RESEARCH

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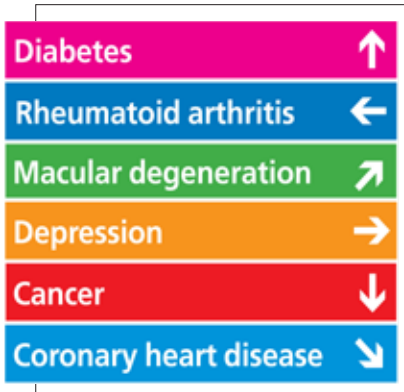

11 **RESEARCH NEWS** All you need to read in the other general medical journals

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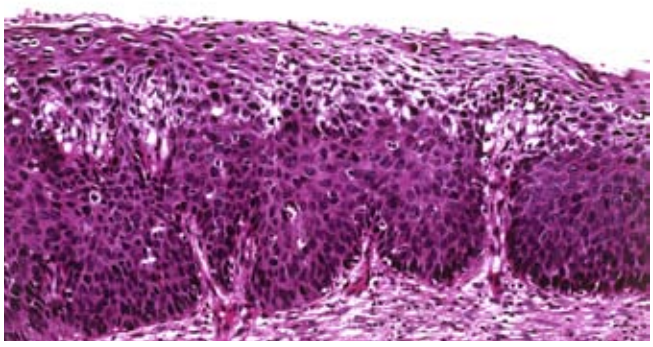
WHAT OUR READERS ARE SAYING

Risk of preterm birth after treatment for cervical intraepithelial neoplasia among women attending colposcopy in England

This analysis of data from 12 NHS hospitals in England (p 15) showed that the risk of preterm delivery in women treated by colposcopy was substantially less than that in many other studies, predominantly from Nordic countries. The authors of a rapid response add:

"Cervical length is an excellent predictor of preterm birth, including in women who have had cervical surgery, and, in combination with fetal fibronectin, can help assess risk accurately. This can reassure large numbers of women who have had cervical treatments (or colposcopy) and appropriately direct further management to women who are truly at risk.

The findings suggest an urgent need to evaluate the role of surveillance in these women, along with directed interventions to reduce the risk of preterm birth. As treatment may not influence cervical mechanical function in most women, commonly used interventions that reinforce the cervix, such as cerclage or vaginal pessaries, may not necessarily be the most appropriate treatment. If cervical intraepithelial neoplasia influences endocervical integrity and therefore antimicrobial peptides and the vaginal microbiome, other interventions such as probiotics, natural antimicrobials, or anti-inflammatory agents may be valuable and need to be investigated."



BIOPHOTO ASSOCIATES/SPL

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

Exposure to diagnostic radiation and risk of breast cancer among carriers of BRCA1/2 mutations

In this retrospective cohort study in 1993 European women carrying BRCA1/2 mutations, exposure to diagnostic radiation before age 30 was associated with an increased risk of breast cancer at dose levels considerably lower than those at which increases have been found in other cohorts exposed to radiation. These results support the use of non-ionising radiation imaging techniques as the main tool for surveillance in young women with BRCA1/2 mutations, the authors conclude.

MAURO FERMARIELLO/SPL

Elevated rheumatoid factor and long term risk of rheumatoid arthritis

In this cohort study, including 9712 individuals without rheumatoid arthritis recruited from the general population of Copenhagen, participants with elevated rheumatoid factor had up to 26 times the long term risk of rheumatoid arthritis and, in absolute terms, the highest 10 year risk of rheumatoid arthritis was 32%. These findings may lead to revision of guidelines for early referral to a rheumatologist and early arthritis clinics, say the researchers.

Use of relative and absolute effect measures in reporting health inequalities

The authors of this structured review found that health inequalities are most commonly reported using only relative measures of effect, which may influence readers' judgments of their magnitude, direction, significance, and implications. They conclude that following existing recommendations by reporting both absolute and relative measures will increase transparency, reduce systematic reporting biases, and improve the evidence base for policies aimed at reducing health inequalities.

Managing patients with multimorbidity: systematic review of interventions in primary care and community settings

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EDITORIAL by Mercer et al

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- Multimorbidity and the inverse care law in primary care (*BMJ* 2012;344:e4152)
- Multimorbidity's many challenges (*BMJ* 2007;334:1016)
- Ordering the chaos for patients with multimorbidity (*BMJ* 2012;345:e5915
- Better training is needed to deal with increasing multimorbidity (*BMJ* 2012;344:e3336)

STUDY QUESTION

How effective are interventions designed to improve outcomes in patients with multimorbidity in primary care and community settings?

SUMMARY ANSWER

Evidence on the care of patients with multimorbidity is limited, despite the prevalence of multimorbidity and its impact on patients and healthcare systems. Interventions to date have had mixed effects, although they are more likely to be effective if targeted at risk factors or specific functional difficulties.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Multimorbidity has an important effect on patients and healthcare systems and research to date has focused on epidemiology and impact rather than on interventions.
A need exists to identify patients with multimorbidity at particular risk and to develop cost effective and specifically targeted interventions that can improve health outcomes.

Selection criteria for studies

Multimorbidity was defined as two or more chronic conditions in the same individual. All included studies were randomised controlled trials reporting on interventions to improve outcomes for people with multimorbidity in primary care and community settings. We searched Medline, Embase, CINAHL, CAB Health, the Cochrane central register of controlled trials, the database of abstracts of reviews of effectiveness, and the Cochrane EPOC (effective practice and organisation of care) register (searches updated in April 2011).

Primary outcomes

Outcomes included any validated measure of physical or mental health, quality of life, and wellbeing, and measures of disability or functional status. We also included measures of patient and provider behaviour, including drug adherence, utilisation of health services, acceptability of services, and costs.

Main results and role of chance

Ten studies examining a range of complex interventions and totalling 3407 patients with multimorbidity were identified. Two studies described interventions for patients with specific comorbidities. The remaining eight studies focused on multimorbidity, generally in older patients. Consideration of the impact of socioeconomic deprivation was minimal. All studies involved complex interventions with multiple components. In six of the 10 studies the predominant component was a change to the organisation of care delivery, usually through case management or enhanced multidisciplinary team work. In the remaining four studies, intervention components were predominantly patient oriented. Overall, the results were mixed, with a trend towards improved prescribing and drug adherence. The results indicated that it is difficult to improve outcomes in this population but that interventions focusing on particular risk factors in comorbid conditions or functional difficulties in multimorbidity may be more effective.

Bias, confounding, and other reasons for caution

All included studies were randomised controlled trials with a low risk of bias.

Study funding/potential competing interests

This was a systematic review carried out within the Cochrane Collaboration without specific external funding. We have no competing interests.

Characteristics of studies included in systematic reviews

Participants	Interventions
Aged >50, depression and hypertension (n=64)	Care manager, structured visits and telephone contact, patient care plans
Aged >65, multiple conditions and high service use (n=904)	Guided care nurse managers, enhanced multidisciplinary team, home assessments and monthly monitoring, patient care plans; education of nurse mangers; patient self management support
Aged >50, at least two conditions and at risk of experiencing adverse outcome (n=241)	Enhanced multidisciplinary team with structured home visit, drug review, patient care plans
Depression and diabetes or coronary heart disease, or both (n=214)	TEAMcare nurses, structured visits, patient care plans and treatment targets, weekly team meetings, use of electronic registry to track patient progress; education of nurse managers; patient support for self care
Aged >65, at least two conditions (n=332)	Pharmaceutical patient care plan created by pharmacist during structured care visit and implemented by practice team
Aged >65, at least two conditions (n=543)	Senior Care Connections: enhanced multidisciplinary team including social worker, home assessment and patient care plans, and training of care coordinators
Multimorbidity defined as at least two conditions (n=175)	Patient self management support, diet, exercise intervention delivered by health educator. Organisational: structured visits and telephone contact
Aged >70, multiple conditions and reported difficulties with activities of daily living (n=319)	Advancing Better Living for Elders (ABLE): occupational therapy and physiotherapy home based intervention including balance and muscle strengthening and fall recovery techniques, and problem solving techniques
Aged >65, at least two of seven chronic conditions (n=79)	Patient engagement intervention led by "coaches" with focus on making most of healthcare
Aged >40, at least two of heart disease, lung disease, arthritis, or stroke (n=536)	Patient (weekly community based meetings led by trained volunteer lay leaders focusing on self management and peer support)

bmj.com Osteoarthritis updates from BMJ Group at http://www.bmj.com/specialties/osteoarthritis

Risk of preterm birth after treatment for cervical intraepithelial neoplasia among women attending colposcopy in England: retrospective-prospective cohort study

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EDITORIAL by Kyrgiou et al

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STUDY QUESTION

Does treatment of cervical intraepithelial neoplasia increase the risk of preterm delivery, and if so by how much?

SUMMARY ANSWER

6.7% of all singleton births in England are preterm compared with 8.8% in women attending colposcopy. Women attending colposcopy had a greater risk of preterm delivery regardless of whether the delivery was before or after the colposcopy or whether they had a diagnostic biopsy or treatment. After adjustment for the timing of the birth relative to colposcopy and the type of procedure at colposcopy, the risk of preterm delivery was not increased after treatment.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Observational studies have found that women t reated at colposcopy have about twice the risk of preterm delivery than women in general. The increased risk is substantially less in women treated in quality managed colposcopy clinics and may all be as a result of confounding.

Participants and setting

Women with cervical histology samples taken between 1987 and 2009 in 12 National Health Service hospitals in England. We linked these women to hospital obstetric records between 1998 and 2009 by hospital episode statistics to identify singleton live births between 20 and 43 gestational weeks.

Summary of analyses and results

Analyses	Total No of births	Crude rate (%) (preterm)	Excess risk per 100 (95% CI)	Relative risk (95% CI)
England	510 660	6.7	—	—
External (versus England)				
All cohort	18 441	8.8	2.08 (1.66 to 2.49)	1.31 (1.25 to 1.37)
All post-histology	14 265	9.0	2.31 (1.84 to 2.79)	1.35 (1.28 to 1.42)
Post-treatment	4776	9.4	2.71 (1.88 to 3.54)	1.41 (1.29 to 1.54)
Internal*				
All post-histology	9368	8.9	—	—
Versus all pre-histology	3569	7.5	2.13 (0.99 to 3.27)	1.32 (1.13 to 1.53)
Post-treatment:	3095	9.1	—	—
Versus pre-treatment	1045	7.8	2.31 (0.34 to 4.33)	1.33 (1.04 to 1.70)
Versus post-biopsy	4770	8.3	1.49 (0.05 to 2.95)	1.19 (1.01 to 1.41)
Adjusted	—	—	−0.25 (−2.61 to 2.11)	0.91 (0.66 to 1.26)

*Excess risk and relative risk adjusted by study site, parity, and maternal age at delivery.

Design, size, and duration

Retrospective-prospective cohort study of 44 210 women who had a cervical biopsy at colposcopy followed for up to 10 years (including retrospectively) for singleton births (18 441). We studied the proportion of preterm births (<37 weeks).

Main results and the role of chance

The relative risk of a delivery being preterm after colposcopy (1284/14 265) compared with before colposcopy (332/4176) was 1.32; and the relative risk in women who previously had treatment (449/4776) compared with those who only had a punch biopsy (586/7263) was 1.19. However, the relative risk of a delivery being preterm in a birth before colposcopy when women who subsequently had treatment (98/1173) were compared with those who subsequently had a punch biopsy (119/1736) was 1.33. Thus the risk ratio of treatment after adjustment for colposcopy procedure and timing was 0.91 (about 1.19/1.33) with an upper limit of the 95% confidence interval of 1.26 corresponding, in this cohort, to at most one additional preterm delivery for every 47 singleton births.

Bias, confounding, and other reasons for caution

The design linking prospectively recorded data should eliminate bias. Comparisons with population statistics do not adjust for confounding. We identified three possible sources: factors predisposing to both cervical disease and preterm deliveries; factors affecting both disease severity and obstetric outcome; and the possibility that the disease, rather than its treatment, causes preterm delivery. In our analyses we attempted to take all three into account. Nevertheless, information on smoking and ethnicity was not available and the type of procedure at colposcopy was missing for 20% of women. The main reason for caution is that we had no information on the size of the excised cone in treated women, and extensive excision could carry substantial risk.

Generalisability to other populations

The results should be generalisable to other populations with colposcopy guidelines and quality management.

Study funding/potential competing interests

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Prevalence of abnormalities in knees detected by MRI in adults without knee osteoarthritis: population based observational study (Framingham Osteoarthritis Study)

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STUDY QUESTION

What is the prevalence of structural osteoarthritic lesions detected by magnetic resonance imaging (MRI) in knees with no radiographic evidence of osteoarthritis?

SUMMARY ANSWER

MRI lesions in the tibiofemoral joint are found in most middle aged and older people whose knee radiographs show no osteoarthritis features, regardless of pain.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Conventional radiography cannot detect all features of knee osteoarthritis, and about half of people with knee pain have no abnormalities on radiography. MRI shows that osteoarthritic changes are commonly present in the knees of most people aged 50 and over who have no radiographic evidence of tibiofemoral osteoarthritis. Osteoarthritic features detected by MRI are common in people with and without knee pain, suggesting the questionable clinical significance of such findings.

Participants and setting

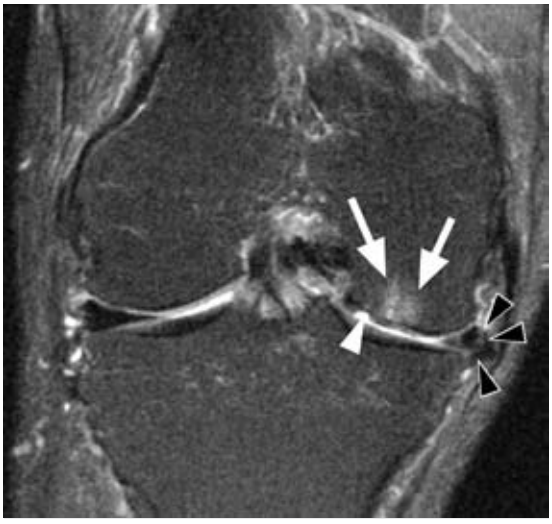
710 people aged over 50 with no radiographic evidence of knee osteoarthritis (Kellgren-Lawrence grade 0) who underwent magnetic resonance imaging (MRI) of the knee in the Framingham community cohort.

Design

Population based observational study.

Primary outcomes

Prevalence of findings on MRI that indicate knee osteoarthritis (including osteophytes, cartilage damage, bone marrow lesions, etc) in all participants and after stratification by age, sex, body mass index (BMI), and the presence of knee pain. Pain was assessed with three questions and by Western Ontario McMaster University arthritis index questionnaire.



Coronal fat suppressed proton density weighted image shows several features of early OA detectable only by MRI. White arrowhead shows focal full thickness cartilage defect at central weight bearing part of medial femur. White arrows show adjacent subchondral bone marrow lesion presenting as area of ill defined hyperintensity. Black arrowheads show meniscal extrusion at medial joint line causing bulging of neighbouring medial collateral ligament

Main results and the role of chance

In people with no signs of knee osteoarthritis on radiography, MRI shows a high prevalence of osteoarthritic features. Of the 710 participants, 393 (55%) were women, 660 (93%) were white, and 206 (29%) had knee pain in the past month. The mean age was 62.3 years, and the mean BMI was 27.9. The prevalence of "any abnormality" was 89% (631/710) overall. Osteophytes were the most common feature among all participants (74%, 524/710), followed by cartilage damage (69%, 492/710). The higher the age, the higher the prevalence of all types of abnormalities detected by MRI. The prevalence of "any abnormality" was high in people with painful (90-97%, depending on pain definition) and painless (86-88%) knees.

Bias, confounding, and other reasons for caution

Most participants were white, reflecting the population of Framingham. There were too few people from other racial or ethnic groups for comparisons. Ideally, intra-articular pathology should be confirmed by direct visualisation during arthroscopy, which is neither feasible nor ethical in large scale population based studies. Arthroscopy cannot visualise some osteoarthritis disease processes seen on MRI such as subchondral bone marrow lesions. We did not include the evaluation of radiographic patellofemoral joint pathology because we used the posteroanterior radiograph to classify the tibiofemoral joint of the knee. We dealt with this by including only subregions of the knee that correspond to the tibiofemoral joint for MRI analysis.

Generalisability to other populations

Our prevalence estimates cannot be generalised to adults aged under 50. In particular, meniscal lesions in young active otherwise healthy adults are more likely to be caused by trauma than the degenerative process seen in middle aged and older people.

Study funding/potential competing interests

This study was funded by the National Institutes of Health (AG18393 and AR47785) and the Arthritis Foundation. AG is the president of Boston Imaging Core Lab (BICL), LLC, and a consultant to Merck Serono, Stryker, Genzyme, AstraZeneca, and Novartis; FWR a vice president and shareholder of BICL and is a consultant to Merck Serono and the National Institutes of Health.

Risk of lung cancer associated with domestic use of coal in Xuanwei, China: retrospective cohort study

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STUDY QUESTION

What is the risk of lung cancer associated with domestic use of different types of coal in rural Xuanwei County, China?

SUMMARY ANSWER

For residents of Xuanwei aged less than 70 years the absolute risks of death from lung cancer associated with using bituminous ("smoky") coal were 18% for men and 20% for women, compared with less than 0.5% for both sexes among users of anthracite ("smokeless") coal.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The risk of lung cancer associated with household coal burning shows substantial heterogeneity by geographical location due to the use of different coal types. In Xuanwei the domestic use of smoky coal rather than smokeless coal is associated with a more than 30-fold increase in the relative risk of developing lung cancer and is likely to represent one of the strongest effects of environmental pollution reported for cancer risk in any population to date.

Participants and setting

Participants in our study were residents in Xuanwei County, Yunnan Province, China, who used either bituminous coal ("smoky coal") or anthracite coal ("smokeless coal") in domestic stoves during their entire life.

Design, size, and duration

This was a retrospective cohort study of 37 272 individuals followed from 1976 to 1996. Information on the type of coal used was based on a questionnaire administered in 1992 to all cohort members. The primary outcomes were absolute and relative risk of death from lung cancer among the users of different types of coal. Survival analysis was used to estimate the absolute risk of lung cancer, while Cox regression models adjusting for potential confounders were constructed to compare mortality hazards for lung cancer between users of smoky coal and users of smokeless coal.

Main results and the role of chance

Lung cancer mortality was substantially higher among smoky coal users than smokeless coal users. The absolute risks of death from lung cancer before the age of 70 years were 18% for men using smoky coal and 20% for women using smoky coal, compared with less than 0.5% among users of smokeless coal of both sexes. Lung cancer alone accounted for about 40% of all deaths before the age of 60 among individuals using smoky coal. Compared with smokeless coal, use of smoky coal was associated with a substantial increase in the risk of developing lung cancer (see table).

Effect of lifelong use of different types of coal in household stoves on risk of lung cancer in Xuanwei, China

Sex and coal used	Hazard ratio (95% CI)	
	Unadjusted	Adjusted*
Men:		
Smokeless coal	1 (reference)	1 (reference)
Smoky coal	41.6 (23.6 to 73.5)	36.2 (20.3 to 64.7)
Women:		
Smokeless coal	1 (reference)	1 (reference)
Smoky coal	115.8 (43.4 to 309.0)	98.8 (36.8 to 265.6)

*Hazard ratios are adjusted for demographic factors, residential history, type of household stove and fuel used, occupation, smoking, cooking practices, time spent indoors and outdoors, medical history, and family history of lung cancer.

Bias, confounding, and other reasons for caution

One possible limitation of the study is recall bias related to surrogate respondents. However, analyses using only data collected from participants who were alive at the time of the interview were consistent with the results of the primary analysis, suggesting only a small role, if any, of recall bias. Also, there is some evidence that during the 1970s lung cancer may have been underdiagnosed in rural China. Thus, it is possible that the absolute risks from lung cancer in the cohort are underestimated.

Generalisability to other populations

The chemical and physical composition of smoky coal differs widely in different geographical locations, and it is possible that smoky coal in Xuanwei is relatively more carcinogenic than smoky coal mined from other parts of China.

Study funding/potential competing interests

The study was supported by the Chinese Academy of Preventive Medicine, Beijing, China; Yunnan Province Antiepidemic Station, Kunming, China; Environmental Protection Agency, USA; and Intramural Research Program of the National Cancer Institute, National Institutes of Health, USA.

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- Effectiveness of provider incentives for anaemia reduction in rural China: a cluster randomised trial (*BMJ* 2012;345:e4809)
- Impact of China's New Rural Cooperative Medical Scheme and its implications for rural primary healthcare (*BMJ* 2010;341:c5617)
- China's excess males, sex selective abortion, and one child policy: analysis of data from 2005 national intercensus survey (*BMJ* 2009;338:b1211)

Reporting of conflicts of interest from drug trials in Cochrane reviews: cross sectional study

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STUDY QUESTION

To what extent did Cochrane reviews of drug trials published in 2010 report conflicts of interest from included trials, including trial funding sources, trial author-industry financial ties, and trial author-industry employment and, among reviews that reported this information, where was it found in the review document?

SUMMARY ANSWER

Most Cochrane reviews of drug trials published in 2010 did not report information on conflicts of interest from included trials. When Cochrane reviews did report on this, the location where the information was reported was inconsistent across reviews.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

A study reported that only 7% of meta-analyses of drug trials published in high impact biomedical journals reported trial funding sources, and none noted trial author-industry financial ties or employment. Although Cochrane reviews reported information on conflicts of interest from included trials at somewhat higher rates, most did not report this information and when they did, it was not consistently reported in the same location across reviews.

Selection criteria for studies

We searched the *Cochrane Database of Systematic Reviews* for Cochrane reviews of drug trials published in 2010, with review content classified as up to date in 2008 or later and with results from at least one randomised controlled trial. We restricted the search to this one year period to obtain recent systematic reviews, with or without meta-analyses, to reflect relatively current reporting practices.

Primary outcomes

For each Cochrane review, we recorded whether the review reported information on trial funding sources, trial author-industry financial ties, and trial author-industry employment. For each of these types of conflicts of interest from included trials, we coded reviews as reporting fully (for all included trials), partially (for some, but not all, included trials), or not reporting conflicts of interest from included trials.

Main results and the role of chance

Of 151 included Cochrane reviews, 46 (30%, 95% confidence interval 24% to 38%) reported information on the funding sources of included trials, including 30 (20%, 14% to 27%) that reported trial funding information for all included trials and 16 (11%, 7% to 17%) that reported for some, but not all, trials. Only 16 of the 151 Cochrane reviews (11%, 7% to 17%) provided information on trial author-industry financial ties or trial author-industry employment for at least some included trials. Information on trial funding and trial author-industry ties was reported in one to seven locations within each review, with no consistent reporting location observed.

Bias, confounding, and other reasons for caution

We searched the *Cochrane Database of Systematic Reviews* using the MeSH term "drug therapy," to identify Cochrane reviews of drug trials. It is possible that our search strategy might have missed some potentially eligible reviews, although we have no reason to believe that this would have biased the results.

Study funding/potential competing interests

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Reporting of trial funding sources, trial author financial ties to the pharmaceutical industry, and trial author employment by the pharmaceutical industry among 151 Cochrane reviews of drug trials published in 2010

	No of reviews reporting		
Type of conflict of interest	Fully (for all included trials)	Partially (for some included trials)	Fully or partially
Trial funding sources	30	16	46
Trial author-industry financial ties	2	9	11
Trial author-industry employment	0	10	10