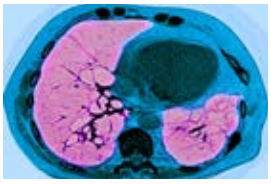
research



Many asymptomatic adults have potentially serious incidental findings on MRI p 311

Low carbohydrate diets may increase the effectiveness of obesity treatment p 312

Energy control and food source mediate effect of fructose on glycaemic control p 313

Rotating shift work and unhealthy lifestyle associated with higher risk of type 2 diabetes p 314

ORIGINAL RESEARCH Systematic review and meta-analysis

Potentially serious incidental findings on brain and body magnetic resonance imaging of apparently asymptomatic adults

Gibson LM, Paul L, Chappell FM, et al

Cite this as: *BMJ* 2018;363:k4577
Find this at: http://dx.doi.org/10.1136/bmj.k4577

Study question What is the prevalence of potentially serious incidental findings in apparently asymptomatic adults undergoing magnetic resonance imaging (MRI) of the brain, thorax, abdomen, or brain and body (brain, thorax, and abdomen combined)?

Methods The authors searched Medline and Embase (from inception to 25 April 2017), citations of relevant articles, and authors' files for published studies of the prevalence and types of incidental findings among apparently asymptomatic adults undergoing MRI of the brain, thorax, abdomen, or brain and body (that is, brain, thorax, and abdomen combined). Data on study population and methods, prevalence and types of incidental findings, and final diagnoses were extracted. Pooled prevalence was estimated by random effects meta-analysis, and heterogeneity was determined by τ^2 statistics.

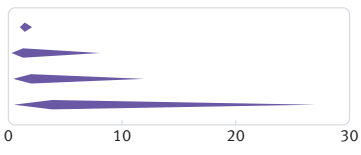
Study answer and limitations Pooled prevalences of potentially serious incidental findings from 32 studies of 27 643 participants were 1.4% (95% confidence interval 1.0% to 2.1%) on brain MRI, 1.3% (0.2% to 8.1%) on thoracic MRI, 1.9% (0.3% to 12.0%) on abdominal MRI, and 3.9% (0.4% to 27.1%) on brain and body MRI. Pooled prevalence rose when including incidental findings of uncertain potential seriousness (1.7% (1.1% to 2.6%), 3.0% (0.8% to 11.3%), 4.5% (1.5% to 12.9%), and 12.8% (3.9% to 34.3%), respectively). Around half of potentially serious incidental findings were suspected malignancies (brain, 0.6% (95% confidence interval 0.4% to 0.9%); thorax, 0.6% (0.1% to 3.1%); abdomen, 1.3% (0.2% to 9.3%); brain and body, 2.3% (0.3% to 15.4%)). There was substantial heterogeneity among included studies, but few informative data on potential sources of between-study variation. Limited follow-up data suggested that relatively few people (48/234, 20.5%) had serious final diagnoses.

What this study adds A substantial proportion of apparently asymptomatic adults will have potentially serious incidental findings on MRI, but little is known of their final diagnoses or health consequences. Systematic, long term follow-up studies are needed to better inform on these and the implications for policies on feedback of potentially serious incidental findings.

Funding, competing interests, and data sharing LMG is funded by a Wellcome Trust Clinical Research Training Fellowship (107190/Z/15/Z) and receives personal fees from UK Biobank, outside the submitted work. CLMS is the chief scientist of UK Biobank. None of the remaining authors report competing interests. The full dataset is available at http://dx.doi.org/10.7488/ds/2100 with open access.

Study registration Prospero CRD42016029472.

Region imaged	Sample size	Potentially serious incidental findings in apparently asymptomatic adults on MRI* No	Prevalence (%) (95% CI)
Brain	27 349	688	1.4 (1.0 to 2.1)†
Thorax	5111	238	1.3 (0.2 to 8.1)†
Abdomen	4817	412	1.9 (0.3 to 12.0)†
Brain and body	4817	786	3.9 (0.4 to 27.1)†



Pooled prevalence estimates of potentially serious incidental findings detected on magnetic resonance imaging (MRI), by imaged region. *Pooled prevalence results of random effects meta-analyses, which modelled within-study variance as binomial. †τ^2=0.8 brain, 5.1 thorax, 4.2 abdomen, and 5.7 brain and body. τ^2 is an estimate of between-study variance on the logit scale (zero represents no variance)

Effects of a low carbohydrate diet on energy expenditure during weight loss maintenance

Ebbeling CB, Feldman HA, Klein GL, et al

Cite this as: *BMJ* 2018;363:k4583
Find this at: http://dx.doi.org/10.1136/bmj.k4583

Study question Do diets differing in carbohydrate to fat ratio affect total energy expenditure during weight loss maintenance, as predicted by the carbohydrate-insulin model of obesity?

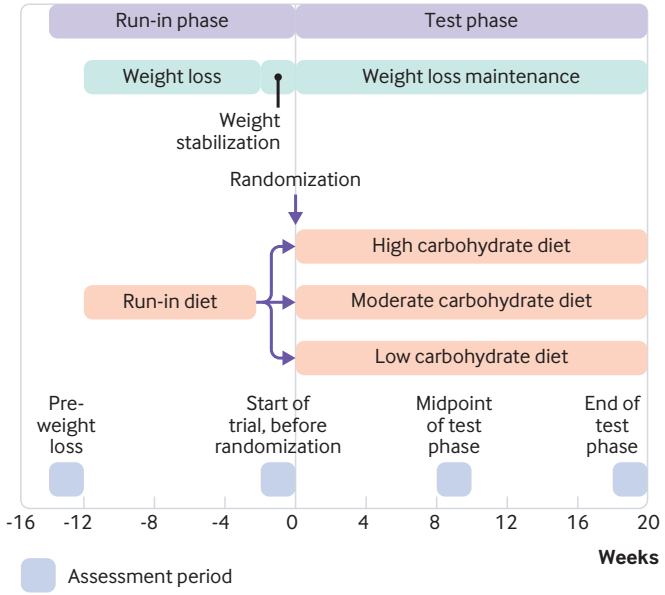
Methods The Framingham State Food Study, a randomised trial, was carried out between August 2014 and May 2017 in two US sites. The study sample comprised 164 adults with a body mass index of 25 or more. After 12% (within 2%) weight loss, participants were randomly assigned to a high (n=54), moderate (n=53), or low (n=57) carbohydrate diet (60%, 40%, or 20% of total energy) for 20 weeks. These diets were controlled for protein and were energy adjusted to maintain weight loss within 2 kg. The primary outcome was total energy expenditure, measured with doubly labelled water, by intention-to-treat analysis. A per protocol analysis included participants who maintained target weight loss, potentially providing a more precise effect estimate.

Study answer and limitations Total energy expenditure differed by diet in the intention-to-treat analysis (n=162, P=0.002), with a linear trend of 52 kcal/d (95% confidence interval 23 to 82) for every 10% decrease in the contribution of carbohydrate to total energy intake (1 kcal=4.18 kJ=0.00418 MJ). Change in total energy expenditure was 91 kcal/d (−29 to 210) greater in participants assigned to the moderate carbohydrate diet and 209 kcal/d (91 to 326) greater in those assigned to the low carbohydrate diet compared with those assigned to the high carbohydrate diet. In the per protocol analysis (n=120, P<0.001), the respective differences were 131 kcal/d (−6 to 267) and 278 kcal/d (144 to 411). Among participants in the highest third of pre-weight loss insulin secretion, the difference between the low carbohydrate and high carbohydrate diet was 308 kcal/d in the intention-to-treat analysis and 478 kcal/d in the per protocol analysis (P<0.004). Ghrelin, a hormone thought to lower energy expenditure, was significantly lower in participants assigned to the low carbohydrate compared with high carbohydrate diet (P=0.004). Study limitations are potential measurement error, non-compliance, and generalisability.

What this study adds A low carbohydrate diet could increase total energy expenditure during weight loss maintenance, an effect that might improve the effectiveness of obesity treatment.

Funding, competing interest, and data sharing See full paper on bmj.com for funding. DSL was supported by a mid-career mentoring award from the National Institute of Diabetes and Digestive and Kidney Diseases (K24DK082730) and received royalties for books on obesity and nutrition that recommend a low glycaemic load diet. The full dataset is available at Open Science Framework (https://osf.io/rvbuy/).

Study registration ClinicalTrials.gov NCT02068885.



Study design

Ghrelin, a hormone thought to lower energy expenditure, was significantly lower in participants assigned to the low carbohydrate compared with the high carbohydrate diet

Food sources of fructose-containing sugars and glycaemic control

Choo VL, Viguiliouk E, Blanco Mejia S, et al

Cite this as: *BMJ* 2018;363:k4644
Find this at: http://dx.doi.org/10.1136/bmj.k4644

Study question Does the evidence supporting reductions in free sugars, especially fructose-containing sugars from sugars-sweetened beverages, hold for all food sources of these sugars in relation to glycaemic control?

Methods Medline, Embase, and the Cochrane library were searched up to 25 April 2018. We included controlled intervention studies of at least seven days' duration in people with and without diabetes that assessed the effect of different food sources of fructose-containing sugars on glycaemic control. This assessment was made at one of four levels of energy control: substitution (sugars in energy matched comparisons), addition (energy from sugars added to diet), subtraction (energy from sugars subtracted from diet), or ad libitum (energy from sugars freely replaced). Outcomes were glycated haemoglobin (HbA_{1c}), fasting glucose, and fasting insulin. Four independent reviewers extracted data and assessed risk of bias. Data were pooled by use of random effects models. The GRADE (grading of recommendations assessment, development, and evaluation) approach was used to assess the certainty of the evidence.

Study answer and limitations 155 controlled intervention studies (n=5086) were included. Although total fructose-containing sugars had no harmful effect on any outcome in substitution or subtraction studies with a decrease in HbA_{1c} (mean difference −0.22%, 95% confidence interval −0.35% to −0.08%), a harmful effect was seen on fasting insulin in addition studies (4.68 pmol/L, 1.40 to 7.96) and ad libitum studies (7.24 pmol/L, 0.47 to 14.00). An interaction by food source was seen with specific food sources, showing beneficial effects (fruit and fruit juice) or harmful effects (sweetened milk and mixed sources) in substitution studies, and harmful effects (sugars-sweetened beverages and fruit juice) in addition studies on at least one outcome. The majority of the evidence was low quality.

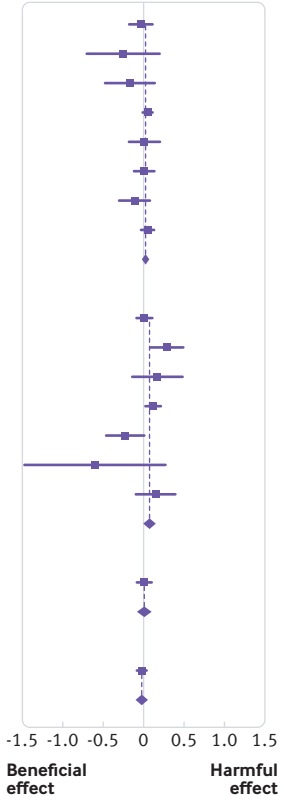
What this study adds

Most food sources of fructose-containing sugars do not have a harmful effect on glycaemic control in energy-matched substitutions for other macronutrients, but sweetened drinks and some other foods that add excess "nutrient poor" energy to diets may have harmful effects.

Competing interests, funding, and data sharing Full details of competing interests and funding are on bmj.com. No additional data are available.

Study registration ClinicalTrials.gov NCT02716870.

Comparison	Studies	No of participants: Intervention	No of participants: Control	Mean difference (95% CI)	Weight (%)	Mean difference (95% CI)	Heterogeneity: I^2 (%)	Heterogeneity: P value	P value
Substitution studies									
Fruit	11	327	296		12.6	-0.04 (-0.35 to -0.03)	76	<0.001	0.62
Dried fruit	4	105	79		1.5	-0.25 (-0.17 to 0.02)	28	0.24	0.28
Fruit juice	1	39	39		1.0	-0.17 (-1.21 to 0.07)	-	-	0.28
Sugars-sweetened beverages	20	318	312		32.2	0.05 (-1.12 to 0.12)	76	<0.001	0.18
Sweetened low fat milk	2	91	96		4.4	0.01 (-2.41 to 0.30)	68	0.08	0.92
Baked goods, sweets, and desserts	10	118	119		5.9	0.01 (-0.38 to 0.40)	0	0.74	0.93
Added sweeteners	12	157	147		8.8	-0.11 (-0.35 to -0.08)	66	<0.001	0.28
Mixed sources	39	781	785		33.5	0.05 (0.13 to 1.07)	58	<0.001	0.26
Total	99	1936	1873		100.0	0.02 (-0.28 to 1.08)	65	<0.001	0.40
Addition studies									
Fruit	7	86	74		22.5	0.01 (-0.79 to 0.44)	0	0.52	0.76
Fruit juice	2	33	40		6.4	0.29 (-0.41 to 0.50)	0	0.81	<0.01
Fruit drinks	3	48	47		11.7	0.17 (-0.04 to 0.14)	82	<0.001	0.28
Sugars-sweetened beverages	11	129	128		47.0	0.12 (-0.04 to 0.14)	74	<0.001	0.01
Sweetened chocolate	1	39	39		3.8	-0.23 (-0.38 to 0.42)	-	-	0.05
Added sweeteners	3	66	63		4.9	-0.60 (-0.38 to 0.42)	57	0.10	0.17
Mixed sources	1	12	11		3.7	0.15 (-0.38 to 0.42)	-	-	0.23
Total	28	413	402		100.0	0.07 (-0.38 to 0.42)	71	<0.001	0.06
Subtraction studies									
Sugars-sweetened beverages	4	346	239		100.0	0.01 (-0.07 to 0.10)	59	0.06	0.79
Total	4	346	239		100.0	0.01 (-0.07 to 0.10)	59	0.06	0.79
Ad libitum studies									
Mixed sources	6	198	279		100.0	-0.02 (-0.07 to 0.04)	0	0.48	0.56
Total	6	198	279		100.0	-0.02 (-0.07 to 0.04)	0	0.48	0.56



Summary plot of the effect of food sources of fructose-containing sugars on fasting blood glucose. Data are weighted mean differences (95% confidence intervals) for summary effects of individual food sources and total food sources on fasting blood glucose. Analyses conducted by generic, inverse variance random effects models (at least five trials available) or fixed effects models (fewer than five trials available). Interstudy heterogeneity was tested by the Cochran's Q statistic (I^2) at a significance level of P<0.10

Rotating night shift work and adherence to unhealthy lifestyle in predicting risk of type 2 diabetes

Shan Z, Li Y, Zong G, et al

Cite this as: *BMJ* 2018;363:k4641
Find this at: http://dx.doi.org/10.1136/bmj.k4641

Study question What are the joint associations of duration of rotating night shift work and unhealthy lifestyle factors with risk of type 2 diabetes?

Methods This study included data for 143 410 female nurses from two large prospective cohorts, the Nurses' Health Study and Nurses' Health Study II. Rotating night shift work was defined as at least three night shifts per month in addition to day and evening shifts in that month. Unhealthy lifestyles included current smoking, physical activity levels below 30 min/day at moderate to vigorous intensity, diet in the bottom three fifths of the Alternate Healthy Eating Index, and body mass index of 25 or higher. Incident cases of type 2 diabetes were identified through self report and validated by a supplementary questionnaire.

Attributing effects to additive interaction between rotating night shift work and lifestyle on risk of type 2 diabetes

	Nurses' Health Study	Nurses' Health Study II	Pooled results*	P for heterogeneity†
Main effects, hazard ratio (95% CI)				
Shift work duration (per 5 years)	1.25 (1.15 to 1.37)	1.38 (1.24 to 1.54)	1.31 (1.19 to 1.44)	0.17
Unhealthy lifestyle‡ (per unit increase)	2.08 (1.98 to 2.18)	2.56 (2.43 to 2.70)	2.30 (1.88 to 2.83)	<0.001
Joint effect	2.46 (2.37 to 2.55)	3.26 (3.15 to 3.37)	2.83 (2.15 to 3.73)	<0.001
Relative excess risk (95% CI) due to interaction				
Relative excess risk due to interaction	0.13 (0.09 to 0.17)	0.32 (0.21 to 0.42)	0.20 (0.09 to 0.48)	<0.001
P value	<0.001	<0.001	<0.001	-
Attributable proportion, % (95% CI)				
Shift work	17.3 (11.9 to 22.7)	16.9 (12.7 to 21.1)	17.1 (14.0 to 20.8)	0.91
Unhealthy lifestyle‡	73.7 (68.1 to 79.2)	69.1 (64.5 to 73.7)	71.2 (66.9 to 75.8)	0.22
Additive interaction	9.0 (7.2 to 10.9)	14.0 (11.4 to 16.5)	11.3 (7.3 to 17.3)	0.002

Multivariable adjusted for age, calendar year, ethnicity (white, African-American, Hispanic, or Asian), marital status (married, divorced/separated/single, or widowed); living status (alone or not), family history of diabetes (yes or no), menopausal status (premenopausal or postmenopausal; never, past, or current menopausal hormone use), oral contraceptive use (never, past, or current use (NHS II only)), alcohol drinking (0, 0.1-4.9, 5.0-14.9, 15.0-19.9, 20.0-29.9, or ≥30 g/day), and total energy intake (fifths); all covariates, except ethnicity and family history of diabetes, were time varying.
*Results were pooled by using random effects model.
†Tests for heterogeneity between studies were quantified using Cochran's Q statistic and I^2 statistic.
‡Unhealthy lifestyles include current smoking, physical activity levels <30 min/day at moderate to vigorous intensity, diet in bottom three fifths of Alternate Healthy Eating Index score, and body mass index ≥25.

Study answer and limitations During more than 20 years of follow-up, 10 915 cases of incident type 2 diabetes occurred. Duration of rotating night shift work and unhealthy lifestyle were independently and jointly associated with a higher risk of type 2 diabetes (P for interaction <0.001). The multivariable adjusted hazard ratios for type 2 diabetes were 1.31 (95% confidence interval 1.19 to 1.44) per five year increment of rotating night shift work duration, 2.30 (1.88 to 2.83) per unhealthy lifestyle factor, and 2.83 (2.15 to 3.73) for their joint effect. The participants were all female nurses and mostly white, which limits the generalisability of the findings to other populations.

What this study adds This study suggests that most cases of type 2 diabetes could be prevented by adherence to a healthy lifestyle, and the benefits could be larger in rotating night shift workers.

Funding, competing interests, data sharing This study was supported by research grants from the National Institutes of Health.