

performed too soon after mergers to judge whether or not they met their objectives, given the length of time taken to achieve considerable change in healthcare organisations. The results from the second stage of our data collection for the case study, which took place during the organisations' third year of operation (data are currently being analysed), may show that the merged trusts are closer to meeting the mergers' objectives. The longer the timeframe used, however, the more difficult it is to attribute effects—for example, the impact on service developments—to the merger process, given the context of a turbulent environment of change within the NHS.

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What is already known on this topic

Research suggests that effectiveness increases as the amount of activity by specialised units in certain clinical specialities increases

Little empirical research has looked at the impact of mergers; most studies focus on financial variables

Mergers result in short term disruption caused by difficulties in integrating services and personnel

What this study adds

Important drivers for NHS mergers that are not stated publicly have implications for the process and impact of mergers

Mergers have positive effects, as well as unintended negative consequences that disrupt services and set back developments in services

Perceived differences in organisational culture impede bringing organisations together

Mergers do not achieve target savings in management costs in first two years after merger

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Association between competing interests and authors' conclusions: epidemiological study of randomised clinical trials published in the *BMJ*

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Abstract

Objective To assess the association between competing interests and authors' conclusions in randomised clinical trials.

Design Epidemiological study of randomised clinical trials published in the *BMJ* from January 1997 to June 2001. Financial competing interests were defined as funding by for profit organisations and other competing interests as personal, academic, or political.

Studies 159 trials from 12 medical specialties.

Main outcome measures Authors' conclusions defined as interpretation of extent to which overall results favoured experimental intervention. Conclusions appraised on 6 point scale; higher scores favour experimental intervention.

Results Authors' conclusions were significantly more positive towards the experimental intervention in trials funded by for profit organisations alone compared with trials without competing interests (mean difference 0.48 (SE 0.13), $P=0.014$), trials funded by both for profit and non-profit organisations (0.30 (SE 0.10), $P=0.003$), and trials with other competing interests (0.45 (SE 0.13), $P=0.006$). Other competing interests and funding from both for profit and non-profit organisations were not significantly associated with authors' conclusions. The association between financial competing interests and authors' conclusions was not explained by methodological quality, statistical power, type of experimental intervention (pharmacological or non-pharmacological), type of control intervention



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(for example, placebo or active drug), or medical specialty.

Conclusions Authors' conclusions in randomised clinical trials significantly favoured experimental interventions if financial competing interests were declared. Other competing interests were not significantly associated with authors' conclusions.

Introduction

Financial and other competing interests have recently received increasing attention.¹ In a study of trials of multiple myeloma the authors' conclusions—that is, the authors' reported interpretation of the overall trial results—were more positive towards the benefit of experimental interventions in those trials that were funded by the pharmaceutical industry compared with trials that were funded by non-profit organisations.² In a systematic review on antipsychotic drugs for schizophrenia, trials were more likely to show a benefit of treatment if they were funded by drug companies.³ It is not known whether the association between financial competing interests and authors' conclusions is limited to certain specialties or whether it is a general problem. It is also not known whether personal, academic, or political interests are associated with authors' conclusions.

Unlike most journals, the *BMJ* requires authors to declare funding as well as other competing interests. Trials in the *BMJ* therefore offer a unique opportunity to assess the potential impact of competing interests. We analysed the association between financial and other competing interests and authors' conclusions in randomised clinical trials published in the *BMJ*. We performed the analyses with and without adjustment for potential confounders, including the methodological quality, statistical power, type of experimental intervention, type of control intervention, and specialty.

Methods

We included all original randomised clinical trials published in the *BMJ* from 1997 to June 2001. From each trial, we gathered data on authors' conclusions, competing interests, methodological quality, sample size (number of patients per intervention arm), whether the preset sample size was estimated and reached, specialty, type of intervention (pharmacological or non-pharmacological), and type of control (drug, placebo, no intervention, nursing, or surgery).

We defined authors' conclusions as the original investigators' reported interpretation of the extent to which the overall trial results favoured the experimental over the control intervention. We graded authors' conclusions according to phrasing in the abstract and the summarised conclusion on a previously validated 6 point scale² (box). Higher scores indicate more positive conclusions towards the experimental intervention: scores of 1-3 favoured the control and scores of 4-6 favoured the experimental intervention.

We defined competing interests as anything that may influence professional judgment. We considered funding from for profit organisations—that is, companies that may incur financial gain or loss depending on the outcome—to be financial competing interests. Trials funded by for profit organisations alone and trials funded by both for profit and non-profit organi-

Scale used to grade authors' conclusions

Experimental intervention highly preferred and should now be considered the standard intervention in all patients or similar (6 points)

Experimental intervention preferred to standard but further trials still indicated; may be more costly or similar disclaimer (5 points)

Experimental and control intervention about equal but experimental intervention successful because of minor advantage (4 points)

Experimental and control intervention about equal, but experimental intervention (3 points) disappointing as control intervention had some minor advantage

Control intervention preferred to experimental intervention but experimental intervention might be promising under some circumstances or similar (2 points)

Control intervention highly preferred and is best alternative; should be considered the standard intervention in all patients or similar (1 point)

sations were analysed separately. Other competing interests were defined as personal, academic, political, or similar competing interests declared by authors.

We assessed the methodological quality by looking at three components⁴⁻⁶: generation of allocation sequence (adequate, unclear (not reported), or inadequate (quasi-randomised)); concealment of allocation (adequate, unclear (not reported), or inadequate); and blinding (adequate, unclear, or not performed).

Results

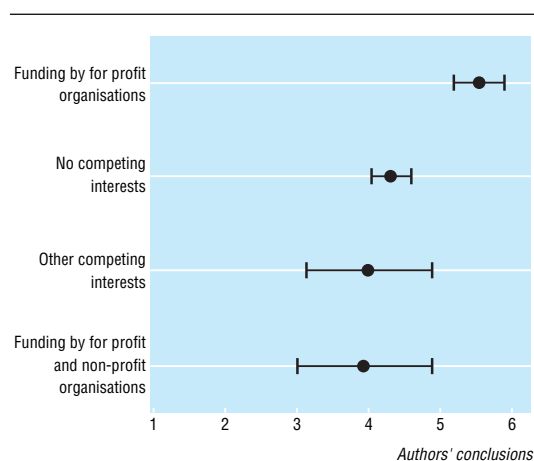
We identified 159 randomised clinical trials that fulfilled our inclusion criteria. The trials were in psychiatry, palliative care/nursing, infections, cardiology, gastroenterology, gynaecology/obstetrics, stroke, pain, allergy, obstructive lung diseases, alcohol/drug abuse, and orthopaedic surgery. The experimental intervention was pharmacological in 99 trials and non-pharmacological in 60 trials. The control intervention was nursing in 29 trials, drugs in 27 trials, surgery in 5 trials, placebo in 31 trials, and nothing in 67 trials.

In 94 of these trials authors declared that they had no competing interests. In 65 trials authors had competing interests because they had received funding from for profit organisations (27 trials), funding by both for profit and non-profit organisations (19 trials), or other competing interests—for instance, personal, academic, or political (19 trials). In most trials, authors' conclusions favoured the experimental intervention (table).

Authors conclusions in 159 randomised clinical trials published from January 1997 to June 2001 in the *BMJ*

Score for conclusions*	No (%) of trials
1	10 (6)
2	5 (3)
3	33 (21)
4	21 (13)
5	39 (25)
6	51 (32)

*Higher scores favour experimental intervention (see box).



Source of funding and authors' conclusions assessed by 6 point scale (higher scores favour experimental intervention). Points are means with 95% confidence intervals

The unadjusted analyses showed a significant association between competing interests and authors' conclusions ($r^2=0.10$; $P=0.001$). Authors' conclusions were not significantly different in trials without competing interests, trials funded by both for profit and non-profit organisations, and trials with other competing interests. As shown in the figure, authors' conclusions in trials funded by for profit organisations alone significantly favoured experimental interventions compared with trials without competing interests (mean difference 0.48 (SE 0.13), $P=0.014$), trials funded by both for profit and non-profit organisations (0.30 (SE 0.10), $P=0.003$), and trials with other competing interests (0.45 (SE 0.13), $P=0.006$). Adjustment for potential confounders did not affect the association between competing interests and authors' conclusions ($r^2=0.11$; $P=0.002$). None of the extracted confounders was significantly associated with authors' conclusions.

Discussion

In a sample of randomised clinical trials published in the *BMJ* from January 1997 to June 2001 we found that authors' conclusions were positively associated with financial competing interests. We included trials published in the *BMJ* after the introduction of the CONSORT statement.⁷ We chose this sample because of the consistent reporting of competing interests in the *BMJ* and to avoid confounding by editorial policies, language bias, and variations in methodological quality. We cannot exclude that some competing interests were not revealed by authors. Furthermore, given the declared editorial policies,¹ the *BMJ* may be considered one of the leading medical journals with respect to the reporting of competing interests. It is possible that the requirement to disclose competing interests will discourage authors with competing interests from submitting biased trials to the *BMJ*. Accordingly, we may have underestimated the general association between competing interests and authors' conclusions. Conversely, apart from random error, we have not been able to identify any reasons why the results of the present study should be false positive.

The *BMJ* publishes fewer pharmacological trials than other general medical journals.⁸ According to our

adjusted analyses, the association between financial competing interests and authors' conclusions was significant in pharmacological as well as non-pharmacological trials. Our findings may be relevant only to trials published in the *BMJ*, although we cannot identify any reason why this should be the case.

Our results increase the external validity of previous evidence.²⁻³ In accordance with Djulbegovic and colleagues,² we found that trials sponsored by for profit organisations significantly more often compared the experimental interventions with placebo or no intervention (data not shown). However, according to our adjusted analyses, this did not explain why authors' conclusions were more favourable towards experimental interventions in trials funded by for profit organisations. Our results also concur with a systematic review by Wahlbeck and colleagues, who showed that the quantitative results of trials were significantly more favourable towards antipsychotic drugs if they were funded by for profit organisations.³ The combined evidence supports suggestions that systematic reviews should include sensitivity analyses with regard to funding.³

Mechanisms and implications

Our results cannot show the causes of the association between financial competing interests and authors' conclusions. Profit organisations, by skill or by chance, may fund only those trials in which the experimental intervention is significantly better than the control intervention.

Previous evidence indicates that trials sponsored by industry are more likely to be affected by publication bias.⁹ Publication bias could therefore explain the findings of the present study.

What is already known on this topic

Financial competing interests may influence authors' conclusions—for instance, interpretation of whether results favour the experimental or control intervention

Trials of antipsychotic drugs for schizophrenia funded by drug companies were more likely to show a benefit of treatment

It is not known whether other competing interests, such as personal, academic, or political, are associated with authors' conclusions.

What this study adds

In pharmacological and non-pharmacological randomised clinical trials from 12 specialties financial competing interests were significantly associated with authors' conclusions

The association did not reflect inadequate methodological quality, greater statistical power, or use of inactive control interventions

Personal, academic, and political competing interests were not significantly associated with authors' conclusions.

Some have argued that industrial funding has undue influence on the research agenda.¹⁰ Others state that a submitted manuscript should be considered the intellectual property of authors, not the study sponsor.¹¹ A reliable assessment of this question depends on the transparency of the reporting.¹ The CONSORT statement^{8,12} and similar standardised reporting guidelines could consider the importance of adequate reporting of funding. The reader can make an assessment only if the information is clearly presented.

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Effect of prenatal exposure to oestrogen on quality of semen: comparison of twins and singleton brothers

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Figure A shows how the study groups were established and table A gives characteristics of the participants.

The decline in sperm count and increase in disorders of the male reproductive tract may be due to high concentrations of prenatal exposure to oestrogens.¹⁻² As the concentration of free oestrogens in plasma is much greater in twin pregnancies from the first weeks of gestation, and greater for dizygotic twins than monozygotic twins,³⁻⁴ we studied sperm count in twins and singleton brothers to see if twin brothers have lower sperm counts and if the lowest values are for dizygotic twins.

Participants, methods, and results

From the population based Danish twin registry, we selected 250 monozygotic and 250 dizygotic pairs of twin brothers and from the Danish civil registration 500 pairs of singleton brothers. All the men were 20-45 years old and born in Denmark.

Of the 2000 men, 778 (38.9%) agreed to participate (40% of the singletons (396), 39% of the dizygotic twins (197), and 37% of the monozygotic twins(185)).

Characteristics of semen and sex hormones. Values are medians (interquartile range) unless otherwise indicated

Characteristic	Singletons (n=105)	Monozygotic twins (n=104)	Dizygotic twins (n=107)	P value*		
				Singletons v monozygotic twins	Singletons v dizygotic twins	Singletons v all twins
Sperm concentration (millions/ml)	60.0 (26.0-99.0)	71.5 (26.5-115.0)	55.0 (25.0-103.0)	0.65	0.78	0.42
Sperm volume (ml)	3.5 (2.8-4.5)	3.4 (2.6-4.0)	3.5 (2.5-4.5)	0.76	0.33	0.67
Sperm total count (millions)	185 (96-367)	237 (78-434)	208 (84-328)	0.83	0.86	0.47
No (%) of men with sperm concentration <20 million/ml (% within each group)	17 (16)	15 (14)	18 (16)	0.72	0.90	0.90
% of sperm with normal morphology†	15 (10-21)	12 (6-17)	12 (7-18)	0.03	0.70	0.16
Sex hormone concentrations:						
Testosterone (nmol/l)	22.8 (17.2-26.4)	19.8 (15.9-23.4)	20.7 (16.7-24.1)	0.16	0.99	0.34
Follicle stimulating hormone (IU/l)	3.9 (2.9-5.1)	3.6 (2.1-6.2)	4.4 (3.2-5.9)	0.07	0.39	0.23
Luteinising hormone (IU/l)	2.3 (1.5-2.9)	2.3 (1.6-3.0)	2.4 (1.8-3.4)	0.12	0.04	0.04
Inhibin B (pg/ml)	195 (155-255)	155 (120-243)	165 (131-210)	0.004‡	0.43‡	0.07‡

*Adjusted for duration of sexual abstinence, urogenital disorders, alcohol, age, smoking, season, and birth weight.

†Morphology scored according to the World Health Organization's 1999 guidelines.

‡Also adjusted for sampling time.