



Brief Report

Financial relationships with industry among guideline authors for the management of acute ischemic stroke

Joshua D. Niforatos, MTS^a, Richard M. Pescatore, DO^{b,*}^a Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH, United States of America^b Department of Emergency Medicine, Crozer-Keystone Health System, Upland, PA, United States of America

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ABSTRACT

Objective: To characterize the prevalence of industry relationships among authors of acute ischemic stroke (AIS) guidelines and its association with graded evidence.

Methods: A cross-sectional study of five policy papers on AIS published by the American Heart Association (AHA)/American Stroke Association (ASA), American Academy of Emergency Physicians (AAEM), and American College of Emergency Physicians (ACEP). Financial conflicts of interest (FCOI) data were obtained using the Open Payments Database for the years 2013 through 2017. A search of publicly available information was done to determine post-guideline employment. We characterized the prevalence of FCOI, as well as employment with industry engaged in thrombolysis or neurointerventional treatment of AIS after guideline publication.

Results: 76 unique authors were identified in 5 policy statements. The prevalence of FCOI among authors of AAEM, ACEP, and AHA/ASA guidelines was 0%, 0%, and 35%, respectively. Post-publication increase in FCOI was 0% for authors of the AAEM and ACEP guidelines, and a 300% increase for authors of the 2013 AHA/ASA guidelines with data unavailable to assess post-publication FCOI for authors of the 2018 AHA/ASA guidelines. 2 authors were found to engage in new industry employment following recommendation publication. Finally, 9% (n = 3) authors of the 2013/2018 AHA/ASA guidelines were employees of the Genentech Speakers Bureau.

Conclusions: Our results suggest an association between current Graded Evidence and FCOI of major academic societies for the management of AIS. Due to the bias inherent to such conflicts, future recommendation groups should take steps to insulate against FCOI both during and following guideline publication.

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1. Introduction

The use of thrombolytic therapy for patients with acute ischemic stroke (AIS) remains controversial [1,2]. This controversy is in part due to conflicting policy statements published by the American Heart Association (AHA)/American Stroke Association (ASA) and the American Academy of Emergency Medicine (AAEM) and American College of Emergency Physicians (ACEP) [3–7]. Some suggest this difference in interpretation is secondary to physicians' financial conflicts of interest (FCOI) with industry, such as Genentech's potential influence in the Thrombolysis in Myocardial Infarction (TIMI) trial, the National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Stroke Study Group, and The Re-Examining Acute Eligibility for Thrombolysis (TREAT) Task Force [1,2]. Concerns related to industry bias permeating practice guidelines panels and FDA Advisory Committees has been researched previously [8–11]. To our knowledge, however, there is no recent assessment of the prevalence of FCOI among guideline authors

of stroke guidelines using data from the publicly available Open Payments Database (OPD) provision of the Affordable Care Act (ACA), which has tracked physician-industry transactions since 2013.

2. Materials and methods

2.1. Study design and human subjects

We conducted a cross-sectional study of five policy papers on the management of AIS published from 2013 to 2018 by AHA/ASA, AAEM, and ACEP [3–7]. Authors' names and Graded Evidence were manually extracted from each paper. FCOI data was obtained for each author using the OPD (<https://openpaymentsdata.cms.gov/search/>) for the years 2013 through 2017.

As the “revolving door” between industry and academia has previously been described as a subtle form of FCOI [12], we assessed the prevalence of authors with new relevant industry employment following publication of guidelines recommendations. We searched publicly available information from LinkedIn, social media, and PubMed to ascertain employment following publication of AIS guidelines using methods previously described [12].

* Corresponding author at: Department of Emergency Medicine, 1 Medical Center Blvd, Upland, PA 19013, United States of America.

E-mail address: Richard.Pescatore@crozer.org (R.M. Pescatore).

Table 1
Graded evidence and prevalence of financial conflicts of interest with industry in acute ischemic stroke guidelines.

Characteristics	Organization				
	ACEP (n = 10)	ACEP (n = 29)	AAEM (n = 9)	AHA/ASA (n = 15)	AHA/ASA (n = 19)
Policy year	2013	2015 [†]	2017	2013	2018
Graded evidence for tPa < 3 h	A	B	N/A	A	A
Graded evidence for tPa between 3 and 4.5 h	B	B	N/A	B	B
FCOI before/year of publication – tPA, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	2 (11)
FCOI after publication – tPA, n (%)	0 (0)	0 (0)	0 (0)	4 (27)	N/A
FCOI before/year of publication – neurointerventional, n (%)	0 (0)	0 (0)	0 (0)	2 (13)	3 (16)
FCOI after publication – neurointerventional, n (%)	0 (0)	0 (0)	0 (0)	4 (27)	N/A
Overall FCOI, n (%)	0 (0)	0 (0)	0 (0)	6 (22)	6 (32)
Later employment with industry, n (%) [*]	1 (10)	0 (0)	0 (0)	0 (0)	1 (5)

Abbreviations: ACEP, American College of Emergency Physicians; AAEM, American Academic of Emergency Physicians; AHA, American

Heart Association; ASA, American Stroke Association; tPa, tissue plasminogen activator; FCOI, financial conflict of interest; N/A, not available, which here implies that the AAEM did not directly provide a Graded Evidence in the policy statement.

^{*} Later employment was defined as an employee of a pharmaceutical or device manufacture.

[†] In 2013, the ACEP guidelines were published with the American Academy of Neurology (AAN) and endorsed by the Emergency Nurses Association and the Neurocritical Care Society. American Association of Neurology. Where, the 2015 ACEP guidelines were published without the neurological organizations.

2.2. Data source and data processing

Using the OPD, three kinds of payments can be received by authors: (1) general payments, defined as payments not associated with a research study, which included food and beverages, travel and lodging, consulting fees, honoraria, education, and non-educational speaking fees; (2) research payments, which included research funding and associated payments; (3) and ownership payments, which included amount invested and interest in a company. An in-depth description of these categories can be found at the OPD website (<https://www.cms.gov/openpayments/about/natures-of-payment.html>).

We included those FCOI (1) directly related to the treatment of AIS—i.e., conflicts associated with thrombolytic therapy and neuroendovascular interventions—and (2) deemed a ‘significant financial conflict of interest’, which was defined as an aggregate of greater than or equal to \$5000 from a single company over a 12 month period [13]. Thus, FCOI were coded as binary categorical variables (0 = no FCOI greater than or equal to \$5000, 1 = FCOI greater than or equal to \$5000).

2.3. Outcome measures

The primary outcomes of this study were to characterize (1) the prevalence of FCOI of guideline authors of the AHA/ASA, AAEM, and ACEP both before, at the time of, and after the publication of the aforementioned guidelines and its association with Graded Evidence, and (2) employment with industry engaged in the thrombolysis or neurointerventional treatment of AIS after publication of guidelines.

2.4. Analysis

The study sample and types of FCOI were described using descriptive statistics. This study of publicly available information was conducted December 2018 and did not require institutional review board review and approval.

3. Results

3.1. Results

We identified 76 unique authors in the 5 policy statements. Table 1 provides information related to the graded evidence and frequency of FCOI for thrombolytic therapy and neuroendovascular intervention the year(s) before or during, as well as year(s) after, the year of the guidelines publication. The AAEM did not provide graded evidence,

while the ACEP evidence changed to B recommendations in 2015 for the administration of tPa before 3 h and between 3 and 4.5 h. The 2013 and 2018 AHA/ASA guidelines provided grade A and B evidence for the administration of tPa before 3 h and between 3 and 4.5 h, respectively. Despite the time differences between the ACEP and AHA/ASA recommendations, no high-quality phase 3 RCTs were published in the intervening years that explain discordant recommendations.

None of the 48 authors of the three ACEP and AAEM guidelines had significant FCOI with industry related to the treatment of AIS between the years 2013 and 2017. The overall prevalence of FCOI among authors of the 2013/2018 AHA/ASA guidelines was 35% (n = 12). Specifically of the 2013 AHA/ASA authors, 0 (0%) and 2 (13%) had significant FCOI with thrombolytic therapy and neuroendovascular intervention, respectively, during the year the guideline was published. After publications of the 2013 AHA/ASA guidelines, 4 (27%) and 4 (27%) of authors had significant FCOI related to thrombolytic therapy and neuroendovascular intervention, respectively, which represents a 300% increase in FCOI. During the year before the publication of the 2018 AHA/ASA guidelines, 2 (11%) and 3 (16%) of authors had significant FCOI related to thrombolytic therapy and neuroendovascular intervention, respectively. Data related to FCOI in 2018 is not yet available in the OPD.

Revolving door employment was low among all policy statements, with only 2 authors found to engage in new industry employment following recommendation publication, 1 (11.1%) author from the 2017 AAEM guideline and 1 (5.3%) author from the 2018 AHA/ASA guidelines. Finally, 3 (9%) authors of the 2013/2018 AHA/ASA guidelines were employees of the Genentech Speakers Bureau.

3.2. Limitations

FCOI data was limited to those payments properly reported under the ACA. Most significantly, FCOIs for non-physician contributors (e.g. nurses and non-clinician scientists) may not be reported, as they do not necessarily fall under the OPD purview as it varies by state. Assessment of “revolving door employment” was limited by publicly available data through the described methods, and may underestimate the rate of new industry engagement following recommendation publication. Finally, this study of FCOI and its association with graded evidence provides evidence for correlation but not causation.

4. Discussion

Discrepancies in interpretation of the evidence supporting the administration of tPA in AIS have driven controversy in both the medical and lay literature, as well as at the point of care. FCOI has been well-demonstrated to introduce bias [14] and may represent a problematic

confounder when comparing policy statements and guidelines from various academic societies. In this important instance, emergency medicine organizations have successfully eliminated FCOI from most of their guideline writing groups. Major national vascular organizations (AHA and ASA) continue to have a significant number of guideline writers with FCOI. This data fit with previous reports demonstrating an increased likelihood of favorable reporting among those subject to FCOI [10,15]. Furthermore, our results demonstrate an increase in FCOI following authorship in guidelines with more favorable recommendations. Due to the bias inherent to such conflicts, future recommendation groups should take steps to insulate against FCOI both during and following guideline publication.

Author contributions

The work was performed via online collaboration. Mr. Niforatos designed the study. Dr. Pescatore and Mr. Niforatos collected the study data and performed the data analysis. Both authors contributed substantially to drafting of the manuscript. All authors have reviewed and approved the final manuscript.

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None.

Declarations of interest

None.

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