The Big Four Bulletin
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BMJ (4-11 August 2018, Vol. 362, No. 8163)

Association between population mean and distribution of deviance in demographic surveys from 65 countries: Cross sectional study
Fahad Razak, SV Subramanian, Shohinee Sarma, et al.
BMJ 2018; 362 (Published 03 August 2018)
https://www.bmj.com/content/362/bmj.k3147

Abstract
Objectives To examine whether conditions related to scarcity at the left side of the distribution (anaemia, severe chronic energy deficiency, and underweight) are as strongly related to population means as conditions of excess at the right side of the distribution (overweight and obesity).
Design Observational study.
Setting 65 countries, with nationally representative cross sectional data from 1994 to 2014 obtained from the Demographic Health Surveys.
Participants Non-pregnant women aged 20-49. Sample of 65 countries and n=524 380 for analysis of BMI; sample of 44 countries and n=316 465 for analysis of haemoglobin.
Main outcome measures The association between mean and prevalence of each category. For BMI, prevalence of severe chronic energy deficiency (SCED, BMI <16.0), underweight (BMI <18.5), overweight (BMI >25) and obese (BMI >30.) were measured; for haemoglobin, prevalence of anaemia (haemoglobin <12.0 g/dL) and severe anaemia (haemoglobin <8.0 g/dL) were examined.
Results There was a strong association between mean BMI and prevalence of overweight (r^2=0.98; r=0.99; β=8.3 (8.0 to 8.6)) and obesity (r^2=0.93; r=0.97; β=4.2 (3.9 to 4.5)). For left sided conditions, a moderate to strong association was found between mean BMI and prevalence of underweight (r^2=0.67; r=−0.82; β=−2.7 (−3.1 to −2.2)), and a weaker association for SCED (r^2=0.38; r=−0.61; β=−0.32 (−0.43 to −0.22)). There was a moderate association between mean haemoglobin and prevalence of anaemia (r^2=0.46; r=−0.68; β=−10.8 (−14.5 to −7.1)) and a weaker association with severe anaemia (r^2=0.30; r=-0.55; β=−0.55 (−0.81 to −0.29)).
Conclusions The associations between population means and prevalence of conditions of scarcity such as low BMI and anaemia were substantially weaker than the associations of mean BMI with conditions of excesses such as overweight and obesity.

Alcohol consumption and risk of dementia: 23 year follow-up of Whitehall II cohort study

Séverine Sabia, Aurore Fayosse, Julien Dumurgier, et al.

BMJ 2018; 362 (Published 01 August 2018)
https://www.bmj.com/content/362/bmj.k2927

Abstract

Objective To examine the association between alcohol consumption and risk of dementia.

Design Prospective cohort study.

Setting Civil service departments in London (Whitehall II study).

Participants 9087 participants aged 35-55 years at study inception (1985/88).

Main outcome measures Incident dementia, identified through linkage to hospital, mental health services, and mortality registers until 2017. Measures of alcohol consumption were the mean from three assessments between 1985/88 and 1991/93 (midlife), categorised as abstinence, 1-14 units/week, and >14 units/week; 17 year trajectories of alcohol consumption based on five assessments of alcohol consumption between 1985/88 and 2002/04; CAGE questionnaire for alcohol dependence assessed in 1991/93; and hospital admission for alcohol related chronic diseases between 1991 and 2017.

Results 397 cases of dementia were recorded over a mean follow-up of 23 years. Abstinence in midlife was associated with a higher risk of dementia (hazard ratio 1.47, 95% confidence interval 1.15 to 1.89) compared with consumption of 1-14 units/week. Among those drinking >14 units/week, a 7 unit increase in alcohol consumption was associated with a 17% (95% confidence interval 4% to 32%) increase in risk of dementia. CAGE score >2 (hazard ratio 2.19, 1.29 to 3.71) and alcohol related hospital admission (4.28, 2.72 to 6.73) were also associated with an increased risk of dementia. Alcohol consumption trajectories from midlife to early old age showed long term abstinence (1.74, 1.31 to 2.30), decrease in consumption (1.55, 1.08 to 2.22), and long term consumption >14 units/week (1.40, 1.02 to 1.93) to be associated with a higher risk of dementia compared with long term consumption of 1-14 units/week. Analysis using multistate models suggested that the excess risk of dementia associated with abstinence in midlife was partly explained by cardiometabolic disease over the follow-up as the hazard ratio of dementia in abstainers without cardiometabolic disease was 1.33 (0.88 to 2.02) compared with 1.47 (1.15 to 1.89) in the entire population.

Conclusion The risk of dementia was increased in people who abstained from alcohol in midlife or consumed >14 units/week. In several countries, guidelines define thresholds for harmful alcohol consumption much higher than 14 units/week. The present findings encourage the downward revision of such guidelines to promote cognitive health at older ages.

Trends in outpatient antibiotic use and prescribing practice among US older adults, 2011-15: Observational study

Scott W Olesen, Michael L Barnett, Derek R MacFadden, et al.

BMJ 2018; 362 (Published 27 July 2018)
https://www.bmj.com/content/362/bmj.k3155

Abstract

Objective To identify temporal trends in outpatient antibiotic use and antibiotic prescribing practice among older adults in a high income country.

Design Observational study using United States Medicare administrative claims in 2011-15.

Setting Medicare, a US national healthcare program for which 98% of older adults are eligible.
Participants 4.5 million fee-for-service Medicare beneficiaries aged 65 years old and older.
Main outcome measurements Overall rates of antibiotic prescription claims, rates of potentially appropriate and inappropriate prescribing, rates for each of the most frequently prescribed antibiotics, and rates of antibiotic claims associated with specific diagnoses. Trends in antibiotic use were estimated by multivariable regression adjusting for beneficiaries' demographic and clinical covariates.
Results The number of antibiotic claims fell from 1364.7 to 1309.3 claims per 1000 beneficiaries per year in 2011-14 (adjusted reduction of 2.1% (95% confidence interval 2.0% to 2.2%)), but then rose to 1364.3 claims per 1000 beneficiaries per year in 2015 (adjusted reduction of 0.20% over 2011-15 (0.09% to 0.30%)). Potentially inappropriate antibiotic claims fell from 552.7 to 522.1 per 1000 beneficiaries over 2011-14, an adjusted reduction of 3.9% (3.7% to 4.1%). Individual antibiotics had heterogeneous changes in use. For example, azithromycin claims per beneficiary decreased by 18.5% (18.2% to 18.8%) while levofloxacin claims increased by 27.7% (27.2% to 28.3%). Azithromycin use associated with each of the potentially appropriate and inappropriate respiratory diagnoses decreased, while levofloxacin use associated with each of those diagnoses increased.
Conclusion Among US Medicare beneficiaries, overall antibiotic use and potentially inappropriate use in 2011-15 remained steady or fell modestly, but individual drugs had divergent changes in use. Trends in drug use across indications were stronger than trends in use for individual indications, suggesting that guidelines and concerns about antibiotic resistance were not major drivers of change in antibiotic use.

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JAMA: Journal of the American Medical Association (14 August 2018, Vol. 320, No. 6)

Effect of Cell-Free DNA Screening vs Direct Invasive Diagnosis on Miscarriage Rates in Women With Pregnancies at High Risk of Trisomy 21: A Randomized Clinical Trial

Valérie Malan, Laurence Bussières, Norbert Winer, et al.
JAMA. 2018; 320 (6): 557-565.
https://jamanetwork.com/journals/jama/article-abstract/2697008

Abstract

Importance Cell-free DNA (cfDNA) tests are increasingly being offered to women in the first trimester of pregnancies at a high risk of trisomy 21 to decrease the number of required invasive fetal karyotyping procedures and their associated miscarriages. The effect of this strategy has not been evaluated.
Objective To compare the rates of miscarriage following invasive procedures only in the case of positive cfDNA test results vs immediate invasive testing procedures (amniocentesis or chorionic villus sampling) in women with pregnancies at high risk of trisomy 21 as identified by first-trimester combined screening.
Design, Setting, and Participants Randomized clinical trial conducted from April 8, 2014, to April 7, 2016, in 57 centers in France among 2111 women with pregnancies with a risk of trisomy 21 between 1 in 5 and 1 in 250 following combined first-trimester screening.
Interventions Patients were randomized to receive either cfDNA testing followed by invasive testing procedures only when cfDNA tests results were positive (n = 1034) or to

receive immediate invasive testing procedures (n = 1017). The cfDNA testing was performed using an in-house validated method based on next-generation sequencing.
Main Outcomes and Measures The primary outcome was number of miscarriages before 24 weeks' gestation. Secondary outcomes included cfDNA testing detection rate for trisomy 21. The primary outcome underwent 1-sided testing; secondary outcomes underwent 2-sided testing.
Results Among 2051 women who were randomized and analyzed (mean age, 36.3 [SD, 5.0] years), 1997 (97.4%) completed the trial. The miscarriage rate was not significantly different between groups at 8 (0.8%) vs 8 (0.8%), for a risk difference of −0.03% (1-sided 95% CI, −0.68% to ∞; *P* = .47). The cfDNA detection rate for trisomy 21 was 100% (95% CI, 87.2%-100%).
Conclusions and Relevance Among women with pregnancies at high risk of trisomy 21, offering cfDNA screening, followed by invasive testing if cfDNA test results were positive, compared with invasive testing procedures alone, did not result in a significant reduction in miscarriage before 24 weeks. The study may have been underpowered to detect clinically important differences in miscarriage rates.

Fixed Low-Dose Triple Combination Antihypertensive Medication vs Usual Care for Blood Pressure Control in Patients With Mild to Moderate Hypertension in Sri Lanka: A Randomized Clinical Trial

Ruth Webster, Abdul Salam, H. Asita de Silva, et al. for the TRIUMPH Study Group
JAMA. 2018; 320 (6): 566-579.
https://jamanetwork.com/journals/jama/article-abstract/2697010

Abstract
Importance Poorly controlled hypertension is a leading global public health problem requiring new treatment strategies.
Objective To assess whether a low-dose triple combination antihypertensive medication would achieve better blood pressure (BP) control vs usual care.
Design, Setting, and Participants Randomized, open-label trial of a low-dose triple BP therapy vs usual care for adults with hypertension (systolic BP >140 mm Hg and/or diastolic BP >90 mm Hg; or in patients with diabetes or chronic kidney disease: >130 mm Hg and/or >80 mm Hg) requiring initiation (untreated patients) or escalation (patients receiving monotherapy) of antihypertensive therapy. Patients were enrolled from 11 urban hospital clinics in Sri Lanka from February 2016 to May 2017; follow-up ended in October 2017.
Interventions A once-daily fixed-dose triple combination pill (20 mg of telmisartan, 2.5 mg of amlodipine, and 12.5 mg of chlorthalidone) therapy (n = 349) or usual care (n = 351).
Main Outcomes and Measures The primary outcome was the proportion achieving target systolic/diastolic BP (<140/90 mm Hg or <130/80 mm Hg in patients with diabetes or chronic kidney disease) at 6 months. Secondary outcomes included mean systolic/diastolic BP difference during follow-up and withdrawal of BP medications due to an adverse event.
Results Among 700 randomized patients (mean age, 56 years; 58% women; 29% had diabetes; mean baseline systolic/diastolic BP, 154/90 mm Hg), 675 (96%) completed the trial. The triple combination pill increased the proportion achieving target BP vs usual care at 6 months (70% vs 55%, respectively; risk difference, 12.7% [95% CI, 3.2% to 22.0%]; *P* < .001). Mean systolic/diastolic BP at 6 months was 125/76 mm Hg for the triple combination pill vs 134/81 mm Hg for usual care (adjusted difference in postrandomization BP over the entire follow-up: systolic BP, −9.8 [95% CI, −7.9 to −11.6] mm Hg; diastolic BP, −5.0 [95% CI, −3.9 to −6.1] mm Hg; *P* < .001 for both comparisons). Overall, 419

adverse events were reported in 255 patients (38.1% for triple combination pill vs 34.8% for usual care) with the most common being musculoskeletal pain (6.0% and 8.0%, respectively) and dizziness, presyncope, or syncope (5.2% and 2.8%). There were no significant between-group differences in the proportion of patient withdrawal from BP-lowering therapy due to adverse events (6.6% for triple combination pill vs 6.8% for usual care).

Conclusions and Relevance Among patients with mild to moderate hypertension, treatment with a pill containing low doses of 3 antihypertensive drugs led to an increased proportion of patients achieving their target BP goal vs usual care. Use of such medication as initial therapy or to replace monotherapy may be an effective way to improve BP control.

Association Between Traumatic Brain Injury and Risk of Suicide

Trine Madsen, Annette Erlangsen, Sonja Orlovska, et al.

JAMA. 2018; 320 (6): 580-588.
https://jamanetwork.com/journals/jama/article-abstract/2697009

Abstract

Importance Traumatic brain injuries (TBIs) can have serious long-term consequences, including psychiatric disorders. However, few studies have assessed the association between TBI and risk of suicide.

Objective To examine the association between TBI and subsequent suicide.

Design, Setting, and Participants Retrospective cohort study using nationwide registers covering 7 418 391 individuals (≥10 years) living in Denmark (1980-2014) with 164 265 624 person-years' follow-up; 567 823 (7.6%) had a medical contact for TBI. Data were analyzed using Poisson regression adjusted for relevant covariates, including fractures not involving the skull, psychiatric diagnoses, and deliberate self-harm.

Exposure Medical contacts for TBI recorded in the National Patient Register (1977-2014) as mild TBI (concussion), skull fracture without documented TBI, and severe TBI (head injuries with evidence of structural brain injury).

Main Outcomes and Measures Suicide recorded in the Danish Cause of Death register until December 31, 2014.

Results Of 34 529 individuals who died by suicide (mean age, 52 years [SD, 18 years]; 32.7% women; absolute rate 21 per 100 000 person-years [95% CI, 20.8-21.2]), 3536 (10.2%) had medical contact: 2701 with mild TBI, 174 with skull fracture without documented TBI, and 661 with severe TBI. The absolute suicide rate was 41 per 100 000 person-years (95% CI, 39.2-41.9) among those with TBI vs 20 per 100 000 person-years (95% CI, 19.7-20.1) among those with no diagnosis of TBI. The adjusted incidence rate ratio (IRR) was 1.90 (95% CI, 1.83-1.97). Compared with those without TBI, severe TBI (absolute rate, 50.8 per 100 000 person-years; 95% CI, 46.9-54.6) was associated with an IRR of 2.38 (95% CI, 2.20-2.58), whereas mild TBI (absolute rate, 38.6 per 100 000 person-years; 95% CI, 37.1-40.0), and skull fracture without documented TBI (absolute rate, 42.4 per 100 000 person-years; 95% CI, 36.1-48.7) had an IRR of 1.81 (95% CI, 1.74-1.88) and an IRR of 2.01 (95% CI, 1.73-2.34), respectively. Suicide risk was associated with number of medical contacts for TBI compared with those with no TBI contacts: 1 TBI contact, absolute rate, 34.3 per 100 000 person-years (95% CI, 33.0-35.7; IRR, 1.75; 95% CI, 1.68-1.83); 2 TBI contacts, absolute rate, 59.8 per 100 000 person-years (95% CI, 55.1-64.6; IRR, 2.31; 95% CI, 2.13-2.51); and 3 or more TBI contacts, absolute rate, 90.6 per 100 000 person-years (95% CI, 82.3-98.9; IRR, 2.59; 95% CI, 2.35-2.85; all $P < .001$ for the IRR's). Compared with the general population, temporal proximity

since the last medical contact for TBI was associated with risk of suicide (*P*<.001), with an IRR of 3.67 (95% CI, 3.33-4.04) within the first 6 months and an incidence IRR of 1.76 (95% CI, 1.67-1.86) after 7 years.
Conclusions and Relevance In this nationwide registry-based retrospective cohort study individuals with medical contact for TBI, compared with the general population without TBI, had increased suicide risk.

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The Lancet (11 August 2018, Vol. 392, No. 10146)

Excess mortality and cardiovascular disease in young adults with type 1 diabetes in relation to age at onset: A nationwide, register-based cohort study
Araz Rawshani, Naveed Sattar, Stefan Franzén, et al.
The Lancet: Volume 392, ISSUE 10146, P477-486, August 11, 2018
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31506-X/fulltext

Summary
Background
People with type 1 diabetes are at elevated risk of mortality and cardiovascular disease, yet current guidelines do not consider age of onset as an important risk stratifier. We aimed to examine how age at diagnosis of type 1 diabetes relates to excess mortality and cardiovascular risk.
Methods
We did a nationwide, register-based cohort study of individuals with type 1 diabetes in the Swedish National Diabetes Register and matched controls from the general population. We included patients with at least one registration between Jan 1, 1998, and Dec 31, 2012. Using Cox regression, and with adjustment for diabetes duration, we estimated the excess risk of all-cause mortality, cardiovascular mortality, non-cardiovascular mortality, acute myocardial infarction, stroke, cardiovascular disease (a composite of acute myocardial infarction and stroke), coronary heart disease, heart failure, and atrial fibrillation. Individuals with type 1 diabetes were categorised into five groups, according to age at diagnosis: 0–10 years, 11–15 years, 16–20 years, 21–25 years, and 26–30 years.
Findings
27 195 individuals with type 1 diabetes and 135 178 matched controls were selected for this study. 959 individuals with type 1 diabetes and 1501 controls died during follow-up (median follow-up was 10 years). Patients who developed type 1 diabetes at 0–10 years of age had hazard ratios of 4·11 (95% CI 3·24–5·22) for all-cause mortality, 7·38 (3·65–14·94) for cardiovascular mortality, 3·96 (3·06–5·11) for non-cardiovascular mortality, 11·44 (7·95–16·44) for cardiovascular disease, 30·50 (19·98–46·57) for coronary heart disease, 30·95 (17·59–54·45) for acute myocardial infarction, 6·45 (4·04–10·31) for stroke, 12·90 (7·39–22·51) for heart failure, and 1·17 (0·62–2·20) for atrial fibrillation. Corresponding hazard ratios for individuals who developed type 1 diabetes aged 26–30 years were 2·83 (95% CI 2·38–3·37) for all-cause mortality, 3·64 (2·34–5·66) for cardiovascular mortality, 2·78 (2·29–3·38) for non-cardiovascular mortality, 3·85 (3·05–4·87) for cardiovascular disease, 6·08 (4·71–7·84) for coronary heart disease, 5·77 (4·08–8·16) for acute myocardial infarction, 3·22 (2·35–4·42) for stroke, 5·07 (3·55–7·22) for heart failure, and 1·18 (0·79–1·77) for atrial fibrillation; hence the excess risk differed by up to five times across the diagnosis age groups. The highest overall incidence rate, noted for all-cause mortality, was 1·9 (95% CI 1·71–2·11) per 100 000 person-years for people with type 1 diabetes. Development of type 1 diabetes before 10 years of age resulted in a

loss of 17·7 life-years (95% CI 14·5–20·4) for women and 14·2 life-years (12·1–18·2) for men.

Interpretation

Age at onset of type 1 diabetes is an important determinant of survival, as well as all cardiovascular outcomes, with highest excess risk in women. Greater focus on cardioprotection might be warranted in people with early-onset type 1 diabetes.

Analysis of clinical benefit, harms, and cost-effectiveness of screening women for abdominal aortic aneurysm

Michael J Sweeting, Katya L Masconi, Edmund Jones, et al.
The Lancet: Volume 392, ISSUE 10146, P487-495, August 11, 2018
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31222-4/fulltext

Summary

Background

A third of deaths in the UK from ruptured abdominal aortic aneurysm (AAA) are in women. In men, national screening programmes reduce deaths from AAA and are cost-effective. The benefits, harms, and cost-effectiveness in offering a similar programme to women have not been formally assessed, and this was the aim of this study.

Methods

We developed a decision model to assess predefined outcomes of death caused by AAA, life years, quality-adjusted life years, costs, and the incremental cost-effectiveness ratio for a population of women invited to AAA screening versus a population who were not invited to screening. A discrete event simulation model was set up for AAA screening, surveillance, and intervention. Relevant women-specific parameters were obtained from sources including systematic literature reviews, national registry or administrative databases, major AAA surgery trials, and UK National Health Service reference costs.

Findings

AAA screening for women, as currently offered to UK men (at age 65 years, with an AAA diagnosis at an aortic diameter of ≥3·0 cm, and elective repair considered at ≥5·5cm) gave, over 30 years, an estimated incremental cost-effectiveness ratio of £30 000 (95% CI 12 000–87 000) per quality-adjusted life year gained, with 3900 invitations to screening required to prevent one AAA-related death and an overdiagnosis rate of 33%. A modified option for women (screening at age 70 years, diagnosis at 2·5 cm and repair at 5·0 cm) was estimated to have an incremental cost-effectiveness ratio of £23 000 (9500–71 000) per quality-adjusted life year and 1800 invitations to screening required to prevent one AAA-death, but an overdiagnosis rate of 55%. There was considerable uncertainty in the cost-effectiveness ratio, largely driven by uncertainty about AAA prevalence, the distribution of aortic sizes for women at different ages, and the effect of screening on quality of life.

Interpretation

By UK standards, an AAA screening programme for women, designed to be similar to that used to screen men, is unlikely to be cost-effective. Further research on the aortic diameter distribution in women and potential quality of life decrements associated with screening are needed to assess the full benefits and harms of modified options.

Urinary sodium excretion, blood pressure, cardiovascular disease, and mortality: A community-level prospective epidemiological cohort study

Andrew Mente, Martin O'Donnell, Sumathy Rangarajan, et al.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31376-X/fulltext

Summary

Background

WHO recommends that populations consume less than 2 g/day sodium as a preventive measure against cardiovascular disease, but this target has not been achieved in any country. This recommendation is primarily based on individual-level data from short-term trials of blood pressure (BP) without data relating low sodium intake to reduced cardiovascular events from randomised trials or observational studies. We investigated the associations between community-level mean sodium and potassium intake, cardiovascular disease, and mortality.

Methods

The Prospective Urban Rural Epidemiology study is ongoing in 21 countries. Here we report an analysis done in 18 countries with data on clinical outcomes. Eligible participants were adults aged 35–70 years without cardiovascular disease, sampled from the general population. We used morning fasting urine to estimate 24 h sodium and potassium excretion as a surrogate for intake. We assessed community-level associations between sodium and potassium intake and BP in 369 communities (all >50 participants) and cardiovascular disease and mortality in 255 communities (all >100 participants), and used individual-level data to adjust for known confounders.

Findings

95 767 participants in 369 communities were assessed for BP and 82 544 in 255 communities for cardiovascular outcomes with follow-up for a median of 8·1 years. 82 (80%) of 103 communities in China had a mean sodium intake greater than 5 g/day, whereas in other countries 224 (84%) of 266 communities had a mean intake of 3–5 g/day. Overall, mean systolic BP increased by 2·86 mm Hg per 1 g increase in mean sodium intake, but positive associations were only seen among the communities in the highest tertile of sodium intake (p<0·0001 for heterogeneity). The association between mean sodium intake and major cardiovascular events showed significant deviations from linearity (p=0·043) due to a significant inverse association in the lowest tertile of sodium intake (lowest tertile <4·43 g/day, mean intake 4·04 g/day, range 3·42–4·43; change –1·00 events per 1000 years, 95% CI –2·00 to –0·01, p=0·0497), no association in the middle tertile (middle tertile 4·43–5·08 g/day, mean intake 4·70 g/day, 4·44–5.05; change 0·24 events per 1000 years, –2·12 to 2·61, p=0·8391), and a positive but non-significant association in the highest tertile (highest tertile >5·08 g/day, mean intake 5·75 g/day, >5·08–7·49; change 0·37 events per 1000 years, –0·03 to 0·78, p=0·0712). A strong association was seen with stroke in China (mean sodium intake 5·58 g/day, 0·42 events per 1000 years, 95% CI 0·16 to 0·67, p=0·0020) compared with in other countries (4·49 g/day, –0·26 events, –0·46 to –0·06, p=0·0124; p<0·0001 for heterogeneity). All major cardiovascular outcomes decreased with increasing potassium intake in all countries.

Interpretation

Sodium intake was associated with cardiovascular disease and strokes only in communities where mean intake was greater than 5 g/day. A strategy of sodium reduction in these communities and countries but not in others might be appropriate.

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The New England Journal of Medicine (8 August 2018, Vol. 379, No. 6)

Labor Induction versus Expectant Management in Low-Risk Nulliparous Women

William A. Grobman, Madeline M. Rice, Uma M. Reddy, et al. for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network
N Engl J Med 2018; 379: 513-523 August 9, 2018
https://www.nejm.org/doi/full/10.1056/NEJMoa1800566

Abstract
Background
The perinatal and maternal consequences of induction of labor at 39 weeks among low-risk nulliparous women are uncertain.
Methods
In this multicenter trial, we randomly assigned low-risk nulliparous women who were at 38 weeks 0 days to 38 weeks 6 days of gestation to labor induction at 39 weeks 0 days to 39 weeks 4 days or to expectant management. The primary outcome was a composite of perinatal death or severe neonatal complications; the principal secondary outcome was cesarean delivery.
Results
A total of 3062 women were assigned to labor induction, and 3044 were assigned to expectant management. The primary outcome occurred in 4.3% of neonates in the induction group and in 5.4% in the expectant-management group (relative risk, 0.80; 95% confidence interval [CI], 0.64 to 1.00). The frequency of cesarean delivery was significantly lower in the induction group than in the expectant-management group (18.6% vs. 22.2%; relative risk, 0.84; 95% CI, 0.76 to 0.93).
Conclusions
Induction of labor at 39 weeks in low-risk nulliparous women did not result in a significantly lower frequency of a composite adverse perinatal outcome, but it did result in a significantly lower frequency of cesarean delivery.

Outcomes of Cardiac Screening in Adolescent Soccer Players
Aneil Malhotra, Harshil Dhutia, Gherardo Finocchiaro, et al.
N Engl J Med 2018; 379: 524-534 August 9, 2018
https://www.nejm.org/doi/full/10.1056/NEJMoa1714719

Abstract
Background
Reports on the incidence and causes of sudden cardiac death among young athletes have relied largely on estimated rates of participation and varied methods of reporting. We sought to investigate the incidence and causes of sudden cardiac death among adolescent soccer players in the United Kingdom.
Methods
From 1996 through 2016, we screened 11,168 adolescent athletes with a mean (±SD) age of 16.4±1.2 years (95% of whom were male) in the English Football Association (FA) cardiac screening program, which consisted of a health questionnaire, physical examination, electrocardiography, and echocardiography. The FA registry was interrogated to identify sudden cardiac deaths, which were confirmed with autopsy reports.
Results
During screening, 42 athletes (0.38%) were found to have cardiac disorders that are associated with sudden cardiac death. A further 225 athletes (2%) with congenital or valvular abnormalities were identified. After screening, there were 23 deaths from any cause, of which 8 (35%) were sudden deaths attributed to cardiac disease.

Cardiomyopathy accounted for 7 of 8 sudden cardiac deaths (88%). Six athletes (75%) with sudden cardiac death had had normal cardiac screening results. The mean time between screening and sudden cardiac death was 6.8 years. On the basis of a total of 118,351 person-years, the incidence of sudden cardiac death among previously screened adolescent soccer players was 1 per 14,794 person-years (6.8 per 100,000 athletes).

Conclusions

Diseases that are associated with sudden cardiac death were identified in 0.38% of adolescent soccer players in a cohort that underwent cardiovascular screening. The incidence of sudden cardiac death was 1 per 14,794 person-years, or 6.8 per 100,000 athletes; most of these deaths were due to cardiomyopathies that had not been detected on screening.

Vitamin D Supplementation in Pregnancy and Lactation and Infant Growth

Daniel E. Roth, Shaun K. Morris, Stanley Zlotkin, et al.
N Engl J Med 2018; 379: 535-546 August 9, 2018
https://www.nejm.org/doi/full/10.1056/NEJMoa1800927

Abstract

Background

It is unclear whether maternal vitamin D supplementation during pregnancy and lactation improves fetal and infant growth in regions where vitamin D deficiency is common.

Methods

We conducted a randomized, double-blind, placebo-controlled trial in Bangladesh to assess the effects of weekly prenatal vitamin D supplementation (from 17 to 24 weeks of gestation until birth) and postpartum vitamin D supplementation on the primary outcome of infants' length-for-age z scores at 1 year according to World Health Organization (WHO) child growth standards. One group received neither prenatal nor postpartum vitamin D (placebo group). Three groups received prenatal supplementation only, in doses of 4200 IU (prenatal 4200 group), 16,800 IU (prenatal 16,800 group), and 28,000 IU (prenatal 28,000 group). The fifth group received prenatal supplementation as well as 26 weeks of postpartum supplementation in the amount of 28,000 IU (prenatal and postpartum 28,000 group).

Results

Among 1164 infants assessed at 1 year of age (89.5% of 1300 pregnancies), there were no significant differences across groups in the mean (±SD) length-for-age z scores. Scores were as follows: placebo, −0.93±1.05; prenatal 4200, −1.11±1.12; prenatal 16,800, −0.97±0.97; prenatal 28,000, −1.06±1.07; and prenatal and postpartum 28,000, −0.94±1.00 (P=0.23 for a global test of differences across groups). Other anthropometric measures, birth outcomes, and morbidity did not differ significantly across groups. Vitamin D supplementation had expected effects on maternal and infant serum 25-hydroxyvitamin D and calcium concentrations, maternal urinary calcium excretion, and maternal parathyroid hormone concentrations. There were no significant differences in the frequencies of adverse events across groups, with the exception of a higher rate of possible hypercalciuria among the women receiving the highest dose.

Conclusions

In a population with widespread prenatal vitamin D deficiency and fetal and infant growth restriction, maternal vitamin D supplementation from midpregnancy until birth or until 6 months post partum did not improve fetal or infant growth.

Closed-Loop Insulin Delivery for Glycemic Control in Noncritical Care
Lia Bally, Hood Thabit, Sara Hartnell, et al.
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Abstract

Background

In patients with diabetes, hospitalization can complicate the achievement of recommended glycemic targets. There is increasing evidence that a closed-loop delivery system (artificial pancreas) can improve glucose control in patients with type 1 diabetes. We wanted to investigate whether a closed-loop system could also improve glycemic control in patients with type 2 diabetes who were receiving noncritical care.

Methods

In this randomized, open-label trial conducted on general wards in two tertiary hospitals located in the United Kingdom and Switzerland, we assigned 136 adults with type 2 diabetes who required subcutaneous insulin therapy to receive either closed-loop insulin delivery (70 patients) or conventional subcutaneous insulin therapy, according to local clinical practice (66 patients). The primary end point was the percentage of time that the sensor glucose measurement was within the target range of 100 to 180 mg per deciliter (5.6 to 10.0 mmol per liter) for up to 15 days or until hospital discharge.

Results

The mean (±SD) percentage of time that the sensor glucose measurement was in the target range was 65.8±16.8% in the closed-loop group and 41.5±16.9% in the control group, a difference of 24.3±2.9 percentage points (95% confidence interval [CI], 18.6 to 30.0; P<0.001); values above the target range were found in 23.6±16.6% and 49.5±22.8% of the patients, respectively, a difference of 25.9±3.4 percentage points (95% CI, 19.2 to 32.7; P<0.001). The mean glucose level was 154 mg per deciliter (8.5 mmol per liter) in the closed-loop group and 188 mg per deciliter (10.4 mmol per liter) in the control group (P<0.001). There was no significant between-group difference in the duration of hypoglycemia (as defined by a sensor glucose measurement of <54 mg per deciliter; P=0.80) or in the amount of insulin that was delivered (median dose, 44.4 U and 40.2 U, respectively; P=0.50). No episode of severe hypoglycemia or clinically significant hyperglycemia with ketonemia occurred in either trial group.

Conclusions

Among inpatients with type 2 diabetes receiving noncritical care, the use of an automated, closed-loop insulin-delivery system resulted in significantly better glycemic control than conventional subcutaneous insulin therapy, without a higher risk of hypoglycemia.

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Sources

BMJ: British Medical Journal	http://www.bmj.com/theBMJ
JAMA: The Journal of the American Medical Association	http://jama.ama-assn.org/
The Lancet	www.thelancet.com
The New England Journal of Medicine	http://content.nejm.org/

The British Medical Journal (BMJ), JAMA and the New England Journal of Medicine (NEJM) can be accessed in full-text through your NHS Athens account. Unfortunately the national subscription to The Lancet has been cancelled.	https://www.evidence.nhs.uk/nhs-evidence-content/journals-and-databases or http://www.openathens.net/
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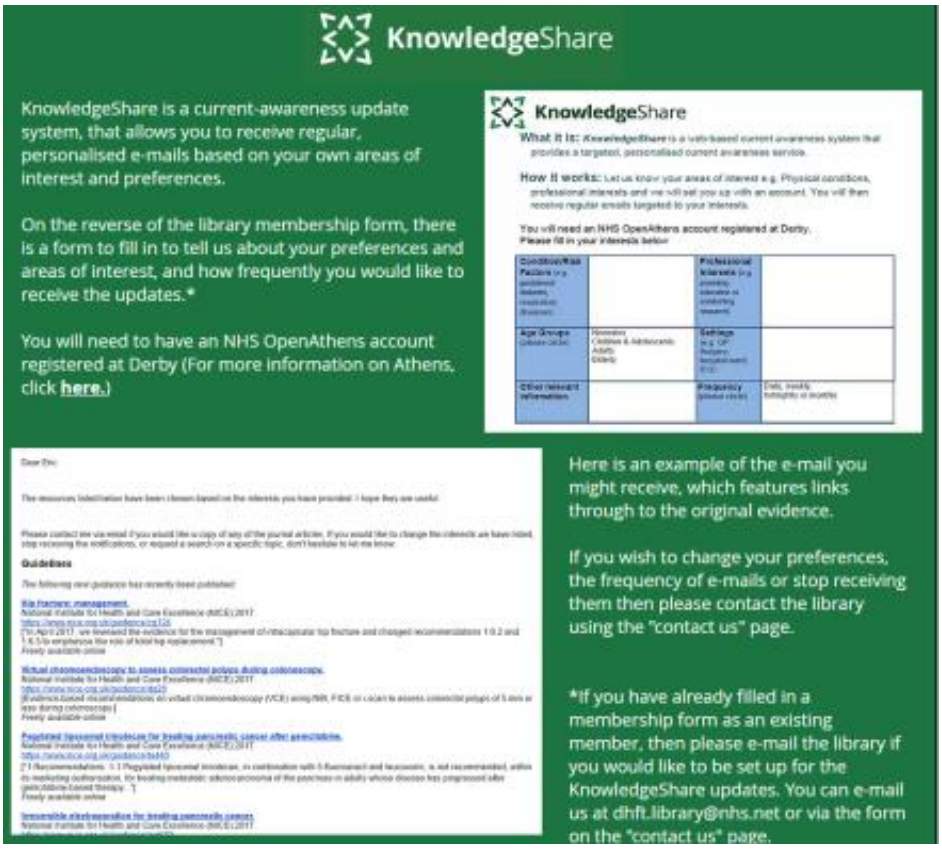

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