JAMA Internal Medicine | Special Communication

Sugar Industry and Coronary Heart Disease Research
A Historical Analysis of Internal Industry Documents

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Early warning signals of the coronary heart disease (CHD) risk of sugar (sucrose) emerged in the 1950s. We examined Sugar Research Foundation (SRF) internal documents, historical reports, and statements relevant to early debates about the dietary causes of CHD and assembled findings chronologically into a narrative case study. The SRF sponsored its first CHD research project in 1965, a literature review published in the *New England Journal of Medicine*, which singled out fat and cholesterol as the dietary causes of CHD and downplayed evidence that sucrose consumption was also a risk factor. The SRF set the review's objective, contributed articles for inclusion, and received drafts. The SRF's funding and role was not disclosed. Together with other recent analyses of sugar industry documents, our findings suggest the industry sponsored a research program in the 1960s and 1970s that successfully cast doubt about the hazards of sucrose while promoting fat as the dietary culprit in CHD. Policymaking committees should consider giving less weight to food industry–funded studies and include mechanistic and animal studies as well as studies appraising the effect of added sugars on multiple CHD biomarkers and disease development.

JAMA Intern Med. 2016;176(11):1680-1685. doi:10.1001/jamainternmed.2016.5394
Published online September 12, 2016. Corrected on October 3, 2016.

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In the 1950s, disproportionately high rates of coronary heart disease (CHD) mortality in American men led to studies of the role of dietary factors, including cholesterol, phytosterols, excessive calories, amino acids, fats, carbohydrates, vitamins, and minerals in influencing CHD risk.[1] By the 1960s, 2 prominent physiologists were championing divergent causal hypotheses of CHD[2,3]: John Yudkin identified added sugars as the primary agent, while Ancel Keys identified total fat, saturated fat, and dietary cholesterol. However, by the 1980s, few scientists believed that added sugars played a significant role in CHD, and the first *1980 Dietary Guidelines for Americans*[4] focused on reducing total fat, saturated fat, and dietary cholesterol for CHD prevention.

Although the contribution of dietary sugars to CHD is still debated, what is clear is that the sugar industry, led by the Sugar Association, the sucrose industry's Washington, DC–based trade association,[5] steadfastly denies that there is a relationship between added sugar consumption and CVD risk.[6,7] This Special Communication uses internal sugar industry documents to describe how the industry sought to influence the scientific debate over the dietary causes of CHD in the 1950s and 1960s, a debate still reverberating in 2016.

Methods

The Sugar Association evolved from the Sugar Research Foundation (SRF), founded in 1943.[8] We located correspondence between the SRF and Roger Adams, a professor who served on the SRF's scientific advisory board (SAB) between 1959 and 1971, in the University of Illinois Archives[9] (319 documents totaling 1551 pages). We located correspondence between the SRF and D. Mark Hegsted, professor of nutrition at the Harvard School of Public Health and co-director of the SRF's first CHD research project from 1965 to 1966,[10] in the Harvard Medical Library[11] (27 documents totaling 31 pages).

We collected additional SRF materials through a WorldCat search including annual reports, symposium proceedings, and internal reviews of research. We reviewed historical reports and statements contextualizing scientific debates in the 1950s and 1960s on dietary factors causally related to CHD published by the National Academy of Sciences–National Research Council (NAS-NRC), US Public Health Service, the American Heart Association (AHA), and American Medical Association (AMA). Findings were assembled chronologically into a narrative case study.

Results

SRF's Interest in Promoting a Low-Fat Diet to Prevent CHD

Sugar Research Foundation president Henry Hass's 1954 speech, "What's New in Sugar Research,"[12] to the American Society of Sugar Beet Technologists identified a strategic opportunity for the sugar industry: increase sugar's market share by getting Americans to eat a lower-fat diet: "Leading nutritionists are pointing out the chemical connection between [American's] high-fat diet and the formation of cholesterol which partly plugs our arteries and capillaries, restricts the flow of blood, and causes high blood pressure and heart trouble… if you put [the middle-aged man] on a low-fat diet, it takes just five days for the blood cholesterol to get down to where it should be… If the carbohydrate industries were to recapture this 20 percent of the calories in the US diet (the difference between the 40 percent which fat has and the 20 percent which it ought to have) and if sugar main-

tained its present share of the carbohydrate market, this change would mean an increase in the per capita consumption of sugar more than a third with a tremendous improvement in general health."[12]

The industry would subsequently spend $600 000 ($5.3 million in 2016 dollars) to teach "people who had never had a course in biochemistry… that sugar is what keeps every human being alive and with energy to face our daily problems."[12]

Growing Evidence That Sucrose Elevates Serum Cholesterol Level

In 1962, the SRF became concerned with evidence showing that a low-fat diet high in sugar could elevate serum cholesterol level. At its November 1962 SAB meeting,[13] the SRF considered an AMA Council on Foods and Nutrition report, *The Regulation of Dietary Fat*,[14] that, according to the SRF, "indicate[d] that, in low fat diets, the kind of carbohydrate ingested may have an influence on the formation of serum cholesterol."[13] The SAB concluded, "that research developments in the [CHD] field should be watched carefully."[13] The SRF's vice president and director of research, John Hickson, started closely monitoring the field.[15]

In December 1964, Hickson reported to an SRF subcommittee[15] that new CHD research was a cause for concern: "From a number of laboratories of greater or lesser repute, there are flowing reports that sugar is a less desirable dietary source of calories than other carbohydrates, eg,—Yudkin."[15] Since 1957, British physiologist John Yudkin[16] had challenged population studies singling out saturated fat as the primary dietary cause of CHD and suggested that other factors, including sucrose, were at least equally important.[17,18]

Hickson proposed that the SRF "could embark on a major program" to counter Yudkin and other "negative attitudes toward sugar."[15] He recommended an opinion poll "to learn what public concepts we should reinforce and what ones we need to combat through our research and information and legislative programs" and a symposium to "bring detractors before a board of their peers where their fallacies could be unveiled."[15] Finally, he recommended that SRF fund CHD research: "There seems to be a question as to whether the [atherogenic] effects are due to the carbohydrate or to other nutrient imbalance. We should carefully review the reports, probably with a committee of nutrition specialists; see what weak points there are in the experimentation, and replicate the studies with appropriate corrections. Then we can publish the data and refute our detractors."[15]

In 1965, the SRF asked Fredrick Stare, chair of the Harvard University School of Public Health Nutrition Department[19] to join its SAB as an ad hoc member.[20] Stare was an expert in dietary causes of CHD and had been consulted by the NAS,[1] National Heart Institute,[21] and AHA,[22] as well as by food companies and trade groups.[19] Stare's industry-favorable positions and financial ties would not be widely questioned until the 1970s.[23]

Link Between Sucrose and Elevated Serum Triglyceride Level

On July 1, 1965, the SRF's Hickson visited D. Mark Hegsted, a faculty member of Stare's department,[24,25] after publication of articles in *Annals of Internal Medicine* in June 1965[26-29] linking sucrose to CHD. The first 2 articles[26,27] reported results from an epidemiological study suggesting that blood glucose levels were a better predictor of atherosclerosis than serum cholesterol level or hypertension. The third[28(p210)] demonstrated that sucrose, more than starches, aggravated carbohydrate-induced hypertriglyceridemia and hypothesized that "perhaps fructose, a constituent of sucrose but not of starch, [was] the agent mainly responsible." An accompanying editorial[29(p1330)] argued that these findings corroborated Yudkin's research and that if elevated serum triglyceride levels were a CHD risk factor, then "sucrose must be atherogenic."

On July 11, 1965, the *New York Herald Tribune* ran a full-page article on the *Annals* articles stating that new research "threatened to tie the whole business [of diet and heart disease] in a knot."[30] It explained that, while sugar's association with atherosclerosis was once thought to be theoretical and supported by limited studies, the new research strengthened the case that sugar increased the risk of heart attacks.

SRF Funds Project 226: A Literature Review on Sugars, Fats, and CHD

On July 13, 1965, 2 days after the *Tribune* article, the SRF's executive committee approved Project 226,[31] a literature review on "Carbohydrates and Cholesterol Metabolism" by Hegsted and Robert McGandy, overseen by Stare.[10] The SRF initially offered $500 ($3800 in 2016 dollars) to Hegsted and $1000 ($7500 in 2016 dollars) to McGandy, "half to be paid when you start work on the project, and the remainder when you inform me that the article has been accepted for publication."[31] Eventually, the SRF would pay them $6500[32] ($48 900 in 2016 dollars) for "a review article of the several papers which find some special metabolic peril in sucrose and, in particular, fructose."[31]

On July 23, 1965, Hegsted asked Hickson to provide articles relevant to the review.[33] Most of the articles Hickson sent[34-40] contained findings that could threaten sugar sales, which suggests that the industry expected the review authors to critique them. Hickson also sent the *Tribune* article[30] and a letter to the editor that criticized findings questioning the therapeutic value of corn oil.[41,42]

On July 30, 1965, Hickson emphasized the SRF's objective for funding the literature review to Hegsted: "Our particular interest had to do with that part of nutrition in which there are claims that carbohydrates in the form of sucrose make an inordinate contribution to the metabolic condition, hitherto ascribed to aberrations called fat metabolism. I will be disappointed if this aspect is drowned out in a cascade of review and general interpretation."[34]

In response, Hegsted assured Hickson that "We are well aware of your particular interest in carbohydrate and will cover this as well as we can."[43]

Nine months into the project, in April 1966, Hegsted told the SRF that the review had been delayed because of new evidence linking sugar to CHD: "Every time the Iowa group publishes a paper *we have to rework a section in rebuttal* [emphasis added]."[44] The "Iowa group" included Alfredo Lopez, Robert Hodges, and Willard Krehl, who had reported a positive association between sugar consumption and elevated serum cholesterol level.[45]

It is not clear whether the SRF commented on or edited drafts of the review. However, on September 6, 1966, Hickson asked Hegsted, "Am I going to get another copy of the draft shortly?"[40] suggesting Hickson had been involved. Hegsted responded on September 29, "I expect to get it down to you within a week or two."[46] Hickson received the final draft on October 25, 1966, a few days before Hegsted intended to submit it for publication.[47] On November 2, Hickson told Hegsted, "Let me assure you this is quite what we had in mind and we look forward to its appearance in print."[47]

Publication of Project 226

Project 226 resulted in a 2-part literature review by McGandy, Hegsted, and Stare "Dietary Fats, Carbohydrates and Atherosclerotic Disease," in the *New England Journal of Medicine* (*NEJM*) in 1967.[48,49] Industry and nonindustry funding of the review authors' experimental research was disclosed, but the SRF's funding and participation in the review was not. Evidence reported in the review was relevant to 2 questions: (1) Does the high sucrose content of the American diet cause CHD? and (2) What is the comparative effectiveness of interventions modifying the sucrose or saturated fat content of the diet for the prevention of CHD? The review concluded there was "no doubt" that the only dietary intervention required to prevent CHD was to reduce dietary cholesterol and substitute polyunsaturated fat for saturated fat in the American diet.[49(p246)]

High Sucrose Content of the American Diet and CHD

The review summarized findings from epidemiologic, experimental, and mechanistic studies examining the role of sucrose in CHD (see eTable 1 in the Supplement). It reported that epidemiologic studies showed a positive association between high sucrose consumption and CHD outcomes[48(pp187-189)] and that experimental studies showed that sucrose caused serum cholesterol and serum triglyceride levels to rise in healthy individuals,[48(pp190-192)] and serum triglyceride levels to rise in those with hypertriglyceridemia.[49(pp242-243)] Finally, it reported that mechanistic studies demonstrated the biological plausibility of (1) sucrose affecting serum cholesterol level mediated through changes to the intestinal microbiome,[49(p243)] and (2) fructose, a component of sucrose, affecting serum triglyceride levels mediated through endogenous lipogenesis in the liver, adipose tissues, and other organs.[49(pp244-246)]

The review evaluated the quality of individual studies, including the work of Yudkin and the Iowa Group[48(pp187-188)] (see eTables 1 and 2 in the Supplement), investigators whom the SRF had identified as threatening before initiating the review[15] and in correspondence while it was being prepared.[34,44] The review discounted these studies on the grounds that they contained questionable data or incorrect interpretation.[48(pp187-189)49(pp242-243)] It questioned whether entire classes of evidence were relevant (see eTables 1 and 3 in the Supplement). It discounted epidemiologic evidence for identifying dietary causes of CHD because of multifactorial confounding[48(p188)] and experimental evidence from short-term studies using large doses of sucrose because they were not comparable with amounts typically consumed in the American diet.[48(pp191-192)] It discounted mechanistic studies conducted with fructose or glucose, not sucrose,[49(p244)] and animal evidence because of species differences and because people rarely consumed low-fat diets typically fed to rats.[49(pp243-244)] Overall, the review focused on possible bias in individual studies and types of evidence rather than on consistency across studies and the coherence of epidemiologic, experimental and mechanistic evidence.

Comparative Effectiveness of Dietary Interventions for the Prevention of CHD

The *NEJM* review summarized findings from human randomized clinical trials (RCTs) evaluating the effect of sucrose interventions on serum cholesterol and triglyceride levels in healthy and hypertriglyceridemic individuals, and the effect of fat interventions on serum cholesterol levels in healthy persons (see eTable 4 in the Supplement). Regarding sucrose interventions, it argued that substituting fat for sucrose caused a large improvement in serum triglyceride levels in healthy individuals,[48(p190)] substituting starch for sucrose caused a large improvement in serum triglyceride levels in patients with hypertriglyceridemia,[49(pp242-243)] and that substituting leguminous vegetables for sucrose caused a large improvement in serum cholesterol levels in healthy individuals.[48(pp190-191)] Finally, it reported that substituting starch for sucrose caused a small improvement in serum cholesterol levels in healthy individuals.[48(pp190-191)] Regarding fat interventions, the review reported that reducing dietary cholesterol and substituting polyunsaturated fat for saturated fat caused a large improvement in serum cholesterol level in healthy persons.[48(pp189-190)]

The review discounted RCTs that had shown that substituting starch for sucrose had a large effect on improving serum triglyceride levels and implied that only studies that had used serum cholesterol level as a biomarker of CHD risk should be used to compare the efficacy of sucrose interventions to fat interventions (see eTable 4 in the Supplement). The review then discounted RCTs that had shown that substituting fat or vegetables for sucrose had a large effect on improving serum cholesterol level, by arguing this intervention was infeasible[48(p191)] (see eTables 4 and 5 in the Supplement). Substituting refined starches (sweetened with artificial sweeteners) for sucrose, despite being feasible, was dismissed because the magnitude of effect on serum cholesterol level was minimal compared with reducing dietary cholesterol level and substituting polyunsaturated for saturated fat.[48(pp190-191)]

Unlike its summary of sucrose intervention RCTs, the review reported few study characteristics and no quantitative results in its summary of fat intervention RCTs.[48(pp189-190)] Consulting the original fat intervention RCTs reveals that the review overstated the consistency of studies (see eTable 6 in the Supplement). Only 1 RCT, conducted by Hegsted et al,[50] concluded that reducing dietary cholesterol and substituting polyunsaturated fat for saturated fat substantially improved serum cholesterol levels. Consulting the original clinical studies cited to substantiate reducing dietary cholesterol and substituting polyunsaturated fat for saturated fat reveals that they were not well controlled. Despite arguing earlier in the review that epidemiologic evidence was irrelevant to determining dietary causes of CHD,[48(pp187-189)] the review implied that the epidemiologic evidence pointed to dietary cholesterol and saturated fat as the primary dietary causes of CHD.[49(p246)] The review argued that the lack of mechanistic evidence confirming the biological plausibility that dietary cholesterol and saturated fat raised serum cholesterol levels was unimportant.[49(p246)] Finally, the review emphasized that polyunsaturated fats were readily available and would be well accepted as substitute for saturated fats in the American diet.[49(p246)]

Discussion

These internal documents show that the SRF initiated CHD research in 1965 to protect market share and that its first project, a literature review, was published in *NEJM* in 1967 without disclosure of the sugar industry's funding or role. The *NEJM* review served the sugar industry's interests by arguing that epidemiologic, animal, and mechanistic studies associating sucrose with CHD were limited, implying they should not be included in an evidentiary assessment of the CHD risks of sucrose. Instead, the review argued that the only evidence modality needed to yield a definitive answer to the question of how to modify

the American diet to prevent CHD was RCTs that exclusively used serum cholesterol level as a CHD biomarker. Randomized clinical trials using serum cholesterol level as the CHD biomarker made the high sucrose content of the American diet seem less hazardous than if the entire body of evidence had been considered.

Following the *NEJM* review, the sugar industry continued to fund research on CHD and other chronic diseases "as a main prop of the industry's defense."[51] For example, in 1971, it influenced the National Institute of Dental Research's National Caries Program to shift its emphasis to dental caries interventions other than restricting sucrose.[8] The industry commissioned a review, "Sugar in the Diet of Man," which it credited with, among other industry tactics, favorably influencing the 1976 US Food and Drug Administration evaluation of the safety of sugar.[51] These findings, our analysis, and current Sugar Association criticisms of evidence linking sucrose to cardiovascular disease[6,7] suggest the industry may have a long history of influencing federal policy.

This historical account of industry efforts demonstrates the importance of having reviews written by people without conflicts of interest and the need for financial disclosure. Scientific reviews shape policy debates, subsequent investigations, and the funding priorities of federal agencies.[52] The *NEJM* has required authors to disclose all conflicts of interest since 1984,[53] and conflict of interest disclosure policies have been widely implemented since the sugar industry launched its CHD research program. Whether current conflict of interest policies are adequate to withstand the economic interests of industry remains unclear.[54]

Many industries sponsor research to influence assessments of the risks and benefits of their products.[55-57] The influence of industry sponsorship on nutrition research is receiving increased scrutiny.[58] Access to documents not meant for public consumption has provided the public health community unprecedented insight into industry motives, strategies, tactics, and data designed to protect companies from litigation and regulation.[59] This insight has been a major factor behind successful global tobacco control policies.[60] Our analysis suggests that research using sugar industry documents has the potential to inform the health community about how to counter this industry's strategies and tactics to control information on the adverse health effects of sucrose.

Study Limitations

The Roger Adams papers and other documents used in this research provide a narrow window into the activities of 1 sugar industry trade association; therefore, it is difficult to validate that the documents gathered are representative of the entirety of SRF internal materials related to Project 226 from the 1950s and 1960s or that the proper weight was given to each data source. There is no direct evidence that the sugar industry wrote or changed the *NEJM* review manuscript; the evidence that the industry shaped the review's conclusions is circumstantial. We did not analyze the role of other organizations, nutrition leaders, or food industries that advocated that saturated fat and dietary cholesterol were the main dietary cause of CHD. We could not interview key actors involved in this historical episode because they have died.

Conclusions

This study suggests that the sugar industry sponsored its first CHD research project in 1965 to downplay early warning signals that sucrose consumption was a risk factor in CHD. As of 2016, sugar control policies are being promulgated in international,[61] federal,[62,63] state, and local venues.[64] Yet CHD risk is inconsistently cited as a health consequence of added sugars consumption. Because CHD is the leading cause of death globally, the health community should ensure that CHD risk is evaluated in future risk assessments of added sugars. Policymaking committees should consider giving less weight to food industry–funded studies, and include mechanistic and animal studies as well as studies appraising the effect of added sugars on multiple CHD biomarkers and disease development.[65]

ARTICLE INFORMATION

Correction: This article was corrected online October 3, 2016, to include additional information regarding funding and additional contributions.

Accepted for Publication: July 2, 2016.

Published Online: September 12, 2016. doi:10.1001/jamainternmed.2016.5394

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Author Contributions: Drs Kearns and Glantz had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of data analysis.
Study concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Kearns.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Glantz.
Obtained funding: Glantz.
Administrative, technical, or material support: Kearns, Glantz.
Study supervision: Schmidt, Glantz.

Conflict of Interest Disclosures: None reported.

Funding/Support: This work was supported by the UCSF Philip R. Lee Institute for Health Policy Studies, a donation by the Hellmann Family Fund to the UCSF Center for Tobacco Control Research and Education, the UCSF School of Dentistry Department of Orofacial Sciences and Global Oral Health Program, National Institute of Dental and Craniofacial Research grant DE-007306 and National Cancer Institute grant CA-087472. We also thank Gary Taubes, MS, co-founder of Nutrition Science Initiative, for providing funding for travel to the Harvard Medical Library.

Role of the Funder/Sponsor: The funders had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Additional Contributions: We thank Kimber Stanhope, PhD, RD, for advice on the analysis of the SRF-funded *NEJM* review and the original studies it cited. No compensation was received for her contribution. We also thank Gary Taubes, MS, co-founder of Nutrition Science Initiative, for photographing documents in the D. Mark Hegsted papers at the Harvard Medical Library.

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Invited Commentary

HEALTH CARE POLICY AND LAW

Food Industry Funding of Nutrition Research
The Relevance of History for Current Debates

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Industry-sponsored nutrition research, like that of research sponsored by the tobacco, chemical, and pharmaceutical industries, almost invariably produces results that confirm the benefits or lack of harm of the sponsor's products, even when independently sponsored research comes to opposite conclusions.[1] Although considerable evidence demonstrates that those industries deliberately influenced the design, results, and interpretation of the studies they paid for,[2] much less is known about the influence of food-company sponsorship on nutrition research. Typically, the disclosure statements of sponsored nutrition studies state that the funder had no role in their design, conduct, interpretation, writing, or publication. Without a "smoking gun" it is difficult to prove otherwise.

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In this issue of *JAMA Internal Medicine*, Kearns and colleagues[3] report on having found a smoking gun. From a deep dive into archival documents from the 1950s and 1960s, they have produced compelling evidence that a sugar trade association not only paid for but also initiated and influenced research expressly to exonerate sugar as a major risk factor for coronary heart disease (CHD). Although studies at that time indicated a relationship between high-sugar diets and CHD risk, the sugar association preferred scientists and policymakers to focus on the role of dietary fat and cholesterol. The association paid the equivalent of more than $48 000 in today's dollars to 3 nutrition professors—at Harvard no less—to publish a research review that would refute evidence linking sugars to CHD.

The sponsored review appeared in 2 parts in the *New England Journal of Medicine* in 1967. Its authors acknowledged support from the industry-funded Nutrition Foundation, but they did not mention the sugar association's specific funding of their review. Their first article demonstrates a close correlation between sugar and fat "consumption" (actually amounts in the food supply) and mortality in 14 countries (**Figure**).[4] To minimize the association with sugar, the authors seem to have cherry-picked existing data. Despite their having previously published studies linking both fats and sugars to CHD risk, their review gave far more credence to studies implicating saturated fat than it did to those implicating sugars.

The documents leave little doubt that the intent of the industry-funded review was to reach a foregone conclusion. The investigators knew what the funder expected, and produced it. Whether they did this deliberately, unconsciously, or because they genuinely believed saturated fat to be the greater threat is unknown. But science is not supposed to work this way. The documents make this review seem more about public relations than science.

This 50-year-old incident may seem like ancient history, but it is quite relevant, not least because it answers some questions germane to our current era. Is it really true that food companies deliberately set out to manipulate research in their favor? Yes, it is, and the practice continues. In 2015, the *New York Times* obtained emails revealing Coca-Cola's cozy relationships with sponsored researchers who were conducting studies aimed at minimizing the effects of sugary drinks on obesity.[5] Even more recently, the Associated Press obtained emails showing how a candy trade association funded and influenced