RESEARCH

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14 **RESEARCH NEWS** All you need to read in the other general medical journals

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CHRISTIAN DARKIN/SPL

Specialty in the spotlight—the cardiology portal

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- Visit the cardiology portal at www.bmj.com/specialties/cardiovascular-medicine

Recently published

- Management of the failing Fontan circulation http://goo.gl/oae5g
- Predicting the 10 year risk of cardiovascular disease in the United Kingdom http://www.bmj.com/content/344/bmj.e4181
- Atrial fibrillation: diagnosis and management http://goo.gl/mmjmC

What our readers think

Low carbohydrate-high protein diet and incidence of cardiovascular diseases in Swedish women: prospective cohort study (see also p 16)

This study, which reported an increased cardiovascular risk in regular users of such diets, resulted in a lot of press coverage when it was published online two days ago. Several rapid respondents disagree with the findings: "This study does not allow us to conclude anything about low carbohydrate diets, for or against. It is just another partisan shot in the long-running ideological war between the proponents of low fat and low carbohydrate diets."

"Important data are lacking (for example, fat consumption, diet composition) and the presentation of the results is exaggerated."

"I would like to see a subgroup analysis for women who were obese and smoked, with regard to the dietary effect on cardiovascular events…Furthermore, neither information on medication use nor anything on the presence of glucose metabolism abnormalities is available. Another objection is for the absence of information on dietary salt intake, which may be higher in women eating more protein. That could also be confounding."

- Read more, and submit your own response, at www.bmj.com/content/344/bmj.e4026?tab=responses

RESEARCH ONLINE: For this and other new research articles see www.bmj.com/research

Effect of telehealth on use of secondary care and mortality: findings from the Whole System Demonstrator cluster randomised trial

This study evaluated the effect of remote exchange of data between patients and healthcare professionals as part of patients' diagnosis and management ("telehealth") in 179 general practices in three areas in England. Telehealth was associated with lower mortality and emergency admission rates. The reasons for the short term increases in admissions for the control group are not clear, but the trial recruitment processes could have had an effect, say the authors.

Low carbohydrate-high protein diet and incidence of cardiovascular diseases in Swedish women: prospective cohort study

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STUDY QUESTION

What are the long term consequences of low carbohydrate diets, generally characterised by concomitant increases in protein intake, on cardiovascular health?

SUMMARY ANSWER

Low carbohydrate-high protein diets, used on a regular basis and without consideration of the nature of carbohydrates or the source of proteins, are associated with increased risk of cardiovascular disease.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Three European cohort studies relying on mortality provided evidence that low carbohydrate-high protein diets can increase the risk of cardiovascular disease, but a US cohort study based on incidence indicated no association. In the Swedish Women's Lifestyle and Health Cohort, compelling evidence shows that low carbohydrate-high protein diets may increase cardiovascular risk.

Participants and setting

We studied women, aged 30-49 years at baseline, from a random population sample of the Uppsala healthcare region in Sweden.

Design, size, and duration

In a prospective cohort study, 43 396 Swedish women completed an extensive dietary questionnaire and were followed-up for an average of 15.7 years. We evaluated the association of incident cardiovascular diseases, overall and by diagnostic category, with decreasing carbohydrate intake (in tenths), increasing protein intake (in tenths), and an additive combination of these variables (low carbohydrate-high protein score, from 2 to 20), with adjustment for intake of energy, intake of saturated and unsaturated fat, and several non-dietary variables. We identified incident cases of cardiovascular disease through linkage with nationwide Swedish registries.

Main results and the role of chance

A one tenth decrease in carbohydrate intake or increase in protein intake or a 2 unit increase in the low carbohydrate-high protein score were all statistically significantly associated with increasing incidence of cardiovascular disease overall, with incidence rate ratio estimates of 1.04 (95% confidence interval 1.00 to 1.08), 1.04 (1.02 to 1.06), and 1.05 (1.02 to 1.08). We found no heterogeneity in the association of any of these scores with the five studied cardiovascular outcomes. We found a suggestion that the incidence rate ratios tended to be higher among women whose protein intake was mainly of animal rather than plant origin, although the formal tests for interaction were generally non-significant.

Bias, confounding, and other reasons for caution

Among the weaknesses of the study are concerns about misclassification of dietary exposures, particularly as diet was assessed at enrolment only, which, however, is more likely to generate non-differential misclassification and, thus, attenuate the evaluated association. As in all observational studies, residual confounding cannot be confidently excluded.

Generalisability to other populations

The results of the study are particularly relevant to relatively young women, who often resort to weight control regimens that encourage restriction of carbohydrates with unavoidable increases in protein intake, without consideration of the nature of carbohydrates (complex versus refined) or the source of proteins (plant versus animal).

Study funding/potential competing interests

The study was supported by grants from the Swedish Cancer Society and the Swedish Research Council.

Incidence rate ratios for overall cardiovascular diseases and main diagnostic subcategories, per decreasing tenth of carbohydrate intake, increasing tenth of protein intake, and their addition in Swedish Women's Lifestyle and Health Cohort

	Incidence rate ratios* (95% CI)		
Condition (no of cases)	Low carbohydrate score (per tenth)	High protein score (per tenth)	LCHP score (per 2 units)
All cardiovascular diseases (1268)	1.04 (1.00 to 1.08)	1.04 (1.02 to 1.06)	1.05 (1.02 to 1.08)
Ischaemic heart disease (701)	1.04 (0.99 to 1.09)	1.03 (1.00 to 1.06)	1.04 (1.00 to 1.08)
Ischaemic stroke (294)	1.05 (0.98 to 1.14)	1.05 (1.01 to 1.10)	1.07 (1.00 to 1.13)
Haemorrhagic stroke (70)	1.00 (0.86 to 1.17)	1.05 (0.96 to 1.14)	1.05 (0.93 to 1.18)
Subarachnoid haemorrhage (121)	1.07 (0.95 to 1.21)	1.05 (0.98 to 1.12)	1.07 (0.97 to 1.17)
Peripheral arterial disease (82)	1.04 (0.90 to 1.21)	1.04 (0.95 to 1.13)	1.04 (0.93 to 1.17)

LCHP=low carbohydrate-high protein.
*Incidence rate ratios per indicated increase in corresponding score. Poisson models, using attained age as timescale in 2 year intervals, and adjusting for height, body mass index, smoking status, physical activity, education, diagnosis of hypertension, energy intake, unsaturated lipid intake, saturated lipid intake, and alcohol intake.

Frequency and risk factors for prevalent, incident, and persistent genital carcinogenic human papillomavirus infection in sexually active women: community based cohort study

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STUDY QUESTION

What are the frequency and risk factors for prevalent, incident, and persistent genital carcinogenic human papillomavirus (HPV) infection in sexually active female students?

SUMMARY ANSWER

The prevalence and estimated annual incidence of genital carcinogenic HPV infection were 18% and 13%, and infection was most common in women reporting multiple sexual partners in the past year. Of women with a carcinogenic HPV infection at baseline, one in seven had infection with the same genotype detected after 12–28 months, nearly half of them with carcinogenic genotypes not included in current vaccines.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Persistent carcinogenic HPV infection can lead to cervical cancer, and immunisation against HPV types 16 and 18 prevents cervical cancer due to these genotypes. Since infection with non-vaccine carcinogenic genotypes is common, and these genotypes cause around 30% of cervical cancers, both vaccinated and unvaccinated women continue to need cervical screening.

Participants and setting

We studied sexually active female students in London, mean age 21 years (range 16–27), 38% from ethnic minorities, who took part in the POPI (prevention of pelvic infection) chlamydia screening trial in 2004-8 before the introduction of immunisation against HPV types 16 and 18 for schoolgirls.

Design, size, and duration

In this cohort study 2185 women provided self taken vaginal swabs and completed questionnaires at baseline; and 821 (38%) returned further samples by post after a median of 16 months. In 2009-10, the stored samples were tested for HPV.

Main results and the role of chance

At baseline, samples from 404 (18.5% (95% CI 16.9% to 20.2%)) women were positive for carcinogenic HPV, including 327 (15.0%) positive for non-vaccine carcinogenic genotypes. Reporting two or more sexual partners in the previous year and concurrent *Chlamydia trachomatis* or bacterial vaginosis were independent risk factors for prevalent HPV infection. The estimated annual incidence of carcinogenic HPV in women who returned follow-up samples was 12.9% (11.0% to 15.0%). Incident infection was more common in women reporting multiple sexual partners in the previous year, aged <20 years, of black ethnicity, or with chlamydia infection at baseline. Having multiple partners was the only independent risk factor for incident infection (adjusted relative risk 1.99 (95% CI 1.46 to 2.72)). Of the 143 women with baseline carcinogenic HPV infection who returned a follow-up sample, 20 (14% (8.3% to 19.7%)) had infection with the same carcinogenic HPV genotype(s) detected in the second sample. Thirteen of these women (65%) had redetected or persistent infection with HPV types 16 or 18, or both, and nine (45%) had non-vaccine carcinogenic HPV genotypes.

Bias, confounding, and other reasons for caution

Compared with non-responders, the women who returned follow-up samples were slightly older and less likely to be of black ethnicity, to smoke, to use condoms, or to have bacterial vaginosis at baseline. In women with redetected infection we could not distinguish between persistent infection and reinfection with the same genotype.

Generalisability to other populations

Findings may not be applicable to women in developing countries or those attending genitourinary or hospital clinics.

Study funding/potential competing interests

The study was funded by the BUPA Foundation and Medical Research Council. Gen-Probe provided the Aptima test kits for vaginosis analysis. HPV testing was supported by GlaxoSmithKline. RHJ was funded by the Policy Research Programme in the Department of Health. PO, STS, and PEH are members of the eSTI2 consortium funded by the UK Clinical Research Collaboration.

Prevalence, incidence, and persistence or redetection of infection with carcinogenic HPV types in female students

Carcinogenic HPV genotype	% Prevalence (95% CI)*	% Incidence (95% CI)†		% Persistence or redetection (95% CI)‡
		Total	Estimated annual	
Any	18.5 (16.9 to 20.2)(n=404/2185)	17.7 (15.1 to 20.4)(n=145/821)	12.9 (11.0 to 15.0)	14 (8.3 to 19.7)(n=20/143)
Vaccine types:				
16	5.4 (4.5 to 6.4)(n=118/2185)	5.8 (4.3 to 7.7)(n=45/775)	4.2 (3.1 to 5.6)	24 (12.6 to 38.8)(n=11/46)
16, 18, or both	7.3 (6.2 to 8.4)(n=159/2185)	6.6 (4.9 to 8.6)(n=50/758)	5.3 (4.0 to 6.9)	21 (11.5 to 32.7)(n=13/63)
Non-vaccine types	15.0 (13.5 to 16.5)(n=327/2185)	13.4 (11.1 to 15.9)(n=110/821)	9.8 (8.1 to 11.7)	9 (4.0 to 15.8)(n=9/104)

*Frequency of infection at baseline in 2185 women.
†Frequency of new infection acquired during follow-up of 11-32 months (median 16) from baseline in 821 women.
‡Frequency of infection with same HPV type at follow-up among women infected with the same HPV type at baseline.

Derivation and validation of updated QFracture algorithm to predict risk of osteoporotic fracture in primary care in the United Kingdom: prospective open cohort study

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EDITORIAL by Cooper and Harvey

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Research: Predicting risk of osteoporotic and hip fracture in the United Kingdom (*BMJ* 2011;342:d3651)

STUDY QUESTION

Is an updated version of the QFracture algorithm more effective than previous algorithms at estimating the risk of osteoporotic fracture or hip fracture in a primary care population?

SUMMARY ANSWER

Updated algorithms were better at identifying patients at high risk of fracture in primary care in the United Kingdom, compared with previous algorithms reported in 2009.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

International guidelines recommend a targeted approach to the prevention of osteoporosis by identifying high risk patients who are likely to benefit from interventions, based on a 10 year absolute risk of fracture. The updated QFracture algorithm accounts for ethnic origin, previous fragility fracture, care home residence, additional diseases, and use of specific drugs; validation statistics suggested that the updated algorithms were more effective than previous algorithms at identifying high risk patients.

Participants and setting

The derivation and validation cohorts included 3 142 673 and 1 583 373 patients, respectively, who were aged 30-100 years, registered with eligible general practices at some time between 1 January 1993 and 1 October 2011, and contributed 23 608 337 and 11 732 106 person years of observation, respectively.

Design, size, and duration

Prospective open cohort study using routinely collected data from QResearch general practices in England and Wales (data last updated October 2011). We used 420 general practices to develop the scores and a separate set of 207 practices to validate the scores. Cox's proportional hazards models were used in the derivation cohort to derive risk equations that could be evaluated at five and 10 years. Outcomes were incident diagnosis of osteoporotic fracture (vertebral, distal radius, proximal humerus, or hip) and incident hip fracture recorded in general practice records or linked cause of death records.

Main results and the role of chance

We recorded 59 772 incident diagnoses of osteoporotic fracture in the derivation cohort and 28 685 in the validation cohort during follow-up. We found significant independent associations with osteoporotic fracture risk in women for age, body mass index, ethnic origin, alcohol intake, smoking status, chronic obstructive pulmonary disease or asthma, any cancer, cardiovascular disease, dementia, diagnosis or treatment for epilepsy, history of falls, chronic liver disease, Parkinson's disease, rheumatoid arthritis or systemic lupus erythematosus, chronic renal disease, type 1 diabetes, type 2 diabetes, previous fracture, endocrine disorders, gastrointestinal malabsorption, any antidepressants, corticosteroids, unopposed hormone replacement therapy, and parental history of osteoporosis. Risk factors for hip fracture in women were similar, except gastrointestinal malabsorption and parental history of osteoporosis were not significantly associated. Risk factors for men were largely the same as those for women but also included care home residence. The updated algorithm explained 71.7% (95% confidence interval 71.1% to 72.3%) of the variation in women and 70.4% (69.3% to 71.5%) in men. D statistic values for hip fracture were high for women and men, and higher than those for osteoporotic fracture; values for the area under the receiver operating characteristics curve (ROC) were also higher for hip fracture than those for osteoporotic fracture (table). The updated algorithms performed better than the 2009 algorithms (table).

Bias, confounding, and other reasons for caution

Limitations included lack of formally adjudicated outcomes, information bias, missing data, and potential for residual confounding.

Generalisability to other populations

We developed the algorithms in one large primary care cohort and validated them in a separate large cohort that was representative of the patients who would probably be considered for preventative measures.

Study funding/potential competing interests

The study received no external funding. JH-C is professor of clinical epidemiology at the University of Nottingham, codirector of QResearch, and a paid director of ClinRisk Limited. CC is associate professor of medical statistics at the University of Nottingham and a paid consultant statistician for ClinRisk Limited.

Validation statistics of QFracture algorithms. Higher values indicate better discrimination

	Osteoporotic fracture (mean (95% CI))		Hip fracture (mean (95% CI))	
Statistic	Age 30-85 years, 2009 algorithm	Age 30-100 years, updated algorithm	Age 30-85 years, 2009 algorithm	Age 30-100 years, updated algorithm
Women				
R^2 (%)	44.9 (43.1 to 46.7)	51.9 (51.2 to 52.6)	63.9 (62.1 to 65.8)	71.7 (71.1 to 72.3)
D	1.85 (1.78 to 1.91)	2.13 (2.10 to 2.15)	2.73 (2.62 to 2.83)	3.26 (3.21 to 3.31)
ROC	0.788 (0.786 to 0.790)	0.790 (0.787 to 0.793)	0.890 (0.889 to 0.892)	0.893 (0.890 to 0.896)
Men				
R^2 (%)	30.0 (22.2 to 37.8)	38.2 (36.9 to 39.6)	63.2 (60.8 to 65.6)	70.4 (69.3 to 71.5)
D	1.34 (1.09 to 1.59)	1.61 (1.56 to 1.66)	2.68 (2.55 to 2.82)	3.15 (3.06 to 3.24)
ROC	0.688 (0.684 to 0.692)	0.711 (0.703 to 0.719)	0.856 (0.851 to 0.860)	0.875 (0.868 to 0.883)

Effect of editors' implementation of CONSORT guidelines on the reporting of abstracts in high impact medical journals: interrupted time series analysis

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Potential competing interests: SH, IB, and PR are members of the CONSORT Group.

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STUDY QUESTION

Does implementation of the CONSORT for Abstracts guidelines improve the quality of reported abstracts of randomised trials in medical journals?

SUMMARY ANSWER

Based on five high impact medical journals, our findings show that journal endorsement and active implementation by journal editors of the CONSORT guidelines can improve the reporting of randomised trial abstracts.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Problems in the accuracy and quality of abstracts can seriously mislead a reader's interpretation of trial findings. Although authors of randomised trials bear the main responsibility for implementing the CONSORT guidelines, journals can, and should, also have an important role in implementing them.

Selection criteria for studies

We randomly selected up to 60 primary reports of randomised trials per journal per year from five high impact, leading general medical journals, published between January 2006 and December 2009 and indexed in PubMed with an electronic abstract. We excluded any secondary trial publications or economic analyses. Two authors extracted data independently using the CONSORT for Abstracts checklist.

Design

We did an interrupted time series analysis. The study period had 48 monthly intervals: 25 before publication of the CONSORT guidelines (January 2008), three during a transition period to accommodate a gradual implementation (February 2008 to April 2008), and 20 after the intervention (which we considered to begin in May 2008).

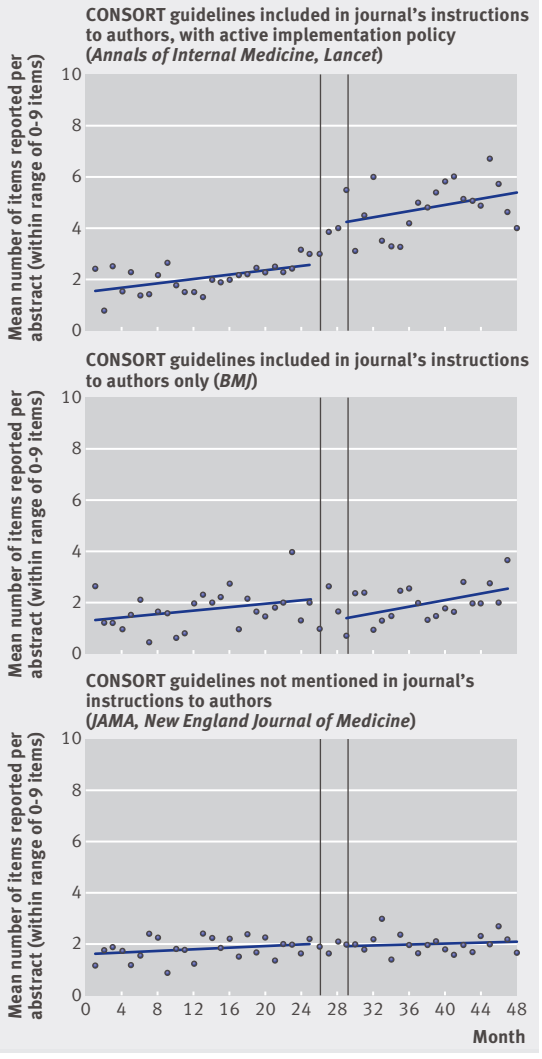
Primary outcome

The mean number of CONSORT items reported in selected abstracts, among nine items reported in fewer than 50% of abstracts across the five journals in 2006.

Main results

We assessed 955 reports of abstracts of randomised trials. Journals with an active policy to enforce the CONSORT guidelines showed an immediate increase in the level of mean number of items reported (increase of 1.50 items; P=0.0037). At 23 months after publication of the guidelines, the mean number of items reported per abstract was 5.41 of nine items, a 53% increase compared with the expected level estimated on the basis of pre-intervention trends. The change in level or trend did not increase in journals with no policy to enforce the guideline.

Change in primary outcome before and after introduction of CONSORT for Abstracts guidelines



Bias, confounding, and other reasons for caution

The overall quality of reporting of abstracts published in these five high impact journals might be higher than in other less well known journals. The primary outcome was a composite outcome assuming that each of the nine CONSORT items was equally important, which might not always be the case. The transition period in the study might have been longer for some articles, since they can take longer than three months to pass through the editorial process.

Generalisability to other populations

We analysed abstracts in journals with considerable resources to support their work. The resources and procedures available for these journals might not be the same for others.

High reprint orders in medical journals and pharmaceutical industry funding: case-control study

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- Head to head: Should journals sell reprints? Yes (*BMJ* 2011;343:d6428)
- Head to head: Should journals sell reprints? No (*BMJ* 2011;343:d6448)

STUDY QUESTION

To what extent are research funding and study design associated with high reprint orders in medical journals?

SUMMARY ANSWER

Funding of research by the pharmaceutical industry is associated with high numbers of reprint orders.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Reprint orders are an important source of income for many medical journals. Of the seven journals assessed in this study, industry sponsored articles were significantly over-represented among those most frequently requested as reprints.

Participants and setting

High reprint articles by the *Lancet*, *Lancet Neurology*, *Lancet Oncology* (Lancet Group), *BMJ*, *Gut*, *Heart*, and *Journal of Neurology, Neurosurgery & Psychiatry* (BMJ Group) each matched to a contemporaneous article not in the list of high reprint orders.

Design, size, and duration

We analysed 339 high reprint articles matched to 339 control articles in a case-control study design. We included articles published between 2002 and 2009. Our analysis was done in Stata using logistic regression.

Primary outcomes, risks, exposures

For each article we extracted the study design (randomised controlled trial or other) and type of funding (pharmaceutical industry, mixed, other or none).

Main results and the role of chance

Papers with high reprint orders were more likely to be funded by the pharmaceutical industry than were control papers (industry funding versus other or none: odds ratio 8.64, 95% confidence interval 5.09 to 14.68, and mixed funding versus other or none: 3.72, 2.43 to 5.70).

Bias, confounding, and other reasons for caution

Several medical journals declined our request for data and so the extent to which industry funding might be associated with high reprint orders in other journals is unknown. Also, it is not known how many reprints were ordered for articles in our control group, only that these did not feature in the list of highest reprints for that journal.

Generalisability to other populations

It is unknown how similar the journals studied are to other medical journals.

Study funding/potential competing interests

We did not receive any specific funding for this study. All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that BG has written articles and books on the activities of the pharmaceutical industry.

Multiple logistic regression analysis showing likelihood of articles being in high reprint versus control groups by design and funding. Values are odds ratios (95% CIs) unless stated otherwise

Journal	Randomised controlled trial *v* other design	P value	Industry funding *v* other or none	Mixed funding *v* other or none	P value
Lancet	1.27 (0.50 to 3.23)	0.62	12.43 (4.63 to 33.38)	5.13 (1.75 to 15.04)	<0.001
Lancet Neurology	0.87 (0.11 to 7.12)	0.89	15.73 (0.93 to 264.88)	4.06 (0.96 to 17.12)	0.03
Lancet Oncology	0.55 (0.11 to 2.64)	0.46	27.36 (2.43 to 307.97)	2.64 (0.56 to 12.37)	0.003
BMJ	0.88 (0.35 to 2.21)	0.78	15.64 (1.75 to 139.48)	2.76 (1.16 to 6.60)	0.001
Gut	3.70 (1.03 to 13.31)	0.045	4.31 (1.02 to 18.25)	2.54 (0.83 to 7.78)	0.07
Heart	5.38 (0.98 to 29.36)	0.052	6.00 (1.08 to 33.33)	4.79 (1.07 to 21.41)	0.02
Journal of Neurology, Neurosurgery & Psychiatry	1.32 (0.23 to 7.69)	0.31	Not applicable	10.15 (2.79 to 36.88)	<0.001
Combined journals	1.04 (0.70 to 1.54)	0.85	8.64 (5.09 to 14.68)	3.72 (2.43 to 5.70)	<0.001