2011 (OR 139.2; 95% CI 25.6–2612.8) and 2016 (OR 101.7; 95% CI 19.3–1887.6) as compared to 2001, more frequent in higher quartile of IF (OR of 4.26; 95% CI 1.72–1.11) and in open access journals (OR 2.28; 95% CI 1.03–5.39). No correlations or interactions between the explanatory variables were detected and variance inflation factor was lower than 1.5 for all of the included variables. Hosmer–Lemeshow goodness of fit C-stat test was performed (*P* value = 0.40) and area under the receiver operating characteristic (ROC) curve of the model was of 0.85. Other variables significantly associated with COI in univariate analysis were not retained in the final model.

**Table 1 Characteristics of journals and studies according to publication period [reported as number (%) or median (IQR)]**

| | 2001 *n* = 23 | 2006 *n* = 77 | 2011 *n* = 113 | 2016 *n* = 161 | *P* value |
|---|---|---|---|---|---|
| Journal and publisher characteristics | | | | | |
| Continent | | | | | < 0.001 |
| Africa | 0 (0.0%) | 1 (1.7%) | 0 (0.0%) | 0 (0.0%) | |
| Asia | 0 (0.0%) | 6 (10.0%) | 2 (2.4%) | 4 (2.5%) | |
| Australia | 0 (0.0%) | 2 (3.3%) | 0 (0.0%) | 2 (1.2%) | |
| Europe | 10 (43.5%) | 19 (31.7%) | 38 (45.2%) | 66 (41.0%) | |
| N. America | 13 (56.5%) | 31 (51.7%) | 42(50.0%) | 74 (45.0%) | |
| Oceania | 0 (0.0%) | 0 (0.0%) | 2 (2.4%) | 3 (1.9%) | |
| South America | 0 (0.0%) | 1 (1.7%) | 0 (0.0%) | 12 (7.5%) | |
| Focus of the journal | | | | | < 0.001 |
| Generalist | 10 (43.5%) | 15 (19.5%) | 38 (33.6%) | 77 (47.8%) | |
| ICU | 7 (30.4%) | 18 (23.4%) | 52 (46.0%) | 35 (21.7%) | |
| Other | 6 (26.1%) | 12 (15.6%) | 23 (20.4%) | 0 (0.0%) | |
| Specialist non ICU | 0 (0.0%) | 32 (41.6%) | 0 (0.0%) | 49 (30.4%) | |
| Open access journal | 1 (4.3%) | 11 (14.9%) | 18 (15.9%) | 53 (32.9%) | < 0.001 |
| Impact factor | 1.96 (0.52, 2.31) | 1.27 (0.00, 2.44) | 2.13 (1.50, 4.61) | 1.98 (1.31, 3.27) | 0.001 |
| Article characteristics | | | | | |
| Type of study | | | | | 0.637 |
| Other | 23 (100.0%) | 75 (97.4%) | 107 (94.7) | 154 (95.7%) | |
| RCT | 0 (0.0%) | 1 (1.3%) | 3 (2.7%) | 6 (3.7%) | |
| SR/MA | 0 (0.0%) | 1 (1.3%) | 3 (2.7%) | 1 (0.6%) | |
| Focus of the study | | | | | < 0.001 |
| Device | 1 (4.3%) | 7 (9.1%) | 11 (9.7%) | 14 (8.7%) | |
| Drugs | 1 (4.3%) | 14 (18.2%) | 6 (5.3%) | 5 (3.1%) | |
| Other | 11 (47.8%) | 49 (63.6%) | 55 (48.7%) | 104 (64.6%) | |
| Strategy | 10 (43.5%) | 7 (9.1%) | 41 (36.3%) | 38 (23.6%) | |
| Review or editorial | 11 (47.8%) | 0 (0.0%) | 4 (3.5%) | 27 (16.8%) | < 0.001 |
| Study sample | 10 (0, 494.5) | 247 (66, 1249) | 224 (48, 1007) | 134 (27, 739) | 0.004 |
| Observed statistical significance | 9 (39.1%) | 9 (11.7%) | 46 (40.7%) | 34 (21.1%) | < 0.001 |
| Number of authors | 3 (1.5, 6.5) | 4.00 (2, 6) | 5.00 (4, 6) | 5 (4, 7) | 0.001 |
| Study endorsed by a trial group | 3 (13.0%) | 8 (10.4%) | 5 (4.4%) | 14 (8.7%) | 0.327 |
| Conflict of interest and authors affiliated to industry | | | | | |
| COI Statement | | | | | < 0.001 |
| Declared COI | 1 (4.3%) | 1 (1.3%) | 10 (8.8%) | 17 (10.6%) | |
| Declared absence of COI | 0 (0.0%) | 8 (10.4%) | 88 (77.9%) | 118 (73.3%) | |
| No statement | 22 (95.7%) | 68 (88.3%) | 15 (13.3%) | 26 (16.1%) | |
| Type of COI | | | | | < 0.001 |
| Academic | 1 (4.3%) | 0 (0.0%) | 2 (1.8%) | 1 (0.6%) | |
| Financial/industry | 0 (0.0%) | 1 (1.3%) | 8 (7.1%) | 17 (10.6%) | |
| None | 0 (0.0%) | 8 (10.4%) | 88 (77.9%) | 117 (72.7%) | |
| Unknown | 22 (95.7%) | 68 (88.3%) | 15 (13.3%) | 26 (16.1%) | |
| Funding statement | | | | | < 0.001 |
| No funding | 0 (0.0%) | 1 (1.3%) | 22 (19.5%) | 27 (16.8%) | |
| No funding statement | 19 (82.6%) | 59 (76.6%) | 41 (36.3%) | 66 (41.0%) | |
| Declared funding | 4 (17.4%) | 17 (22.1%) | 50 (44.2%) | 68 (42.2%) | |
| Type of funding | | | | | < 0.001 |
| Academic | 1 (6.2%) | 3 (3.9%) | 4 (5.4%) | 26 (24.5%) | |
| Academic and industry | 0 (0.0%) | 1 (1.3%) | 10 (13.5%) | 4 (3.8%) | |
| Industry | 3 (8.8%) | 13 (16.9%) | 36 (48.6%) | 59 (55.7%) | |

**Table 1 continued**

| | 2001 *n* = 23 | 2006 *n* = 77 | 2011 *n* = 113 | 2016 *n* = 161 | *P* value |
|---|---|---|---|---|---|
| None | 0 (0.0%) | 1 (1.3%) | 22 (29.7%) | 17 (16.0%) | |
| Not declared | 12 (75.0%) | 59 (76.6%) | 2 (2.7%) | 0 (0.0%) | |
| Number of grant declared | 0.00 (0.00, 0.00) | 0.00 (0.00, 0.00) | 1.00 (0.00, 2.00) | 1.00 (0.00, 1.00) | < 0.001 |
| Number of authors affiliated with industry | 0.00 (0.00, 0.50) | 0.00 (0.00, 0.00) | 0.00 (0.00, 0.00) | 0.00 (0.00, 0.00) | < 0.001 |

*IQR* inter-quartile range, *ICU* intensive care unit, *RCT* randomized controlled trial, *SR/MA* systematic review/meta-analysis, *COI* conflict of interest

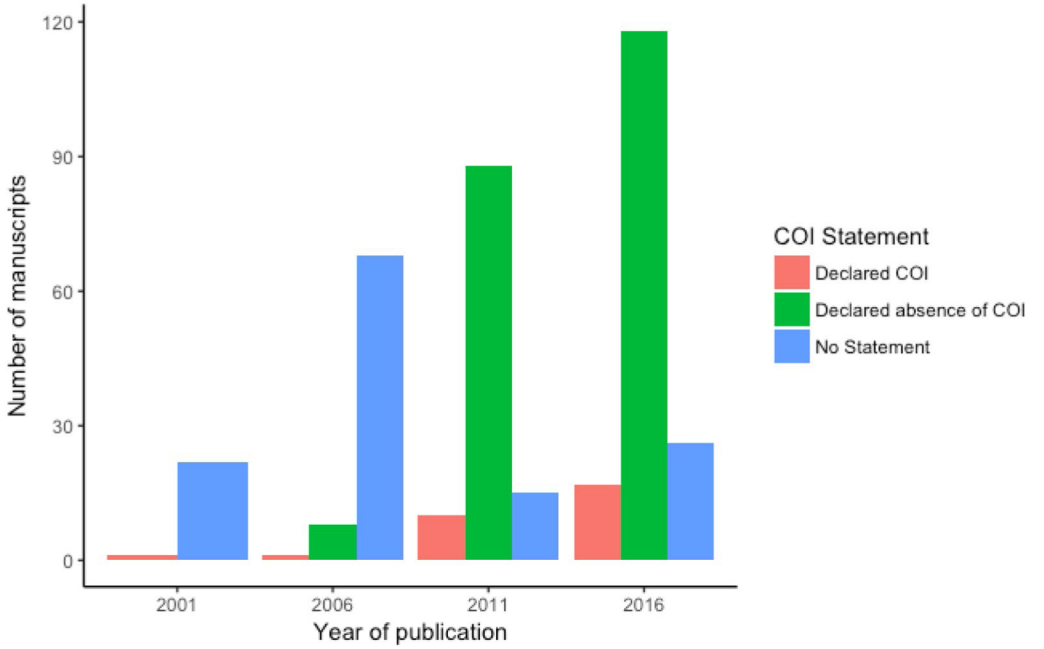


**Fig. 2** Rate of statements (declared COI, declared absence of COI and absence of statement) by publication year

### Factors independently associated with declared COI

In order to assess factors independently associated with declared COI (Fig. 5), and as the number of events was limited, the year variable was transformed into a binary variable (before and after 2010). After adjustment for potential confounders, declared COI were more frequent in 2011–2016 (OR 4.06; 95% CI 1.15–25.79) and in the fourth quartile of IF (OR of 16.73; 95% CI 3.28–306.20). No correlation or interaction between explanatory variables was detected and variance inflation factor was lower than 1.5. Hosmer–Lemeshow goodness of fit C-stat test was performed (*P* value = 0.99).

### Sensitivity analyses

A sensitivity analysis was conducted. Three variables were one by one forced into the primary model, particularly: focus of the study, country of the first author and/or endorsement of the study by a trial group. This did not change the final model and the results.

### Post hoc sensitivity analysis in a larger dataset

The limited sample size in 2001 and 2006 was unexpected. We, therefore, conducted a post hoc sensitivity analysis in which we added two additional months for the 2001 period and 1 month for the 2006 period. Overall, 120 and 134 articles were analyzed for 2001 and 2006, respectively (Fig. S4 and table S2). Relatively to the rate and independent predictors of COI statement, results were similar to those obtained with the main analysis (Figs. S5, S6, and S7).

## Discussion

The main findings of our study is that COI disclosures in critical care studies increased over the past 15 years, but also the rate of COI among these declarations. COI statements were thus found in two thirds of the evaluated studies, which is lower than previously reported [18, 19]. Qureshi et al. [18] evaluated 1574 articles published in 2009 and found a COI statement in 77% of the articles,

**Table 2 Characteristics of journals and studies according to COI statement [reported as number (%) or median (IQR)]**

| | Declared COI *n* = 29 | No COI declared *n* = 214 | No statement *n* = 131 | *P* value |
|---|---|---|---|---|
| Year of publication | | | | < 0.001 |
| 2001 | 1 (3.4%) | 0 (0.0%) | 22 (16.8%) | |
| 2006 | 1 (3.4%) | 8 (3.7%) | 68 (51.9%) | |
| 2011 | 10 (34.5%) | 88 (41.1%) | 15 (11.5%) | |
| 2016 | 17 (58.6%) | 118 (55.1%) | 26 (19.8%) | |
| Journal and publishers' characteristics | | | | |
| Continent | | | | 0.013 |
| Africa | 0 (0.0%) | 1 (0.5%) | 0 (0.0%) | |
| Asia | 0 (0.0%) | 6 (3.2%) | 6 (5.3%) | |
| Australia | 0 (0.0%) | 3 (1.6%) | 1 (0.9%) | |
| Europe | 12 (44.4%) | 81 (43.3%) | 40 (35.1%) | |
| N. America | 14 (51.3%) | 86 (46.0%) | 60 (52.7%) | |
| Oceania | 0 (0.0%) | 2 (1.1%) | 3 (2.6%) | |
| South America | 1 (3.7%) | 8 (4.3%) | 4 (3.5%) | |
| Type of journal | | | | 0.001 |
| Generalist | 14 (48.3%) | 90 (42.1%) | 36 (27.5%) | |
| ICU | 13 (44.8%) | 64 (29.9%) | 35 (26.7%) | |
| Other | 1 (3.4%) | 23 (10.7%) | 17 (13.0%) | |
| Non ICU specialist | 1 (3.4%) | 37 (17.3%) | 43 (32.8%) | |
| Open journal | 8 (27.6%) | 58 (27.1%) | 17 (13.3%) | 0.010 |
| Impact factor | 4.42 (2.31, 6.60) | 2.06 (1.42, 3.56) | 1.46 (0.35, 2.28) | < 0.001 |
| Study characteristics | | | | |
| Type of study | | | | 0.043 |
| Other | 25 (86.2%) | 205 (95.8%) | 129 (98.5%) | |
| RCT | 3 (10.3%) | 6 (2.8%) | 1 (0.8%) | |
| SR/MA | 1 (3.4%) | 3 (1.4%) | 1 (0.8%) | |
| Focus of the study | | | | 0.084 |
| Device | 4 (13.8%) | 19 (8.9%) | 10 (7.6%) | |
| Drugs | 0 (0.0%) | 11 (5.1%) | 15 (11.5%) | |
| Other | 18 (62.1%) | 121 (56.5%) | 80 (61.1%) | |
| Strategy | 7 (24.1%) | 63 (29.4%) | 26 (19.8%) | |
| Review or editorial | 1 (3.4%) | 25 (11.7%) | 16 (12.2%) | 0.380 |
| Study sample | 359 (99.5, 6225.5) | 150 (33.5, 746.5) | 127.5 (23, 1016) | 0.061 |
| Statistical significance | 14 (48.3%) | 64 (29.9%) | 20 (15.3%) | < 0.001 |
| Number of authors | 6 (5, 10) | 5.00 (4, 6) | 4 (2, 6) | < 0.001 |
| Study endorsed by trial group | 5 (17.2%) | 14 (6.5%) | 11 (8.4%) | 0.135 |
| CoI and funding | | | | |
| Type of COI | | | | < 0.001 |
| Academic | 4 (13.8%) | 0 (0.0%) | 0 (0.0%) | |
| Financial/industry | 25 (86.2%) | 1 (0.5%) | 0 (0.0%) | |
| None | 0 (0.0%) | 213 (99.5%) | 0 (0.0%) | |
| Unknown | 0 (0.0%) | 0 (0.0%) | 131 (100.0%) | |
| Funding statement | | | | < 0.001 |
| No funding | 1 (3.4%) | 46 (21.5%) | 3 (2.3%) | |
| No statement | 4 (13.8%) | 80 (37.4%) | 101 (77.1%) | |
| Funding declared | 24 (82.8%) | 88 (41.1%) | 27 (20.6%) | |
| Type of funding | | | | < 0.001 |
| Academic | 7 (28.0%) | 21 (13.8%) | 6 (6.2%) | |
| Academic and industry | 5 (20.0%) | 9 (5.9%) | 1 (1.0%) | |

**Table 2 continued**

| | Declared COI *n* = 29 | No COI declared *n* = 214 | No statement *n* = 131 | *P* value |
|---|---|---|---|---|
| Industry | 12 (48.0%) | 79 (52.0%) | 20 (20.8%) | |
| None | 1 (4.0%) | 36 (23.7%) | 3 (3.1%) | |
| Unknown | 0 (0.0%) | 7 (4.6%) | 66 (68.8%) | |
| Number of declared grant | 1.00 (1.00, 2.00) | 1.00 (0.00, 1.00) | 0.00 (0.00, 1.00) | < 0.001 |
| Number of authors affiliated to industry | 0.00 (0.00, 2.00) | 0.00 (0.00, 0.00) | 0.00 (0.00, 0.00) | < 0.001 |

*IQR* inter-quartile range, *ICU* intensive care unit, *RCT* randomized controlled trial, *SR/MA* systematic review/meta-analysis, *COI* conflict of interest

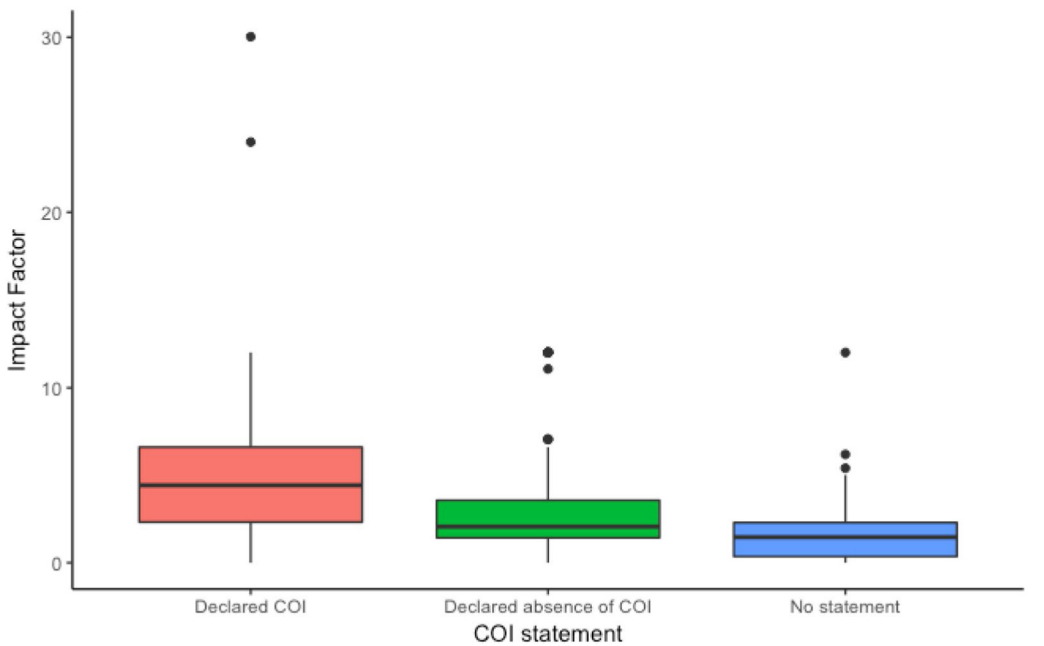


**Fig. 3** Boxplot reporting impact factor of journal according to COI statement

while Hakoum et al. [19]. included 200 randomized controlled trials published in 2015 and showed that 94% had COI statements. Disclosures of COI were, however, found to widely vary across specialties [19]. The methods (survey versus systematic review), the type of articles considered (RCT, meta-analyses or guidelines), the year of publication and the perception about what constitutes a conflict of interest may account for this variations in prevalence of COI disclosure [20, 21].

Not surprisingly, we found a significant increase in the reporting of COI over time. While statements were nearly non-existent in 2001 and 2006, they have widely increased over the last decade. This is consistent with two successive studies in leading journals of gastroenterology and hepatology [18, 22]. This increase probably resulted from several organizations developing guidelines for the handling of COI in biomedical research, including WAME [9]. Nevertheless, the rate of missing statements about funding sources and COI disclosures remains high in 2016 (41.0% and 16.1%, respectively).

Our results also highlight the significant reduction in the discrepancy between disclosed COI and affiliation with industry over time, which may be a result of more rigorous COI policies by scientific journals. Although no direct comparison of COI statement with actual COI was feasible, COI under-declaration was suggested by the rate of discordance between declared affiliation to industry and declared COI.

In the present systematic review, one of the factors independently associated with COI statements was publication in the most recent years (2011 and 2016). Not only did COI disclosure increase over time, but also the rate of COI among these declarations. Indeed, 2011 and 2016 were independently associated with increased rate

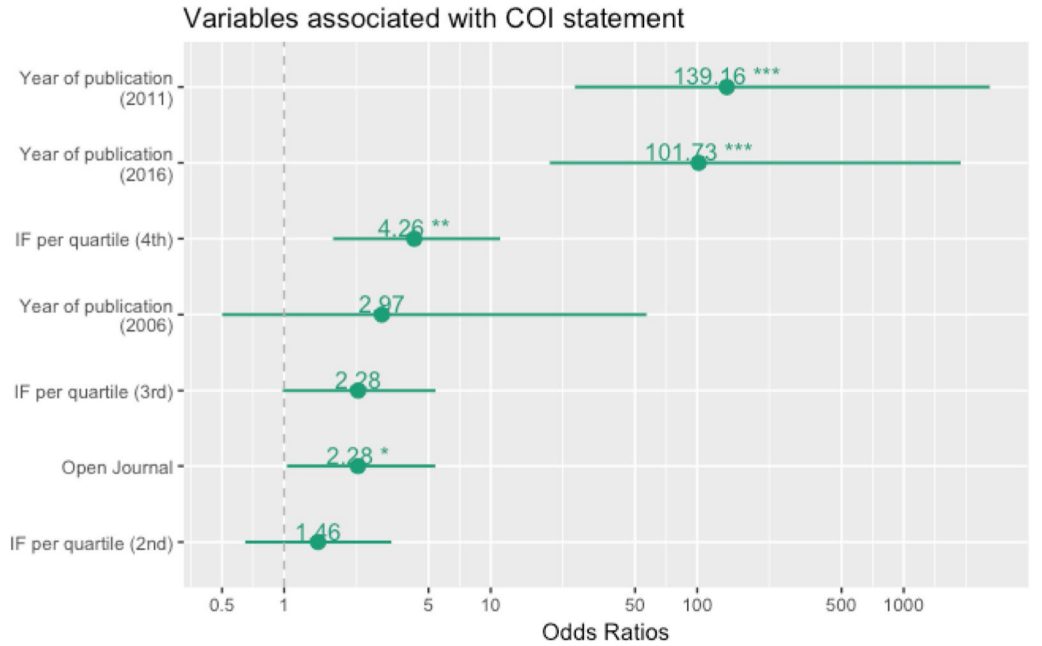


**Fig. 4** Forest plot reporting adjusted odds ratios (ORs) (95% CI) of variables ultimately retained in the logistic regression model assessing presence of COI statement. Area under the ROC curve of the final model was 0.85

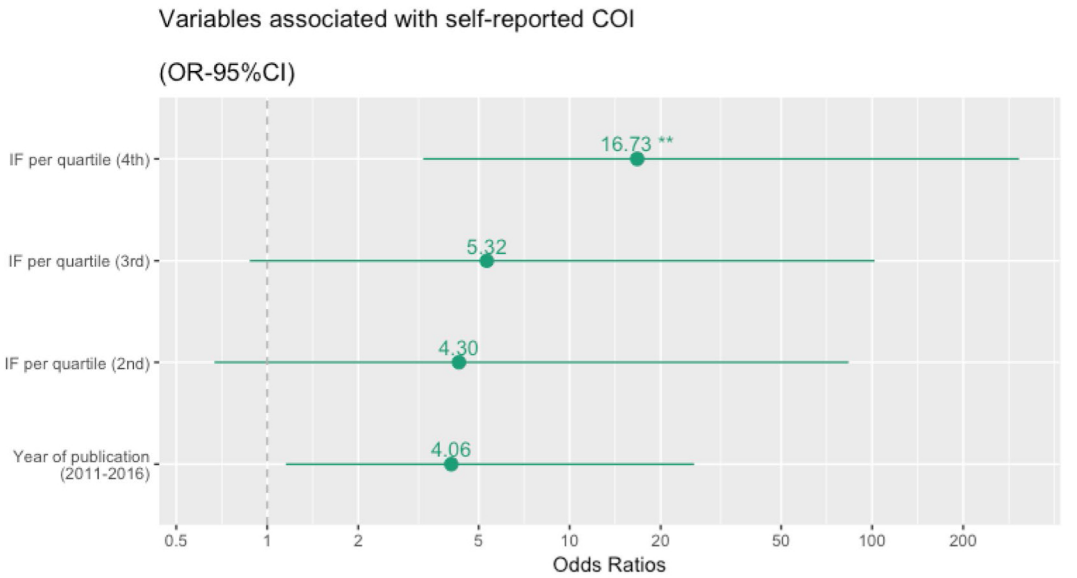


**Fig. 5** Forest plot reporting adjusted odds ratios (95% CI) of variables ultimately retained in the logistic regression model assessing presence of self-reported COI

of COI. This finding along with the lower rate of discordance suggests that COI were underreported in 2001 and 2006, and indirectly reflects an under-reporting of actual COI. Our results on the reporting of financial COI are consistent with other recent surveys. Hakoum et al. [19] compared 19 surveys on COI of authors from several types of trials and showed discrepancies between surveyed field, with highest COI disclosures in oncology research. Beyari et al. [23] also reported that papers published more recently were more likely to report on the

presence or absence of a conflicts of interest. In the present study, the COI rate was much lower than previously reported [19]. Hakoum et al. indeed showed as much as 57% of the 188 trials having at least one author reporting at least one COI and the totality of these trials having at least one author reported financial COI [19]. The results suggest a selection bias in these studies reporting high-quality RCTs, published in higher rank journal having a higher rate of COI statement. Our study included only ten RCTs of 374 included articles. Despite the small sample, there was an increased proportion of declared COI compared to other ICU articles. Interestingly, disclosures about both academic and financial COI and funding have considerably increased over time, although academic COI remain less frequently reported than financial ones. In line with our findings, several already older studies reported rate of spontaneous under-reporting and impact of recommendations in other specialties [6, 24–27].

Not surprisingly, the higher the impact factor was, the higher the rates of COI statements and of COI declared, which is consistent with previous data [19]. This association results probably from more stringent disclosure policies in journals with higher impact factors, constraining the authors to declare their COI. Most of the large multicenter trials have authors reporting COI, which may be acceptable as long as COI are clearly disclosed.

Rose et al. [28] showed that authors who performed key roles in the design, analysis, and reporting of oncology clinical trials are more likely to have financial ties to industry. However, industry may be involved in some trial design, reporting and decision to publish, which should be clearly established, as it has been clearly shown that there were significant associations between industry sponsorship and pro-industry conclusions and restrictions on publication [4].

The strengths of our study include the following: we included a large number of intensive care studies (374 articles), and we assessed the quality of the data extractions by cross-checking 10% of the sample; also, the long time-period (15 years) considered allowed for data collection across numerous specialized and non-specialized journals, thus limiting the risk of the results being skewed by some practices or journals; finally, all the studies included were published after 2000, allowing for a recent assessment of COI and research funding practices in intensive care.

Our study also has limitations. First, the broad inclusion criteria were meant to include a sample representative of all ICU research. However, the inclusion of a large number of studies published in lower IF journals, as well as the few RCTs and reviews among the included studies, may have influenced our findings and may at least partly explain the low rate of COI reported. In addition, the increasing number of monthly published manuscript resulted in a limited sample size during the early years. We tried to acknowledge this by conducting a post hoc analysis in which we included a larger sample size for the years 2001 and 2006. Although the overall quality of our dataset was good, some variables were at least partly subjective and were found to be poorly reliable. Our study report a decrease in rate of missing COI statement and in discrepancy between declared COI and authors affiliation to industry, suggesting under-reporting of COI. Nevertheless, an increased rate of COI triggered by increased involvement of industry in research over time may have participated to the observed results and should probably be taken into account when interpreting our results. Moreover, the last part of our analysis was performed in 2016, very early after launch of sunshine act in various countries [8]. Our study was, therefore, unable to assess impact of this initiative on COI reporting. Last, our study focused on financial COI although non-financial COI may occurs and are uncommonly reported. Importance of these non-financial COI, as well as their influence on study finding may deserve to be assessed by future studies.

Our study suggests COI reporting to have been unintuitive to most investigators and unreliable before ICMJE statements, and that strong incentives are needed to implement adequate reporting of COI. Considerable efforts should therefore be made in the next years to implement careful reporting of conflicts of interest of authors in intensive care studies and much work remains to be done to make disclosures uniform across journals. Several avenues for research emerge from our study. First, specific data regarding reliability of COI remain to be assessed and influence of COI on other actors of the editorial process (including peer reviewers and editors) to be evaluated. In addition, the high rate of COI in open access journals in our study was unexpected and may deserve further investigations. Last, the influence of initiative aiming to transparently report COI via dedicated website [8] on COI statements accuracy could not be assessed by this study. Future studies may be required as this regard.

**Abbreviations**

CI: Confidence interval; COI: Conflict of interest; ICMJE: International Committee of Medical Journal Editors; ICU: Intensive care unit; IF: Impact factor; IOM: Institute of Medicine; IQR: Interquartile range; RCT: Randomized clinical trial; MESH: Medical subject headings; OR: Odds ratio; PRISMA: Preferred reporting items for systematic reviews and meta-analyses; ROC: Receiver operating characteristic; SE: Standard error; SR/MA: Systematic review/meta-analysis; WAME: World Association of Medical Editors.

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