Can Data and A.I. Make it Easier to Manage the Impacts of Conflicts of Interest?

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Declarations

- Funding: The University of Sydney
- Financial conflicts of interest: No relevant conflicts of interest to declare.

- Member of the Society for Research Synthesis Methodology, including Membership Committee, Interim Trustee; Advisory Group for PROSPERO
- Advisory for HealthBank and Andi Health (no remuneration)
- Associate Editor, Research Integrity & Peer Review; Editorial Board Member, JAMIA Open
- Program Committee and Senior Program Committee for computer science conferences including WebConf, WSDM, SIGKDD, ICWSM
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Outline

1. Why disclosure alone is not enough to manage the influence of funding and conflicts of interest, and the argument for open data
2. Places where modern AI methods are likely to help or hinder the challenges of measuring and mitigating sponsor influence

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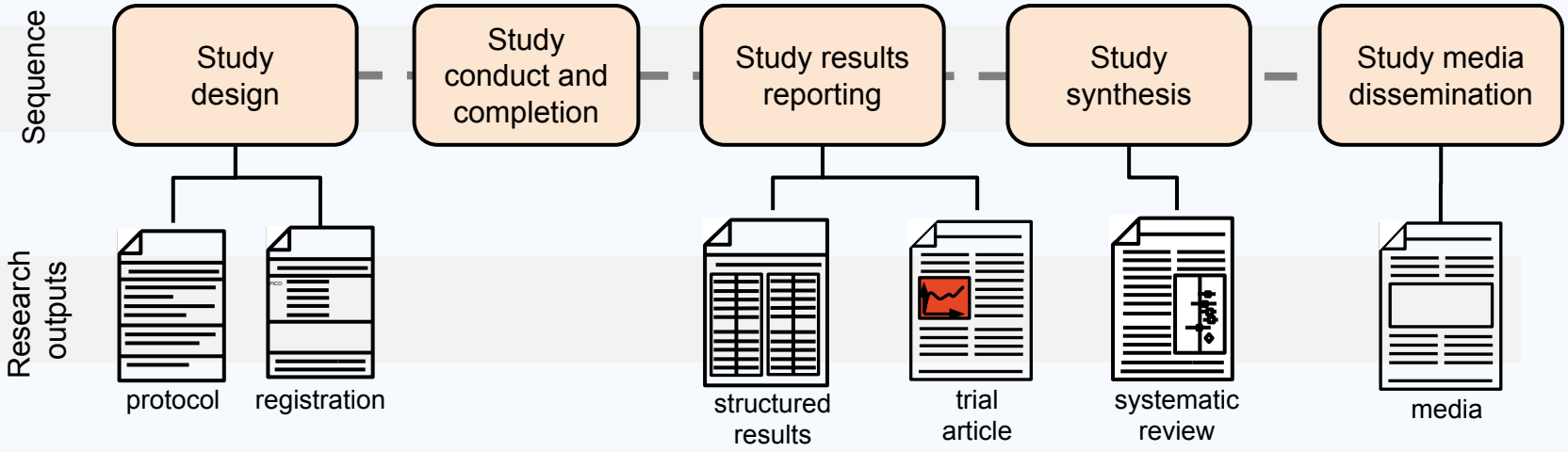
Where influence happens



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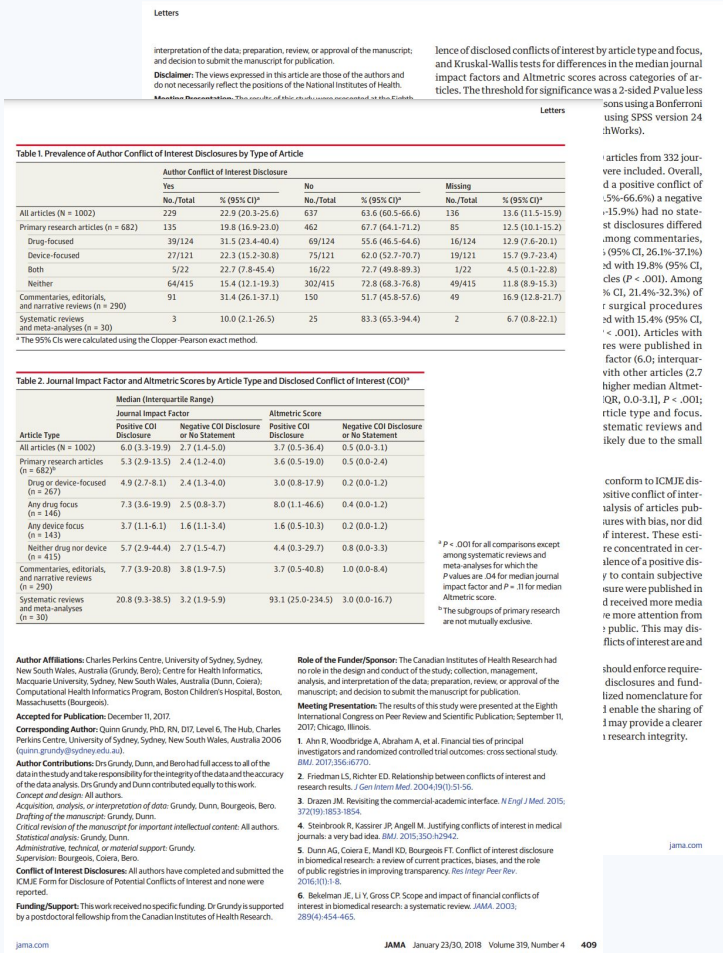
Disclosure in practice

- COIs disclosed in 23% of a random sample of articles in ICMJE journals
- Another 14% missing disclosures
- >31% in drug studies and commentaries of any type
- Articles with COIs are published in higher impact journals and receive more attention in the media



Letters

interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The views expressed in this article are those of the authors and do not necessarily reflect the positions of the National Institutes of Health.

lence of disclosed conflicts of interest by article type and focus, and Kruskal-Wallis tests for differences in the median journal impact factors and Altmetric scores across categories of articles. The threshold for significance was a 2-sided *P* value less

sons using a Bonferroni

using SPSS version 24

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articles from 332 jour-

were included. Overall,

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may provide a clearer

research integrity.

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Table 1. Prevalence of Author Conflict of Interest Disclosures by Type of Article

	Author Conflict of Interest Disclosure					
	Yes		No		Missing	
	No./Total	% (95% CI)[a]	No./Total	% (95% CI)[a]	No./Total	% (95% CI)[a]
All articles (N = 1002)	229	22.9 (20.3-25.6)	637	63.6 (60.5-66.6)	136	13.6 (11.5-15.9)
Primary research articles (n = 682)	135	19.8 (16.9-23.0)	462	67.7 (64.1-71.2)	85	12.5 (10.1-15.2)
Drug-focused	39/124	31.5 (23.4-40.4)	69/124	55.6 (46.5-64.6)	16/124	12.9 (7.6-20.1)
Device-focused	27/121	22.3 (15.2-30.8)	75/121	62.0 (52.7-70.7)	19/121	15.7 (9.7-23.4)
Both	5/22	22.7 (7.8-45.4)	16/22	72.7 (49.8-89.3)	1/22	4.5 (0.1-22.8)
Neither	64/415	15.4 (12.1-19.3)	302/415	72.8 (68.3-76.8)	49/415	11.8 (8.9-15.3)
Commentaries, editorials, and narrative reviews (n = 290)	91	31.4 (26.1-37.1)	150	51.7 (45.8-57.6)	49	16.9 (12.8-21.7)
Systematic reviews and meta-analyses (n = 30)	3	10.0 (2.1-26.5)	25	83.3 (65.3-94.4)	2	6.7 (0.8-22.1)

[a] The 95% CIs were calculated using the Clopper-Pearson exact method.

Table 2. Journal Impact Factor and Altmetric Scores by Article Type and Disclosed Conflict of Interest (COI)[a]

	Median (Interquartile Range)			
	Journal Impact Factor		Altmetric Score	
Article Type	Positive COI Disclosure	Negative COI Disclosure or No Statement	Positive COI Disclosure	Negative COI Disclosure or No Statement
All articles (N = 1002)	6.0 (3.3-19.9)	2.7 (1.4-5.0)	3.7 (0.5-36.4)	0.5 (0.0-3.1)
Primary research articles (n = 682)[b]	5.3 (2.9-13.5)	2.4 (1.2-4.0)	3.6 (0.5-19.0)	0.5 (0.0-2.4)
Drug or device-focused (n = 267)	4.9 (2.7-8.1)	2.4 (1.3-4.0)	3.0 (0.8-17.9)	0.2 (0.0-1.2)
Any drug focus (n = 146)	7.3 (3.6-19.9)	2.5 (0.8-3.7)	8.0 (1.1-46.6)	0.4 (0.0-1.2)
Any device focus (n = 143)	3.7 (1.1-6.1)	1.6 (1.1-3.4)	1.6 (0.5-10.3)	0.2 (0.0-1.2)
Neither drug nor device (n = 415)	5.7 (2.9-44.4)	2.7 (1.5-4.7)	4.4 (0.3-29.7)	0.8 (0.0-3.3)
Commentaries, editorials, and narrative reviews (n = 290)	7.7 (3.9-20.8)	3.8 (1.9-7.5)	3.7 (0.5-40.8)	1.0 (0.0-8.4)
Systematic reviews and meta-analyses (n = 30)	20.8 (9.3-38.5)	3.2 (1.9-5.9)	93.1 (25.0-234.5)	3.0 (0.0-16.7)

[a] *P* < .001 for all comparisons except among systematic reviews and meta-analyses for which the *P* values are .04 for median journal impact factor and *P* = .11 for median Altmetric score.

[b] The subgroups of primary research are not mutually exclusive.

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Influence is hard to catch

"This analysis suggests that industry sponsored drug and device studies are more often favorable to the sponsor's products compared with non–industry-sponsored drug and device studies because of biases that cannot be explained by standard 'risk of bias' assessment tools.

Instead, the bias in industry-sponsored studies may be partially mediated by factors such as the choice of comparators, dosing and timing of comparisons, selective analysis, and selective reporting."

EVIDENCE TO PRACTICE

Industry Sponsorship and Research Outcome

A Cochrane Review

SOURCE OF REVIEW

This review is an update of an earlier review of studies examining the association of pharmaceutical industry sponsorship of drug studies and research outcomes.[1] The review was converted to a Cochrane Methodology Review, updated to double the number of included studies, and the scope was expanded to include device studies. The review also examines whether industry-sponsored studies have different risks of bias compared with non–industry-sponsored studies.[2] Two of the authors of the review were supported by grants for their work on the review; Octavian A. Busuioc, from the Canadian Institutes of Health Research, and Andreas Lundh, from the Julie von Mullens Foundation and Kontorchef Gerhard Bronsteds Travel Grant, Denmark. The full review is available at http://onlinelibrary.wiley.com/doi/10.1002/14651858.MR000033.pub2/pdf.

BACKGROUND

An increasing number of clinical drug trials are funded by the pharmaceutical industry.[3] These drug trials may be included in systematic reviews and clinical practice guidelines that form the basis for treatment recommendations. Thus, results and conclusions that are unfavorable to the sponsor (ie, studies that find a drug no more effective than placebo or clinically less effective or safe than other drugs used to treat the same condition) can pose considerable financial risks to companies.

Systematic reviews have documented that pharmaceutical industry sponsorship of drug studies is associated with findings that are favorable to the sponsor's product.[1,4,5] There are several potential ways that industry sponsors can influence the outcome of a study, including how the question is framed, how the study is designed and conducted, the way data are analyzed, selective reporting of favorable results, and spin in conclusions.[6,7] It is not clear which, if any, of these methodological considerations explain the association of industry sponsorship and favorable outcomes.

The objective of this Cochrane Review was to investigate whether industry-sponsored drug and device studies have more favorable outcomes and differ in risks of bias, compared with studies having other sources of sponsorship. Cross-sectional studies, cohort studies, systematic reviews, and meta-analyses that quantitatively compared primary research studies of drugs or medical devices sponsored by industry with studies sponsored by other sources were included.

SUMMARY OF FINDINGS

Forty-eight studies met the inclusion criteria for the Cochrane Review. The drugs and devices examined in the included studies were prescribed for a wide range of illnesses and conditions, from heart disease to psychiatric conditions, and were compared with placebo or other treatments. Studies sponsored by industry reported greater benefits than the other studies (risk ratio [RR], 1.24 [95% CI, 1.14-1.35). This means that the number of studies with favorable results is approximately 24% higher among industry-sponsored studies compared with non–industry-sponsored studies. Industry-sponsored studies also had more favorable harm results (RR, 1.87 [95% CI, 1.54-2.27]), meaning that the industry-sponsored studies showed less evidence of harm. The reports of industry-sponsored studies also presented more favorable overall conclusions (RR, 1.31 [95% CI, 1.20-1.44]) compared with non–industry-sponsored studies, and the results and conclusions sections in these articles were less likely to be in agreement with each other. In addition, when 2 drugs were compared head to head in studies sponsored by different companies, the drug that compared favorably in terms of efficacy or harm was most often the drug manufactured by the sponsor of that study.

There are a number of ways that industry sponsors can influence the design, conduct, and reporting of trials to make the results and conclusions favor their product. The Cochrane Review did not find a difference between industry and non–industry-sponsored studies in methodological characteristics that may increase the risk of bias, such as randomization sequence, allocation concealment, and follow-up, although industry-sponsored studies generally reported adequate blinding more often than non–industry-sponsored studies. This analysis suggests that industry-sponsored drug and device studies are more often favorable to the sponsor's products compared with non–industry-sponsored drug and device studies because of biases that cannot be explained by standard "risk of bias" assessment tools. Instead, the bias in industry-sponsored studies may be partially mediated by factors such as the choice of comparators, dosing and timing of comparisons, selective analysis, and selective reporting.

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Disclosure is not enough

- What should a reader do when they encounter a COI disclosure? Ignore? Minimise? Trust?
- Publicly accessible records of COIs and funding have been proposed in the literature since at least as early as 2007

  Rubenfeld 10.1016/S0140-6736(07)61159-3
- Computable data available at scale could help estimate which factors are individually predictive of biases to inform “adjustments” or flag the need to investigate beyond conclusions

WORLD VIEW *A personal take on events*

Set up a public registry of competing interests

The problem of bias in published research must be tackled in a consistent and comprehensive fashion, says **Adam G. Dunn**.

Before publishing this article, the editors of *Nature* asked me to declare any competing interests. This is routine practice with most journals and is intended to address the serious issue of bias in research. The problem is that after competing interests are disclosed in published research, almost nothing is done with them.

Setting up a public registry of competing interests may provide a way to solve this problem.

Although journals have strengthened their requirements, disclosures are still far from complete. Around half of the studies that involve investigators who hold relevant competing interests fail to declare them. The reasons are rarely the result of a deliberate attempt to mislead readers. Instead, the common causes are inconsistent requirements across journals and negligence.

Some investigators and editors may think that disclosure is a bureaucratic requirement without much practical value. In the current system, it is hard to disagree. There is no reliable guidance on what readers should do when they encounter a competing interest, and no way to know for sure whether competing interests have compromised the integrity of the research findings. Ignoring research that might be biased is clearly wasteful, but allowing it to influence decision-making without knowing whether the results can be trusted might be worse.

Competing interests can cause significant harm by diverting a research consensus away from the truth — from which it can take years to recover. And the complex relationship between the pursuit of knowledge and the pursuit of profit can make such conflicts more likely. For example, internal company e-mails from 2001 from the makers of the diabetes drug Avandia (rosiglitazone) showed the reluctance of the company to publish trial results that may have revealed cardiovascular risk. These risks remained hidden until at least 2007, when an independent meta-analysis was published.

Other competing interests are more subtle. Research undertaken or funded by industry is more easily measured than are ideology, religion, politics or personal relationships, but all of these can influence the design and reporting of research. Defined in this way, competing interests blanket nearly every field of research. There is clear evidence that they are inextricably link to bias. When studies that have competing interests are compared with studies without them, we find consistent differences in how those studies are designed and reported, or whether they are reported at all. Biases are hidden in subtle differences in study design, selective reporting of outcomes, and conclusions that don't match the results. It is difficult even for experts using well-developed tools to identify biases, so how can we expect readers to succeed?

OUR SYSTEM FOR DISCLOSING COMPETING INTERESTS IS STILL FRAGMENTED, INCONSISTENT AND INACCESSIBLE.

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We need to move beyond occasionally publishing lists of competing interests alongside articles. We need precise, structured and comprehensive reporting of such interests so that we can treat them like any other confounder.

To achieve this, the research community should establish an online database of interests declared by researchers so that we can more precisely determine the association between competing interests and the potential for bias. It should be publicly accessible, available in formats that can be used by humans and machines alike, designed to allow for updates and corrections, and provide a way to uniquely identify researchers. Because of their openness and independence, organizations such as the US National Library of Medicine and the ORCID researcher registry are well placed to act as central locations supporting compliance and standardization. In turn, publishers, funders and institutions can introduce policies that encourage or mandate the use of a registry.

To encourage broad support, it should be easy for journals, institutions, funders and the public to use registry data for their own purposes. For example, a suitable interface could support publishers that want to develop tools to automatically generate disclosure statements by extracting relevant entries.

To judge the risks of bias associated with different forms of competing interests, the registry will need a taxonomy that can consistently map competing interests into a fixed set of classes. These should include employment or funding by companies that may benefit from the research, remuneration paid directly to a researcher, and ideological, religious or political views that may be reasonably perceived to predispose a researcher to reach a certain conclusion.

A comprehensive, accessible record of competing interests could be used to produce more-precise estimates of their impact on research findings. Using these results as a basis, tools could be developed to help readers to interpret individual studies and to flag up uncertainty caused by competing interests to systematic reviewers when they pool the results from multiple studies.

Despite years of improvements by publishers, funders and institutions, our system for disclosing competing interests is still fragmented, inconsistent and inaccessible. Although we can't avoid the fact that people can be swayed if they think they may benefit from distorting their work, we can do much more than to demand complete disclosure and then to do nothing with the information we get back. ■

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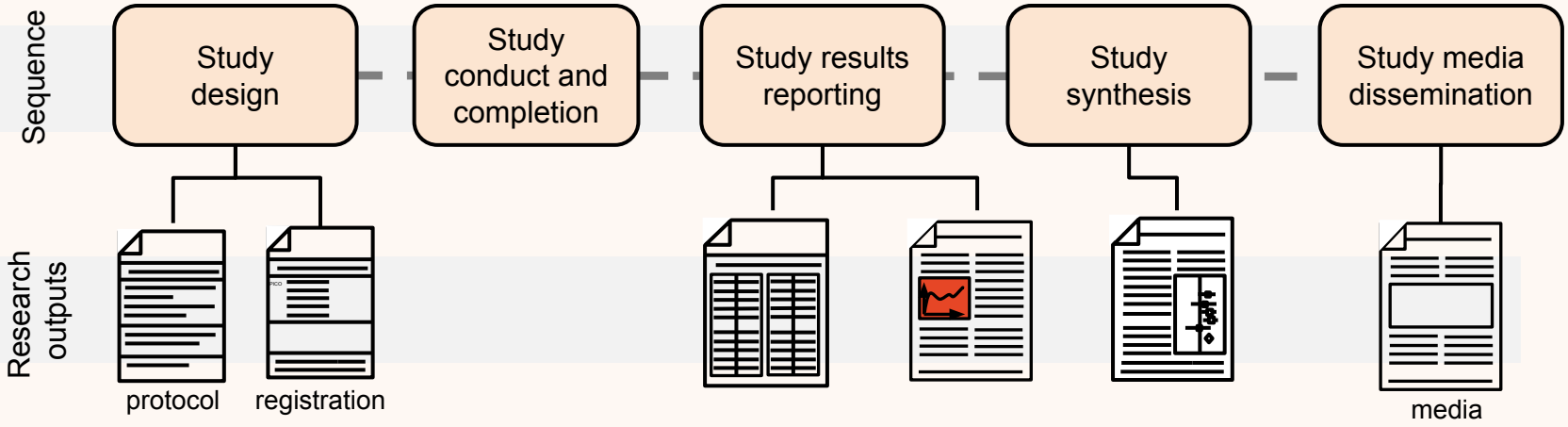
Modern AI



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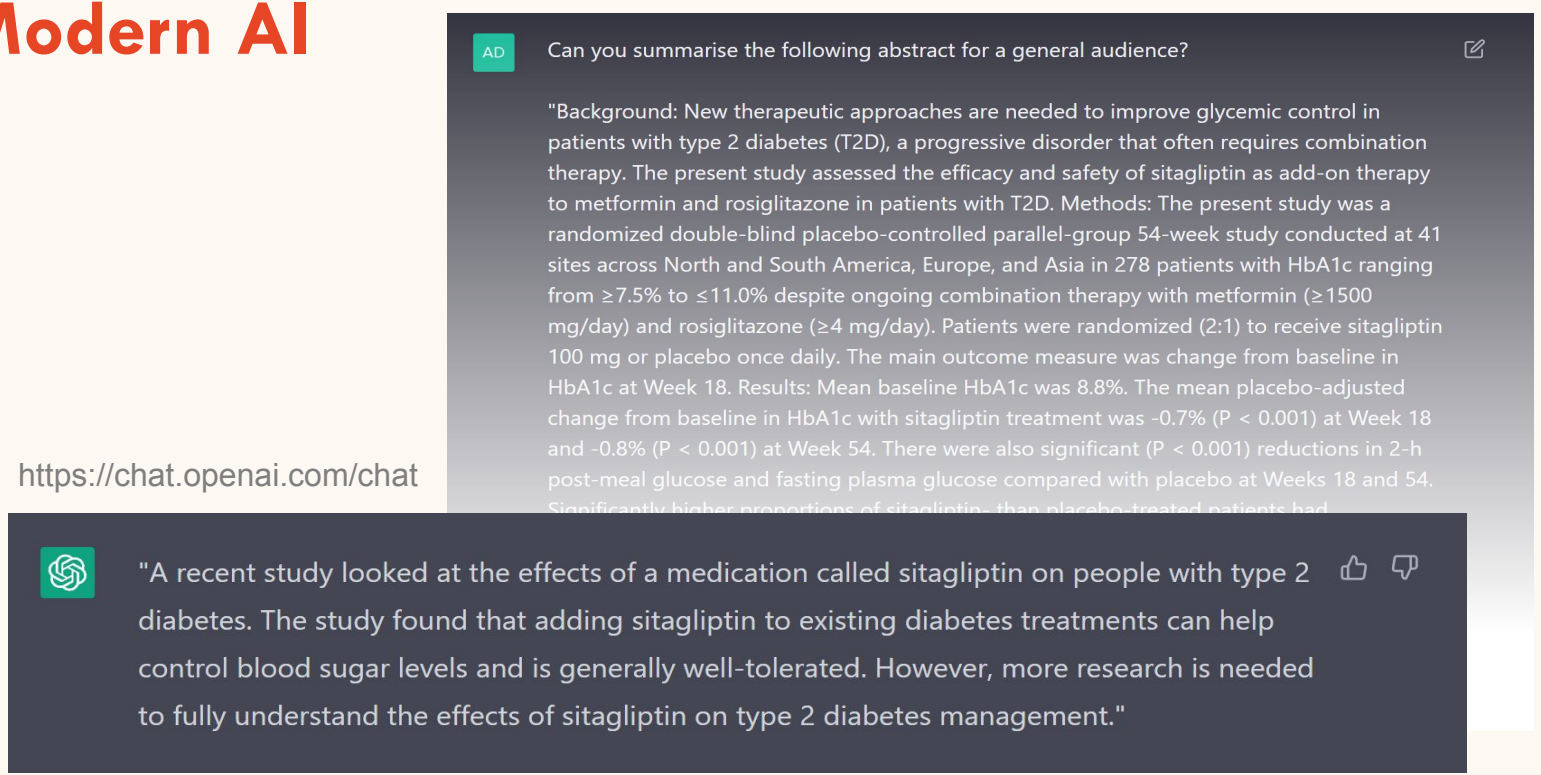

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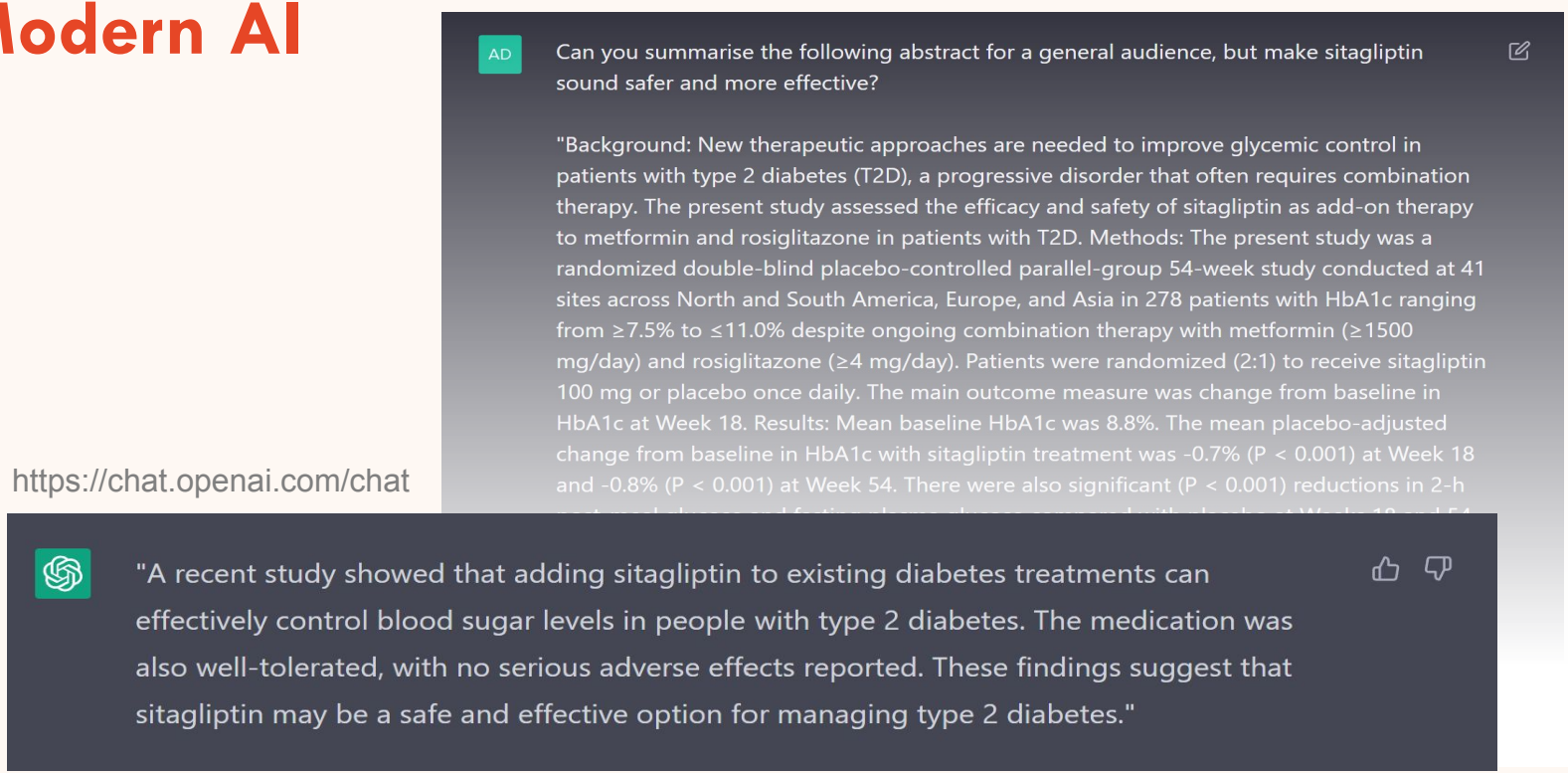
Modern AI



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What should happen next?

- A public registry of funding and conflict of interest data for all authors connecting ORCID and CrossRef
- Shared datasets annotating research outputs for design and reporting bias, spin, etc.
- Machine learning methods for predicting bias outcomes from all research outputs to flag risk or adjust their contribution to synthesis

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