RESEARCH

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SPL

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

THIS WEEK'S RESEARCH QUESTIONS

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18 Does the presence of hyperglycaemia or diabetes on admission to hospital influence mortality in patients with community acquired pneumonia?

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20 How scattered across journals are reports of randomised trials and systematic reviews in different medical specialties?

Specialty in the spotlight—the *BMJ* Olympics portal

As Olympic athletes are preparing for London 2012 we will be publishing more about sports medicine than usual across our many publications and products. The BMJ Olympics portal features selected material from the *BMJ*, BMJ Journals, BMJ Learning, doc2doc, blogs, and podcasts and videos. From now until the end of the Olympics and Paralympics you can access some of our best resources on sports medicine in one place. Join in the discussions on our Olympics forum and catch up with the latest on the track and other Olympic venues with our tweets, by visiting bmj.com/olympics

Latest Olympics stuff on portal

A doctor's lifelong campaign to revive the Olympic games
BMJ 2012;344:e3691

Olympics' public health surveillance scheme will be retained after games, agency says
BMJ 2012;344:e3620

Passport to clean competition
BMJ 2012;344:e2077

What can we learn from asthma in elite athletes?
BMJ 2012;344:e2556

Reactions to *BMJ* research

Facilitated physical activity as a treatment for depressed adults: randomised controlled trial

This study was published on bmj.com on 6 June and triggered a heated debate in the media. Here's what some of our rapid responders said:

"Expecting para-professional staff using a previously untested approach to increasing physical activity to bring about significant improvements in mood in a moderate to severely depressed group of patients was unrealistic."

"I am not sure exactly what the intended aim of this study is. While it might be said that this study does not show an increased improvement in depression in exercise, are we really going tell patients not to exercise?"

"While the media have taken their share of criticism over this, the research itself and the way it was presented did little to bring clarity to an important topic."

Read more at http://tinyurl.com/d4abq86

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

Use of pioglitazone and the risk of bladder cancer in people with type 2 diabetes

In this nested case-control study including 600 general practices in the United Kingdom, the use of pioglitazone was associated with an increased risk of incident bladder cancer among people with type 2 diabetes. The accompanying editorial cautions that the risks seem to outweigh benefits as yet more evidence emerges.

Relation between volume and outcome for patients with severe sepsis in United Kingdom: retrospective cohort study

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EDITORIAL by Wallace and Khan

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bmj.com/blogs
David Payne: Playing the sepsis game

STUDY QUESTION

Does a volume-outcome relation exist for admissions with severe sepsis to adult general critical care units in the United Kingdom?

SUMMARY ANSWER

No association was found between volume and outcome in admissions with severe sepsis treated in adult general critical care units in the UK.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Two small studies have suggested the presence of a volume-outcome relation for critically ill patients with severe sepsis.
No relation was found between volume and acute hospital mortality for patients with severe sepsis admitted to adult general critical care units in the UK, and no significant interaction was found between volume and either severity of illness or receipt of mechanical ventilation.

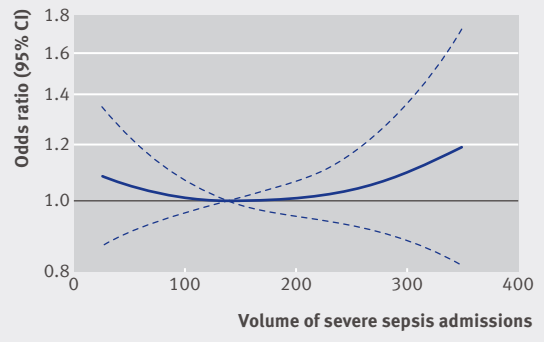
Participants and setting

We selected patients, aged 16 years or older and participating in the case mix programme, who met objective, standardised criteria for severe sepsis in the first 24 hours after admission to critical care units.

Design, size, and duration

This was a retrospective cohort study of 33 538 admissions with severe sepsis to 170 critical care units participating in the case mix programme for 2008-09. The case mix programme database is a high quality clinical database containing pooled case mix and outcome data on consecutive admissions to adult, general critical care units in England, Wales, and Northern Ireland. The primary exposure of interest was volume of admissions with severe sepsis per unit per year, and the primary outcome was ultimate acute hospital mortality.

Odds ratio (95% CI) for effect of volume on acute hospital mortality



Main results and the role of chance

We did a multivariable logistic regression analysis, using generalised estimating equations, to assess the association between volume, modelled using fractional polynomials, and ultimate acute hospital mortality, with adjustment for potential confounders. We found no relation between volume and outcome for admissions with severe sepsis to adult general critical care units in the UK (P=0.65). Subgroup analyses tested for interactions between the effect of volume and acute severity of illness and receipt of mechanical ventilation. We found no significant interactions (P=0.46 for acute severity of illness, P=0.42 for receipt of mechanical ventilation).

Bias, confounding, and other reasons for caution

Bias may have arisen from misclassification of severe sepsis cases. However, we based identification of severe sepsis on raw physiological and diagnostic data, using objective, standardised criteria across units. A second potential source of bias is residual confounding from the case mix of patients. This is unlikely given that we made adjustments by using the validated Intensive Care National Audit & Research Centre (ICNARC) physiology score from the ICNARC model plus other known confounders.

Generalisability to other populations

The study was based on a large sample of adult general critical care units across the UK (more than 80% of all adult, general units), and the results are therefore generalisable to the whole of the UK. The findings may not be generalisable to critical care units outside the UK.

Study funding/potential competing interests

This research received no specific funding. JS was funded through a bursary provided by the Fonds de Recherche du Québec-Santé.

Hospital volume and patient outcomes after cholecystectomy in Scotland: retrospective, national population based study

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STUDY QUESTION

Does hospital volume influence patient outcomes after cholecystectomy in Scotland?

SUMMARY ANSWER

The relative risk of death, reoperation, and readmission is reduced in high volume centres; although absolute risk differences between volume groups were clinically significant for elderly patients and patients with comorbidity, they were negligible for those at average risk.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Associations between hospital volume and outcome after specialist surgery are well defined, but less is known about these associations after low risk, high volume surgery such as cholecystectomy. For high risk patients, particularly those who are elderly or with comorbidity, hospital choice could be important even for elective procedures.

Participants and setting

All patients undergoing cholecystectomy in Scotland between 1 January 1998 and 31 December 2007, in a locally validated administrative dataset covering all NHS hospitals.

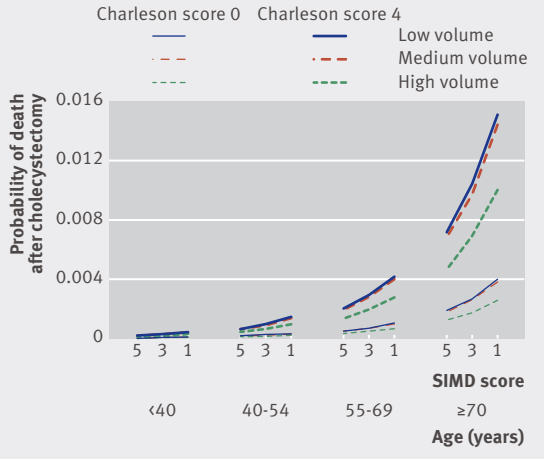
Design, size, and duration

Retrospective, national population based study using multilevel modelling and simulation. We identified 59 918 patients who had a cholecystectomy in one of 37 hospitals: five with high volumes (>244 cholecystectomies/year), 10 with medium volumes (173-244), and 22 with low volumes (<173). Main outcomes were mortality, 30 day reoperation rate, 30 day readmission rate, and length of stay.

Main results and the role of chance

Compared with low and medium volume hospitals, high volume hospitals performed more procedures non-electively (17.1% and 19.5% *v* 32.8%), completed more procedures laparoscopically (64.7% and 73.8% *v* 80.9%), and used more operative cholangiography (11.2% and 6.3% *v* 21.2%; x^2 test, all P<0.001). In a well performing multivariable analysis with bias correction for a low event rate, the odds ratio for death was greater in both the low volume (1.45, 95% confidence interval 1.06 to 2.00, P=0.022) and medium volume (1.52, 1.11 to 2.08, P=0.010) groups than in the high volume group. However, in simulation studies, absolute risk differences between hospital volume groups were clinically negligible for patients with average risk (number needed to treat to harm (low *v* high volume comparison) 3871, 1963 to 17 118), but became significant in patients with higher risk. Figure 1 shows the probability of death after elective cholecystectomy against hospital volume, age, deprivation (Scottish Index of Multiple Deprivation (SIMD) score), and comorbidity (Charlson score). In models accounting for the hierarchical structure of patients within hospitals, those in medium volume hospitals were more likely to undergo reoperation (odds ratio 1.74, 1.31 to 2.30, P<0.001) or be readmitted (1.17, 1.04 to 1.31, P=0.008) after cholecystectomy than those in high volume hospitals. Length of stay was shorter in high volume hospitals than in low (hazard ratio for discharge 0.78, 0.76 to 0.79, P<0.001) or medium volume hospitals (0.75, 0.74 to 0.77, P<0.001). These differences were also only of clinical significance in patients at higher risk.

Risk modelling using simulation procedures



Bias, confounding, and other reasons for caution

Although case mix was controlled with several factors, illness severity was not accounted for, which could explain some of the differences seen between hospital volume groups. We also have not sought to explain the differences in outcome between study groups by the inclusion of variables describing hospital structure and process, which is the focus of ongoing work.

Generalisability to other populations

This population based study covered all of Scotland and as such, generalisability to other population groups in the United Kingdom should be high, since both the distribution of risk factors for gallbladder disease and for hospital resources and structure are probably similar. However, care may be needed before generalising these results to other settings.

Study funding/potential competing interests

This study was funded by the University of Edinburgh, which had no direct role in the study. MD, SP-B, SJW, and OJG work as consultant surgeons in one of the institutions included in this study, constituting a non-financial interest that may be relevant to the submitted work.

Serum glucose levels for predicting death in patients admitted to hospital for community acquired pneumonia: prospective cohort study

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STUDY QUESTION

Does the presence of hyperglycaemia or diabetes on admission to hospital influence mortality in patients with community acquired pneumonia?

SUMMARY ANSWER

Serum glucose levels on admission predict death in patients with community acquired pneumonia without pre-existing diabetes. Patients with diabetes have an increased risk of death independent of serum glucose level on admission.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Community acquired pneumonia, one of the leading infectious diseases in more economically developed countries, is associated with considerable morbidity and mortality. Hyperglycaemia is a known risk factor for premature death from different causes, including infectious diseases. This study shows that the presence of mild to moderate hyperglycaemia on admission to hospital has a major impact on mortality in patients with community acquired pneumonia and previously undiagnosed diabetes mellitus.

Participants and setting

6891 patients with community acquired pneumonia included in the German community acquired pneumonia competence network (CAPNETZ) study between 2003 and 2009.

Design, size, and duration

Prospective cohort study with over 7000 recruited patients. The study is ongoing.

Main results and the role of chance

An increased serum glucose level on admission to hospital in participants with community acquired pneumonia and no pre-existing diabetes was a predictor of death at 28 and 90 days. Compared with participants with normal serum glucose levels on admission, those with mild acute hyperglycaemia (serum glucose concentration 6-10.99 mmol/L) had a significantly increased risk of death at 90 days (1.56, 95% confidence interval 1.22 to 2.01; P<0.001), and this risk increased to 2.37 (1.62 to 3.46; P<0.001) when serum glucose concentrations were ≥14 mmol/L. In sensitivity analyses the predictive value for death of serum glucose levels on admission was confirmed at 28 days and 90 days. Patients with pre-existing diabetes had a significantly increased overall mortality compared with those without diabetes (crude hazard ratio 2.47, 95% confidence interval 2.05 to 2.98; P<0.001). Owing to the large number of patients included, the risk of a chance finding was relatively low.

Bias, confounding, and other reasons for caution

We used multivariate analysis to account for confounding.

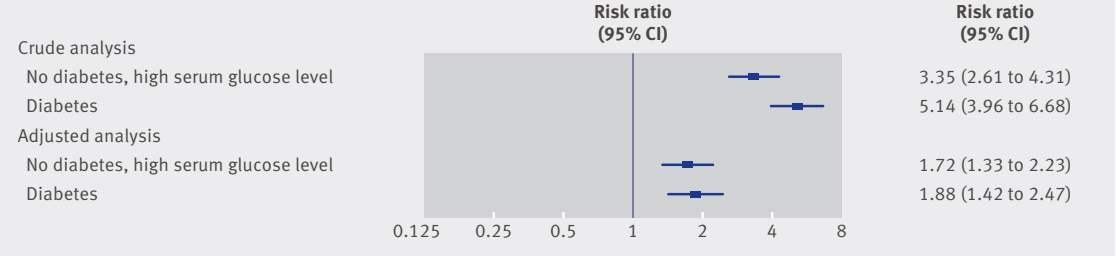
Generalisability to other populations

The mechanisms leading to hyperglycaemia in acutely ill patients should be similar in other populations with community acquired pneumonia. A pooled analysis of 97 prospective studies showed that hyperglycaemia is a risk factor for premature death from various causes.

Study funding/potential competing interests

The German Ministry of Education and Research (Bundesministerium für Bildung und Forschung) funds the German community acquired pneumonia competence network, CAPNETZ. We have no competing interests.

Crude and adjusted analyses of cohorts with highest mortality (P<0.001 for all)



Effect of pre-diabetes on future risk of stroke: meta-analysis

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EDITORIAL by Treadwell

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Diabetes resources from BMJ Group http://www.bmj.com/specialties/diabetes

Stroke resources from BMJ Group http://www.bmj.com/specialties/stroke

STUDY QUESTION

Does presence of pre-diabetes predict future risk of stroke?

SUMMARY ANSWER

Pre-diabetes, defined as impaired glucose tolerance or a combination of impaired fasting glucose and impaired glucose tolerance, may be associated with a higher risk of future stroke.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Pre-diabetes is increasingly diagnosed in many developed countries and has been linked to a modest rise in overall cardiovascular risk. In this meta-analysis, people with pre-diabetes on the basis of presence of impaired glucose tolerance had an independent risk of future stroke that was 20% greater than those with normal glycaemia, although the absolute risk would be modest and the findings may reflect unmeasured confounding.

Selection criteria for studies

We searched PubMed, Embase, and the Cochrane Library (all 1947 to 16 July 2011). We selected studies that prospectively collected data within cohort studies or clinical trials, evaluated blood glucose at baseline, assessed stroke event as an endpoint during the follow-up period, had follow-up of at least one year, and reported quantitative estimates of the multivariate adjusted relative risk and 95% confidence interval for future stroke associated with baseline pre-diabetes. Pre-diabetes was defined as impaired fasting glucose (fasting glucose 5.6-6.9 mmol/L or 6.1-6.9 mmol/L) or impaired glucose tolerance (two hour values in the oral glucose tolerance test of 7.8-11.0 mmol/L). The reference group (normoglycaemia) included people with fasting glucose below 5.6 mmol/L, fasting glucose below 6.1 mmol/L, or non-fasting glucose below 7.8 mmol/L.

Primary outcome

The primary outcome was relative risk of future stroke.

Main results and role of chance

The search yielded 15 prospective cohort studies comprising 760 925 participants. In eight studies analysing pre-diabetes defined as fasting glucose 5.6-6.9 mmol/L, the random effects summary estimate did not show increased risk of stroke after adjustment for established cardiovascular risk factors (1.08, 95% confidence interval 0.94 to 1.23; P=0.26). In five studies analysing pre-diabetes defined as fasting glucose 6.1-6.9 mmol/L, the random effects summary estimate showed increased risk of stroke after adjustment for established cardiovascular risk factors (1.21, 1.02 to 1.44; P=0.03). In eight studies with information about impaired glucose tolerance or combined impaired glucose tolerance and impaired fasting glucose, the random effects summary estimate showed increased risk of stroke after adjustment for established cardiovascular risk factors (1.26, 1.10 to 1.43; P=0.0008). When we excluded studies that might have enrolled patients with undiagnosed diabetes, only impaired glucose tolerance or a combination of impaired fasting glucose and impaired glucose tolerance independently raised risk of future stroke (1.20, 1.07 to 1.35; P=0.002).

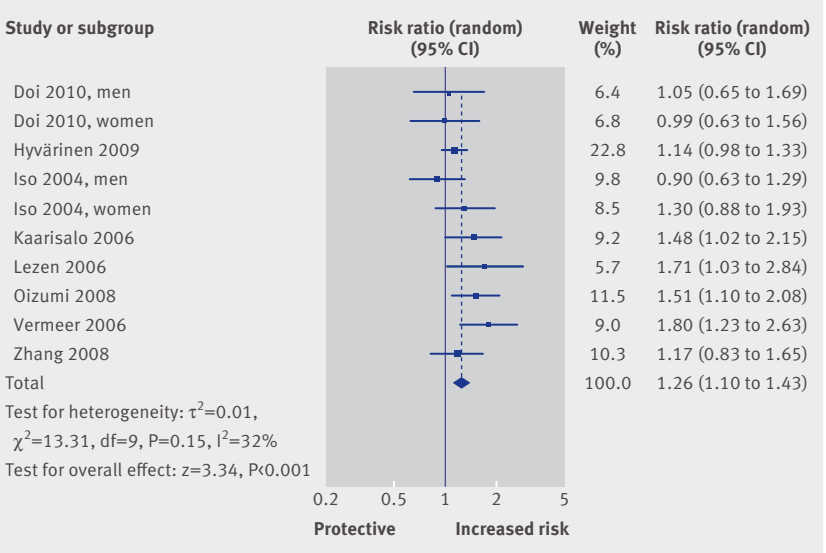
Bias, confounding, and other reasons for caution

Although we preferred studies that measured baseline fasting plasma glucose and oral glucose tolerance test, in the main analysis we did not exclude studies that measured only baseline fasting or non-fasting glucose concentrations. So, for instance, people with a fasting plasma glucose of 7.0 mmol/L or above may have inadvertently been included if only non-fasting glucose was measured, and people with a non-fasting glucose of 11.1 mmol/L or above might have been included if a study measured only fasting glucose. The association of pre-diabetes with risk of stroke was modest and may reflect underlying confounding: effect sizes were attenuated in studies that used adequate adjustment.

Study funding/potential competing interests

ML was supported by a grant from Chang Gung Memorial Hospital, Taiwan; JLS was supported by the specialised programme on translational research in acute stroke award from the National Institutes of Health (NIH); and BO was supported by the NIH.

Baseline impaired glucose tolerance (IGT) or combination of IGT and impaired fasting glucose versus risk of stroke



The scatter of research: cross sectional comparison of randomised trials and systematic reviews across specialties

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STUDY QUESTION

How scattered across journals are reports of randomised trials and systematic reviews relevant to different medical specialties and subspecialties?

SUMMARY ANSWER

Publication rates of specialty relevant trials vary widely, from 1 to 7 trials per day, and are scattered across hundreds of general and specialty journals. This scatter varies considerably among specialties.

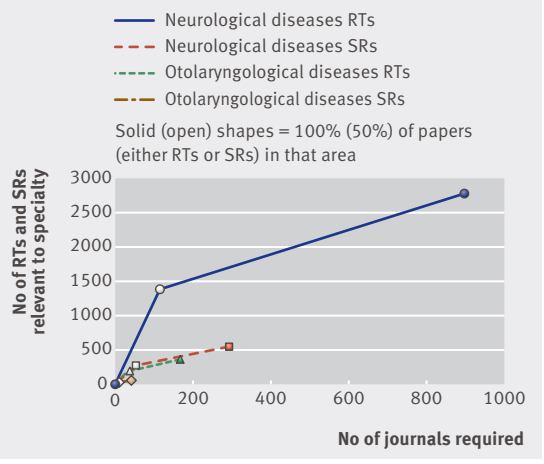
WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Publication of specialty relevant randomised trials and systematic reviews is now scattered across hundreds of general, specialty, and subspecialty journals. To keep up to date, personal journal subscriptions are insufficient and must be supplemented by other methods such as comprehensive and rigorous journal scanning services or systems; however, few existing services seem adequate.

Data sources and study selection

We chose the nine diseases or disorders with the highest burden of disease (depressive disorders, ischaemic heart disease, cerebrovascular disease, dementias, alcohol use disorders, hearing loss, chronic obstructive pulmonary disease, diabetes mellitus, and lung cancer) and the broader category of disease to which each belonged (for example, lung cancer in the category of cancer). For these seven specialties and nine subspecialties, we searched PubMed for all disease relevant randomised trials and systematic reviews that were published in 2009.

Specialties with most and least amount of scatter and number of randomised trials (RTs) and systematic reviews (SRs) published in PubMed in 2009 compared with number of journals in which they were published



Design

The study was a cross sectional analysis of randomised trials and systematic reviews.

Main results

The scatter across journals varied considerably among specialties and subspecialties: otolaryngology had the least scatter (363 trials across 167 journals) and neurology the most (2770 trials across 896 journals). In only three subspecialties were 10 or fewer journals needed to locate 50% of trials. The scatter was less for systematic reviews: hearing loss had the least scatter (10 reviews across nine journals) and cancer the most (670 reviews across 279 journals). For some specialties and subspecialties, the papers were concentrated in specialty journals; whereas for others, few of the top 10 journals were a specialty journal for that area. Generally, there was little overlap between the top 10 journals publishing trials and those publishing systematic reviews. The number of journals required to find all trials or reviews was highly correlated (r=0.97) with the number of papers for each specialty/subspecialty.

Bias, confounding, and other reasons for caution

Our sample of papers was restricted to a single year and the analysis to seven specialties and nine subspecialties. Scatter is likely to be greater in areas of specialty practice that typically concern patients with a wide variety of conditions, such as emergency medicine, primary care, and allied health disciplines. Our search strategy relied on PubMed's publication type to retrieve papers. We may therefore have missed some eligible papers and included some that are not truly systematic reviews or randomised trials, and hence the extent of scatter is an estimate.

Study funding/potential competing interests

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