

research



Dietary fat and diabetes prevention p 227



Dose-response effects of physical activity p 228



China's two child policy p 230

ORIGINAL RESEARCH Systematic review and meta-analysis of RCTs

Omega-3, omega-6, and total dietary polyunsaturated fat for prevention and treatment of type 2 diabetes mellitus

Brown TJ, Brainard J, Song F, Wang X, Abdelhamid A, Hooper L; on behalf of the PUFAH Group
 Cite this as: *BMJ* 2019;366:l4697 Find this at: <http://dx.doi.org/10.1136/bmj.l4697>

Study question What are the effects of increasing omega-3, omega-6, and total polyunsaturated fatty acid (PUFA) on diabetes diagnosis and glucose metabolism?

Methods This was a systematic review and meta-analysis, with searches of Medline, Embase, CENTRAL, and trials registers. It included randomised controlled trials of at least 24 weeks' duration assessing effects of increasing

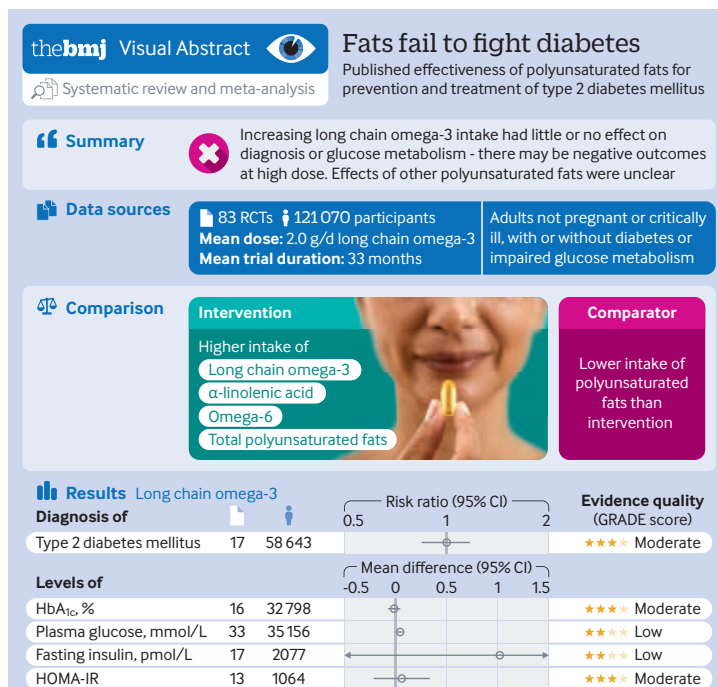
α -linolenic acid, long chain omega-3, omega-6, or total PUFA, which collected data on diagnoses of diabetes, fasting glucose or insulin, glycated haemoglobin (HbA_{1c}), and/or homeostatic model assessment for insulin resistance (HOMA-IR). Statistical analysis included random effects meta-analyses, using relative risk and mean difference, and sensitivity analyses. Risk of bias was assessed using the Cochrane tool and quality of evidence using GRADE.

Study answer and limitations Long chain omega-3 had little or no effect on diagnosis of diabetes (relative risk 1.00, 95% confidence interval 0.85 to 1.17; 58 643 participants; 3.7% developed diabetes) or measures of glucose metabolism. Effects did not differ in sensitivity analyses or in longer duration trials. A suggestion of negative outcomes was seen when the supplemental long chain omega-3 dose was above 4.4 g/d. Increasing α -linolenic acid, omega-6, and total PUFA seemed to have little or no effect on measures of glucose metabolism, but data for these interventions were limited and few trials were at low summary risk of bias.

What this study adds Extensive evidence from randomised controlled trials suggests that increasing long chain omega-3 has little or no effect on prevention and treatment of type 2 diabetes mellitus. Data on effects of α -linolenic acid, omega-6, and total PUFA are less clear, as data were limited.

Funding, competing interests, and data sharing The World Health Organization funded this research. The authors will share their database of trials and have published a companion paper detailing this database.

Systematic review registration PROSPERO CRD42017064110.



Every step you take

ORIGINAL RESEARCH Systematic review and harmonised meta-analysis

Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality

Ekelund U, Tarp J, Steene-Johannessen J, et al

Cite this as: *BMJ* 2019;366:l4570

Find this at: <http://dx.doi.org/10.1136/bmj.l4570>

Study question What is the magnitude and shape of dose-response associations between accelerometer assessed intensities of physical activity and sedentary time and all cause mortality?

Methods This systematic review and harmonised meta-analysis was carried out on prospective cohort studies that measured physical activity and sedentary time by accelerometry. Individual level participant data were harmonised and analysed at study level. Sedentary time, total physical activity, and intensity specific physical activity were categorised by quarters (least active or least sedentary as referent) of physical activity intensity at study level, and Cox proportional hazards regression analyses were used to study specific associations with all cause mortality. Study results were summarised using random effects meta-analysis. Individual level data from eight studies (n=36 383, mean age 62.6 years), with median follow-up of 5.8 years (range 3.0-14.5 years) and 2149 (5.9%) deaths were analysed.

Study answer and limitations Any physical activity, regardless of intensity, was associated with lower risk of mortality, with a non-linear dose-response. Hazards ratios for mortality were 1.00 (referent, least active) in the first quarter, 0.48 (95% confidence interval 0.43 to 0.54) in the second, 0.34 (0.26 to 0.45) in the third, and 0.27 (0.23 to 0.32) in the fourth (most active). Corresponding hazards ratios for light physical activity were 1.00, 0.60 (0.54 to 0.68), 0.44 (0.38 to 0.51), and 0.38 (0.28 to 0.51), and for moderate-to-vigorous physical activity were 1.00, 0.64 (0.55 to 0.74), 0.55 (0.40 to 0.74), and 0.52 (0.43 to 0.61). Time spent sedentary was associated with an increased risk of death. The results are only generalisable to middle aged and older adults in the US and western Europe.

What this study adds The results suggest that all intensities of physical activity, including light intensity, are associated with a substantially reduced risk of death in a dose-response manner.

The observed effect sizes for associations between physical activity and risk of death are about twice as large as those previously reported in studies assessing physical activity by self report and were observed at activity levels achievable for large segments of the population.

Funding, competing interests, and data sharing The funders of the individual studies had no role in this work. No competing interests. Summary data can be obtained from the corresponding author (ulf.ekelund@nih.no).

Study registration PROSPERO CRD42018091808.

COMMENTARY Walk more and sit less: even light exercise is linked to a lower risk of death

In the 1950s the London busman's study found that bus drivers developed a higher rate of coronary heart disease than their bus conductor counterparts.¹ Since then, observational studies have repeatedly suggested that sedentary behaviour is bad and physical activity is good for health and longevity. Guidelines recommend at least 150 minutes of moderate intensity or 75 minutes of vigorous intensity aerobic physical activity each week.^{2,3}

Guideline evidence is mostly based on self report of the amount, intensity, and frequency of activity. Self report is, however, open to recall and reporting bias, potentially resulting in underestimation of low intensity activity and overestimation of overall activity.⁴ Self reports are also imprecise.

The introduction of body-worn sensors in the past decade has enabled more objective and precise data on the amount and intensity of physical activity and considerably advanced the specialty. But inconsistency and uncertainty remain, especially about the magnitude of any effects and the contribution to health of low levels of physical activity.

The systematic review and meta-analysis by Ekelund and colleagues combines high quality studies analysing the effect of sensor measured physical activity and sedentary behaviour on mortality.⁷

The results show non-linear dose-response relations between all activity measures, including sedentary time, and all cause mortality in

Walking is simple, free, achievable even for older adults, and rarely contraindicated

adults. More than 9.5 hours of daily sedentary behaviour, excluding sleeping time, was associated with a statistically significant increased risk of death. In contrast, mortality fell steeply as total volume of physical activity increased up to a plateau at 300 accelerometer counts per minute of wear time. A similarly steep decrease in mortality occurred with increasing duration of light physical activity up to a plateau of about 300 minutes per day.

Bigger benefits

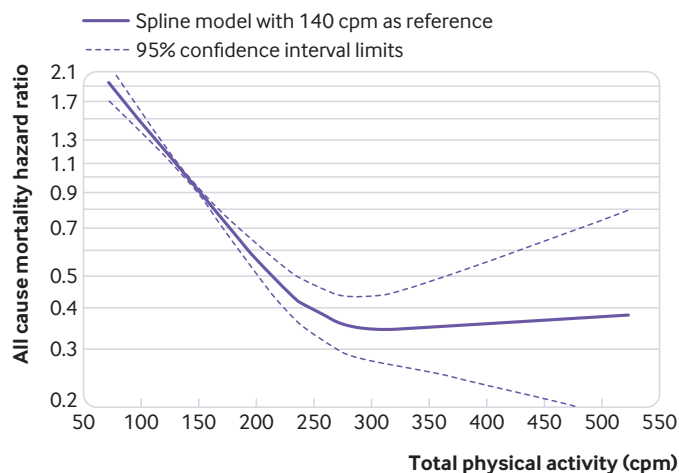
The new meta-analysis clarifies previous findings and confirms that even light activity, such as walking, is beneficial. The observed effect sizes for physical activity and mortality were substantially larger than those reported previously, potentially because of the improved precision of measurement and reduction of variance.

Questions remain, particularly over whether the effect of physical activity continues above a certain threshold. Previous studies using step detection to quantify activity have also reported a plateau after an initially steep decrease in mortality.^{8,9} Furthermore, it is unclear whether the effect of activity simply adds up or whether the distribution and complexity of activity across the day or week is relevant. We do not know if sedentary behaviour and physical activity are independent factors or if they represent two sides of the same coin. New statistical approaches such as compositional analyses are required to explore these interdependencies.¹⁰

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Dose-response associations between total physical activity and all cause mortality. Modelling performed using restricted cubic splines with knots at 25th, 50th, and 75th centiles of exposure specific distribution from medians of quarters (least to most active). The exposure reference is set as the median of the medians in the reference group (least active). Counts per minute (cpm) is a measure of total physical activity averaged over the measurement period by dividing the total accumulated movement (physical activity) measured by the accelerometer by the time (minutes) the monitor was worn by the participant

The current analysis assumes that physical activity levels remain constant over time, which does not reflect reality. Changes in the duration and intensity of physical activity occur over the whole life span. Longitudinal data and novel methods examining activity trajectories are needed. This is also important to eliminate the risk of reverse causation whereby disease causes reduced activity, not the other way around.

Besides these details, the clinical message for general practitioners, public health professionals, policy makers, and the public seems straightforward: every step counts and even light activity is beneficial. Developing ways to limit sedentary time and increase activity at any level could considerably improve health and reduce mortality.

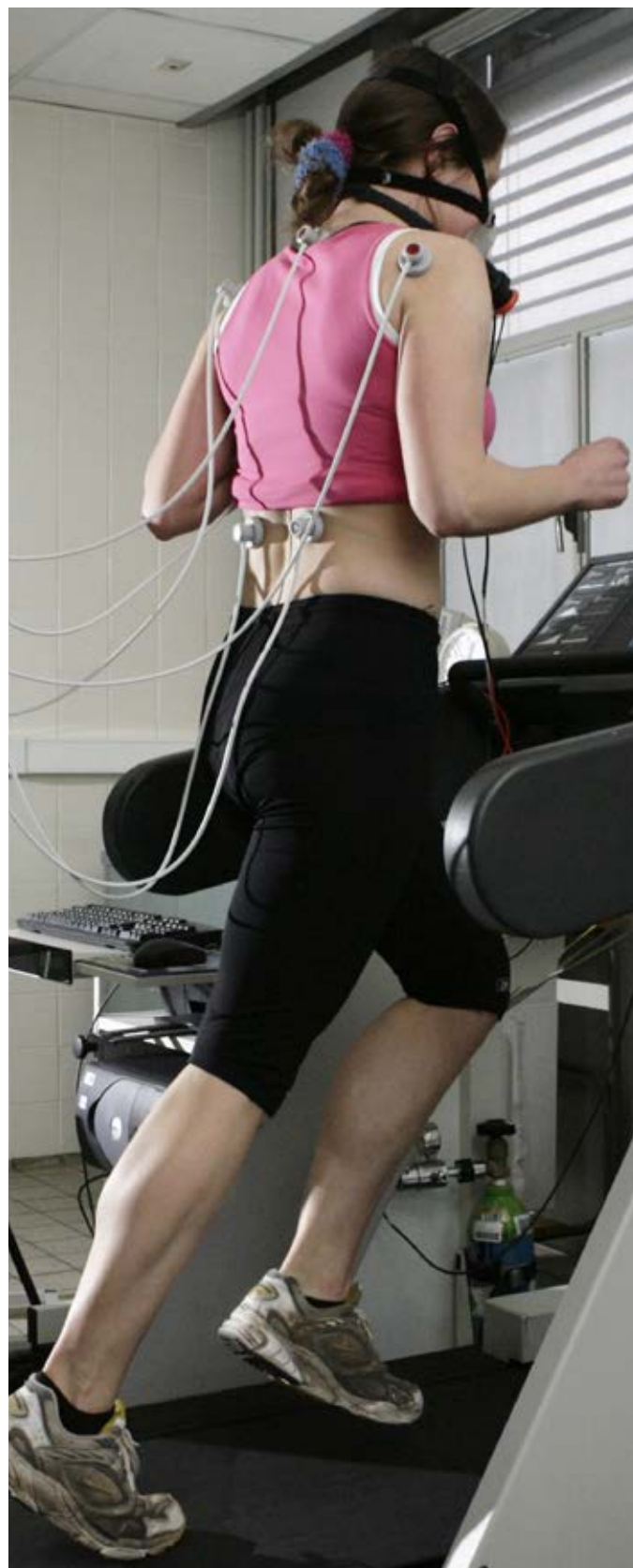
Effective interventions include prescriptions for activity from primary care practitioners, particularly with community follow-up.¹¹ Health coaches also show promise.¹² Activity prescribing is cheaper than many pharmaceutical interventions for cardiovascular disease and more effective at improving quality adjusted life years.¹³

Increasing activity at the population level is challenging, and sustained behaviour change is the holy grail of primary care and public health.¹⁴ Walking is one promising target for intervention.¹⁵ It is simple, affordable (free), achievable even for older adults, and rarely contraindicated.

In conclusion, Ekelund and colleagues' findings are important and easy to interpret: we should all move more and sit less and should encourage others to do the same.

Cite this as: *BMJ* 2019;366:l5051

Find the full version with references at <http://dx.doi.org/10.1136/bmj.l5051>

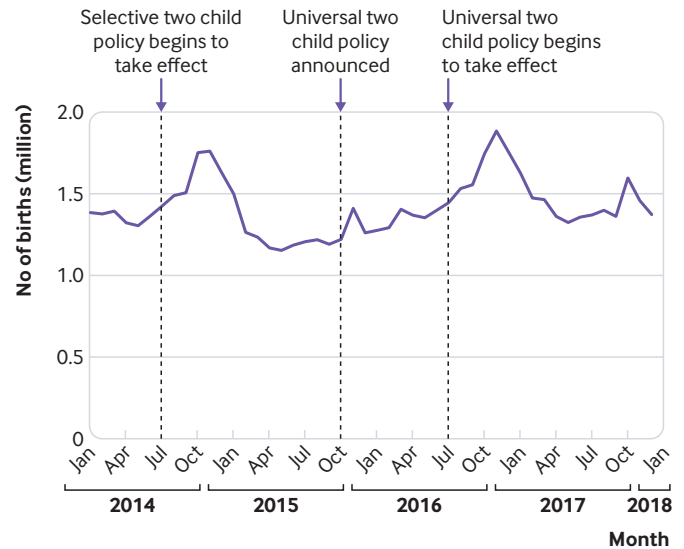


Association of China's universal two child policy with changes in births and birth related health factors

Li H, Xue M, Hellerstein S, et al

Cite this as: *BMJ* 2019;366:l4680

Find this at: <http://dx.doi.org/10.1136/bmj.l4680>



Number of births in mainland China during January 2014 and December 2017, by month (information taken from county level monthly aggregated data). Both selective and universal two child policies were assumed to take effect about nine months after being announced

Study question What changes in births have been associated with China's universal two child policy, announced in October 2015?

Methods Using two national databases (county level monthly aggregated data on births covering the period from January 2014 to December 2017 and individual level delivery information records from January 2015 to December 2017), researchers quantified the number of births attributable to the policy using a difference-in-differences approach—that is, assuming that the policy would affect births to multiparous mothers but not to nulliparous mothers (control). Included data covered 28 of the 31 provinces in mainland China. Changes in the proportion of multiparous mothers and mothers aged 35 and older, preterm deliveries, and caesarean deliveries were also examined.

Study answer and limitations The estimated number of additional births attributable to the universal two child policy between July 2016 and December 2017 was 5.40 (95% confidence interval 4.34 to 6.46) million. The monthly mean percentage of multiparous mothers and

mothers aged 35 and over increased by 9.1 percentage points (95% confidence interval 6.4 to 11.7) and 5.8 percentage points (5.2 to 6.4), respectively. This increase in older mothers, however, was not associated with a concurrent increase in the overall rate of preterm birth. The monthly mean caesarean delivery rate among multiparous mothers increased by 1.2 percentage points (0.8 to 1.6), from 39.7% to 40.9%, and decreased by 3.0 percentage points (−3.5 to −2.5) among nulliparous mothers, from 39.6% to 36.6%. Lack of additional clinically meaningful measures of health outcomes was a limitation of the study.

What this study adds This study investigates the impact of China's universal two child policy using national data. Results suggest that births increased in response to the policy, albeit not as much as some policymakers had hoped.

Funding, competing interests, and data sharing Jointly funded by the National Key Research and Development Program of China, National Health Commission of China, and National Natural Science Foundation of China. No competing interests declared. No additional data available.

the **bmj** Visual summary

See our infographics page for a visual explanation of trends in China's birth rates after introduction of the two child policy

<http://bit.ly/BMJinfographics>

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