

# research update

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## Fish oil omega 3 fatty acids improve heart muscle recovery after MI

• (BMJ 2016;354:i4240)

Taking high dose omega 3 fatty acids from fish oil improves heart muscle function and reduces cardiac scarring after a myocardial infarction (MI), a randomised trial published in *Circulation* has shown. Previous studies have shown benefits from omega 3 fatty acids, but their effects on patients receiving the latest evidence based treatment after an MI have been less clear. The new study randomly allocated 358 patients with acute MI attending three hospitals in Boston, USA, to six months' treatment with omega 3 fatty acids (four 1 g capsules a day of a preparation containing 465 mg of ethyl esters of eicosapentaenoic acid and 375 mg of docosahexaenoic acid) or to placebo containing corn oil.

• Heydari B, Abdullah S, Pottala JV, et al. Effect of omega-3 acid ethyl esters on left ventricular remodeling after acute myocardial infarction: the OMEGA-REMODEL randomized clinical trial. *Circulation* 2016;doi:10.1161/CIRCULATIONAHA.115.019949.

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(Richard Lehman is away)

## One in 10 young people experiences a distressing sexual problem

• (BMJ 2016;354:i4272)

A sizeable minority of people aged 16 to 21 experience distressing sexual function problems but very few seek professional help, research published in the *Journal of Adolescent Health* has found. The third National Survey of Sexual Attitudes and Lifestyles included a nationally representative sample of 1875 sexually active and 517 sexually inactive participants and found that 36% of men and 42% of women who reported one or more sexual problems had sought help; however, this was rarely from a professional source but rather from family and friends, the media, or the internet. Only 4% of young men and 8% of young women who reported a sexual problem had consulted a general practitioner, sexual health professional, or psychiatrist.

• Mitchell KR, Geary R, Graham C, et al. Sexual function in 16- to 21-year-olds in Britain. *J Adolesc Health* 2016;doi:10.1016/j.jadohealth.2016.05.017.

## Eating more plant protein is associated with lower risk of death

• (BMJ 2016;354:i4243)

Eating more protein from plant sources is associated with a lower risk of death, and animal protein is associated with a higher risk of death, in people with at least one lifestyle risk factor such as smoking or being overweight, research published in *JAMA Internal Medicine* has shown. The prospective cohort study included 131 342 participants from the Nurses' Health Study and the Health Professionals Follow-Up Study. Diet and other lifestyle data were collected every two years, and participants were followed up for as long as 32 years.

• Song M, Fung TT, Hu FB, et al. Association of animal and plant protein intake with all-cause and cause-specific mortality. *JAMA Intern Med* 2016;doi:10.1001/jamainternmed.2016.4182.

## Most read research on thebmj.com

Exercise therapy versus arthroscopic partial meniscectomy for degenerative meniscal tear in middle aged patients

• (BMJ 2016;354:i3740)

Surgeon specialization and operative mortality in the US

• (BMJ 2016;354:i3571)

Change in fracture risk and fracture pattern after bariatric surgery

• (BMJ 2016;354:i3794)

Adverse inpatient outcomes during the transition to a new electronic health record system

• (BMJ 2016;354:i3835)

Trajectory of body shape in early and middle life and all cause and cause specific mortality

• (BMJ 2016;353:i2195)

## Latest research comments

"Body mass index (BMI) is not a direct measure of body fat, but rather a surrogate measure that calculates excess weight after adjusting for height. There are inherent limitations associated with BMI, specifically in relation to body composition."

Thomas A Cappadona, responding to Trajectory of body shape in early and middle life and all cause and cause specific mortality (doi:10.1136/bmj.i2195)

"The paper regarding surgeon specialisation was interesting, and I suspect in line with the current vogue for super-specialisation by surgeons. The one big omission was no mention of an anaesthetic or anaesthetist being associated with any of the procedures."

David Price, responding to Surgeon specialization and operative mortality in United States (doi:10.1136/bmj.i3571)

"Are you sure this is a case-control study? Is not a case-control study one where cases with some outcome, eg, fracture, are compared to controls without the outcome, no fracture, concerning the presence or absence of some putative risk factor, eg, bariatric surgery?"

Martin Bland, responding to Change in fracture risk and fracture pattern after bariatric surgery (doi:10.1136/bmj.i4117)

# Studying the link between physical activity and health

**ORIGINAL RESEARCH** Systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013

## Physical activity and risk of breast cancer, colon cancer, diabetes, ischaemic heart disease, and ischaemic stroke events

Kyu HH, Bachman VF, Alexander LT, et al

Cite this as: *BMJ* 2016;354:i3857

Find this at: <http://dx.doi.org/10.1136/bmj.i3857>

**Study question** What are the dose-response associations between total physical activity and risks of breast cancer, colon cancer, diabetes, ischaemic heart disease, and ischaemic stroke events?

**Methods** PubMed and Embase were searched for articles published from 1980 to 27 February 2016. Reference lists of included studies in previous systematic reviews of these outcomes were also reviewed. Prospective cohort studies examining the associations of physical activity (any domain) with at least one of the five chosen diseases were eligible for inclusion in this Bayesian dose-response meta-analysis.

**Study answer and limitations** Higher levels of total physical activity are strongly associated with lower risk of breast cancer, colon cancer, diabetes, ischaemic heart disease, and ischaemic stroke, with most health gains occurring at a total activity level of 3000-4000 metabolic equivalent (MET) minutes/week. MET represents the ratio of the working metabolic rate to the resting metabolic rate. One MET is defined as the amount of oxygen consumed while a person is sitting quietly and is about 3.5 mL O<sub>2</sub>/kg body weight/min. Climbing stairs for 10 minutes, vacuuming for 15 minutes, gardening for 20 minutes, running for 20 minutes, and walking or cycling for transportation for 25 minutes on a daily basis would together achieve about 3000 MET minutes a week. Because the analysis relied on the data reported by the cohort studies, the potential for residual confounding or effect modification could not be addressed.

**What this study adds** This is the first dose-response meta-analysis focusing on total physical activity across different domains of life (leisure time, occupation, domestic,



transportation), and it includes about three to five times more prospective cohort studies than previous dose-response meta-analyses that focused on only a single domain of activity. The continuous risk curves for the associations between total physical activity and breast cancer, colon cancer, diabetes, ischaemic heart disease, and ischaemic stroke show that, although the risks of these diseases decrease by increasing the level of total activity, most health gains occur at relatively lower levels of activity (up to 3000-4000 MET minutes/week), with diminishing returns at higher levels of activity.

**Funding, competing interests, data sharing** This study was funded by the Bill and Melinda Gates Foundation. The authors declare no competing interests. The full dataset is available from the corresponding author.

## COMMENTARY Future studies must streamline measurement and reporting for real gains in knowledge

Physical activity is good for health. Few would oppose this contention. But, curiously, we do not definitively know how much the type and quantity of physical activity reduces the risk of common conditions. This imprecision stems essentially from the myriad different ways physical activity has been appraised in epidemiological studies. Some studies investigated physical activity as a whole, while others concentrated on specific types of activity. The metabolic equivalent of tasks (MET) is a standardised metric that expresses the energy spent during a specific activity. The MET is defined as the ratio of the metabolic rate during that activity to the metabolic rate when resting.<sup>1</sup> For example, skipping has a MET of 10, which means that someone skipping for one hour spends 10 times the energy spent during an hour of rest.

Kyu and colleagues<sup>7</sup> carried out a quantitative meta-analysis of the association between the amount of total physical activity

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### This study represents an advance in the handling of disparate data on a lifestyle factor

and the risk of certain diseases: breast and colorectal cancers and diabetes, ischaemic heart diseases, and ischaemic stroke. To overcome the heterogeneity in reporting, the authors relied on elaborate data handling to convert the results of all epidemiological studies into a single metric—MET minutes/week. The study found two phased reductions in the risk of the five conditions of interest: quick drops in risk from 600 to 4000 MET minutes/week, followed by slow steady reductions from 4000 to 10000 MET minutes/week. These amounts might seem enormous, but the study is about the total physical activity of adults.

This study represents an advance in the handling of disparate data on a lifestyle factor that has considerable importance for the prevention of chronic diseases.<sup>7</sup> Nonetheless, because it is based on the MET—a measure of volumes of activity

combining intensity, frequency, and duration—it cannot tell us whether risk reductions would be different with short duration intense physical activity or longer duration light physical activity. The less steep risk reductions seen above 4000 MET minutes/week could be a consequence of the imputation of the amount of a specific activity when it was not reported in studies. Lastly, this study cannot identify those factors likely to modify the association between physical activity and health outcomes. For instance, a recent study showed that the apparently moderate risk reduction observed for breast cancer could be due to the influence of hormone replacement therapy (HRT).<sup>8</sup>

The way forward for improving our knowledge on health benefits associated with physical activity is for future studies to rely on standardised internationally validated questionnaires like the International Physical Activity Questionnaire (IPAQ).<sup>9</sup>

Cite this as: *BMJ* 2016;354:i4200

Find this at: <http://dx.doi.org/10.1136/bmj.i4200>

## Congenital Zika syndrome with arthrogryposis

van der Linden V, Filho ELR, Lins OG, et al

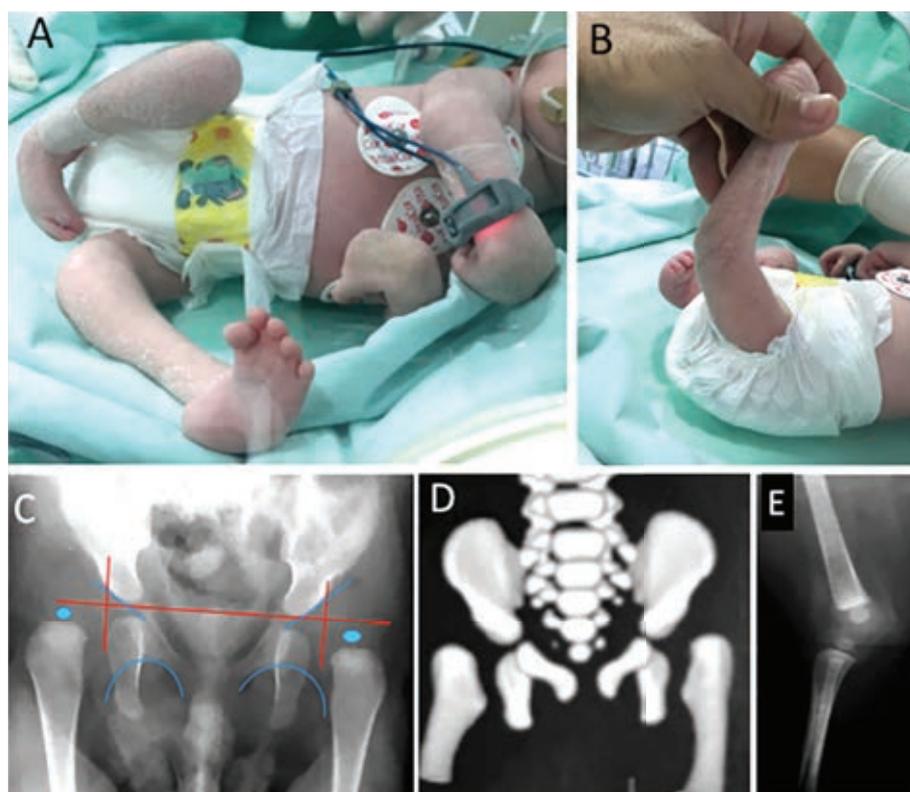
Cite this as: *BMJ* 2016;354:i3899

Find this at: <http://dx.doi.org/10.1136/bmj.i3899>

**Study question** What are the clinical, radiological, and electromyographic features of children with arthrogryposis (joint contractures) associated with congenital infection presumably caused by Zika virus?

**Methods** In this retrospective case series the authors reviewed the medical records of seven children with arthrogryposis associated with congenital infection presumably caused by Zika virus during the Brazilian microcephaly epidemic. All the children underwent neurological and orthopaedic evaluation along with clinical examination and additional investigations: radiography, brain imaging with computerised tomography or magnetic resonance imaging (MRI), high definition ultrasonography of the joints, nerve conduction studies, and needle electromyography. Four children underwent spinal MRI.

**Study answer and limitations** Changes were seen on the brain images of all seven children, with calcifications predominantly in cortex and subcortical white matter (especially in the junction between the cortex and white matter), with abnormalities of cortical development and hypoplasia of the brainstem and cerebellum. Test results for evaluation of the arthrogryposis were consistent with a neurogenic pattern, with electromyography and spinal MRI suggesting involvement of the lower motor neurones. Microcephaly and craniofacial disproportion have been common with Zika virus infection but were not observed in all cases in this study. Further research is needed



(A) Joint deformities; (B) hyperextension and dislocation of knee; (C) anteroposterior radiographs of hips showing features compatible with dislocation: interrupted Shenton's arc, hypoplastic proximal femoral epiphysis, acetabular index of 35 degrees, and right and left proximal femoral epiphysis located laterally on side and bottom quadrant ombredanne; (D) 3D computed tomography showing bilateral dislocation of hips; (E) radiograph showing subluxation of knee (arrows)

to study the neurological abnormalities behind arthrogryposis with a larger number of cases, including histopathology of autopsy samples or tissue from stillborn babies.

**What this study adds** The clinical, imaging, and electromyographic findings suggest that the arthrogryposis was unrelated to the joint abnormalities themselves, but might be of neurogenic origin, with chronic involvement of central and peripheral motor neurones, or

due to vascular change affecting these two segments.

**Funding, competing interests, data sharing** The study received no external funding. The authors have no competing interests. No additional data are available. The authors obtained written consent from parents for publication of the images. All mothers gave consent for neuroimaging studies to be performed as part of the Brazilian microcephaly outbreak protocol or clinical indication. All cases have been deidentified, and *The BMJ* decided to proceed with publication in the interests of public health.

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## Blood pressure and complications in individuals with type 2 diabetes and no previous cardiovascular disease

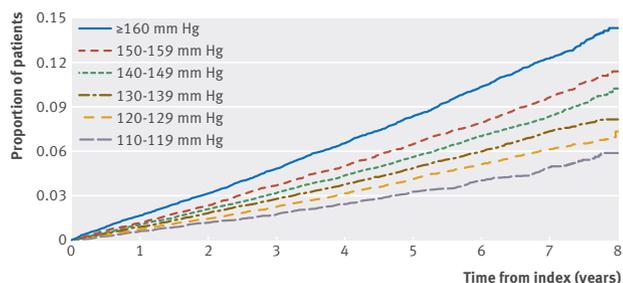
Adamsson Eryd S, Gudbjörnsdóttir S, Manhem K, et al

Cite this as: *BMJ* 2016;354:i4070

Find this at: <http://dx.doi.org/10.1136/bmj.i4070>

**Study question** What are the risks associated with a systolic blood pressure that meets current recommendations (<140 mm Hg) compared with the risks of lower levels of blood pressure in patients who have type 2 diabetes and no previous cardiovascular disease?

**Methods** This observational study used the Swedish national diabetes register. Inclusion criteria were presence of type 2 diabetes for at least one year, age 75 or younger, and no previous cardiovascular or other major disease. Baseline systolic blood pressure was measured and clinical events were obtained from the hospital discharge and death registers, with respect to acute myocardial infarction, stroke, a composite of acute myocardial infarction and stroke (cardiovascular disease), coronary heart disease, heart failure, and total mortality. Hazard ratios were estimated for different levels of systolic blood pressure with clinical characteristics and drug prescription data as



Kaplan-Meier analysis of non-fatal cardiovascular events

No at risk	110-119 mm Hg	120-129 mm Hg	130-139 mm Hg	140-149 mm Hg	150-159 mm Hg	≥160 mm Hg
110-119 mm Hg	11 151	11 012	9732	8362	6951	5422
120-129 mm Hg	31 748	31 325	27 909	24 068	20 086	15 800
130-139 mm Hg	43 114	42 472	38 115	33 112	27 712	22 109
140-149 mm Hg	37 628	37 007	33 575	29 616	25 203	20 390
150-159 mm Hg	18 598	18 251	16 666	14 770	12 721	10 417
≥160 mm Hg	19 554	19 059	17 466	15 494	13 334	10 933

covariates. The mean follow-up in 187 106 patients was five years.

**Study answer and limitations** Participants in the lowest systolic blood pressure group (110-119 mm Hg) had a significantly lower risk of acute myocardial infarction, cardiovascular disease, and non-fatal coronary heart disease than those in the reference group (130-139 mm Hg). Overall, there were no indications of a J shaped relation between systolic blood pressure and the endpoints, with the exception of heart failure and total mortality. The study did not evaluate the effect of intensive antihypertensive treatment and did not include patients with previous cardiovascular disease or other major diseases or those older than 75.

**What this study adds** Lower systolic blood pressure than currently recommended is associated with significantly lower risk of cardiovascular events in patients with type 2 diabetes. The association between low blood pressure and increased mortality could be due to concomitant disease rather than antihypertensive treatment.

**Funding, competing interests, data sharing** This study was supported by grants from the Region Västra Götaland in Sweden, the Swedish Heart and Lung Foundation, Diabetes Wellness, the Swedish Diabetes Foundation, the Swedish Council for Working Life and Social Research (Epilife), and the Swedish Research Council. The authors declared no competing interest, and there are no data to share.

## RESEARCH METHODS AND REPORTING A systematic and transparent approach to making well informed healthcare choices

### GRADE Evidence to Decision (EtD) frameworks

GRADE Working Group

Cite this as: *BMJ* 2016;353:i2016

Find this at: <http://dx.doi.org/10.1136/bmj.i2016>

Cite this as: *BMJ* 2016;353:i2089

Find this at: <http://dx.doi.org/10.1136/bmj.i2089>

The GRADE Working Group has developed Evidence to Decision (EtD) frameworks to support the process of moving from evidence to decisions. The EtD frameworks provide a systematic and transparent approach to making well informed healthcare choices. Their main purpose is to help groups of people (panels) use evidence in a structured and transparent way to inform decisions about clinical recommendations, coverage, health systems, and public health interventions.

EtD frameworks help panels to be

more systematic and explicit about the judgments that they make, the evidence used to inform each of those judgments, additional considerations, and the basis for their recommendations or decisions. EtD frameworks can help to ensure the trustworthiness of recommendations and decisions, enable users of recommendations and those affected by decisions to appraise the basis for the recommendations or decisions, and facilitate adaptation of recommendations or decisions to different settings.

EtD frameworks include three main sections that reflect the main steps in going from evidence to a decision: formulating the question, making an assessment, and drawing conclusions. The assessment entails use of an explicit set of criteria and decision making on each criterion that is informed by the best available research evidence and other considerations.

Different types of decisions and different perspectives require different criteria, although most of the criteria are similar. Consequently, we have developed different frameworks for clinical recommendations from an individual patient perspective, clinical recommendations from a population perspective, coverage decisions, recommendations or decisions about tests, and health system or public health recommendations and decisions. All of the frameworks include criteria that address whether the problem is a priority, the magnitude of the desirable and undesirable effects, the certainty of the evidence, consideration of how patients or others who are affected value the main outcomes, the balance between desirable and undesirable effects, resource use, acceptability, and feasibility. All of the frameworks that take a population perspective also include consideration of effects on equity.