

RESEARCH

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Specialty in the spotlight—the cardiology portal

BMJ Group's cardiology portal includes discussions from our online cardiology forum and the latest research, review articles, and online learning modules. You can see abstracts on cardiology from all of our journal articles, including those from *Heart*. The portal also links to our cardiology discussion (http://doc2doc.bmj.com/forums/open-clinical_cardiology) forum on doc2doc, our global clinical community.

The cardiology portal is led by Sadia Khan, a consultant cardiologist at West Middlesex University Hospital, London. Her interests are cardiac imaging, particularly echocardiography, and heart failure. Her blogs include topics such as "What's in a name," on the role of nurse consultants.

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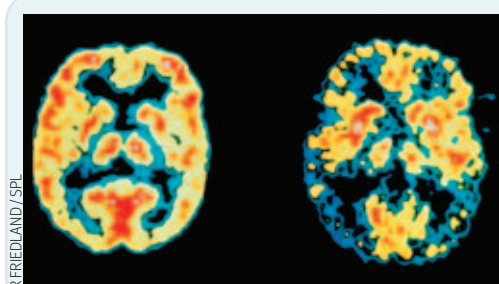
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Plasma asymmetric dimethylarginine in patients with acute decompensation of chronic heart failure

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Heart transplantation: organisational aspects and current trends in immunosuppression—a view from Spain

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Effectiveness of dementia follow-up care by memory clinics or general practitioners

This randomised controlled trial of 175 patients with a new diagnosis of mild to moderate dementia found no evidence that memory clinics were more effective than general practitioners with regard to post-diagnosis treatment and coordination of care.

Effects of interventions in pregnancy on maternal weight and obstetric outcomes: meta-analysis of randomised evidence

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EDITORIAL by Poston and Chapell

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STUDY QUESTION

What effects do dietary and lifestyle interventions in pregnancy have on maternal and fetal outcomes related to weight and pregnancy?

SUMMARY ANSWER

Dietary and lifestyle interventions in pregnancy can reduce maternal gestational weight gain. Interventions based on diet are most effective and are also associated with improved obstetric outcomes compared with alternative interventions.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Excessive weight gain in pregnancy is associated with adverse maternal and fetal outcomes. Diet and lifestyle interventions in pregnancy are effective in reducing maternal weight gain in pregnancy. There is no significant overall effect on outcomes related to fetal weight. Diet based interventions are the most effective in reducing maternal gestational weight gain with no associated increase in the risk of having babies who are small for gestational age.

Selection criteria for studies

We searched Medline, Embase, BIOSIS, LILACS, Science Citation Index, Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE), the Health Technology Assessment Database (HTA), and PsychInfo from inception to January 2012. We included randomised controlled trials that evaluated any dietary or lifestyle interventions with potential to influence maternal and fetal weight related outcomes.

Primary outcome

The primary outcomes were maternal and fetal outcomes related to weight (weight gain in pregnancy and birth weight), and other outcomes were critically important outcomes in pregnancy.

Main results and role of chance

Forty four randomised trials (7278 women) reported the effects of dietary and lifestyle interventions in pregnancy. Compared with control, there was a reduction in weight gain of 1.42 kg in pregnancy with interventions (95% confidence interval 0.95 to 1.89 kg). The largest reduction in weight gain was observed with dietary intervention (3.84 kg, 2.45 to 5.22 kg). There was no significant reduction in the birth weight (mean difference -50 g, 95% confidence interval -100 to 0 g) for all interventions

compared with control. There was no significant difference in the incidence of large for gestational age (relative risk 0.85, 0.66 to 1.09) or small for gestational age (1.00, 0.78 to 1.28) babies. Interventions were associated with a reduced risk of pre-eclampsia (0.74, 0.60 to 0.92) and shoulder dystocia (0.39, 0.22 to 0.70), with no significant effect on other critically important outcomes.

Among interventions, dietary intervention resulted in the largest reduction in maternal gestational weight gain (3.84 kg, 2.45 to 5.22 kg) and was associated with a significant reduction in pre-eclampsia (relative risk 0.67, 0.53 to 0.85), gestational diabetes (0.39, 0.23 to 0.69), gestational hypertension (0.30, 0.10 to 0.88), and preterm delivery (0.68, 0.48 to 0.96). Physical activity was associated with reduced birth weight (mean difference -60 g, -120 to -10 g). The interventions based on physical activity and mixed approaches did not show a difference in obstetric outcomes when compared with the control.

Bias, confounding, and other reasons for caution

We observed heterogeneity for beneficial effects of interventions on maternal weight gain that persisted after accounting for the type of intervention, body mass index (BMI), and diabetic status. Further information is needed on patients' characteristics such as age, ethnicity, socioeconomic status, parity, and underlying medical conditions and characteristics of the intervention such as frequency, duration, and intensity that could influence the outcomes.

The quality across various outcomes assessed by GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) was moderate for benefit observed with gestational weight gain but low to very low for other important obstetric outcomes such as pre-eclampsia, gestational diabetes, gestational hypertension, and preterm delivery. This weakens the inferences for these outcomes. The reasons for low evidence rating were the considerable heterogeneity observed in the effect size, deficiencies in the quality of the individual studies, and risk of publication and related biases.

Study funding

The review was funded by the National Institute for Health Research (NIHR) HTA (Health Technology Assessment) UK programme 09/27/06, to whom the report is submitted. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the HTA programme, NIHR, NHS, or the Department of Health.

Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis

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STUDY QUESTION

What is the effect of tranexamic acid on blood transfusion, thromboembolic events, and mortality in surgical patients?

SUMMARY ANSWER

There is strong evidence that tranexamic acid reduces blood transfusion in surgery but its effect on thromboembolic events and mortality remains uncertain.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

95 randomised controlled trials reported the effect of tranexamic acid on blood transfusion in surgical patients, and more trials are under way. We found that about a decade ago tranexamic acid was shown to reduce blood transfusion in surgery and that large trials to assess its effect on thromboembolic events and mortality are now needed.

Selection criteria for studies

Our selection criteria were randomised controlled trials comparing tranexamic acid with no tranexamic acid or placebo in surgical patients (irrespective of language or publication status). We searched the Cochrane central register of controlled trials, Medline, and Embase from inception to September 2011, along with the World Health Organization International Clinical Trials Registry Platform and the reference lists of relevant articles.

Primary outcomes

Blood transfusion, thromboembolic events, and mortality.

Main results and role of chance

Use of tranexamic acid reduces the probability of receiving a blood transfusion by about one third (risk ratio 0.62, 95% confidence interval 0.58 to 0.65; $P<0.001$). This effect was also evident when the analysis was restricted to trials with adequate allocation concealment (0.68, 0.62 to 0.74; $P<0.001$). There was uncertainty about the effect of tranexamic acid on myocardial infarction (0.68, 0.43 to 1.09; $P=0.11$), stroke (1.14, 0.65 to 2.00; $P=0.65$), deep vein thrombosis (0.86, 0.53 to 1.39; $P=0.54$), and pulmonary embolism (0.61, 0.25 to 1.47; $P=0.27$). Although fewer deaths occurred in the tranexamic acid group (0.61, 0.38 to 0.98; $P=0.04$), when the analysis was restricted to trials with adequate concealment there was remaining uncertainty (0.67, 0.33 to 1.34; $P=0.25$).

Bias, confounding, and other reasons for caution

The effect of tranexamic acid on blood transfusion in surgery seems to be valid and the estimate is precise. The validity of the estimated effect of tranexamic acid on thromboembolic events and mortality remains questionable due to the possibility of bias from selective outcome reporting. The point estimates for thromboembolic events and mortality are imprecise and larger clinical trials are needed.

Study funding/potential competing interests

This study received no external funding. IR is a senior investigator for the National Institute for Health Research. We have no competing interests.

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Research: Intraoperative use of tranexamic acid to reduce transfusion rate in patients undergoing radical retropubic prostatectomy
(*BMJ* 2011;343:d5701)

Meta-analysis of effect of tranexamic acid on blood transfusion, thromboembolic events, and mortality		
Outcomes	Pooled risk ratio (95% CI)	P value (test for effect)
Blood transfusion:		
All trials	0.62 (0.58 to 0.65)	<0.001
Well concealed trials	0.68 (0.62 to 0.74)	<0.001
Myocardial infarction:		
All trials	0.68 (0.42 to 1.09)	0.11
Well concealed trials	0.70 (0.39 to 1.25)	0.22
Stroke:		
All trials	1.14 (0.65 to 2.00)	0.65
Well concealed trials	1.18 (0.36 to 3.83)	0.78
Deep vein thrombosis:		
All trials	0.86 (0.53 to 1.39)	0.54
Well concealed trials	0.92 (0.45 to 1.85)	0.81
Pulmonary embolism		
All trials	0.61 (0.25 to 1.47)	0.27
Well concealed trials	0.52 (0.10 to 2.75)	0.44
Mortality:		
All trials	0.61 (0.38 to 0.98)	0.04
Well concealed trials	0.67 (0.33 to 1.34)	0.25

Prevention of acute knee injuries in adolescent female football players: cluster randomised controlled trial

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Research: Comprehensive warm-up programme to prevent injuries in young female footballers
(*BMJ* 2008;337:a2469)

Research: Neuromuscular training and the risk of leg injuries in female football players: cluster randomised controlled study
(*BMJ* 2008;337:a295)

Research: Exercises to prevent lower limb injuries in youth sports
(*BMJ* 2005;330:449)

STUDY QUESTION

Does a neuromuscular warm-up programme reduce the rate of anterior cruciate ligament injury in adolescent female football players?

SUMMARY ANSWER

The neuromuscular warm-up programme reduced the overall rate of anterior cruciate ligament injury by 64%.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Knee injuries are common in football regardless of the playing level, and adolescent female players are more susceptible to anterior cruciate ligament injury than their male counterparts. Almost two thirds of anterior cruciate ligament injuries in adolescent female football players can be prevented with a 15 minute neuromuscular warm-up programme.

Design

This study was a stratified cluster randomised controlled trial, with randomisation using a computer generated list of random numbers. The intervention was a coach led 15 minute neuromuscular warm-up programme (targeting core stability, balance, and proper knee alignment) to be carried out twice a week throughout the competitive season in 2009 (seven months). Clubs in the control group trained as usual. Individual playing time and acute knee injuries causing loss of time from play were recorded during the season. Physiotherapists and physicians supplied to all clubs evaluated and recorded acute knee injuries.

Participants and setting

We randomised 309 clubs in Sweden with female players aged 12-17 years; 18 clubs were dissolved before the study started and were excluded. Of the 291 clubs that entered the study, 230 (79%) clubs (121 in the intervention group, 109 in the control group) with 4564 players (intervention 2479, control 2085) were included in the analysis.

Primary outcome

The primary outcome was the rate of anterior cruciate ligament injury.

Main results and the role of chance

Seven (0.28%) players in the intervention group and 14 (0.67%) in the control group had an anterior cruciate ligament injury during the study. By intention to treat analysis, we found a 64% reduction in the rate of anterior cruciate ligament injury in the intervention group (rate ratio 0.36, 95% confidence interval 0.15 to 0.85). The number needed to treat was 14. We found no significant rate reductions for secondary outcomes (rates of severe knee injury and any acute knee injury). Subgroup analyses of players who carried out the neuromuscular warm-up programme at least once a week showed significant reductions in all outcomes.

Harms

No injury occurred during the execution of the warm-up programme.

Bias, confounding, and other reasons for caution

Although this is the largest randomised controlled trial in prevention of sports injury to date, the number of anterior cruciate ligament injuries recorded was limited. Contributing factors included recruitment not reaching the pre-trial estimated sample size, a 21% dropout rate, and a lower than expected rate of anterior cruciate ligament injury.

Generalisability to other populations

Whether the preventive effect of the neuromuscular warm-up programme on anterior cruciate ligament injury in adolescent female football players shown in our study can be generalised to other age groups, male football players, or other team sports is uncertain. However, similar neuromuscular training programmes have shown preventive effects on knee and lower extremity injuries in other team sports.

Study funding/potential competing interests

The study was supported by grants from the Swedish Football Association, the Folksam Insurance Company, and the Swedish National Centre for Research in Sports. MW and MH have worked as the medical staff of the Swedish male under 19 national football team.

Trial registration number

Clinical trials NCT00894595.

Effectiveness of intervention on primary and secondary outcomes			
Outcome	No (%) of players		Rate ratio (95% CI)
	Intervention group (n=2479)	Control group (n=2085)	
Anterior cruciate ligament injury	7 (0.28)	14 (0.67)	0.36 (0.15 to 0.85)
Severe knee injury	26 (1.05)	31 (1.49)	0.70 (0.42 to 1.18)
Any acute knee injury	48 (1.94)	44 (2.11)	0.92 (0.61 to 1.40)

Evaluation of the national Cleanyourhands campaign to reduce *Staphylococcus aureus* bacteraemia and *Clostridium difficile* infection: four year, prospective, ecological, interrupted time series study

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STUDY QUESTION How successful was the national Cleanyourhands campaign in England and Wales in improving hand hygiene in hospitals, and how did it affect rates of healthcare associated infections?

SUMMARY ANSWER The campaign was associated with sustained increases in hospital procurement of alcohol rub and soap, which were strongly associated with reduced rates of some healthcare associated infections, even after adjustment for other national infection control interventions.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Hand hygiene campaigns aim to reduce healthcare associated infections through sustained improvements in hand hygiene, although it is not known whether national campaigns are effective. This study suggests that in the context of a high profile political drive, a national campaign could make a significant and independent contribution to reductions in selected infections.

Participants and settings

Acute hospital trusts in England and Wales implementing the national Cleanyourhands campaign (installation of bedside alcohol hand rub, materials promoting hand hygiene and institutional engagement, and regular hand hygiene audits) from 1 December 2004.

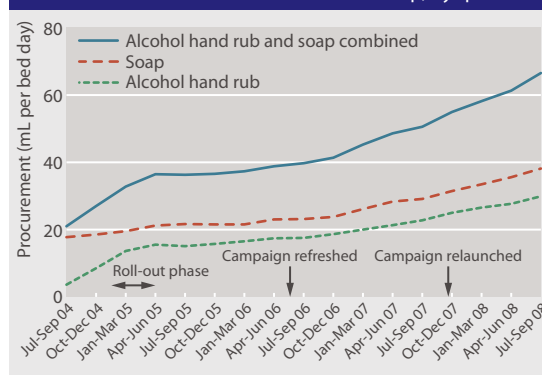
Design, size, and duration

Prospective, ecological, interrupted time series study of 187 trusts from 1 July 2004 to 30 June 2008. Main outcome measures were each trust's quarterly procurement rates of alcohol hand rub and liquid soap (from central NHS supply agencies), and rates of *Staphylococcus aureus* bacteraemia (meticillin resistant (MRSA) and meticillin sensitive (MSSA)) and *Clostridium difficile* infections (from the national mandatory reporting scheme database). We assessed associations between procurement and infection rates by a mixed effect Poisson regression model (accounting for bed occupancy, length of stay, hospital type, and timing of other national interventions targeting these infections).

Main results and the role of chance

Combined procurement of soap and alcohol hand rub tripled from 21.8 to 59.8 mL per patient bed day; procurement rose in association with each phase of the campaign. Rates fell for MRSA bacteraemia (1.88 to 0.91 cases per 10 000 bed days) and *C difficile* infection (16.75 to 9.49 cases). MSSA bacteraemia rates did not fall. Increased procurement of soap was independently associated with reduced *C difficile* infection throughout the study (adjusted incidence rate ratio for 1 mL

Estimated use of alcohol hand rub and soap, by quarter



increase per patient bed day 0.993 (95% confidence interval 0.990 to 0.996; $P < 0.0001$). Increased procurement of alcohol hand rub was independently associated with reduced MRSA bacteraemia, but only in the last four quarters of the study (0.990, 0.985 to 0.995; $P < 0.0001$). Publication of the Health Act 2006 was strongly associated with reduced MRSA bacteraemia (0.86, 0.75 to 0.98; $P = 0.02$) and *C difficile* infection (0.75, 0.67 to 0.84; $P < 0.0001$). Trust visits by Department of Health improvement teams were also associated with reduced MRSA bacteraemia (0.91, 0.83 to 0.99; $P = 0.03$) and *C difficile* infection (0.80, 0.71 to 0.90; $P = 0.01$), for at least two quarters after each visit.

Bias, confounding, and other reasons for caution

Our analysis allowed us to control confounding at the trust level (instead of national level) to identify independent associations. The study was limited by the policy imperative to roll out the campaign quickly, which precluded more robust designs and collection of potentially important but unavailable trust level data, in particular, antibiotic prescription. However, a strong correlation would be needed between rises in procurement and decreases in selected antibiotics to abolish the strong independent associations reported.

Generalisability

The campaign took place in the context of a high profile political drive and other national interventions to reduce MRSA bacteraemia and *C difficile* infection. It received central sustained funding and coordination. The World Health Organization currently offers a very similar intervention as part of its Save Lives initiative. Although caution should be exercised when extrapolating from these results, the campaign could offer a model for other countries to adopt or adapt. National infection control interventions, including an effective hand hygiene campaign, can successfully reduce selected healthcare associated infections.