



## Review Article

# A conflict of interest is strongly associated with tobacco industry–favourable results, indicating no harm of e-cigarettes

Charlotta Pisinger<sup>a,b,\*</sup>, Nina Godtfredsen<sup>c,d</sup>, Anne Mette Bender<sup>e</sup>

<sup>a</sup> Center for Clinical Research and Prevention, Bispebjerg and Frederiksberg Hospital, The Capital Region of Denmark, Hovedvejen, Entrance 5, Nordre Fasanvej 57, DK-2000 Frederiksberg, Denmark

<sup>b</sup> University of Copenhagen, Faculty of Health Sciences, Department of Public Health, Denmark

<sup>c</sup> Department of Pulmonary Medicine, Hvidovre University Hospital, Hvidovre, Denmark

<sup>d</sup> Institute of Clinical Medicine, University of Copenhagen, Denmark

<sup>e</sup> University of Copenhagen, Faculty of Health Sciences, Department of Public Health, Section of Social Medicine, Denmark

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## ABSTRACT

Researchers reach contradictory results when trying to assess the potential harm of e-cigarettes. This study investigated whether the findings and conclusions in papers published on e-cigarettes and health differ depending on whether the authors had a financial conflict of interest (COI) or not.

A total of 94 studies (identified in a previous systematic review) that investigated the content of fluid/vapor of e-cigarettes or in vitro experiments were included. The type, level and direction of the financial COI were coded. Abstracts were blinded and evaluated by two assessors. Fischer's Test and Logistic regression analyses were used to investigate the associations between findings of harm/conclusions and COI.

All three dimensions of COI showed the same tendency: studies with industry-related COI found potential harm significantly less often than studies without a COI. 95.1% of papers without and 39.4% of papers with a COI found potential harmful effects/substances. Only 7.7% of tobacco industry-related studies found potential harm. The odds of finding of no harm were significantly higher in studies with an industry-related COI (OR 66.92 (95% CI 8.1–552.9)) than in studies without a COI. A strong/moderate COI was associated with very high odds (OR 91.50 (95% CI 10.9–771.4)) of finding of no harm compared with studies with no/weak COI.

This blinded assessment showed that almost all papers without a COI found potentially harmful effects of e-cigarettes. There was a strong association between industry-related COI and tobacco- and e-cigarette industry-favourable results, indicating that e-cigarettes are harmless.

## 1. Introduction

Global e-cigarette use has increased in the last decade (McMillen et al., 2015), especially among young people, and a heated debate about their use is ongoing (McNeill et al., 2015a; McKee and Capewell, 2015). A report by Public Health England concluded that e-cigarettes were 95% safer than conventional cigarettes (McNeill et al., 2015b), and their use is promoted in the United Kingdom. Conversely, most health organisations, including the World Health Organization (WHO), regard their level of harm as uncertain and do not recommend their use. Therefore, it can be difficult for health professionals, lay people and decision makers to figure out what to believe.

Researchers have reached contradictory results when trying to assess the potential harm of e-cigarettes. There are no standardised

testing procedures, there are approximately 500 brands and > 8000 flavours, and the design is changing all the time. Studies have also shown significant variations in puffing topography among users of various models and that the production of harmful substances is influenced by the battery voltage output, the vaporiser and the levels of e-liquid left in the e-cigarette, which further complicates the research (Pisinger and Dossing, 2014). This may partly explain why some studies find harm while others do not.

The e-cigarette market was initially dominated by small manufacturers; however, since 2012, large tobacco companies have entered the market with their own products and have started to buy established brands (Tobacco tactics, n.d.).

Many studies have found a strong association between financial conflict of interest and industry-favourable results. Research sponsored

\* Corresponding author at: Centre for Clinical Research and Prevention, Bispebjerg and Frederiksberg Hospital, The Capital Region of Denmark, Hovedvejen, Entrance 5, Nordre Fasanvej 57, DK-2000 Frederiksberg, Denmark.

E-mail address: [Charlotta.pisinger@regionh.dk](mailto:Charlotta.pisinger@regionh.dk) (C. Pisinger).

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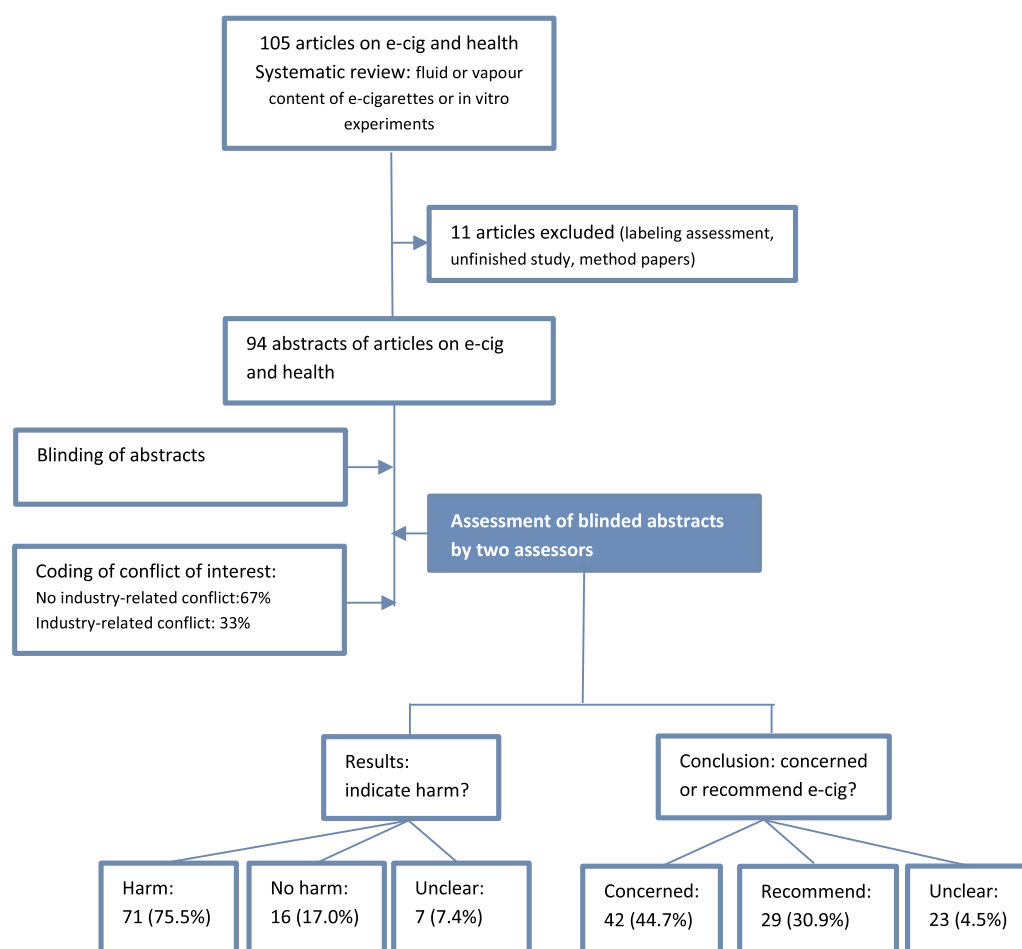


Fig. 1. Flowchart of the blinded assessment of studies assessing the potential harm of e-cigarettes.

\*e-cig = e-cigarettes.

by industries, such as the manufacturers of sweetened beverages (Mandrioli et al., 2016), the chemical industry or pharmaceutical companies (Lexchin et al., 2003), has shown a tendency to draw industry-favourable conclusions. A Cochrane review from 2017 found that the probability of finding a positive effect of a drug was significantly higher in industry-sponsored studies than in studies without a conflict of interest (Lundh et al., 2017). The tobacco industry has a long history of publishing papers showing that tobacco smoke (Cataldo et al., 2010) and environmental tobacco smoke do not cause harm to health (Barnes and Bero, 1998). Thus, the different conclusions on the potential health consequences of e-cigarettes may also be explained by the fact that the authors or sponsors of a study have an interest in reaching a specific conclusion.

On one hand, the tobacco industry and other e-cigarette manufacturers might benefit from findings showing no negative health effects, as this would promote their product; conversely, the manufacturers of conventional smoking cessation products may have an interest in reaching opposite conclusions.

After decades of casting doubt on the health hazards of smoking, the tobacco industry now publicly states that chemicals in the combustion emissions of burned tobacco are toxic and carcinogenic. They recommend “harm reduced” products such as e-cigarettes, snus/snuff or heated tobacco cigarettes as safe alternatives to smoking. However, harm-reducing inventions (i.e., filters and low tar, light, no additive cigarettes) have existed for decades without improving the health of smokers (Harris et al., 2004). Internal documents show that the tobacco industry has deliberately promoted low-tar cigarettes knowing that they would offer false reassurance without the health benefits (Bates

and Rowell, n.d.). Furthermore, they failed to implement an effective method of removing the radioactivity in tobacco leaves because it affected the absorption of nicotine (nicotine kick) (Karagueuzian et al., 2012), and, in an internal note they wrote that a “harm reduced” product “could produce extra business from the smokers who would otherwise quit” (Carpenter et al., 2009). This indicates that the harm reduction discourse of tobacco companies primarily is a tactical adaptation.

The main aim of this paper was to investigate whether the findings and conclusions in papers published on e-cigarettes and health differed depending on whether or not the authors had a conflict of interest, in this context, any financial relation to the tobacco, e-cigarette- or pharmaceutical industry.

## 2. Methods

The study aimed to create a “real life” scenario. Many health and public health professionals find new information on e-cigarettes important; however, it is not their primary field of expertise, they have very little time, and they often end up reading only an abstract. Most journalists, lay people and decision makers reading a study on e-cigarettes will read no more than the abstract, which condenses the findings of the paper and the author's interpretation of them. Thus, we evaluated the association between conflict of interest and abstract conclusions, consistent with other meta-research designs (Buffel du Vaure et al., 2014).

## 2.1. Inclusion of studies

In 2014, CP was a co-author on, to the best of the authors' knowledge, the first systematic review of the health effects of electronic cigarettes (Pisinger and Dossing, 2014). The review was systematically updated for the WHO and published as a background paper in 2016 (Pisinger, 2016). Articles included in the present study are those identified in this previous review; therefore, details on the search strategy, exclusion criteria etc. are provided in the previous paper (Pisinger, 2016). The conflict of interest of each original paper was systematically registered in the review. The stated conflict of interest, funding, acknowledgements and the workplaces of authors were all assessed. In cases without declaration of conflict of interest or if in doubt, authors were contacted, and the internet and eventual previous papers were searched for information. In cases where the authors declared that they had no conflict of interest despite previous studies that showed one being present, a conflict of interest was registered.

This publication concentrated on studies identified in the systematic review (Pisinger, 2016) that investigated the fluid or vapor content of e-cigarettes or in vitro experiments with fluid or vapor (see the online extra material for the table of included studies, Appendix 1). Studies of both active and passive vaping were included. Of the 105 original studies identified, 11 were excluded, as they did not draw conclusions on the health effects (they focussed on the labelling of products or the description of new methods applied to the testing of e-cigarettes or were ongoing studies without final results) (Fig. 1). The remaining 94 studies were published between 2009 and 2015.

## 2.2. The assessment

A university student printed all the abstracts and blinded them so that the author name, affiliation, funding, acknowledgement, journal name and time of publication were not visible. Two assessors (co-authors) were contacted: one was a consultant in pulmonology, and the other had a master's degree in public health. Both had a general interest in e-cigarettes, but they had read only a few papers on e-cigarettes. The assessors (NG and AMB) independently assessed the blinded abstracts without any knowledge of the papers' potential conflict of interest.

Then, the assessors discussed unclear cases/discrepancies and agreed on a coding. Two outcomes were measured:

(a) Do the results indicate potential harm to health? (1. Yes; 2. No or 3. Unclear)

(b) What are the conclusions? (1. Concern that e-cigarettes might harm users' health or public health; 2. No concern that e-cigarettes might harm users' health or public health/recommend them as harm reduction strategies or 3. Unclear).

CP had no influence on the assessment.

## 2.3. The coding of conflict of interest

Strategies for coding of conflict of interest were suggested by CP and discussed with NG. The study focussed on financial conflicts of interest. It did not discriminate between one or more authors having a conflict of interest; if one author had a conflict, then there was conflict. Neither did the study discriminate between author conflict of interest or industry funding. CP coded first, and NG reviewed the coding (independently of the results of the assessment); there was no disagreement in coding. AMB reviewed the final coding and agreed with it.

Conflict of interest was coded in three dimensions: type, level and direction (please see Table 1). For details on studies and their declaration, please see Appendix 2.

(a) Type of industry/sponsor involved: Five categories were created for descriptive analyses (1. Tobacco industry related; 2. E-cigarette industry related; 3. Pharmaceutical industry related; 4. Mixed industry related, 5. No industry).

(b) Level of conflict of interest: Four categories were created for descriptive analyses (1. Strong; 2. Moderate; 3. Weak and 4. No industry conflict).

(c) Direction of conflict of interest: As there are opposite industry interests (e-cigarette and tobacco industry vs. pharma industry), three categories were created (1. Industry benefits if no harm found; 2. Industry benefits if harm found; 3. No industry benefit or divergent benefits).

Additionally, as it has been suggested that some important funding bodies might require some types of data interpretation (negative health consequences of e-cigarettes) to continue funding, all papers without

**Table 1**

Coding of conflict of interest categories, level of conflict of interest and direction of conflict of interest in studies investigating potentially harmful effects of e-cigarettes.

	Definition
Type of industry/sponsor	
1. Tobacco industry related	Study was fully or partially sponsored by tobacco company which also manufactures e-cigarettes or the author had (any) connections with the tobacco industry – if study was sponsored by both tobacco and e-cigarette industry then it was defined as tobacco industry related
2. E-cigarette industry related	Study was fully or partially sponsored by e-cigarette manufacturer or by users and/or vendors of e-cigarettes or author had received research funding/travel expenses/personal fees from e-cigarette industry
3. Pharmaceutical industry related	Study was fully or partially sponsored by pharmaceutical industry or authors had received research funding/travel expenses/personal fees from pharmaceutical industry
4. Mixed industry related	Study was fully or partially sponsored by pharmaceutical industry or e-cig manufacturers or authors had received research funding/travel expenses/personal fees from both the pharmaceutical industry and e-cigarette manufacturers. No tobacco industry involvement.
5. No industry	No industry related conflict of interest found
Level of conflict of interest	
1. Strong	Study was fully sponsored by the industry or vendors of product, author(s) employed by the industry or first author has very strong connections to industry
2. Moderate	Study was partly sponsored by industry, sponsored by users of product, first authors' previous research funded by industry
3. Weak	Author reimbursed for travels or conferences, nonfinancial support only, co-author previously received research grant from industry
4. None	No connections to tobacco-, e-cigarette or pharmaceutical industries
Direction of conflict of interest	
1. Industry benefits if not harmful	Sponsor would probably sell more of their product (e-cigarettes) if results show that e-cigarettes are harmless; users would be reconfirmed that e-cigarettes are harmless
2. Industry benefits if harmful	Sponsor would probably sell more of their product (smoking cessation medication) if results show that e-cigarettes are harmful; users would use smoking cessation medication instead
3. No industry benefit/divergent benefit	No financial benefit expected or benefit in divergent directions (e.g. both increased sale of smoking cessation products and e-cigarettes)

industry-related conflict of interest were coded as: 1. Sponsored by NIH, FDA or WHO or 2. Other funding.

## 2.4. Statistics

Simple calculations using percentages and chi-squared tests were initially performed. For analyses regarding the association between findings indicating harm and conflict of interest, studies were excluded if they were unclear ( $n = 7$ ). This left 87 studies with clear results. In the same way, studies were excluded if they were unclear regarding the conclusions ( $n = 23$ ), which left 71 studies with clear conclusions.

Due to the small number of cases (especially mixed and pharma industries) authors used Fischer's Exact Test to investigate difference in finding of harm. Studies with no conflict of interest were compared with studies with industry-related conflict of interest; one category at a time. Difference in findings of harm between studies funded by FDA, NIH, WHO and studies without conflict of interest funded by other sources was also tested by Fischer's Exact Test. Further, Logistic regression analyses were used to investigate the association between the results and conclusions of the studies and the three dimensions of conflict of interest. Due to low power all three dimensions of conflict of interest were dichotomized:

(a) Type of industry/sponsor involved, dichotomized (1. Any industry/sponsor (original 1–4); 2. No industry (original 5))

(b) Level of conflict of interest, dichotomized (1. High or Moderate (original 1–2); 2. Weak or No conflict (original 3–4)).

(c) Direction of conflict of interest, dichotomized (1. Benefits if no harm found (original 1); 2. No industry benefits/Divergent benefits/Benefits if harm found (original 2–3)).

A Hosmer-Lemeshow test was used as model control.

SPSS version 22 was used for all statistical analyses, and the level of significance was set at 0.05.

## 3. Findings

### 3.1. Descriptive analyses

One-third (33/94, 35.1%) of the studies had industry-related conflict of interest.

Type of industry/sponsor involved: Thirteen studies (13.8%) had a tobacco industry-related conflict of interest, 10 studies (10.6%) had an e-cigarette industry-related conflict of interest, four studies (4.3%) had a mixed (non-tobacco) industry-related conflict of interest, and six studies (6.4%) had a pharmaceutical industry-related conflict of interest.

Level of conflict of interest: More than every sixth study (17.0%) had a strong conflict of interest, 13.8% had a moderate conflict of interest, 3.2% had a weak conflict of interest and 64.9% had no conflict of interest.

Direction of conflict of interest: In 24.5% of studies, the e-cigarette/tobacco industry would benefit if the results showed no harm. In 6.4% of studies, the pharmaceutical industry would benefit if the results showed harmful effects of e-cigarettes.

A total of 75.5% of studies found potentially harmful effects; 17% found no harm of e-cigarettes, while 7.4% were unclear (Fig. 1).

A total of 44.7% of studies were concerned about negative effects on smokers' health or public health; 30.9% were not concerned about negative effects/recommended them as harm reduction strategies, while 24.5% were unclear (Fig. 1).

### 3.2. Relationship between conflict of interest and findings indicating harm

Fig. 2: A higher proportion of non-industry sponsored studies found potentially harmful substances/effects (58/61, 95.1%) compared to industry-sponsored studies (13/33, 39.4%) ( $p < 0.001$ ). Only one (7.7%) of the tobacco industry-related studies found potential harm,

while 70.0% of the e-cigarette industry-related studies, 50.0% of the pharmaceutical industry-related studies and 50.0% of the mixed industry-related studies found potential harm. Studies with a tobacco industry-related conflict of interest ( $p < 0.001$ ) or an e-cigarette industry-related conflict of interest ( $p = 0.044$ ) found no harm significantly more often than studies without a conflict of interest. Studies with a mixed industry-related conflict of interest ( $p = 0.095$ ) or a pharma industry-related conflict of interest ( $p = 0.124$ ) did not differ statistically from studies without a conflict of interest in findings of harm. Studies with strong conflict of interest found harm in only 18.8% of the cases; more than half of studies found harm (53.8%) if the conflict of interest was moderate and two out of three studies found harm if conflict of interest was weak (66.7%).

Ten out of 63 studies without a conflict of interest were funded by NIH, FDA or WHO. Analyses showed that there was no difference in findings of harm between studies funded by one of these bodies (10/10, 100%) and studies without conflict of interest funded by other sources (48/51, 94.1%;  $p = 0.831$ ).

In regression analyses (Table 2), a strong association was found between industry-related conflict of interest and industry-favourable results. The odds of finding no harm of e-cigarettes were 66.92 (95% CI 8.1–552.9) times higher if the study was industry-related. Level of conflict of interest was also significantly associated with higher odds of finding of no harm. Odds were 91.50 (95% CI 10.9–771.4) times higher for papers with a strong or moderate conflict compared with papers with no or weak conflict of interest. The odds of finding no harm of e-cigarettes were 34.16 (95% CI 8.0–146.2) times higher if this finding would benefit the tobacco/e-cigarette industry compared to studies with no conflict of interest, benefit for the pharma industry or divergent industry benefit.

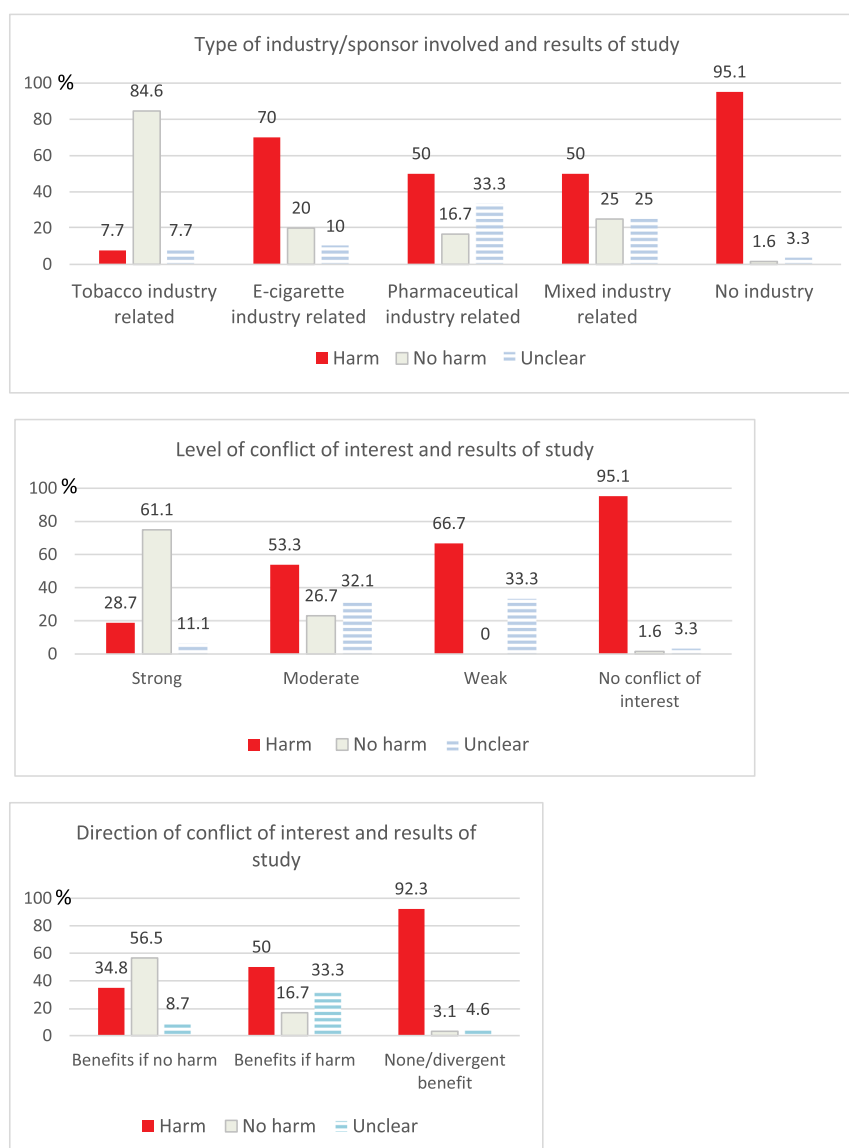
### 3.3. Relationship between conflict of interest and conclusions on studies

Fig. 2: A higher proportion of non-industry sponsored studies expressed concern about smokers' health or negative effects on public health by use of e-cigarettes (37/61, 60.7%) compared to industry-sponsored studies (5/33, 15.2%) ( $p < 0.001$ ). No tobacco industry-related studies expressed concern, while 20.0% of the e-cigarette industry-related studies, 16.7% of the pharmaceutical industry-related studies and 50.0% of the mixed industry-related studies expressed concern.

Industry-related papers significantly more often draw positive conclusions, recommending e-cigarettes, even though potential harm was found in their study. This discordance was found in 71.4% (5/7) of e-cigarette industry-related papers, 33.3% (1/3) of pharma industry-related papers compared to 15.5% (11/71) of papers with no industry-relation. No discordance was found in mixed industry papers (0/2). As the tobacco industry found potential harm in only one study and this study's conclusion was assessed to be unclear, there was no discordance either (0/0).

No studies with strong conflict of interest expressed concern about health effects of e-cigarettes. One out three studies expressed concern (30.8%) if the conflict of interest was moderate or weak (33.3%). In studies where industry would benefit if there was no harm (tobacco/e-cigarette industry), only 8.7% of authors expressed concern (Fig. 3).

In regression analyses (Table 2), a strong association was found between industry-related conflict of interest and industry-favourable conclusions. The odds of no concern/recommendation were 23.26 (95% CI 6.6–82.2) times higher if any industry was involved. Strong or moderate level of conflict of interest was also associated with high odds (24.94 (95% CI 6.7–92.7)) of no concern/recommendation of e-cigarettes compared with no or weak conflict of interest. The odds of recommendation were 32.73 (95% CI 6.6–163.1) times higher if the finding of no harm would benefit the tobacco/e-cigarette industry than if there was no conflict of interest/if it would benefit the pharmaceutical industry or if there were divergent benefits.



**Fig. 2.** Studies' results on potential harm of e-cigarettes by conflict of interest (n = 94\*).

\*13 Tobacco industry related studies, 10 E-cigarette industry related studies, 6 Pharmaceutical industry related studies, 4 Mixed industries studies, 61 studies with no industry related conflict of interest.

**Table 2**

The association between three dimensions of conflict of interest and results and conclusions of studies investigating health effects of e-cigarettes<sup>a</sup>.

	Result = No potentially harmful substances/effects of e-cigarettes found (n = 87)			Conclusion = No concerns about negative health effects of e-cigarettes/ recommendation (n = 71)		
	N	OR	95% CI	N	OR	95% CI
Type of industry/sponsor						
Not industry related	59	1		44	1	
Industry related	28	66.92	8.1–552.9	27	23.26	6.6–82.2
Level of conflict of interest						
No conflict or weak	62	1		46	1	
Strong or moderate	25	91.50	10.9–771.4	25	24.94	6.7–92.7
Direction of conflict of interest						
No industry benefits/divergent benefits/ benefits if harm found <sup>b</sup>	66	1		51	1	
Industry benefits if no harm found <sup>c</sup>	21	34.16	8.0–146.2	20	32.73	6.6–163.1

<sup>a</sup> Studies with unclear results were excluded.

<sup>b</sup> Pharmaceutical industry, mixed industries, no conflict of interest.

<sup>c</sup> Tobacco and e-cigarette industry.

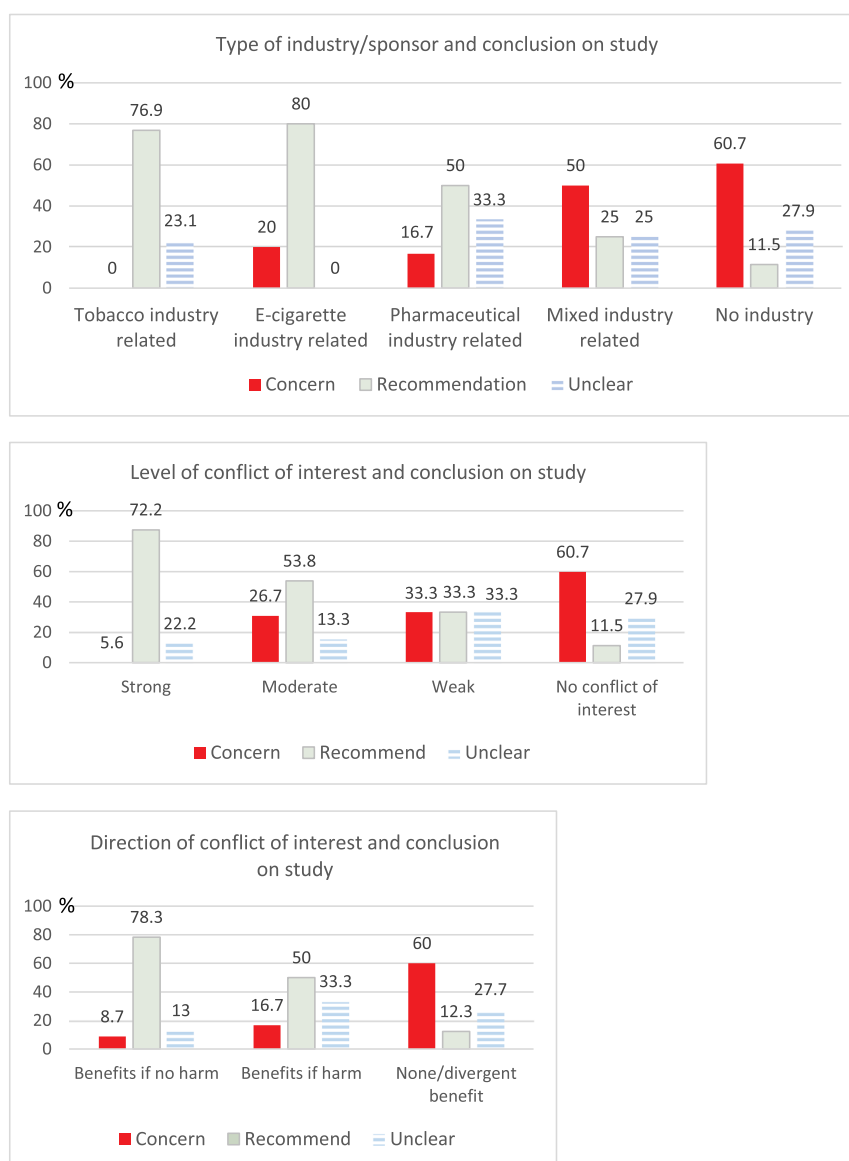


Fig. 3. Studies' conclusion on potential harm of e-cigarettes by conflict of interest (n = 94\*).

\*13 Tobacco industry related studies, 10 E-cigarette industry related studies, 6 Pharma industry related studies, 4 Mixed industries studies, 61 studies with no industry related conflict of interest.

#### 4. Discussion

Three different dimensions of coding showed the same tendency: a strong association between industry-related conflict of interest and industry-favourable results. Almost all papers with no conflict of interest found that e-cigarettes had a potentially harmful effect on health, while < 8% of studies performed by the tobacco industry reported potential harm. Studies with a tobacco industry- or an e-cigarette industry-related conflict of interest found no harm significantly more often than studies without a conflict of interest. Studies with strong or moderate conflict of interest had very high odds of finding no harm. No tobacco industry-related papers expressed concerns about the health effects of e-cigarettes.

Even though e-cigarette industry-related studies did not find potential harm significantly more often than studies without a conflict of interest, surprisingly, 70% of the e-cigarette industry-related studies reported a potentially negative effect on health. This may reflect that the e-cigarette industry is more truthful than the tobacco industry or

that it is less able to “control” the study design than is the tobacco industry (Hong and Bero, 2002). On the other hand, only one out of five e-cigarette industry-related papers expressed concerns regarding e-cigarettes in their conclusion.

It has been claimed that researchers funded by NIH, FDA or WHO are expected to report harmful effects of e-cigarettes, due to ideology. This study showed that there was no difference in results between those funded by one of these bodies and those without conflict of interest funded by other sources. Nor could this study support the claim that pharma industry-related studies report less harm than independent research, as they might have an interest in undermining e-cigarette sales, which competes with sales of conventional smoking cessation products.

Interestingly, authors with pharmaceutical industry-related conflict of interest recommended e-cigarettes significantly more often than authors without a conflict of interest. This might reflect author's personal belief in harm reduction.

#### 4.1. Comparison with previous studies

This study is in full agreement with previous studies in finding a strong association between conflict of interest and industry-favourable results. Studies on sugar-sweetened beverages were shown to be five times more likely to find no association with weight gain if they were industry sponsored (Bes-Rastrollo et al., 2013), the chemical industry has also shown a tendency to draw industry-favourable conclusions, (Fedeli and Mastroangelo, 2011; Neltner et al., 2013) and the probability of finding a positive effect of a drug was shown to be 27% higher in pharmaceutical industry-sponsored studies than in studies without a conflict of interest (Lundh et al., 2017). Previous tobacco industry-sponsored papers more frequently found no harm of smoking (Jackler and Samji, 2012) or of exposure to second-hand smoke (Tong et al., 2005) than papers not sponsored by the tobacco industry. Very concerning is that the tobacco industry papers are cited more often than papers written by independent researchers (Malone et al., 2000).

#### 4.2. How do industry-funded studies reach opposite conclusions to studies without a conflict of interest?

A Cochrane review comparing sponsored and non-sponsored studies found no difference in the risk of the traditionally known biases, except that industry studies often had a lower risk of bias from blinding (Lundh et al., 2017). Furthermore, data do not speak for themselves, and their interpretation is essential. Screening of almost 17,000 clinical trial abstracts revealed that adjectives such as “well tolerated” and “meaningful”, which could result in misperceptions, were used approximately five times more frequently in industry-authored research than in non-industry research (Cepeda et al., 2015), and “mild” was used more than three times as often.

However, although this was true for medical drugs and devices, what is known about tobacco industry research? There is proof that tobacco companies previously created an impression of legitimate and unbiased scientific research (Muggli et al., 2001), designed studies to show specific results (Yano, 2005), failed to publish studies showing unfavourable results (Neeley and Glantz, 2017), deleted unfavourable data (Neilsen and Glantz, 2004) and concealed its involvement in research so that studies would appear to have no conflict of interest (Malone et al., 2000; Diethelm et al., 2005).

#### 4.3. Is a conflict of interest statement sufficient?

Study after study has shown that industry-funded studies find industry-favourable results; therefore, one might ask whether a conflict of interest statement is sufficient to eliminate this industry bias. Many do not read the disclosures, and a low compliance with the conflict of interest disclosure has been described (Forsyth et al., 2014). Penalties to authors who do not disclose correctly have been proposed, and it has been discussed whether there should be stronger restrictions on industry involvement in research. The BMJ, Tobacco Control and PLOS Med have already decided they will not publish tobacco industry-funded research. This paper's authors recommend all journals to follow in their footsteps.

#### 4.4. Strengths and limitations

Due to limited number of studies with conflicts of interest, authors could not include the original categories in regression analyses. Even when merging the categories power was low in the regression analyses and the confidence intervals are broad. The authors believe they have identified most of the conflicts of interest; however, given the well-known problem of the underreporting of competing interests (Dunn et al., 2016), it is possible, and perhaps even likely, that the paper may

underreport authors with such competing interests. The coding of conflict of interest was associated with many decisions and therefore many potential weaknesses, as others may have done it a different way; e.g., the researchers did not discriminate between authors' conflict of interest and industry funding of a study. On the other hand, the three different dimensions of coding showed the same tendency. Other personal interests and sheer ideology were not considered. Neither was a potential institutional conflict of interest investigated (some universities in, for example, the United States, took donations from the tobacco and pharma industries). There were only two blinded assessors, and agreement may have happened solely by chance. Assessors with expertise in e-cigarette research or scientifically literate coders could have been used; however, it was essential to use “random” health professionals without previous knowledge of the studies so that the papers and authors could not be recognized. Finally, it can be seen as a weakness that this paper did not analyse whether differences in conclusions were due to study design or interpretation of the results. It could also be argued that independent researchers exaggerate the dangers and are unrealistic about the negative long-term consequences of the findings.

The strengths of the study are that the design is reminiscent of a real-life scenario and includes assessors without prior expert knowledge of the field. The blinded design and use of more than one assessor are also seen as strengths. Assessors discussed unclear cases and agreed on an assessment. Coding of conflict of interest was done independently of assessment of studies' findings/conclusion. The study addressed three dimensions of the conflict of interest: type of industry, level and direction. Finally, the conflict of interest was based not only on a conflict of interest statement but also on a more thorough exploration of the author's potential connections with the industry. This paper is the first to investigate the association between conflict of interest and e-cigarette research findings.

## 5. Conclusion

A blinded assessment showed that almost all papers without a conflict of interest found potentially harmful effects of e-cigarettes on health. The assessment used three dimensions of conflict of interest and all showed a strong association between an industry-related conflict of interest and tobacco/e-cigarette industry-favourable results, indicating that e-cigarettes are harmless. Some journals have already decided they will not publish tobacco industry-funded research. The present authors recommend all journals to follow in their footsteps.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ypmed.2018.12.011>.

## Author contributions

All authors discussed the study design and data interpretation, contributed to subsequent versions of the manuscript and read and approved the final manuscript. CP suggested a coding of COI, and NG critically reviewed the categories and the coding. AMB reviewed the final coding. CP prepared and analysed the data and wrote the first draft of the manuscript. NG and AMB assessed all abstracts. A special thanks to Caroline Kuhlmann that blinded all the abstracts.

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## Conflicts of interest

CP and AMB state that they have no conflict of interest. NG has accepted several invitations (travel expenses, accommodation and conference fee) from the pharmaceutical industry to take part in international medical conferences in the last five years.

## References

- Barnes, D.E., Bero, L.A., 1998. Why review articles on the health effects of passive smoking reach different conclusions. *JAMA* 279 (19), 1566–1570.
- Bates, C., Rowell, A. Tobacco Explained. The truth about the tobacco industry...in its own words. <http://www.who.int/tobacco/media/en/TobaccoExplained.pdf> (In: ASH, ed.).
- Bes-Rastrollo, M., Schulze, M.B., Ruiz-Canela, M., et al., 2013. Financial conflicts of interest and reporting bias regarding the association between sugar-sweetened beverages and weight gain: a systematic review of systematic reviews. *PLoS Med.* 10 (12), e1001578.
- Buffel du Vaure, C., Boutron, I., Perrodeau, E., et al., 2014. Reporting funding source or conflict of interest in abstracts of randomized controlled trials, no evidence of a large impact on general practitioners' confidence in conclusions, a three-arm randomized controlled trial. *BMC Med.* (12), 69. <https://doi.org/10.1186/1741-7015-12-69>. (published Online First: 2014/05/02).
- Carpenter, C.M., Connolly, G.N., Ayo-Yusuf, O.A., et al., 2009. Developing smokeless tobacco products for smokers: an examination of tobacco industry documents. *Tob. Control.* 18 (1), 54–59. <https://doi.org/10.1136/tc.2008.026583>. (published Online First: 2008/10/25).
- Cataldo, J.K., Prochaska, J.J., Glantz, S.A., 2010. Cigarette smoking is a risk factor for Alzheimer's Disease: an analysis controlling for tobacco industry affiliation. *J. Alzheimers Dis.* 19 (2), 465–480. <https://doi.org/10.3233/jad-2010-1240>. (published Online First: 2010/01/30).
- Cepeda, M.S., Berlin, J.A., Glasser, S.C., et al., 2015. Use of adjectives in abstracts when reporting results of randomized, controlled trials from industry and academia. *Drugs R&D* 15 (1), 85–139. <https://doi.org/10.1007/s40268-015-0085-9>. (published Online First: 2015/03/10).
- Diethelm, P.A., Riehl, J.C., McKee, M., 2005. The whole truth and nothing but the truth? The research that Philip Morris did not want you to see. *Lancet* 366 (9479), 86–92. [https://doi.org/10.1016/s0140-6736\(05\)66474-4](https://doi.org/10.1016/s0140-6736(05)66474-4). (published Online First: 2005/07/05).
- Dunn, A.G., Coiera, E., Mandl, K.D., et al., 2016. Conflict of interest disclosure in biomedical research: a review of current practices, biases, and the role of public registries in improving transparency. *Res. Int. Peer Rev.* 1 <https://doi.org/10.1186/s41073-016-0006-7>. (published Online First: 2016/05/10).
- Fedeli, U., Mastroangelo, G., 2011. Vinyl chloride industry in the courtroom and corporate influences on the scientific literature. *Am. J. Ind. Med.* 54 (6), 470–473. <https://doi.org/10.1002/ajim.20941>. (published Online First: 2011/04/02).
- Forsyth, S.R., Odierna, D.H., Krauth, D., et al., 2014. Conflicts of interest and critiques of the use of systematic reviews in policymaking: an analysis of opinion articles. *Syst. Rev.* 3, 122. <https://doi.org/10.1186/2046-4053-3-122>. (published Online First: 2014/11/25).
- Harris, J.E., Thun, M.J., Mondul, A.M., et al., 2004. Cigarette tar yields in relation to mortality from lung cancer in the cancer prevention study II prospective cohort, 1982–8. *BMJ* 328 (7431), 72. <https://doi.org/10.1136/bmj.37936.585382.44>. (published Online First: 2004/01/13).
- Hong, M.K., Bero, L.A., 2002. How the tobacco industry responded to an influential study of the health effects of secondhand smoke. *BMJ* 325 (7377), 1413–1416.
- Jackler, R.K., Samji, H.A., 2012. The price paid: manipulation of otolaryngologists by the tobacco industry to obfuscate the emerging truth that smoking causes cancer. *Laryngoscope* 122 (1), 75–87. <https://doi.org/10.1002/lary.22358>. (published Online First: 2011/12/21).
- Karagueuzian, H.S., White, C., Sayre, J., et al., 2012. Cigarette smoke radioactivity and lung cancer risk. *Nicotine Tob. Res.* 14 (1), 79–90.
- Lexchin, J., Bero, L.A., Djulbegovic, B., et al., 2003. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. *BMJ* 326 (7400), 1167–1170. <https://doi.org/10.1136/bmj.326.7400.1167>. (published Online First: 2003/05/31).
- Lundh, A., Lexchin, J., Mintzes, B., et al., 2017. Industry sponsorship and research outcome. *Cochrane Database Syst. Rev.* 2, Mr000033. <https://doi.org/10.1002/14651858.MR000033.pub3>. (published Online First: 2017/02/17).
- Malone, R., Boyd, E., Bero, L., Oct. 2000. Science in the news: journalists' constructions of passive smoking as a social problem. *Soc. Stud. Sci.* 30 (5), 713–735.
- Mandrioli, D., Kearns, C.E., Bero, L.A., 2016. Relationship between research outcomes and risk of bias, study sponsorship, and author financial conflicts of interest in reviews of the effects of artificially sweetened beverages on weight outcomes: a systematic review of reviews. *PLoS One* 11 (9), e0162198. <https://doi.org/10.1371/journal.pone.0162198>. (published Online First: 2016/09/09).
- McKee, M., Capewell, S., 2015. Electronic cigarettes: we need evidence, not opinions. *Lancet* 386 (10000), 1239.
- McMillen, R.C., Gottlieb, M.A., Shaefer, R.M., et al., 2015. Trends in electronic cigarette use among U.S. adults: use is increasing in both smokers and nonsmokers. *Nicotine Tob. Res.* 17 (10), 1195–1202.
- McNeill, A., Brose, L.S., Calder, R., et al., 2015a. E-cigarettes: the need for clear communication on relative risks. *Lancet* 386 (10000), 1237. [https://doi.org/10.1016/s0140-6736\(15\)00079-3](https://doi.org/10.1016/s0140-6736(15)00079-3). (published Online First: 2015/09/05).
- McNeill, A., Brose, L.S., Calder, R., et al., 2015b. E-cigarettes: an evidence update. In: England, P.H. (Ed.), A Report Commissioned by Public Health England. PHE publications gateway number: 2015260 August.
- Muggli, M.E., Forster, J.L., Hurt, R.D., et al., 2001. The smoke you don't see: uncovering tobacco industry scientific strategies aimed against environmental tobacco smoke policies. *Am. J. Public Health* 91 (9), 1419–1423.
- Neeley, E.E., Glantz, S.A., 2017. RJ Reynolds has not published a negative randomised clinical trial of Camel Snus for smoking cessation. *Tob. Control.* 26 (3), 357–358. <https://doi.org/10.1136/tobaccocontrol-2016-052913>. (published Online First: 2016/05/22).
- Neilsen, K., Glantz, S.A., 2004. A tobacco industry study of airline cabin air quality: dropping inconvenient findings. *Tob. Control.* 13 (Suppl. 1), i20–i29 (published Online First: 2004/02/27).
- Neltner, T.G., Alger, H.M., O'Reilly, J.T., et al., 2013. Conflicts of interest in approvals of additives to food determined to be generally recognized as safe: out of balance. *JAMA Intern. Med.* 173 (22), 2032–2036. <https://doi.org/10.1001/jamainternmed.2013.10559>. (published Online First: 2013/08/09).
- Pisinger, C., 2016. A Systematic Review of Health Effects of Electronic Cigarettes: Prepared at the Request of WHO Prevention of Noncommunicable Diseases.
- Pisinger, C., Dossing, M., 2014. A systematic review of health effects of electronic cigarettes. *Prev. Med.* 69, 248–260.
- Tobacco tactics E-cigarettes. <http://www.tobaccotactics.org/index.php/E-cigarettes> (The University of Bath [accessed Sept 18 2017]).
- Tong, E.K., England, L., Glantz, S.A., 2005. Changing conclusions on secondhand smoke in a sudden infant death syndrome review funded by the tobacco industry. *Pediatrics* 115 (3), e356–e366.
- Yano, E., 2005. Japanese spousal smoking study revisited: how a tobacco industry funded paper reached erroneous conclusions. *Tob. Control.* 14 (4), 227–233.