

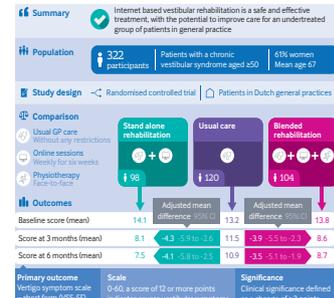
research



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COMMENTARY

Declaring interests and restoring trust in medicine

We need to record and manage conflicts of interest across healthcare

There is a long history of individuals and organisations attempting to fix the biases that arise from conflicts of interests. Such conflicts contribute to a breakdown in research integrity¹ and lead to more favourable outcomes for sponsors,² the withholding of results,³ and an overall lack of trust in research.⁴

Journals disclose authors' potential conflicts of interest to improve the objective assessment of research, increase its credibility, and make peer reviewers, editors, and readers aware of—and account for—the biases that conflicts induce. The International Committee of Medical Journal Editors (ICMJE) considers the purposeful failure to disclose conflicts of interest a form of misconduct. Whether disclosure influences peer reviewers' assessment of the quality of submitted research is, however, unclear.

John and colleagues (p 228) tackled this issue by asking

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Access to disclosures had no impact on reviewers' quality rating of research

whether revealing authors' conflicts at peer review affects the quality rating of submitted manuscripts.⁵ From a sample of 1480 research papers submitted to *Annals of Emergency Medicine*, peer reviewers were randomised to receive a full conflict of interest disclosure or no disclosure. Access to disclosures had no impact on reviewers' quality rating of research.

To many, this result might not be surprising. Little agreement exists on what constitutes effective peer review or the skills required to provide it,⁶ and there is little evidence that peer review does what many think it should do—ensure the quality of research.⁷

Although peer review is highly regarded by researchers and considered essential for publication of research⁸ it has many flaws: in one study, 607 BMJ peer reviewers detected

only one third of major errors inserted into test trial reports, despite training;⁹ in another, 260 readers missed 95% of the 39 discrepancies in a clinical trial report.¹⁰ Peer review itself is of questionable value and could offer false reassurance.

We don't know what should happen when conflicts of interest are disclosed to peer reviewers. It is currently unclear if disclosure identifies, reduces, or avoids biases in research, or if it simply creates false reassurance among reviewers and readers.¹¹ Estimating the impact of conflicts of interest is a difficult task.¹²

Goupil and colleagues (p 228) provide more tangible evidence that gifts from pharmaceutical companies to French general practitioners (GPs) might influence prescribing.¹³ Their retrospective study, using data from the French Transparency in Healthcare and National Health Insurance databases, reports that GPs who received no gifts prescribed cheaper generic drugs and had better drug prescription

efficiency indicators than those in receipt of gifts.

While these results are consistent with previous evidence,¹⁴ they highlight the value of the Transparency in Healthcare database. Without it, gifts to French GPs from pharmaceutical companies would not be readily accessible for analysis.

The French “Sunshine Act” (The Loi Bertrand) established the Transparency in Healthcare database that became publicly accessible in 2018. The law requires health products companies to disclose agreements with healthcare providers publicly within 15 days. Any benefit to the provider exceeding a value of €10.00 (£8.60) in cash or in kind must be disclosed within six months.¹⁵ Although no direct causal link was found between the gifts received and GP prescribing, Goupil and colleagues’ study shows the importance of disclosure legislation: gifts to French GPs are common (36 232/41 257 GPs (87.8%) listed in the database had received gifts) and are associated with poorer prescribing practices and increased costs to the system.

The influence of organisational or individual conflicts on clinical practice demands a system-wide strategy to manage and mitigate such conflicts. Our current understanding of the effects of conflicts of interest is impeded by ineffective strategies to search for, report, and record them. Laws that mandate full transparency—with expectations on both individuals and industry to provide payment data—solve the problems associated with voluntary disclosure and might permit a more thorough understanding of the wide ranging impacts that conflicts of interest have across healthcare. Better data on conflicts would mean better research, a clearer understanding, and more coherent action to reduce harm—a process that might just restore some much needed trust in research.

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Find the full version with references at <http://dx.doi.org/10.1136/bmj.l6236>

Declaring interests and restoring trust in medicine

ORIGINAL RESEARCH Randomised controlled trial

Effect of revealing authors’ conflicts of interests in peer review

John LK, Loewenstein G, Marder A, Callahan ML

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Study question What is the effect of disclosing authors’ conflict of interest (COI) declarations to peer reviewers at a medical journal?

Methods Reviewers (n=838) reviewed manuscripts submitted to *Annals of Emergency Medicine* between 2 June 2014 and 23 January 2018 inclusive (n=1480 manuscripts). Reviewers were randomised to either receive (treatment) or not receive (control) authors’ full International Committee of Medical Journal Editors format COI disclosures before doing their review. Reviewers rated the manuscripts as usual on eight quality ratings and were then surveyed to obtain

Effect of receiving authors’ conflict of interest (COI) disclosures for given manuscript on reviewers’ overall evaluation of manuscripts

Model	No of manuscripts	Mean (SD)		Difference (95% CI)
		Treatment group	Control group	
1. All manuscripts	888	2.74 (1.13)	2.70 (1.11)	0.04 (–0.05 to 0.14)
2. Manuscripts with COIs	319	2.96 (1.16)	2.85 (1.12)	0.11 (–0.05 to 0.26)
3. Manuscripts without COIs	569	2.62 (1.10)	2.62 (1.09)	0.01 (–0.11 to 0.12)

Model 1 denotes overall treatment effect (that is, collapsing across whether authors disclosed versus did not disclose COIs). Model 2 tested for treatment effects among conflicted manuscripts. Model 3 tested for treatment effects among unconflicted manuscripts.

ORIGINAL RESEARCH

Retrospective study using two French databases

Association between gifts from pharmaceutical companies to French general practitioners and their drug prescribing patterns in 2016

Goupil B, Balusson F, Naudet F, et al

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Find this at: <http://dx.doi.org/10.1136/bmj.l6015>

Study question What is the association between gifts from pharmaceutical companies to French general practitioners (GPs) and their prescribing patterns for some drugs?

Methods In this retrospective study, 41 257 GPs who throughout 2016 worked exclusively in the private sector and had at least five registered patients were included and divided in to six groups according to the monetary value of the gifts received from pharmaceutical companies (from none to >€1000). The main outcome measures were the amount reimbursed by the National Health Insurance (the French system that offers healthcare coverage to all citizens) for drug prescriptions per visit and

11 drug prescription efficiency indicators used to calculate the GPs’ performance related financial incentives by the French National Health Insurance. Doctor and patient characteristics were used as adjustment variables.

Study answer and limitations The amount reimbursed by the National Health Insurance for drug prescriptions per visit was lower in the GP group with no gifts reported in the Transparency in Healthcare database in 2016 and since its launch in 2013 (no gift group) compared with the GP groups with at least one gift in 2016 (–€5.33, 99.9% confidence interval –€6.99 to –€3.66 compared with the GP group with gifts valued at €1000 or more reported in 2016; P<0.001). The no gift group also prescribed more frequently generic antibiotics (2.17%, 1.47% to 2.88% compared with the ≥€1000 group), antihypertensives (4.24%, 3.72% to 4.77% compared with the ≥€1000 group), and statins (12.14%, 11.03% to 13.26% compared with the ≥€1000 group) than GPs with at least one gift between 2013 and 2016 (P<0.001). The no gift group also prescribed fewer

“counterfactual scores” (the scores they believed they would have given had they been assigned to the opposite arm), as well as attitudes towards COIs. The primary outcome measure was the overall quality score that reviewers assigned to the manuscript on submitting their review (1-5 scale). The trial had 99% power to detect a 0.4 point difference, determined previously by editors to be the minimal significance threshold for a difference in score that would influence their editorial decision.

Study answer and limitations As currently implemented, COI disclosure had no effect on any quality ratings of real manuscripts being evaluated for publication by real peer reviewers. Reviewers’ mean ratings of manuscript

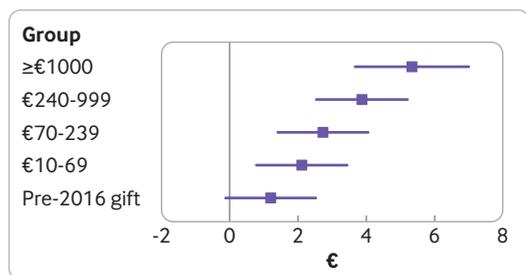
quality were 2.70 (SD 1.11) in the control group versus 2.74 (1.13) in the treatment group (mean difference 0.04, 95% confidence interval -0.05 to 0.14). Limitations include potential generalisability, that no effect was found when the nature of the funding source disclosed was taken into account, and that giving reviewers COI information may have affected downstream measures of editors’ decisions.

What this study adds The findings suggest that authors’ COI disclosures have no effect on peer reviewers’ assessments of the quality of research.

Funding, competing interests, and data sharing This research was funded using LKJ’s annual research budget allocation from Harvard Business School. The authors have no competing interests. No additional data available.



Conflict of interest disclosure had no effect on any quality ratings of real manuscripts being evaluated for publication by real peer reviewers



Adjusted mean differences (99.9% confidence intervals) of amount reimbursed for drug prescriptions per visit according to monetary value of gifts from pharmaceutical companies to five GP groups in 2016 compared with GP group with no gift between 2013 and 2016. Threshold P=0.001

benzodiazepines for more than 12 weeks (-0.68%, -1.13% to -0.23% compared with the €240-999 group) and vasodilators (-0.15%, -0.28% to -0.03% compared with the ≥€1000 group) than GPs with gifts valued at €240 or more reported in 2016, and more angiotensin converting enzyme (ACE) inhibitors compared with all ACE and sartan prescriptions (1.67%, 0.62% to 2.71%) than GPs with gifts valued at €1000 or more reported in 2016 (P<0.001). Differences were not significant for the prescription of aspirin and generic antidepressants and generic proton pump inhibitors. As this is an observational study, it is susceptible

to residual confounding, and no causal relation can be concluded.

What this study adds The findings of this study suggest that French GPs who do not receive gifts from pharmaceutical companies have better drug prescription efficiency indicators and less costly drug prescriptions than those who do receive gifts.

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ORIGINAL RESEARCH Three armed randomised controlled trial

Internet based vestibular rehabilitation with and without physiotherapy support for adults aged 50 and older with a chronic vestibular syndrome in general practice

van Vugt VA, van der Wouden JC, Essery R, et al
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 Find this at: <http://dx.doi.org/10.1136/bmj.l5922>

Study question Is internet based vestibular rehabilitation, with and without physiotherapy support, more effective than usual care in decreasing symptoms of chronic vestibular syndromes in adults in primary care?

Methods This three armed, individually randomised controlled trial in 59 general practices in the Netherlands included 322 adults, aged 50 years and older, with a

Comparison of primary outcome between treatment groups

VSS-SF (intention to treat)*	Mean (SD) score			Adjusted mean difference (95% CI)†	
	Stand alone VR (n=98)	Blended VR (n=104)	Usual care (n=120)	Stand alone VR v usual care (n=218)	Blended VR v usual care (n=224)
Baseline	14.1 (8.9)	13.8 (8.3)	13.2 (8.6)	-	-
3 months	8.1 (7.4)	8.6 (7.1)	11.5 (9.9)	-4.3 (-5.9 to -2.6)	-3.9 (-5.5 to -2.3)
6 months	7.5 (7.8)	8.7 (6.9)	10.9 (9.3)	-4.1 (-5.8 to -2.5)	-3.5 (-5.1 to -1.9)

VR=vestibular rehabilitation; VSS-SF=vertigo symptom scale-short form, range 0-60, clinically relevant difference 3 points.
 *All participants analysed according to allocation.
 †Adjusted for baseline values, repeated measurements within participants, age, sex, level of education, living situation, number of chronic diseases, time since vestibular diagnosis, and presence of a panic disorder, generalised anxiety disorder, or major depressive disorder at baseline.

chronic vestibular syndrome (persisting vestibular symptoms for at least one month and exacerbated or triggered by head movements). Participants received either stand alone vestibular rehabilitation (n=98), blended vestibular rehabilitation (n=104), or usual care (n=120). Stand alone vestibular rehabilitation consisted of a six week, internet based intervention with weekly online sessions and daily exercises. In blended

vestibular rehabilitation, the same internet based intervention was supplemented by face-to-face physiotherapy support. Participants in the usual care group received standard care from their general practitioner, without any restrictions. The primary outcome was vestibular symptoms after six months as measured by the vertigo symptom scale-short form (VSS-SF; clinically relevant difference ≥3 points).

Study answer and limitations After six months, participants in the stand alone and blended vestibular rehabilitation groups reported clinically relevant lower VSS-SF scores than participants in the usual care group (adjusted mean difference -4.1 points, 95% confidence interval -5.8 to -2.5, and -3.5 points, -5.1 to -1.9, respectively). No serious adverse events related to vestibular rehabilitation occurred during the trial. Patients motivated to treat their vestibular symptoms with exercises might have been more likely to participate in the trial.

What this study adds Stand alone and blended internet based vestibular rehabilitation are effective and safe interventions to treat patients aged 50 years and older with a chronic vestibular syndrome. Online vestibular rehabilitation is an easily accessible form of treatment that can potentially improve care for an undertreated group of patients in primary care.

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Trial registration Netherlands Trial Register NTR5712.

