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Alcohol Industry Involvement in the Moderate Alcohol and Cardiovascular Health (MACH) Trial

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Abstract

The National Institutes of Health stopped the Moderate Alcohol and Cardiovascular Health (MACH) trial in 2018 due to institutional failings that led to the biased design of this major study. Drawing on e-mail correspondence among officials, researchers, and alcohol companies, this commentary provides the first detailed analysis of alcohol industry involvement in the MACH trial. Alcohol companies agreed to fund the MACH trial to advance their commercial interests rather than to help answer a major scientific question. Alcohol industry executives seized opportunities presented by discussions of the MACH trial to try to influence this study and wider public health, research, and policy decision-making. The process of soliciting research funding from corporations, which included convincing alcohol companies that the study design supported their commercial interests, was intrinsically biased. Thus, the three parties – research funding officials, researchers, and industry executives – co-produced the biased trial design. A detailed understanding of this episode will be helpful in advancing efforts to protect public health research from biases associated with corporate donations.

The Moderate Alcohol and Cardiovascular Health (MACH) trial, supported by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), began in February 2018 and was designed to investigate the possible cardioprotective effects of alcohol.[1] Approximately two-thirds of the funding for this $100 million dollar trial was provided by five global alcohol producers: Anheuser-Busch InBev, Carlsberg, Diageo, Heineken, and Pernod Ricard.[2,3] Their ability to provide such funding is connected to the concentration of the brewing and distilled spirits industries into a small number of transnational corporations.[4] This has led to a pooling of resources that enables alcohol companies to create “social aspects” organisations for "corporate social responsibility" (CSR) and public relations purposes, including research.[5,6] Researchers have raised concerns about corporate strategies to bias science across a range of health-related topics,[7–9] including industry sponsorship shaping research agendas, as well as particular studies.[10] Following media coverage,[3,11] a National

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Institutes of Health (NIH) investigation[1] led to the termination of the MACH trial in June 2018. This commentary analyses e-mail correspondence made publicly available by the NIH report to explore the role of the alcohol industry in the trial and the implications for public health science.

The significance of the science

The alcohol industry attempts to distance itself from tobacco and other drugs by claiming that low-dose alcohol consumption provides cardiovascular health benefits.[12] Older observational epidemiological studies,[13] including those funded by industry,[14] suggest there is a cardiovascular health benefit, whilst more rigorous Mendelian randomisation studies and other studies adequately correcting for misclassification bias (including former drinkers with current abstainers) find less or no benefit.[15–17] Resolving this uncertainty is a major scientific challenge, and the possible implications for public health, the alcohol industry, and society are quite profound. The MACH trial, the first investigator randomised study on the topic, originated in these circumstances.

The NIH terminated the MACH trial because inappropriate interactions with industry created bias

Concerns about industry involvement in the MACH trial were first raised in the *New York Times* in July 2017[11] and March 2018;[3] the latter report drew from e-mails and travel vouchers obtained via freedom of information requests, as well as interviews with former federal officials. The reporting documented inappropriate interactions between the alcohol industry, researchers, and NIAAA officials. In response, congressional hearings were held[2] and the NIH director requested a review of the trial.[1] Two reviews were undertaken: the Office of Management Assessment review, which has not been published, and the NIH Advisory Committee to the Director Working Group (ACD WG) review, which was published in June 2018.[1]

The main findings from the ACD WG report[1] include: that NIAAA officials sought funding from alcohol companies inappropriately; that NIAAA staff liaised with the principal investigator (PI) and “effectively steered funding to the PI of these staff members’ choosing” (p8);[1] and that collaborations between NIAAA officials and industry actors “appear to intentionally bias the framing of the scientific premise in the direction of demonstrating a beneficial health effect of moderate alcohol consumption” (p3).[1] These findings draw in part on additional peer review of the trial design commissioned by the NIH. This “raised concerns that there are insufficient patients and not enough follow-up time to allow for meaningful assessment of cancer endpoints. It also found that the composite primary endpoint does not include heart failure. Thus, the trial could show benefits while missing harms” (p.3).[1] As a consequence, the ACD WG report recommended that the MACH trial be terminated, and the NIH announced the end of the trial in June 2018.[2]

The e-mail evidence available

Central to the ACD WG's findings were a series of e-mail exchanges among alcohol industry executives, NIAAA officials, and alcohol researchers between June 2013 and February 2015. The report concluded that correspondence among the three parties demonstrated extensive discussions about the scientific planning of the study that went "beyond the norm"(p10) and reflected an apparent attempt by NIAAA officials and the researchers "to persuade industry to support the project" (p3).[1] The focus of the ACD WG report is on the integrity of the process. This commentary explores the role of the alcohol industry in this episode, asking which alcohol industry bodies were involved in discussions about the design and conduct of this trial, how these efforts were organised, and what they sought to influence.

The material used here is publicly available as an appendix in the ACD WG report.[1] We first identified e-mail correspondence (including attached documents) where alcohol industry executives were recipients, senders, or cc'd into e-mails, providing a core dataset that was thematically analysed. This included the creation of an initial coding framework, followed by the construction and revision of themes relevant to our aims.[18] The authors reviewed and discussed the coding until we reached agreement on the main findings. Additionally, the authors examined references to the alcohol industry in both the broader e-mail correspondence and the rest of the NIH report to identify important contextual data. All direct quotes below are from the ACD WG report[1] unless otherwise stated.

The formation and organisation of a tripartite structure

The researchers, two established experts in the field working in prestigious universities, were the first to contact industry about a potential trial on the health benefits of moderate drinking. This occurred in 2013, when the researchers approached Diageo, one of the largest spirits producers in the world.[4] Diageo later involved the Distilled Spirits Council of the United States (DISCUS) and Spirits Europe, both trade associations in which this company is a member. Subsequently, other global beer and spirits companies became involved, which the International Center for Alcohol Policies (ICAP)[19] was key to arranging. ICAP also coordinated, collected, and synthesized scientific input from the producers. NIAAA documentation names the International Alliance for Responsible Drinking (IARD) – the successor organisation formed following a merger of ICAP and the Global Alcohol Producers Group in late 2014 – as having "co-ordinated commitments" from the alcohol industry (p137). The 11 member companies of IARD were all involved in the ICAP-led discussions of the MACH trial design and conduct.

Apart from the Wine Institute, the wine industry was not involved in these discussions. In comparison to beer and spirits, wine producers tend to be small[20] and were less likely potential donors for this reason. A leak from a wine industry source early in the process suggested that the NIH was seeking funding from alcohol companies. This led to much discussion between NIAAA officials about how to manage this unwelcome public disclosure.

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In addition to the correspondence itself, interactions took place via conference calls and in-person (including drinks and meals, and researchers making presentations to industry groups). From the outset, industry executives sought reassurance that NIAAA had a central role in the study; this would increase the likelihood that the wider scientific community viewed the findings as legitimate. The nature of industry interest was clear: the study would be designed to "show the J curve [demonstrate the health benefits of low-level drinking] in all its glory" (p95). NIAAA staff and the researchers held a similar view of the expected outcomes. When alcohol industry executives made requests – to convene conference calls and to have methodological discussions – their requests were accepted, and the information provided. After initial contacts with Diageo, DISCUS, and Spirits Europe, ICAP became the preeminent voice of the alcohol industry in identifying 'questions', 'issues', or 'concerns' about the study. NIAAA officials acknowledged that it was highly unlikely the study could proceed without industry funding. There is, therefore, clear power asymmetry in these interactions, in which NIAAA officials and researchers had to persuade large corporations that this project was in their interests.

The breadth of the scientific issues targeted by alcohol companies

Alcohol companies and trade associations co-ordinated by ICAP engaged with all the key scientific issues raised by the proposed trial design (see particularly ICAP call minutes pp66-91, e-mail correspondence pp100-10 and pp114-5). They discussed:

1) Outcome measures: for example, whether breast cancer would be a secondary outcome

2) Target population: for example, whether to exclude women with a family history of breast cancer in the selection criteria

3) Sample size

4) Compliance with randomised allocation of drinking only one drink per day or none

5) Beverage variation: the decision to include different types of alcohol as chosen by participant

6) Incentives to individuals abstaining from alcohol in the trial

7) Attrition

8) Safety monitoring, including biomarker selection

9) Feasibility and pilot issues

10) Timing issues: including the availability of early data on safety outcomes

11) Interpretation of negative outcomes: how any negative results would be communicated

12) Trial sites chosen to include countries important to a particular company

13) The adequacy of self-reported data

14) Project management issues

Alcohol industry executives required access to a high level of scientific expertise to identify the likelihood of the trial producing results that conflict with commercial interests. Alcohol industry executives not only asked questions but also made several suggestions to alter the design, and by extension the results, of the study. For example, one asked whether there was an "upper age limit cutoff", stating "narrowing the age band would give a tighter cohort. Is this worth doing?" (p105). Researcher responses to industry comments helped reassure industry executives that any commercial risks associated with funding the trial were mitigated due to the study's design. For example, one of the researchers stated "one of the important findings *will be* showing that moderate drinking is safe" (pg. 116, emphasis added).

Windows of opportunity created by discussion of MACH trial funding

Alcohol industry executives used the discussions with NIAAA officials and researchers to gain wider insights into alcohol research relevant to their interests. For example, ICAP requested (and received) a list of attendees at a Research Society on Alcoholism (RSA) symposium (pp102-3). According to an NIAAA official, there were also discussions "on some other issues like the Dietary Guidelines that [industry] keep bugging us (me) on" (p54). Additionally, industry executives sought to advance their influence at the science/policy interface. For example, in November 2013, while the Organisation for Economic Co-operation and Development (OECD) were working on a major report on alcohol policy, a Spirits Europe representative shared a 'note' relating to this meeting with an NIAAA official. This 'note' indicated the Spirits Europe representative's "difficulties with their [OECD] apparent acceptance of the consumption = harm equation" and their "grave concerns about the general nature of that paper" (p95).

The e-mail correspondence revealed instances of industry executives discussing unrelated NIAAA-funded studies with NIAAA officials. For example, an NIAAA staff member reported that a DISCUS executive "hit on me again on our grant studying the effect of privatization on spirits and overall alcohol consumption" (p47). There was also discussion of future projects, such as "the proposed work NIAAA plans on a conference on the benefits of alcohol (within the next year)" (p95). The ACD WG report examined the NIAAA portfolio over time due to the obvious risks revealed to the integrity of its decision-making. A reduction in the funding of some categories of highly policy-relevant research was noted in the report; however, the conclusion reached was that "it is not unusual for Institute research portfolios to evolve over time" (p12). The need to examine the robustness of this conclusion with further investigations of NIAAA decision-making should be clear from the foregoing.

Scientific, health, and policy implications

This commentary moves beyond the findings of the ACD WG report to provide detail on which alcohol industry actors became involved in the MACH trial, how they were organised and which features of the trial design they sought to influence. This industry involvement, alongside NIAAA officials and researchers' efforts to secure industry funding, meant that all three parties co-produced the biased trial design. Despite the termination of the trial,

however, the data analysed suggests that alcohol industry actors benefited from their donations in other ways, including gaining insight into alcohol research and policy both at the U.S. and global level. Concerns have been raised within the scientific community about ICAP and IARD's role in science[21] and policy,[12] and this particular case demonstrates the need for further study of IARD's ongoing activities, especially relationship-building with researchers and officials. We encourage the NIAAA to recognise the need to strengthen the alcohol policy evidence-base by funding research on industry's commercial, political, and scientific activities.

The researchers stand by the scientific integrity of their decision-making,[2] and as far as we are aware, there has been no investigation of their conduct by their universities. The published case for the MACH trial[22] does not make any disclosures pertaining to the interactions with industry executives detailed in the NIH report and has not been withdrawn or corrected. We encourage the journal editors to require that the authors add full disclosures regarding industry interactions, and to withdraw the paper if these are not forthcoming. Further investigation of this case may also aid scientific understanding of research norms and practices in interactions with corporate actors, in order to support strengthening conflict of interest management procedures to secure the ethical conduct of research.

The Foundation for the National Institutes of Health provided the conduit through which large sums could be donated, and there is some evidence available that alcohol industry actors have previously used charities to advance their policy goals.[23] The NIAAA Director remains in position, and it will be interesting to see how far NIAAA learns the lessons available in scrutiny of this episode. We urge the NIH to make all documents associated with the MACH trial publicly available, including the Office of Management Assessment review. This could provide new insights to help manage corporate efforts to influence public research funding bodies and enable the scientific community to develop more robust firewalls between industry and publicly funded institutions.

The major scientific challenge involved in determining whether there are any cardioprotective effects of alcohol remains unresolved, and the MACH trial has involved much wasted effort. This analysis gives further substance to the doubts associated with industry funding of older studies on the subject.[14] Unlike the tobacco industry, there are few accessible internal alcohol company documents that permit direct insights into how strategies are developed and executed to bias science or influence policy.[12,21] Further study of this episode could include broadening the dataset to include related information in the public domain, and identifying ICAP/IARD interactions with the NIAAA, other publicly funded bodies, and relationship building with researchers. Alcohol companies were key actors in the MACH trial, and we know little about their involvement in science more generally.[21] Further study is needed of how relationships between alcohol industry actors, researchers, research funding and other publicly funded bodies develop over time, and the governance issues raised to protect such bodies from inappropriate corporate influence. The consistency between alcohol industry involvement in this case and broader evidence on corporate activities to bias research agendas and distort the evidence-base necessary for effective public policy[7,10] shows that this work is urgently required to protect scientific integrity.

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