RESEARCH

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Charles M Clark Jr has been a diabetes specialist for over 30 years and is a retired associate dean for continuing medical education and professor of medicine at Indiana University School of Medicine. Jose Mario Franco de Oliveira is an associate professor in the Department of Medicine at Universidade Federal Fluminense and senior staff physician in the adults' intensive care unit at Hospital Federal da Lagoa, Rio de Janeiro.

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BMJ 2012;344:e1369

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Evid Based Nurs doi:10.1136/ebnurs-2011-100408

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From Richard Lehman's journal blog

The latest and best meta-analysis of randomised trials of self monitoring of blood glucose in people with non-insulin treated type 2 diabetes uses individual patient data to show once again that use of this expensive technology does not lead to any clinically meaningful improvement in glycaemic control (*BMJ* 2012;344:e486). It's high time that guidelines such as NICE reflected this. We encouraged this practice once, in the belief that it would help patients manage their condition better. Then it became a lucrative scam for the test strip manufacturers who could change their systems every few years to ratchet up costs that are borne by the NHS. Now it's time for a reality check, and for some serious questions about futile spending to be addressed.

www.bmj.com/content/344/bmj.e486

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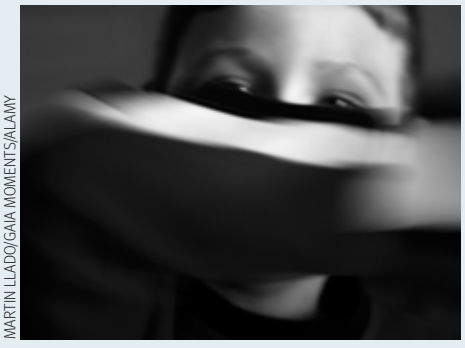
Evaluation of peer led parenting intervention for child disruptive behaviour problems

Children with disruptive behavioural problems and their parents can benefit from peer led parenting classes, according to this community based randomised controlled trial. The rationale of the study was that families would be more likely to seek out and continue treatment if it was delivered by fellow parents in local community settings, rather than professionals working in clinics. The authors conclude that it is a successful way to deliver parenting support for some of the most vulnerable families in society but that research is also needed to evaluate the cost effectiveness of the programme. www.bmj.com/cgi/doi/10.1136/bmj.e1107



MARTIN LLADO/GAIA MOMENTS/ALAMY

Differential risk of death in older residents in nursing homes prescribed specific antipsychotic drugs: population based cohort study

K F Huybrechts,[1] T Gerhard,[2] S Crystal,[2] M Olfson,[3] J Avorn,[1] R Levin,[1] J A Lucas,[4] S Schneeweiss[1]

EDITORIAL by McCleery and Fox

[1]Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02120, USA
[2]Ernest Mario School of Pharmacy, Rutgers University, New Brunswick, NJ 08901
[3]Columbia University, New York, NY 10032
[4]Institute for Health, Health Care Policy and Aging Research, Rutgers University, New Brunswick, NJ 08901
Correspondence to: K F Huybrechts
khuybrechts@partners.org
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STUDY QUESTION

In older people in nursing homes with dementia related behavioural disturbances is the risk of overal and cause specific mortality equal for all antipsychotic drugs?

SUMMARY ANSWER

Compared with risperidone, haloperidol users had an increased risk and quetiapine users a decreased risk of death. The effects were strongest shortly after the start of treatment and remained after adjustment for dose.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Antipsychotics carry a black box warning of increased mortality in elderly patients with behavioural symptoms associated with dementia, but little is known about whether individual drugs differ in their risk. Though the current findings cannot resolve the trade-off between efficacy and safety in the decision to proceed with drug treatment for severe and refractory symptoms, they should help clinicians who are considering use of antipsychotics in patients whose behavioural problems might pose a risk to the patient or others.

Participants and setting

Participants in our study were 75 445 new users of antipsychotics who were aged ≥65, eligible for Medicaid, and living in a nursing home in 45 states in the United States between 2001 and 2005.

Design, size, and duration

We conducted a population based cohort study using linked data from Medicaid, Medicare, the Minimum Data Set, the National Death Index, and a national assessment of nursing home quality. Cox proportional hazards models were used to compare 180 day risks of all cause and cause specific mortality by individual agent, using propensity score adjustment to control for potential confounders. We compared risks associated with haloperidol, aripiprazole, olanzapine, quetiapine, risperidone (reference group), and ziprasidone.

Main results and the role of chance

A total of 6598 residents died from causes other than cancer during the first 180 days after the start of treatment, yielding an event rate of 37.1 per 100 person years (95% confidence interval 36.2 to 38.0). Compared with risperidone, haloperidol users had an increased (adjusted hazard ratio 2.07, 1.89 to 2.26) and quetiapine users a decreased (0.81, 0.75 to 0.88) risk of mortality. The effects were strongest shortly after the start of treatment, remained after adjustment for dose, and were seen for all causes of death examined. No clinically meaningful differences were observed for the other drugs. There was no evidence that the treatment effect differed by the presence of dementia or behavioural disturbances. A dose-response relation was observed for all drugs, except quetiapine.

Bias, confounding, and other reasons for caution

Residual confounding by indication is a factor to consider as an alternative explanation of our findings. We therefore supplemented information on confounders derived from claims data with clinical assessment data and potential indicators of quality of nursing homes. We used multiple methods to mitigate confounding by predefined covariates and by proxies for unobserved factors (high dimensional propensity score) and found results to be consistent. Sensitivity analyses showed that strong risk factors for death that are fairly imbalanced among exposure groups must be unmeasured and uncontrolled to explain the observed associations for deaths from causes other than cancer. Regardless of this, however, causality cannot be shown because of the non-experimental nature of the data, requiring a cautious interpretation of the findings.

Generalisability to other populations

Our study population consisted of patients eligible for Medicaid. As long as socioeconomic status and its correlates do not modify the effect of antipsychotic drugs on short term mortality, the findings should be generalisable.

Study funding/potential competing interests

This study was supported by AHRQ/FDA Awards HS017918 and HS016097.

Hazard ratios for deaths other than from cancer within 180 days of start of treatment with antipsychotic drugs in elderly people in nursing homes

	No of events	Hazard ratio (95% CI)		
		Unadjusted	Adjusted for propensity score	Adjusted for high dimensional propensity score
Haloperidol	745	2.42 (2.21 to 2.65)	2.07 (1.89 to 2.26)	1.81 (1.65 to 1.98)
Aripiprazole	122	0.76 (0.63 to 0.92)	0.88 (0.73 to 1.07)	0.95 (0.78 to 1.15)
Olanzapine	2104	1.01 (0.95 to 1.07)	1.02 (0.96 to 1.08)	1.01 (0.95 to 1.08)
Quetiapine	1120	0.80 (0.74 to 0.86)	0.81 (0.75 to 0.88)	0.83 (0.77 to 0.89)
Ziprasidone	73	0.88 (0.69 to 1.12)	0.92 (0.72 to 1.17)	0.90 (0.69 to 1.17)

Effects of gestational age at birth on health outcomes at 3 and 5 years of age: population based cohort study

Elaine M Boyle,[1] Gry Poulsen,[2] David J Field,[1] Jennifer J Kurinczuk,[2] Dieter Wolke,[3] Zarko Alfirevic,[4] Maria A Quigley[2]

[1]Department of Health Sciences, University of Leicester, Leicester LE1 6TP, UK
[2]National Perinatal Epidemiology Unit, University of Oxford, Oxford OX3 7LF, UK
[3]University of Warwick, Department of Psychology and Division of Mental Health and Wellbeing, Warwick Medical School, Coventry CV4 7AL, UK
[4]University of Liverpool, Department of Women's and Children's Health, Institute of Translational Medicine, Liverpool Women's Hospital, Liverpool L8 7SS, UK
Correspondence to: E M Boyle
eb124@le.ac.uk

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STUDY QUESTION What is the burden of adverse later health status associated with moderate/late preterm (32-36 weeks) and early term (37-38 weeks) birth?

SUMMARY ANSWER Health outcomes of moderate/late preterm and early term babies are worse than those of full term babies, and these babies present a greater burden on public health services than do very preterm babies.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Moderate/late preterm infants have increased neonatal morbidity and mortality compared with those born at 37 weeks or later. A gradient of increasing risk of poorer health outcomes with decreasing gestation extends across all gestations.

Participants and setting

The Millennium Cohort Study (MCS) is a nationally representative prospective cohort study. Infants born in 2000-2 were included if alive and living in the United Kingdom at age 9 months.

Design, size, and duration

The MCS included 18 818 infants. We did a secondary data analysis to investigate effects of gestation at birth on health outcomes at 3 (n=14 273) and 5 years (n=14 056). Outcome measures were growth, hospital admissions, longstanding illness, wheezing, use of prescribed drugs, and parental rating of children's health.

Main results and the role of chance

Measures of general health, hospital admissions, and longstanding illness showed a gradient of increasing risk of poorer outcome with decreasing gestation, suggesting a "dose-response" effect of prematurity. The greatest number with adverse health outcomes was in children born late/moderate preterm or early term. Population attributable fractions for birth at 32-36 and 37-38 weeks were 5.7% (95% confidence interval 2.0% to 10.0%) and 7.2% (1.4% to 13.6%) for having three or more hospital admissions between 9 months and 5 years, compared with 3.8% (1.3% to 6.5%) in children born very preterm. Population attributable fractions for birth at 32-36 and 37-38 weeks were 5.4% (2.4% to 8.6%) and 5.4% (0.7% to 10.5%) for having a limiting longstanding illness at 5 years, compared with 2.7% (1.1% to 4.3%) in children born very preterm.

Bias, confounding, and other reasons for caution

Gestational age was estimated by maternal report, but agreement with hospital records has been shown to be high. Parental report of children's health status may lead to under-reporting or over-reporting of outcomes. Data for severity of illness were unavailable, so bias may have been introduced if parents of sick children responded more frequently than others. Conversely, disproportionately high dropout of children with three or more hospital admissions during the first nine months may lead to underestimation of adverse outcomes. Groups may differ for reasons other than simply gestation; the early term group may contain infants who might be predicted to have a poorer outcome by virtue of intrauterine compromise.

Generalisability to other populations

The MCS cohort is representative of the UK population. Initial recruitment included 85% of eligible families; 78% of families were seen at 3 years and 79% at 5 years. Hospital admission more than three times during the first nine months and birth before 32 weeks were associated with increased dropout. Families with preterm and term infants were equally likely to participate in the MCS, but the small number of very preterm infants with severe neonatal illness may be under-represented.

Study funding/potential competing interests

The study was funded by the BUPA Foundation.

Odds ratios for ≥3 reported hospital admissions between 9 months and 5 years of age and any limiting longstanding illness at 5 years

	Gestation at birth (weeks)				
	<32	32-33	34-36	37-38	39-41
≥3 hospital admissions between 9 months and 5 years					
No (%)	21/147 (13.6)	11/139 (6.9)	44/745 (4.9)	123/2563 (3.9)	285/8989 (2.8)
Adjusted* odds ratio (95% CI)	6.0 (3.2 to 11.4)	3.0 (1.4 to 6.2)	1.9 1.3 to 2.7)	1.4 (1.1 to 1.8)	1
Adjusted* population attributable fraction—% (95% CI)	3.8 (1.3 to 6.5)	1.6 (0.1 to 3.7)	4.1 (1.0 to 7.7)	7.2 (1.4 to 13.6)	–
		5.7 (2.0 to 10.0)			
Any longstanding illness limiting child's activities at 5 years					
No (%)	32/166 (18.6)	21/149 (13.9)	79/855 (8.7)	198/2851 (6.7)	532/9965 (5)
Adjusted* odds ratio (95% CI)	3.9 (2.4 to 6.3)	3.0 (1.7 to 5.2)	1.7 (1.3 to 2.3)	1.3 (1.1 to 1.6)	1
Adjusted* population attributable fraction—% (95% CI)	2.7 (1.1 to 4.3)	1.8 (0.4 to 3.5)	3.6 (1.2 to 6.5)	5.4 (0.7 to 10.5)	–
		5.4 (2.4 to 8.6)			

Percentages and odds ratios are weighted with sampling and non-response weights.
*Adjusted for child's age at interview, sex, and ethnicity; maternal age at birth, marital status, education, and occupation; whether child was mother's firstborn; duration of breast feeding; and maternal smoking and alcohol intake during pregnancy.

Incidence of diabetic retinopathy in people with type 2 diabetes mellitus attending the Diabetic Retinopathy Screening Service for Wales: retrospective analysis

R L Thomas,[1] F Dunstan,[2] S D Luzio,[3] S Roy Chowdhury,[1] S L Hale,[4] R V North,[5] R L Gibbins,[6] D R Owens[1]

[1]Diabetes Research Unit, Centre for Endocrine and Diabetes Sciences, University Hospital of Wales, Cardiff CF14 4XW, UK
[2]Department of Primary Care and Public Health, School of Medicine, Cardiff University, Cardiff
[3]Diabetes Research Group, Swansea University, Swansea, UK
[4]Cardiff and Vale University Health Board, University Hospital of Wales
[5]School of Optometry and Vision Sciences, Cardiff University
[6]Builth Wells, Powys, UK
Correspondence to: D R Owens
owensdr@cardiff.ac.uk

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STUDY QUESTION

For people with type 2 diabetes mellitus attending the Diabetic Retinopathy Screening Service for Wales, what should be the future screening interval for those whose first screening episode indicated no evidence of retinopathy?

SUMMARY ANSWER

In participants with type 2 diabetes and with no evidence of retinopathy at initial screening, the annual incidence of referable retinopathy remained low at 2.02 and 3.54 per 1000 people in the first and fourth follow-up year, respectively.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Screening for diabetic retinopathy is cost effective, although the current policy of screening every person with diabetes each year might not be necessary. The low annual incidence of referable retinopathy seen in participants with no evidence of the disorder at initial screening lends support to the use of risk stratification to define the most appropriate screening interval, with less frequent screening needed in people at low risk of developing retinopathy, therefore allowing more frequent screening in those at high risk.

Participants and setting

49 763 people with type 2 diabetes mellitus and no evidence of diabetic retinopathy attending systematic screening provided by the Diabetic Retinopathy Screening Service for Wales between January 2005 and November 2009.

Design, size, and duration

Retrospective four year analysis of anonymised data for 49 763 participants.

Main results and the role of chance

Cumulative incidence of any and referable retinopathy at four years was 360.27 and 11.64 per 1000 people, respectively (table). Incidence of referable retinopathy was independently associated with known duration of diabetes, age at diagnosis, and use of insulin treatment. The incidence of referable retinopathy varied considerably between subgroups with different levels of risk factors; it was increased in participants receiving insulin treatment and with a duration of diabetes of 10 years or more (cumulative incidence at one and two years, 9.61 and 17.10 per 1000 people, respectively), compared with those receiving a diet treatment with a duration of diabetes of less than 5 years (1.83 and 3.66 per 1000 people, respectively).

Bias, confounding, and other reasons for caution

Our results were restricted to two 45° retinal images per eye and the limited information available on putative risk factors for the development of diabetic retinopathy. We also recorded a relatively high dropout rate (12%) of participants who did not have a second screening event despite being eligible, and we were not able to obtain information for those people who did not participate in screening.

Generalisability to other populations

Our results relate only to people with type 2 diabetes mellitus without diabetic retinopathy at first screening. Further work is needed before the conclusions can be applied to other risk categories of diabetes and degrees of diabetic retinopathy. In the meantime, people who have evidence of diabetic retinopathy should continue to attend annual screenings to avoid any delay in referral to ophthalmologists.

Study funding/potential competing interests

This study was funded by the Welsh Office of Research and Development and by an unrestricted educational grant by Takeda UK. Takeda UK were not sponsors of the research and were not involved in its design, conduct, or reporting of its findings. All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare no conflicts of interest.

Yearly incidence of any and referable diabetic retinopathy in participants without retinopathy at baseline

Time from last negative screen	Any retinopathy		Referable retinopathy	
	Annual incidence	Cumulative incidence	Annual incidence	Cumulative incidence
1 year	124.94 (120.62 to 128.32)	124.94 (120.62 to 128.32)	2.02 (1.63 to 2.44)	2.02 (1.63 to 2.44)
2 years	91.68 (89.67 to 93.66)	216.81 (211.50 to 220.04)	2.82 (2.51 to 3.12)	4.85 (4.29 to 5.43)
3 years	76.96 (74.96 to 79.30)	293.80 (287.34 to 297.76)	3.24 (2.76 to 3.68)	8.09 (7.20 to 8.93)
4 years	66.59 (64.67 to 68.92)	360.27 (352.98 to 366.06)	3.54 (2.89 to 4.21)	11.64 (10.27 to 13.00)

Data are incidence (95% confidence interval) per 1000 people. Incidence of background retinopathy is the difference between the incidences of any and referable retinopathy.

Developing a summary hospital mortality index: retrospective analysis in English hospitals over five years

Michael J Campbell, Richard M Jacques, James Fotheringham, Ravi Maheswaran, Jon Nicholl

ScHARR, University of Sheffield, Sheffield S1 4DA, UK
Correspondence to: M J Campbell
m.j.campbell@sheffield.ac.uk

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STUDY QUESTION

Can a simple, transparent case mix adjustment model be developed to reliably compare hospital mortality rates, which include deaths within hospital and within 30 days of discharge, for all admissions?

SUMMARY ANSWER

A model comprising admission diagnosis, age, sex, type of admission, and Charlson comorbidity score, with the coefficients for these variables estimated separately for each diagnostic group and with no interaction terms, gave good predictions and could be used to compare hospital mortality rates.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Other mortality indices include Dr Foster's hospital standardised mortality ratio (HSMR). These indices, however, are based on in-hospital mortality and a subset of admissions. We describe how a new summary hospital mortality index (SHMI) was derived and tested using deaths in hospital and within 30 days of discharge.

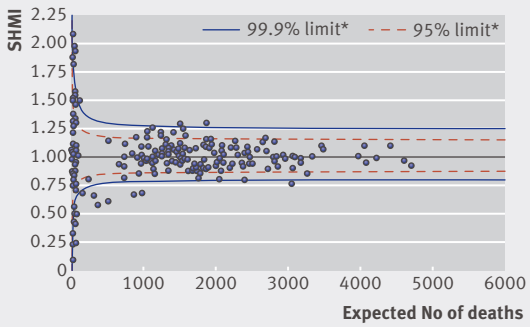
Participants and setting

36.5 million hospital admissions in England, 1 April 2005 to 30 September 2010, with linked mortality data.

Design

Retrospective cross sectional study.

Funnel plot of expected number of deaths and SHMI for 2007/8



* Calculated using random effects model with 10% level of trimming

Primary outcomes

Deaths within hospital or within 30 days of discharge.

Main results and the role of chance

4.2% of males and 4.5% of females admitted to hospital died in hospital or within 30 days of discharge. Predictors used in the final model comprised admission diagnosis, age, sex, type of admission, and Charlson comorbidity score. Given these variables, the relative values of the hospitals were not noticeably changed by adjusting for the index of multiple deprivation and number of previous emergency visits to hospital. There was little evidence that including interaction terms changed the relative ranks by any great amount. The overall C statistic for 2007/8 was 0.911, and the model accounted for 81% of the variability of between hospital mortality. Using the model, we derived the SHMI. We used a random effects funnel plot to identify outlying hospitals. The outliers from the SHMI for 2005-10 have also been identified using other mortality indicators.

Bias, confounding, and other reasons for caution

More advanced comorbidity indices than the Charlson index differentiate between secondary diagnoses for conditions present on admission and newly acquired conditions present on discharge and this may improve prediction. This study has no evidence whether the SHMI is related to quality of care. Pertinent questions to be asked before investigations into the care provided by an outlier on the SHMI include: does the outlying performance persist over time; is this performance sensitive to the methods used—for example, is it sensitive to how the standardisation is carried out or the weightings used; is it sensitive to how the control limits are calculated; is the change in performance associated with changes in the variables used for standardisation; and is there any corroborating evidence from related quality of care indicators?

Generalisability to other populations

This study was restricted to England. It may apply to the countries within the UK's health service, but not to other countries.

Study funding/potential competing interests

This study was funded by the Department of Health.

Observer bias in randomised clinical trials with binary outcomes: systematic review of trials with both blinded and non-blinded outcome assessors

Asbjørn Hróbjartsson,[1] Ann Sofia Skou Thomsen,[1] Frida Emanuelsson,[1] Britta Tendal,[1] Jørgen Hilden,[2] Isabelle Boutron,[3] Philippe Ravaud,[3] Stig Brorson[4]

[1]Nordic Cochrane Centre, Rigshospitalet Department 3343, Blegdamsvej 9, 2100 Copenhagen Ø, Denmark
[2]Department of Biostatistics, University of Copenhagen, Copenhagen
[3]French Cochrane Centre, Assistance Publique (Hotel Dieu), INSERM U738, Université Paris Descartes, France
[4]Department of Orthopaedic Surgery, Herlev University Hospital, Copenhagen
Correspondence to: A Hróbjartsson
ah@cochrane.dk

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STUDY QUESTION

What is the impact of non-blinded outcome assessment on estimated treatment effects in randomised clinical trials with binary outcomes?

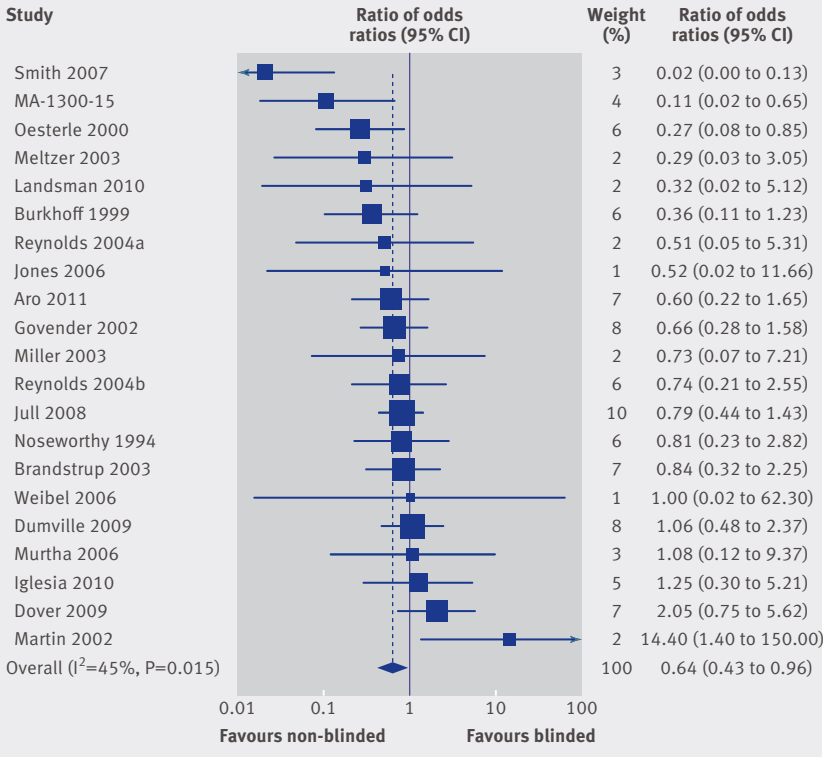
SUMMARY ANSWER

On average, non-blinded outcome assessors generated substantially biased estimates of effect, exaggerating odds ratios by 36%.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The typical degree of observer bias in randomised trials has been unclear, partly because previous studies have been based on indirect comparisons with high risk of confounding. This paper provides empirical evidence of observer bias based on a direct comparison of results from blinded versus non-blinded assessments of the same outcome within the same trial.

Impact of non-blinded assessment of outcome on estimated intervention effects in randomised clinical trials with binary outcomes



Selection criteria for studies

We searched PubMed, Embase, PsycINFO, CINAHL, Cochrane Central Register of Controlled Trials, HighWire Press, and Google Scholar. Randomised clinical trials were included if the same binary outcome had been assessed by both blind and non-blind assessors.

Primary outcome

The ratio of odds ratios—that is, the odds ratio for an unwanted event based on non-blinded assessment relative to the odds ratio based on blinded assessment.

Main results and role of chance

We included 21 trials in the main analysis (4391 patients); eight trials provided individual patient data. The outcomes of the trials were in most cases subjective—for example, qualitative assessments of patients' function, such as severity of angina or neurological deficit. Seventeen trials (81%) scored 4 or 5 for outcome subjectivity on a 1 to 5 scale (5 indicates high degree of subjectivity). The trials were conducted in general surgery, orthopaedic surgery, plastic surgery, cardiology, gynaecology, anaesthesiology, neurology, psychiatry, dermatology, otolaryngology, infectious diseases, and ophthalmology.

The pooled ratio of odds ratios was 0.64 (95% confidence interval 0.43 to 0.96), indicating that the non-blinded odds ratio was exaggerated by an average of 36%. Blinded and non-blinded assessors agreed in a median of 78% of assessments (interquartile range 64-90%) in the 12 trials with available data. The exaggeration of treatment effects associated with non-blinded assessors was induced by the misclassification of a median of 3% of the assessed patients per trial (interquartile range 1-7%).

Bias, confounding, and other reasons for caution

Our results are applicable to trials with subjective outcomes. We would anticipate less observer bias with more objective outcomes. Furthermore, we assume that observer bias in trials with blinded and non-blinded outcome assessors would be similar to that in trials with only non-blinded assessors.

Study funding/potential competing interests

The study was partially funded by the Danish Council for Independent Research: Medical sciences.