RESEARCH

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Specialty in the spotlight—the respiratory medicine portal

If you could cure one respiratory disease today, which one would it be? How do you treat someone you're sure has allergic bronchopulmonary aspergillosis, but the serology result doesn't fit the diagnosis?

BMJ Group's new respiratory medicine portal includes discussions from our online respiratory forum as well as the latest research, review articles, and online learning modules. You can see abstracts on respiratory medicine from all of our journals, including *Thorax*.

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Recent key respiratory medicine articles from BMJ Group:

- What can we learn from asthma in elite athletes? http://www.bmj.com/content/344/bmj.e2556
- Investigating the solitary pulmonary nodule http://www.bmj.com/content/344/bmj.e2759
- Is a blind distal biopsy a transbronchial biopsy by another name? http://doc2doc.bmj.com/forums/open-clinical_respiratory-medicine_blind-distal-biopsy-trans-bronchial-biopsy-another-name

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

This nationwide register based cohort study [http://www.bmj.com/content/344/bmj.e2794] from Denmark found no evidence of an increased risk of fetal death associated with exposure to an adjuvanted pandemic A/H1N1 2009 influenza vaccine during pregnancy. The accompanying editorial [http://www.bmj.com/content/344/bmj.e3091] agrees that the benefits outweigh the risks


CDC

Risk of cardiovascular serious adverse events associated with varenicline use for tobacco cessation: systematic review and meta-analysis

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STUDY QUESTION

What is the risk of treatment emergent, cardiovascular serious adverse events associated with varenicline use for tobacco cessation?

SUMMARY ANSWER

Risk is statistically and clinically insignificant.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Drug safety concerns have been raised in relation to varenicline use for tobacco cessation and the emergence of cardiovascular serious adverse events, although the finding has been called into question owing to the less than optimal methodology used. Our meta-analysis of all published, randomised controlled trials of varenicline use for tobacco cessation included 50% more studies than a previous meta-analysis; used an unbiased summary estimate and compared findings with three other estimates; and examined events that occurred during drug treatment, which is more biologically relevant and obviates problems with differential drop out.

Selection criteria for studies

We included randomised controlled trials of current tobacco users of adult age, comparing use of varenicline with an inactive control drug and reporting adverse events. We searched Medline, the Cochrane Library, and online clinical trials registries, from January 2005 to September 2011. We excluded studies using a quasi-experimental or crossover design, laboratory studies with no follow-up, studies with adolescents or non-smokers, studies in which all participants received varenicline, and comparisons of varenicline with another active drug.

Primary outcome

We defined treatment emergent, cardiovascular serious adverse events as occurring during or within 30 days, drug treatment, and included any ischaemic or arrhythmic event (myocardial infarction, unstable angina, coronary revascularisation, coronary artery disease, arrhythmias, transient ischaemic attacks, stroke, sudden death or cardiovascular related death, or congestive heart failure).

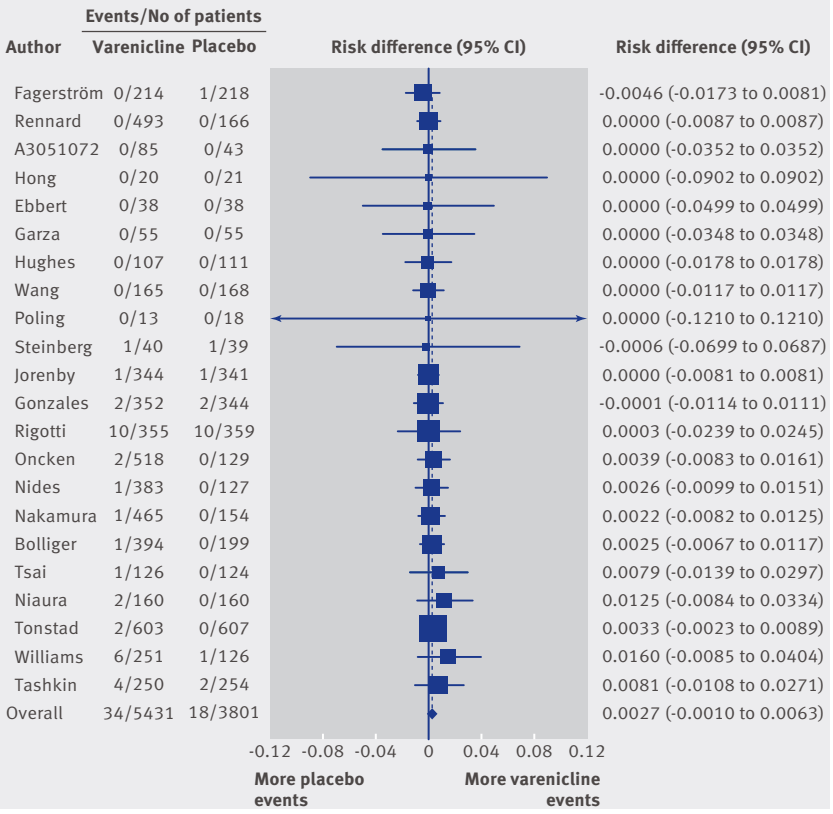
Main results and role of chance

Twenty two trials met criteria for inclusion: two enrolled participants with active cardiovascular disease, 11 enrolled participants with a history of cardiovascular disease, and nine excluded people with a history of cardiovascular disease. Rates of events were 0.63% (34/5431) for participants on varenicline and 0.47% (18/3801) for those on placebo. The risk difference summary estimate, based on all 22 trials, was not clinically or statistically significant (0.27%, 95% confidence interval −0.10 to 0.63; P=0.15; fig). The relative risk (1.40, 0.82 to 2.39; P=0.22), Mantel-Haenszel odds ratio (1.41, 0.82 to 2.42; P=0.22), and Peto odds ratio (1.58, 0.90 to 2.76; P=0.11), all based on 14 trials with at least one event, also indicated no significant difference between active and placebo groups. Study quality was strong, with all 22 trials double blinded; placebo controlled; and adequately describing randomisation, loss to follow-up, and the events. However, only one trial adjudicated the events. We found no evidence of heterogeneity among trials.

Study funding/potential competing interests

Study funding provided by National Institute on Drug Abuse (P50 DA09253) and California Tobacco-Related Disease Research Program (17RT-0077). JJP is principal investigator on National Institute of Mental Health grant R01 MH083684 and an Investigator Initiated Research award WS981308 from Pfizer, and is a collaborator on R34 DA030538 from the National Institute on Drug Abuse and a Cahan Award from the Flight Attendant Medical Research Institute. JFH is coinvestigator on five trials funded by National Institutes of Health and the Agency for Healthcare Research and Quality. The funding sources had no role in the conduct of the research or manuscript preparation.

Difference in risk of cardiovascular serious adverse events associated with varenicline use



Effects of multidisciplinary team working on breast cancer survival: retrospective, comparative, interventional cohort study of 13 722 women

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STUDY QUESTION

Does the introduction of multidisciplinary team working improve the survival of women treated for breast cancer?

SUMMARY ANSWER

After the introduction of multidisciplinary care in one health board area in the west of Scotland, breast cancer mortality was 18% lower and all cause mortality was 11% lower than in neighbouring areas providing conventional care.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Treatment of cancer is increasingly provided by multidisciplinary teams, but the effects of this approach on survival are unclear. We found that multidisciplinary care was associated with greater improvements in breast cancer survival than expected had the approach not been introduced.

Participants and setting

From the Scottish Cancer Registry, we selected women of all ages, diagnosed with symptomatic invasive breast cancer between 1990 and 2000, attending an NHS hospital managed by a health board in the west of Scotland.

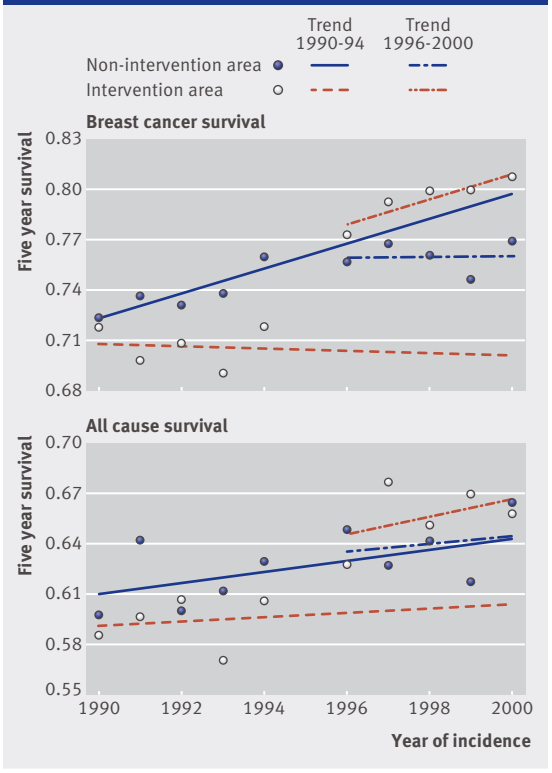
Design, size, and duration

We did a retrospective, comparative, non-randomised, interventional cohort study. The 13 722 eligible women were grouped according to the health board of diagnosis. Multidisciplinary care was formally introduced in 1995 in the intervention area, managed by the Greater Glasgow health board. The non-intervention area, managed by the remaining health boards in the west of Scotland, continued to deliver care using traditional models.

Main results and the role of chance

Before the introduction of multidisciplinary care, mortality specific to breast cancer was 11% higher in the intervention area than in the non-intervention area (hazard ratio adjusted for year of incidence, age at diagnosis, and deprivation 1.11, 95% confidence interval 1.00 to 1.20). After multidisciplinary teams were introduced, mortality was 18% lower in the intervention area than in the non-intervention area (0.82, 0.74 to 0.91). All cause mortality did not differ between areas in the earlier period, but was 11% lower in the intervention area than in the non-intervention area in the later period (0.89, 0.82 to 0.97). Analysis of an interrupted time series showed a significant improvement in breast cancer survival in the intervention area in 1996 (after introduction of the intervention) compared with the expected survival had the pre-intervention trend continued (P=0.004). We saw no corresponding improvement in the non-intervention area (P=0.64), and no significant change in overall survival in either area in 1996.

Five year survival by year of incidence with trends before and after year 1995



Bias, confounding, and other reasons for caution

The observed differences in survival after the introduction of multidisciplinary care in the intervention area might have been due to selection biases or confounding factors. However, selection criteria were applied in the same way to both areas. Where data for tumour size were available, patients in both areas had similar sizes of tumours. No other changes in service provision occurred.

Generalisability to other populations

Owing to the lack of a precise definition of multidisciplinary care, and the variation in provision of and access to specialist health services in countries outside the UK, our results could be difficult to generalise.

Study funding/potential competing interests

The authors have support from NHS Greater Glasgow and Clyde health board (EMK, GMA), NHS Scotland (HJGB), and the University of Glasgow (WDG, DSM) for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

Derivation and validation of a risk adjustment model for predicting seven day mortality in emergency medical admissions: mixed prospective and retrospective cohort study

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STUDY QUESTION

How well does a risk adjustment model for predicting seven day mortality in emergency medical admissions, based on routinely collected data, pre-hospital and emergency department physiological data, and routine blood test results, perform in different settings?

SUMMARY ANSWER

A risk adjustment model for emergency medical admissions based on age, ICD-10 code, active malignancy, and routinely recorded physiological and blood variables can provide excellent prediction of seven day mortality across a range of settings.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Risk adjustment models using routine administrative data can generate hospital standardised mortality rates for use as a performance indicator. Risk prediction was improved by adding active malignancy and physiological and blood variables, but the association between key predictor variables and mortality differed between settings.

Participants and setting

Adults with medical emergencies who were alive and not in cardiac arrest when attended by an ambulance, and either were admitted to hospital or died in the ambulance or emergency department, were studied in acute hospitals and associated ambulance services in England, Australia, and Hong Kong.

Design, size, and duration

This was a mixed prospective and retrospective study of derivation (three hospitals, 5644 patients) and validation (nine hospitals, 13 762 patients) cohorts. Data came from routine sources and extraction from ambulance and emergency department records. We developed risk adjustment models to predict seven day mortality.

Main results and the role of chance

In the derivation phase, a model based on age and ICD-10 (international classification of diseases, 10th revision) code alone had a C statistic of 0.80 (95% confidence interval 0.78 to 0.83), which increased to 0.81 (0.79 to 0.84) with the addition of active malignancy. This was markedly improved only when we added physiological variables (C statistic 0.87, 0.85 to 0.89), blood variables (0.87, 0.84 to 0.89), or both (0.90, 0.88 to 0.92). In the validation phase, the C statistics ranged across centres from 0.80 to 0.91 for the model with physiological variables and from 0.83 to 0.93 for the full model. The rank order of hospitals based on adjusted mortality differed markedly from the rank order based on crude mortality.

Bias, confounding, and other reasons for caution

Key model variables (ICD-10 code, Glasgow coma score, respiratory rate, systolic blood pressure, oxygen saturation, haemoglobin, white cell count, and potassium, urea, creatinine, and glucose concentrations) had statistically significant interactions with hospital. This suggests that the risk associated with these variables varies between centres, and comparing risk adjusted mortality between centres could be misleading.

Generalisability to other populations

We tested the model in a diverse range of settings. Risk prediction varied between settings but was generally good to excellent.

Study funding/potential competing interests

The study was funded by the Medical Research Council.

Summary statistics for models tested in derivation phase

Model	Subset	C statistic (95% CI)	−2 × log likelihood	Likelihood ratio test x^2 (df) and P value
Age and ICD-10 alone	All patients (n=5644)	0.80 (0.78 to 0.83)	2028.91	–
+ active malignancy		0.81 (0.79 to 0.84)	1991.76	35.03 (3); P<0.001
+ active malignancy + physiology		0.87 (0.85 to 0.89)	1720.2	267.12 (15); P<0.001
Age and ICD-10 alone	Those with blood test data (n=3720)	0.81 (0.78 to 0.84)	1232.96	–
+ active malignancy		0.83 (0.80 to 0.85)	1208.22	24.75 (3); P<0.001
+ active malignancy + physiology		0.88 (0.86 to 0.91)	1023.56	184.65 (15); P<0.001
+ active malignancy + bloods		0.87 (0.84 to 0.89)	1085.59	122.062 (20); P<0.001
+ active malignancy + physiology + bloods		0.90 (0.88 to 0.92)	963.16	75.23 (20); P<0.001

Health, employment, and economic change, 1973-2009: repeated cross sectional study

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STUDY QUESTION

How has the moderating effect of self reported limiting long term illness on employment, unemployment, and economic inactivity changed for working age men and women in England and Wales between 1973 and 2009?

SUMMARY ANSWER

The moderating effect has grown during this time period, such that differences in rates of employment and economic inactivity between people with and without limiting long term illness were greater in 2009 than in 1973.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

People of working age with limiting long term illness have higher rates of economic inactivity and lower rates of employment than do working age people without such illness. The gap in employment opportunities between people with and without limiting long term illness has grown substantially since 1973.

Participants and setting

The study population was men and women aged between 18 and 60. The setting was England and Wales.

Design

This was a repeated cross sectional study using data from the General Household Survey.

Primary outcome(s)

The primary outcome was the proportion of respondents who were employed, unemployed, or economically inactive.

Main results and the role of chance

For men of working age, we found a strong inverse correlation between employment and unemployment among those without limiting long term illness; this correlation was much weaker for men with such illness, and instead a strong inverse correlation existed between employment and economic inactivity. For working age women, we found a strong inverse correlation between employment and economic inactivity, with a more modest correlation between employment and unemployment, irrespective of the presence of limiting long term illness. The strength and direction of these correlations also seem to be moderated by occupational group. For men and women, the differences in economic inactivity rates between those with and without limiting long term illness were greatest among those with unskilled/semi-skilled manual occupational backgrounds; these differences have widened substantially since 1973.

Bias, confounding, and other reasons for caution

Annual response rates have varied between 67% and 85%. The potential for non-response bias may exist. As some of the cells used in compiling the results involved small sample sizes, chance will have had an influence. As repeated cross sectional rather than longitudinal data were used, the results cannot be used to infer a causal relation between variables.

Generalisability to other populations

The study population is already very general. It may not be generalised to people not of working age. The generalisability of the results to other nations is unclear.

Study funding/potential competing interests

The study was not funded.

Pearson correlation between employment, unemployment, and economic inactivity for working age men and women, with and without limiting long term illness

	Men			Women		
Category	Employment *v* unemployment	Employment *v* inactivity	Unemployment *v* inactivity	Employment *v* unemployment	Employment *v* inactivity	Unemployment *v* inactivity
Limiting illness:						
Professional/managerial	−0.22	−0.92	−0.17	−0.18	−0.97	−0.07
Intermediate non-manual	0.24	−0/95	−0.52	0.07	−0.94	−0.40
Skilled manual	−0.12	−0.91	−0.32	−0.17	−0.88	−0.32
Semi-skilled and unskilled manual	0.22	−0.88	−0.65	−0.18	−0.87	−0.33
No limiting illness:						
Professional/managerial	−0.75	−0.57	−0.11	−0.36	−0.99	0.24
Intermediate non-manual	−0.92	−0.42	0.03	0.06	−0.99	−0.23
Skilled manual	−0.95	0.02	−0.31	−0.34	−0.99	0.21
Semi-skilled and unskilled manual	−0.94	0.07	−0.40	−0.63	−0.95	0.35