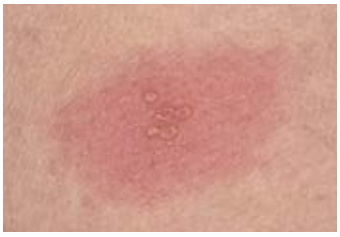
research



Adult exposure to varicella zoster associated with reduction in shingles p 101

Patient groups tend to support commercial sponsors' interests p 102

Blinding in clinical trials: is it necessary? p 104

ORIGINAL RESEARCH Self controlled case series study

Risk of herpes zoster after exposure to varicella to explore the exogenous boosting hypothesis

Forbes H, Douglas I, Finn A, et al

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Study question What are the magnitude and duration of any hypothesised protective effect of household exposure to a child with varicella on the relative incidence of herpes zoster in adults?

Methods This self controlled case series analysis used data from UK general practices contributing to the Clinical Practice Research Datalink. 9604 adults (≥18 years) with a zoster diagnosis (in primary care or hospital records) between 1997 and 2018 were included who, during their observation period, lived with a child (<18 years) diagnosed as having varicella. The relative incidence of zoster was estimated over 20 years after household exposure to a child with varicella, compared with baseline time (that is, all other time, excluding the 60 days before exposure to varicella, to allow for a zoster event resulting in an increased risk of varicella).

Study answer and limitations Evidence suggested that in the two years after exposure to a childhood case of varicella in the household, adults were 33% less likely to develop zoster (incidence ratio 0.67, 95% confidence interval 0.62 to 0.73) and 27% less likely in the 10-20 years after exposure (0.73, 0.62 to 0.87), compared with baseline time. Some evidence suggested that the boosting effect was stronger closer to the time of exposure to varicella. It is possible that some of the children with varicella identified in general practice records had more severe infection.

What this study adds An association was found between household exposure to varicella in adults and a reduced risk of zoster by around 30% over 20 years.

Funding, competing interests, and data sharing

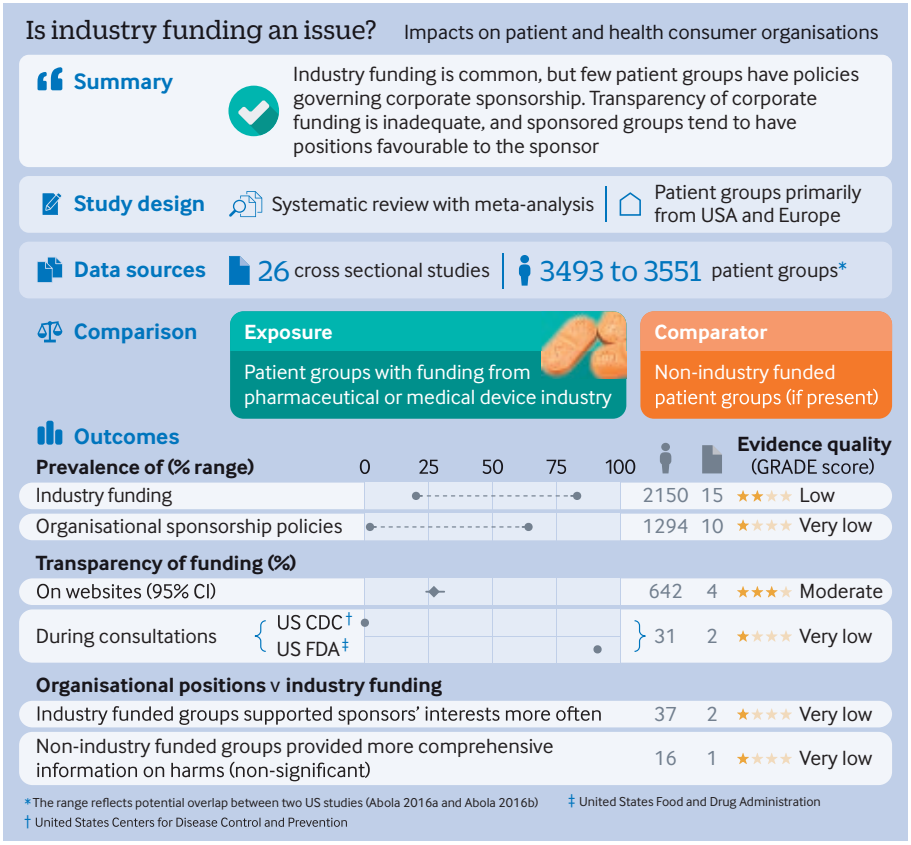
This study was funded by a fellowship to HF from Health Data Research UK. AF has research funding (related to meningococcal carriage) paid to the University of Bristol from GSK.
No additional data available.

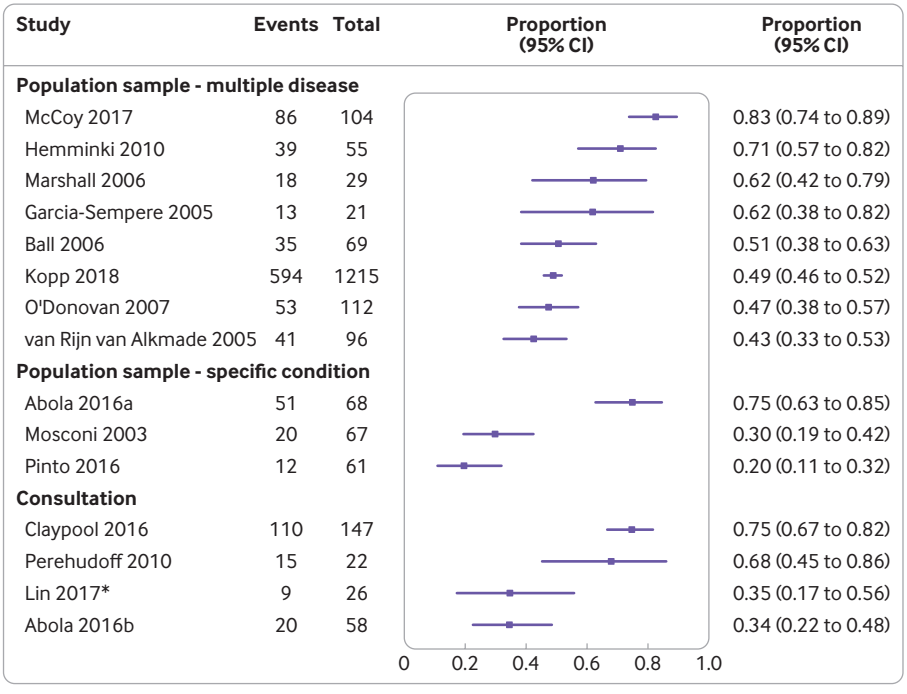
Adjusted incidence ratios for zoster in adults (n=9604) during risk periods after household exposure to a child with varicella

Time period	No of zoster events	Person years of observation	Crude incidence ratio (95% CI)	Age adjusted incidence ratio* (95% CI)	Age, calendar time, and season adjusted incidence ratio* (95% CI)
Baseline†	4116	56 417	1.00	1.00	1.00
60 days pre-exposure	433	1539	3.17 (2.86 to 3.51)	2.89 (2.60 to 3.21)	2.87 (2.58 to 3.19)
Post-exposure risk period (years):					
0-<2	1177	18 031	0.77 (0.72 to 0.82)	0.68 (0.63 to 0.74)	0.67 (0.62 to 0.73)
2-<5	1432	22 2901	0.85 (0.80 to 0.91)	0.70 (0.64 to 0.77)	0.69 (0.63 to 0.76)
5-<10	1546	24 620	0.96 (0.89 to 1.02)	0.70 (0.63 to 0.79)	0.69 (0.61 to 0.77)
10-20	900	13 317	1.25 (1.14 to 1.37)	0.77 (0.65 to 0.90)	0.73 (0.62 to 0.87)

*Age defined by 40 quantiles of age at event (herpes zoster); calendar time defined as 1997-98, 1999-2000, 2001-02, 2003-04, 2005-06, 2007-08, 2009-10, 2011-12, 2013-14, 2015-16, and 2017-18; and season defined as winter (December-February), spring (March-May), summer (June-August), and autumn (September-November).
†All time from observation start to 60 days pre-exposure, and up to 20 years after exposure: seven zoster events occurred after the 20 years after exposure.

Corporate sponsorship of patient groups





Forest plot of prevalence of industry funding of patient groups. *Data received from authors. See full paper on bmj.com for references of studies

Funding, competing interests, and data sharing No specific funding was received for this study. Authors PM and CC report an unconditional grant from GlaxoSmithKline outside the submitted work. PM is a member of the Board of Europa Donna. BM is a member of the European network of Health Action International. BM acted as an expert witness on behalf of plaintiffs in a Canadian class action suit on cardiovascular risks of testosterone. No additional data available.

Systematic review registration PROSPERO CRD42017079265

ORIGINAL RESEARCH

Systematic review with meta-analysis

Industry funding of patient and health consumer organisations

Fabbri A, Parker L, Colombo C, et al

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Study question What are the extent and characteristics of pharmaceutical or medical device industry funding of patient groups?

Methods This systematic review and meta-analysis of observational studies (mainly from the US and Europe) reported at least one of the following outcomes: prevalence of industry funding; proportion of industry funded patient groups that disclosed information about this funding; and association between industry funding and organisational positions on health and policy issues. Data sources were Ovid Medline, Embase, Web of Science, Scopus, and Google Scholar from inception to January 2018, reference lists of eligible studies, and experts in the specialty.

Study answer and limitations 26 cross sectional studies met the inclusion criteria. Of these, 15 studies estimated the prevalence of industry funding, which ranged from 20% (12/61) to 83% (86/104). Among patient organisations that received industry funding, 27% (175/642; 95% confidence interval 24% to 31%) disclosed this information on their websites. Prevalence estimates of organisational policies that govern corporate sponsorship ranged from 2% (2/125) to 64% (175/274). Four studies analysed the relation between industry funding and organisational positions on a range of highly controversial issues. Industry funded groups generally supported sponsors' interests. However, nearly all the studies were conducted in high income countries, therefore findings might not be generalisable to middle or low income settings.

What this study adds Industry funding of patient groups seems to be widespread in high income countries. Few groups have policies that govern industry funding, and transparency is inadequate. Studies that examined associations between funding status and policy positions were limited but reported that industry funded groups generally supported sponsors' interests.

COMMENTARY It's time for mandatory disclosure

Non-profit patient groups provide support services to patients and families, increase public awareness through educational outreach, participate in the development of clinical guidelines, lobby on policies affecting access and care, and invest in novel research on therapeutics. Although many focus on a particular disease, others focus on the needs and interests of healthcare consumers more generally.

Power and influence

Various sources provide financial assistance, including pharmaceutical and medical device companies. Given the considerable power of patient groups to influence healthcare policy and individual medical decision making, and given research documenting the effects of even small payments on physician practices,[1] monetary relationships between patient groups and industry have prompted recent concern.

Fabbri and colleagues provide the first systematic review on this topic to examine the extent of ties between patient groups and industry, the policies of patient groups surrounding corporate sponsorship, and the effect of industry support on the public position statements made by patient groups.[2] This builds on a recent qualitative study in *The BMJ* by Parker and colleagues exploring the attitudes of patient groups towards industry.[3]

Fabbri and colleagues performed a comprehensive meta-analysis of 26 cross sectional studies. Fifteen publications examined the prevalence of corporate sponsorship: between 20% and 83% of patient groups were estimated to have relationships with industry, supplying anywhere from a few per cent to near totality of annual operating expenses. Only a quarter of organisations receiving monetary support disclosed this relationship online, and transparency policies were insufficient. At most, only two thirds had organisational policies to regulate industry funding. The results of four studies examining association between group positions and corporate sponsorship show substantial divergence between funded and non-funded groups, which largely reflect differences in industry versus patient interests.[2]

These results suggest that financial relationships pose real, not potential, conflicts of interest

These findings reveal the breadth and depth of relationships between patient groups and pharmaceutical and medical device companies. The issue is likely even more widespread than portrayed, as included studies only examined relationships with pharmaceutical and medical device companies, excluding connections with the food industry, health insurers, and other companies in the wellness sphere.[2] Additionally, patient groups are not the only patient voices affected—individuals can become corporate sponsored influencers with no public disclosure of their commercial relationships.[4]

More importantly, these results suggest that financial relationships pose real, not potential, conflicts of interest—with alignment between organisational positions and industry interests even when contrary to patient welfare. This is of particular concern given the power of patient groups internationally. When pharmaceutical and medical device companies lobby political leaders, the financial motivation is readily apparent, but when patient groups or individual patients engage in similar efforts, government and society assume they are acting independently in the interests of patients.[5]

Legal channels

Patient groups also may provide a channel through which companies can target patients in the many countries where direct-to-consumer advertising is illegal. As Parker and colleagues noted in their previous study, when a patient group does not already exist, companies have been known to establish one, placing carefully selected leaders at the top. In qualitative interviews with patient group staff, the leaders readily acknowledged the "give and take," transactional nature of corporate sponsorship.[3] Society's sympathy for patients' lived experiences might also underpin hesitancy to legislate in this sphere.

Sunshine acts

Fortunately, the beginnings of a solution have already been developed and implemented by governments in another context. Acknowledging the potential for undue influence as well as the failure of voluntary policies, particularly among those receiving large payments,[7] "sunshine" acts in the US and several European countries mandate disclosure of industry payments to physicians.[8 9] Although not a cure-all, disclosure upholds moral commitments to honesty and integrity while providing a starting point from which governments and the public can begin to recognise and interpret industry's influence.[10]

Fabbri's and Parker's teams provide yet more evidence that conflicts of interest between patient groups and industry are extensive and run deep. Voluntary disclosure is not working. It is time for mandatory disclosure—only then can stakeholders explore how best to respond to disclosed information and develop additional legislative safeguards as needed to fortify public trust.

Bethany Bruno
Susannah Rose roses2@ccf.org
See bmj.com for author details

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Impact of blinding on estimated treatment effects in randomised clinical trials

Moustgaard H, Clayton GL, Jones HE, et al

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Find this at: http://dx.doi.org/10.1136/bmj.l6802

Study question What is the average impact of lack of blinding of patients, healthcare providers, and outcome assessors, on estimated treatment effects in randomised clinical trials?

Methods A meta-epidemiological study included 142 meta-analyses (1153 randomised clinical trials) published in the Cochrane Database of Systematic Reviews (2013-14) on any topic. The average ratio of odds ratios (ROR) was estimated between trials with and without blinding (or unclear blinding) of either patients, healthcare providers, or outcome assessors. ROR values less than 1 indicated exaggerated effect estimates in trials without blinding.

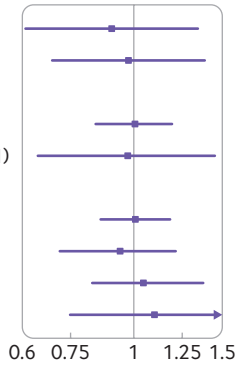
Study answer and limitations No evidence was found of a difference, on average, in estimated treatment effects between randomised clinical trials with and without blinding of patients, between trials with and without blinding of healthcare providers, and between trials with and without blinding of outcome assessors. The ROR for lack of blinding of patients was 0.91 (95% credible interval 0.61 to 1.34) in 18 meta-analyses with patient reported outcomes, and 0.98 (0.69 to 1.39) in 14 meta-analyses with outcomes reported by blinded observers. In 74 meta-analyses of trials not reported as double blind versus those that were double blind, the ROR was 1.02 (0.90 to 1.13). The study was limited by risk of residual confounding and lack of precision.

What this study adds Blinding might be less important than often believed or these results reflect meta-epidemiological study limitations. We suggest replication of this study and no changes to methodological practice at this stage.

Funding, competing interests, and data sharing The study received no specific funding. All authors declare no conflicts of interest. Model code is available in the web appendix, and the dataset from the corresponding author.

ANALYSIS, p 109

Trial group (No of contributing meta-analyses, contributing trials)	Ratio of odds ratios (95% credible interval)	Ratio of odds ratios (95% credible interval)	Increase in standard deviation between trials*	Standard deviation between meta-analyses†
(Ia) Patients - patient reported outcomes (18, 132)		0.91 (0.61 to 1.34)	0.22	0.20
(Ib) Patients - blinded observer reported outcomes (14, 95)		0.98 (0.69 to 1.39)	0.10	0.11
(IIa) Healthcare providers - healthcare provider decision outcomes (29, 173)		1.01 (0.84 to 1.19)	0.06	0.06
(IIb) Healthcare providers - outcomes assessed by blinded observers/patients (13, 91)		0.97 (0.64 to 1.45)	0.10	0.13
(III) Outcome assessor - subjective outcomes (46, 397)		1.01 (0.86 to 1.18)	0.05	0.09
Low (15, 155)		0.94 (0.71 to 1.21)		
Moderate (23, 165)		1.05 (0.83 to 1.38)		
High (8, 77)		1.10 (0.75 to 1.63)		



Estimated ratio of odds ratios and effects on heterogeneity associated with blinding status of patients, healthcare providers, and outcome assessors. Unadjusted analyses. *Increase in standard deviation between trials: (Ia) 0.22 (95% credible interval 0.02 to 0.60), (Ib) 0.10 (0.01 to 0.30), (IIa) 0.06 (0.01 to 0.30), (IIb) 0.10 (0.01 to 0.59), (III) 0.05 (0.01 to 0.22). †Standard deviation between meta-analyses: (Ia) 0.20 (0.01 to 0.74), (Ib) 0.11 (0.01 to 0.55), (IIa) 0.06 (0.01 to 0.26), (IIb) 0.13 (0.01 to 0.82), (III) 0.09 (0.01 to 0.31)