RESEARCH

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- Review: Childhood Cough *BMJ* 2012;344:e1177
- BMJ Careers: A career in respiratory medicine http://careers.bmj.com/careers/advice/view-article.html?id=20000895

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From Richard Lehman's journal blog

[P]erhaps there is a subgroup of diabetic patients who are particularly likely to benefit from treatment with a gliptin, the drug rep or the paid lecturer might argue. Look, in this trial (he says, handing you the reprint), patients with red hair showed a much bigger drop in blood sugar, and moreover their LDL-cholesterol levels were halved. Here are some nice pens and do help yourself to the delicious sandwiches. With Wondagliptin you may be able to meet all your targets for red-headed diabetics, and we can help train your practice nurse to do it with the aid of daily blood glucose monitoring. Do I exaggerate? Not much, I fear. Anyway, back to subgroup analyses. Don't believe them, especially in industry-funded studies. If you are an EBM nerd, or even if you are not, it is worth looking at this systematic review of the credibility of subgroup claims in randomised controlled trials.

www.bmj.com/content/344/bmj.e1553

RESEARCH ONLINE

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

Differences in blood pressure between arms

According to this primary care cohort study [link to http://www.bmj.com/content/344/bmj.e1327], differences in systolic blood pressure between arms can predict an increased risk of cardiovascular events and all cause mortality over 10 years in people with hypertension. This difference could be a valuable indicator of increased cardiovascular risk, say the authors, and bilateral blood pressure measurements should become a routine part of cardiovascular assessment in primary care. Editorialist Dae Hyun Kim cautions [www.bmj.com/content/344/bmj.e2033] that bilateral blood pressure measurement may be diagnostically useful but needs further evaluation as a prognostic marker.

CRISTINA PEDRAZZINI/SPL

Glasgow supported self-management trial (GSuST) for patients with moderate to severe COPD: randomised controlled trial

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EDITORIAL by Currie and Miller

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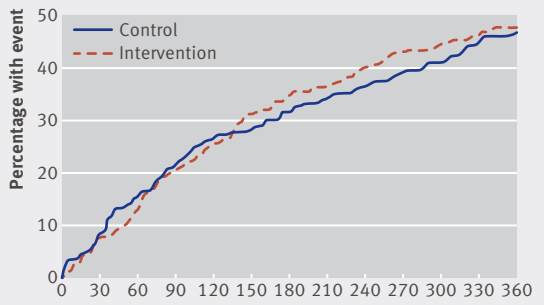
doc2doc
Discuss this article in doc2doc's respiratory medicine forum: http://bit.ly/nMhcH8

STUDY QUESTION Does supported self management for patients with chronic obstructive pulmonary disease (COPD) reduce hospital admissions in the UK healthcare setting?

SUMMARY ANSWER No reduction in hospital admissions was seen with supported self management in COPD.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS The latest Cochrane review concluded that "supported self management" shows benefit in COPD. Although this study found no benefit overall, the 42% of the intervention group who learnt to self manage effectively were significantly less likely to be readmitted to hospital.

Hospital admissions and deaths due to chronic obstructive pulmonary disease



Design
This was a randomised controlled trial comparing supported self management (self management training including recognition and treatment of increased symptoms with prednisolone, antibiotics, or both, with ongoing nurse support) with usual care. Randomisation was stratified to control for key aspects of disease severity and predictors of readmission.

Participants and setting
We included patients in the west of Scotland who had been admitted to hospital with an acute exacerbation of COPD.

Primary outcome(s)
The primary outcome was COPD related hospital admission or death within 12 months.

Main results
In all, 464 patients were randomised, stratified by age, sex, per cent predicted forced expiratory volume in 1 second, recent attendance at pulmonary rehabilitation, smoking status, deprivation category of area of residence, and previous COPD admissions. We found no difference between groups in hospital admissions or death due to COPD (111/232 (48%) *v* 108/232 (47%); hazard ratio 1.05, 95% confidence interval 0.80 to 1.38). Return of health related quality of life questionnaires was poor (n=265; 57%), so no useful conclusions could be made from these data. Pre-planned subgroup analysis showed no differential benefit in primary outcome relating to the disease severity or demographic variables described above. In an exploratory analysis, 42% (75/180) of intervention group patients were classified as successful self managers at study exit, from review of appropriateness of use of self management treatment. Predictors of successful self management on stepwise regression were younger age (P=0.012) and living with others (P=0.010). COPD readmissions/deaths were reduced in successful self managers compared with unsuccessful self managers (20/75 (27%) *v* 51/105 (49%); hazard ratio 0.44, 0.25 to 0.76; P=0.003).

Harms
Harms were not systematically studied, and none was identified.

Bias, confounding, and other reasons for caution
Only 47% of eligible patients agreed to participate; however, as the study showed no benefit, this is unlikely to be important.

Generalisability to other populations
Generalisability is good, with a representative population studied (age, high level of deprivation, moderate to severe COPD) and complete ascertainment of readmissions by record linkage of hospital activity figures for all Scottish hospitals.

Study funding/potential competing interests
Funding came from the Chief Scientist Office, Scottish Health Department (CZH/4/246).

Trial registration number
Clinical trials NCT00706303.

Evaluation of a peer led parenting intervention for disruptive behaviour problems in children: community based randomised controlled trial

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EDITORIAL by Stewart-Brown

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bmj.com/podcasts
Duncan Jarvies talks to some of the parents involved in the initiative

doc2doc
Discuss this article in doc2doc's Journal club: http://bit.ly/FQQFly

STUDY QUESTION To what extent is a peer led parenting intervention acceptable to users and effective at improving child disruptive behaviour for families living in an economically deprived, inner city area?

SUMMARY ANSWER The empowering parents, empowering communities intervention significantly reduced child disruptive behaviour problems and improved positive parenting practices compared with families in a waitlist control condition. Rates of treatment retention and user satisfaction were high.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Families from socially disadvantaged groups often fail to access appropriate care for child behaviour problems. Our study suggests that a peer led format is a highly acceptable method for delivering clinically effective parenting support to families who are hard to reach and may not otherwise engage in mainstream services.

Design
We carried out a randomised controlled trial using a stratified block design with a 1:1 allocation ratio within each block. Fifty nine families were randomised to receive the eight week peer led parenting intervention (based on principles of social learning theory and delivered in a manualised, group format by trained peer facilitators); 57 families were randomised to a waitlist control condition.

Participants and setting
Participants were parental caregivers, mostly from black and ethnic minority groups, seeking help with managing problem behaviours of 116 index children (aged 2-11 years). Treatment was delivered at schools and children's centres in a socially deprived inner London borough.

Primary outcome
Severity of child disruptive behaviour, measured before and after treatment (about 10 weeks apart).

Main results and the role of chance
Significantly greater improvements in child disruptive behaviour and positive parenting practices were observed in the intervention group compared with the waitlist group. Parental stress and children's overall psychological symptoms did not differ significantly between groups. An intention to treat analysis for the primary outcome measure, the parent reported intensity subscale of the Eyberg child behaviour inventory, showed a moderate between group intervention effect size of 0.38 (95% confidence interval 0.01 to 0.75, P=0.01). Acceptability of the treatment was high, with 100% of respondents stating that they were either "a great deal" or "quite a lot" satisfied with the intervention overall.

Harms
The rate of dropout from treatment was low (8.5%).

Bias, confounding, and other reasons for caution
We cannot rule out the possibility of measurement bias due to unblinded follow-up assessments, or shared method bias due to assessment based entirely on parent reported measures.

Generalisability to other populations
The trial was carried out in community settings as part of the routine provision of the peer led parenting intervention, which strengthens the external validity and generalisability of findings. No specific inclusion or exclusion criteria were set for the nature or severity of child problems, other than that the parent was seeking help with managing a child's behaviour in the absence of significant neurodevelopmental problems.

Study funding/potential competing interests
The study was funded by Guy's and St Thomas' Charity and the London Borough of Southwark.

Trial registration number
ISRCTN1962337.

Key outcomes for children and parents. Values are means (standard deviations) unless stated otherwise

	Waitlist control			Peer led parenting intervention			Estimated mean difference (95% CI)†, P value	Effect size (95% CI)
Parent reported measure*	No	Baseline	Follow-up	No	Baseline	Follow-up		
ECBI-I (severity of child disruptive behaviour)	57	111.81 (34.41)	109.26 (28.87)	58	119.29 (34.56)	102.59 (26.41)	−10.57 (−18.56 to −2.59), 0.01	0.38 (0.01 to 0.75)
PS total (positive parenting competencies)	56	3.23 (0.56)	3.26 (0.65)	59	3.34 (0.57)	2.90 (0.62)	−0.44 (−0.63 to −0.26), <0.001	0.69 (0.31 to 1.06)
SDQ total (child psychological symptoms)	47	11.02 (5.77)	10.45 (5.54)	45	12.96 (6.95)	10.09 (5.89)	−1.67 (−3.50 to 0.17), 0.07	0.29 (−0.12 to 0.70)
PSI-SF total (parental stress)	57	85.60 (21.65)	80.86 (18.62)	59	87.88 (22.35)	77.71 (20.77)	−4.38 (−10.52 to 1.77), 0.16	0.22 (−0.15 to 0.58)

ECBI-I=Eyberg child behaviour inventory intensity subscale; PS=parenting scales; SDQ=strengths and difficulties questionnaire; PSI-SF=parenting stress index-short form.
*For all measures, higher scores indicate greater pathology.
†Differences based on intention to treat analysis of covariance, adjusted for baseline score and site.

Screening and cervical cancer cure: population based cohort study

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doc2doc
Read skysteve's blog on detecting cancer early http://bit.ly/xYBZcM

STUDY QUESTION Does the detection of invasive cancer by cervical screening result in better prognosis or merely increase the lead time until death?

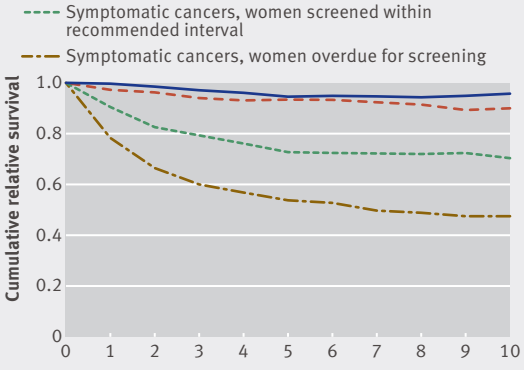
SUMMARY ANSWER Women who receive a diagnosis of cervical cancer based on a smear test (screen detected cancers) have a substantially better prognosis than women whose cancers are detected as a result of symptoms.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS
In addition to reducing the incidence of cervical cancer, cervical screening is associated with improved cure, a finding that is not attributable to lead time bias.

Participants and setting
All 1230 women with invasive cervical cancer diagnosed between 1999 and 2001 in Sweden were followed prospectively as part of the nationwide Swedish cervical cancer audit.

Design, size, and duration
We calculated cure proportions (the level at which the relative survival curve plateaus) and five year relative survival ratios, stratified by screening history, mode of detection, age, histopathological type, and FIGO (International Federation of Gynecology and Obstetrics) stage.

Relative survival ratios of cervical cancer for women of all ages, by screening history and mode of detection of cancers



	Relative survival ratios		
	1 year	5 year	10 year
Screen detected cancers, women overdue for screening	100 (95 to 100)	95 (88 to 98)	96 (89 to 100)
Screen detected cancers, women screened within recommended interval	97 (93 to 99)	94 (88 to 97)	90 (83 to 95)
Symptomatic cancers, women screened within recommended interval	90 (86 to 93)	73 (67 to 78)	70 (63 to 77)
Symptomatic cancers, women overdue for screening	78 (75 to 81)	54 (50 to 58)	47 (42 to 52)

Main results and the role of chance
In the screening ages 23-65, the cure proportion for women with screen detected cancer was 92% (95% confidence interval 75% to 98%) and for symptomatic women was 66% (62% to 70%), a statistically significant difference in cure of 26% (16% to 36%). Among symptomatic women, the cure proportion was significantly higher among women who had been screened according to recommendations (interval cancers) than among those overdue for screening (difference in cure 14%, 95% confidence interval 6% to 23%). Cure proportions were similar for women with all histopathological types except small cell carcinomas, and were closely related to FIGO stage.

Bias, confounding, and other reasons for caution
A major confounder in the evaluation of cancer screening is lead time bias—that is, when detection at an early stage adds time to the follow-up of women but does not prolong life. The cure proportion, however, is a measure that is independent of lead time bias. Length time bias is when screening picks up small indolent carcinomas and the more rapidly growing tumours appear as symptomatic interval cancers with higher associated mortality. However, in our study the cure proportion of women with symptomatic interval cancers was better than that of women with symptomatic cancer and overdue or absent screening. Furthermore, women with cancers detected by screening had an equally excellent relative survival irrespective of whether they had a previous screening test taken in the recommended time, suggesting that determinants of screening attendance did not act as confounders.

Generalisability to other populations
The study comprised all women with a diagnosis of cervical cancer in Sweden during three years and included both organised screening and opportunistic testing, implying that increasing screening attendance is in general associated with a decreased cervical cancer mortality. All women, regardless of previous participation, could be advised that screening will increase the likelihood of cure if an invasive cancer is detected. The assessment of cure proportions should be considered in audits and evaluations of screening programmes.

Study funding/potential competing interests
This work was supported by grants from the Swedish Cancer Society (02-6988 and 2010/900), the Swedish Foundation for Strategic Research (KF 10-0046), Gävle Cancer Fund (2009-09-17), and the Centre for Research and Development, Uppsala University/County Council of Gävleborg, Sweden (CFUG-82261). We have no competing interests.

Risk of atrial fibrillation and stroke in rheumatoid arthritis: Danish nationwide cohort study

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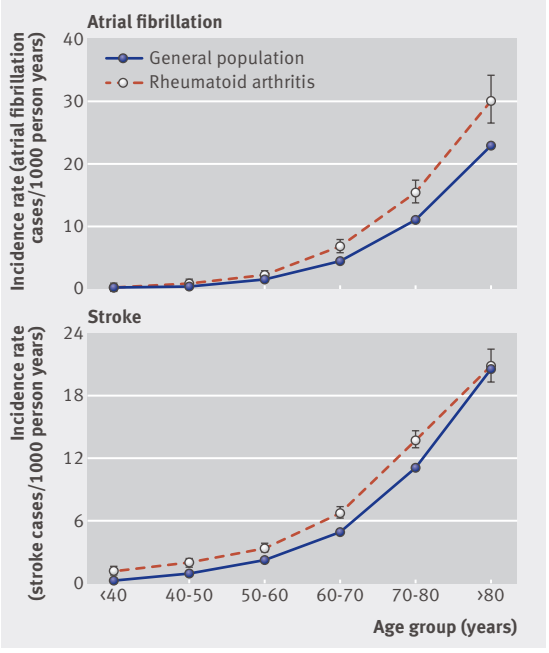
doc2doc
Should we screen for atrial fibrillation? http://bit.ly/FPKks6

STUDY QUESTION Is the risk of atrial fibrillation and stroke increased in people with rheumatoid arthritis?

SUMMARY ANSWER Rheumatoid arthritis was associated with a 40% increase in risk of atrial fibrillation (8.2 cases per 1000 person years compared with 6.0 cases per 1000 person years in age and sex matched controls); the risk of stroke was also significantly greater than in the general population.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS
Patients with rheumatoid arthritis have increased risk of myocardial infarction and cardiovascular death, but evidence on stroke risk is conflicting and the risk of atrial fibrillation is unknown. Rheumatoid arthritis was associated with a significantly increased risk of atrial fibrillation and stroke, suggesting that increased focus on these conditions at the recommended annual cardiovascular risk assessment in patients with rheumatoid arthritis may be appropriate.

Rates of atrial fibrillation and stroke in general population and patients with rheumatoid arthritis



Participants and setting

The study included the entire Danish population aged over 15 years and without rheumatoid arthritis, atrial fibrillation, or stroke before 1997.

Design, size, and duration

The study was a longitudinal register based cohort study based on nationwide data from inpatient and outpatient hospital care in Denmark. Approximately 4.3 million people were characterised by comorbidities and use of prescription drugs. We identified 18 247 people with rheumatoid arthritis by a combination of rheumatoid arthritis diagnoses and treatment. The main outcomes were incidences of atrial fibrillation and stroke in the period 1997 to 2009.

Main results and the role of chance

The rates of atrial fibrillation were 8.2 per 1000 person years in rheumatoid arthritis patients and 6.0 per 1000 person years in age and sex matched individuals in the general population, and the adjusted incidence rate ratio of atrial fibrillation associated with rheumatoid arthritis was 1.41 (95% confidence interval 1.31 to 1.51). The stroke rates were 7.6 and 5.7 per 1000 person years in rheumatoid arthritis patients and the general population, with a resultant stroke rate ratio of 1.32 (1.22 to 1.42). For both atrial fibrillation and stroke, the relative risks were increased in all strata based on sex and age; although the relative risks were higher in younger patients, the absolute risk differences were largest in older patients.

Bias, confounding, and other reasons for caution

We cannot rule out the influence of surveillance bias, which may have increased the detection of atrial fibrillation and stroke among rheumatoid arthritis patients. Unmeasured confounders, such as dyslipidaemia and smoking, may also have biased the results.

Generalisability to other populations

The study used data from complete nationwide registries in Denmark, which reduced selection bias, but we included only patients with rheumatoid arthritis who had received inpatient or outpatient hospital care and were treated with disease modifying antirheumatic drugs. Whether the results can be generalised to other ethnicities is also unclear.

Study funding/potential competing interests

JL received funding from the Danish Rheumatism Association, but the funder had no influence on the initiation or any other aspect of the research presented in this paper.

Mobile phone use and glioma risk: comparison of epidemiological study results with incidence trends in the United States

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STUDY QUESTION How do observed trends in glioma incidence in the United States compare with predicted rates based on two recent reports of increased risk of glioma in relation to mobile phone use?

SUMMARY ANSWER The relatively constant rate of glioma during a period of rising exposure to mobile phones is inconsistent with the substantially increased risk of glioma reported by a 2011 Swedish study, but could be consistent with modest excess risks seen in the 2010 Interphone study.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The International Agency for Research on Cancer recently classified mobile phone exposure as a possible human carcinogen in relation to brain tumour risk, on the basis of two epidemiological studies, a 2011 Swedish study by Hardell et al and the 2010 Interphone study. Our analysis indicates that observed rates in the US are inconsistent with relative risks reported by Hardell et al but could be consistent with the modest excess risks reported in the Interphone study.

Participants and setting

Population based data for glioma incidence in 24 813 non-Hispanic white people diagnosed at age 18 years or older, from 12 registries in the Surveillance, Epidemiology, and End Results (SEER) programme.

Design, size, and duration

We collected data for 1992-2008, combined with data for mobile phone use in the US for 1985-2008.

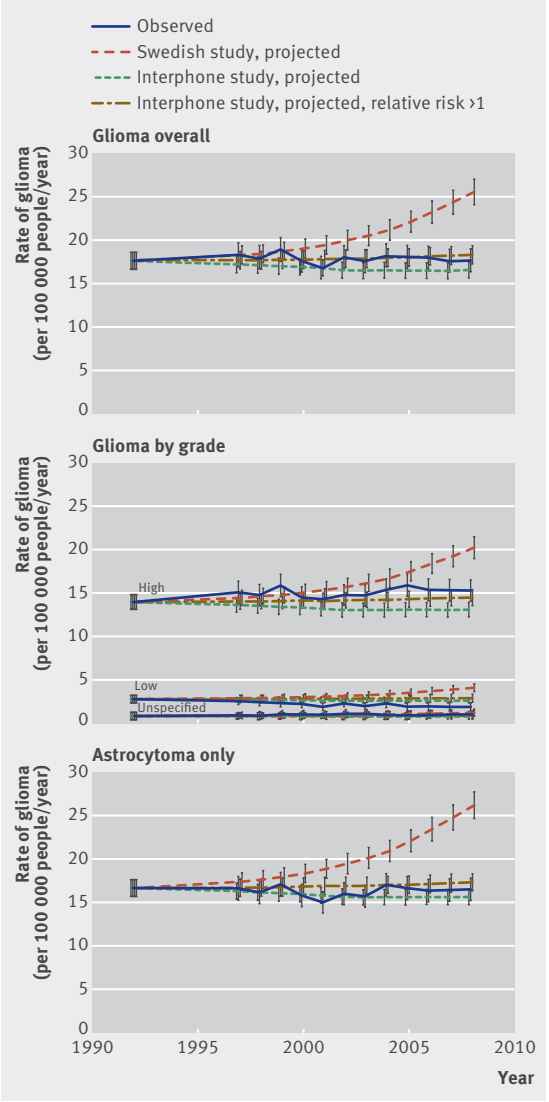
Main results and the role of chance

After taking account of the increasing prevalence of mobile phone use, if we applied the relative risks of glioma reported by the Swedish study to 1992-6 baseline rates, predicted rates should have been at least 40% higher than those observed in 2008 (fig). However, predicted rates based on relative risks in the small proportion of highly exposed people in the Interphone study were statistically consistent with observed rates. Results remained valid if we used either non-regular users or low users of mobile phones as the baseline category, and if we constrained relative risks to be more than 1 (fig).

Bias, confounding, and other reasons for caution

The appropriate exposure measure for brain cancer in relation to mobile phone use is still unclear. We used two models, one comparing "ever versus never use" comparison, and one taking account of the cumulative hours of phone use. The subscription data that we used to determine phone use in the US might not have been completely accurate. The generally flat trend in incidence could have also masked an increasing glioma risk associated with phone use that had been exactly counterbalanced by a fall in incidence for other reasons. Furthermore, the two studies measured cumulative hours of phone use from 1997 to 2004, whereas we predicted glioma incidence trends from 1997 to 2008.

Observed and projected rates (95% CI) of malignant glioma in study population



Generalisability to other populations

We assumed that the relative risks of glioma associated with mobile phone use seen in the Swedish and Interphone studies applied to the US population in the present day.

Study funding/potential competing interests

Funding support from the Intramural Research Program of the National Institutes of Health, and the National Cancer Institute, Division of Cancer Epidemiology and Genetics.