Ce bulletin de veille mensuel signale les articles récents, parus dans des revues scientifiques de renommée internationale, autour des pathologies graves qui devraient représenter les principales causes de mortalité et de handicap en 2030 pour les pays riches et les pays en voie de développement.

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### Pathologies suivies

- Bronchite chronique obstructive
- Cancer du poumon
- Dengue
- Dépression
- Diabète
- Grippe A
- Maladie d’Alzheimer
- Maladies cardio-vasculaires
- Maladies liées à l'alcool
- Paludisme
- Pathologies liées à l'obésité
- Pathologies liées au tabagisme
- SIDA
- Tuberculose

### Revues surveillées

- American journal of epidemiology
- American journal of public health
- BMC public health
- BMJ (Clinical research ed.) - British medical journal
- International journal of epidemiology
- JAMA : the journal of the American Medical Association
- Lancet
- Nature
- Risk analysis : an official publication of the Society for Risk Analysis
- Science
- Social science & medicine
- The New England journal of medicine
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FRIED LP, PIOT P, FRENK JJ, FLAHAULT A, et al. Global public health leadership for the
Sept., vol. 7 Suppl 1, p.S5-S15

Abstract We are at an unprecedented moment in history in terms of the health of populations
around the world. New and old problems all require both short- and long-term solutions, at the
individual, community, national and global levels. Unique solutions for each challenge may not be
feasible or adequately effective or cost-effective. We are confronted by health systems that are
not well matched to current and future needs, both for sustained prevention and chronic care.
Moving forward effectively as a field will benefit from a focus on the changing needs of global
health, and on how changing conditions, globally, should define the next generation of public
health leadership so as to best accomplish global health goals.

Bronchite chronique

(1) CLANCY J, NOBES M. Chronic obstructive pulmonary disease: nature-nurture interactions.
Br J Nurs. 2012 July 12, vol. 21, n° 13, pp.772-781

A person's health status is rarely constant, it is usually subject to continual change as a person
moves from health to illness and usually back to health again; the health-illness continuum
illustrates this dynamism. This highlights the person's various states of health and illness (ranging
from extremely good health to clinically defined mild, moderate and severe illness) and their
fluctuations throughout the life span, until ultimately leading to the pathology associated with the
person's death. Maintenance of a stable homeostatic environment within the body to support the
stability of this continuum depends on a complex series of ultimately intracellular chemical
reactions. These reactions are activated by environmental factors that cause the expression of
genes associated with healthy phenotypes as well as illness susceptibility genes associated with homeostatic imbalances. Obviously, the body aims to support intracellular and extracellular environments allied with health; however, the complexity of these nature-nurture interactions results in illness throughout an individual's life span. This paper will discuss the nature-nurture interactions of chronic obstructive pulmonary disease.


This study included prognostication of the results of daily application of peloids for the treatment of the patients presenting with chronic bronchitis and obstructive pulmonary disease using a mathematical model. It was shown that the individualized selection of the patients for the daily application of peloid preparations taking into consideration the results of mathematical prognostication makes it possible to significantly improve the total efficacy of the treatment (up to 97.7%), accelerate the achievement of positive outcome of peloidotherapy, reduce by a factor of 4 the frequency of moderately severe balneoreactions, and increase the duration of the remission period by 3.5-4 months.


BACKGROUND: Spirometry is used to diagnose chronic obstructive pulmonary disease (COPD). The Impulse oscillometry system (IOS) allows determination of respiratory impedance indices, which might be of potential value in early COPD, although previous experience is limited. We examined pulmonary resistance and reactance measured by IOS in subjects with or without self-reported chronic bronchitis or emphysema or COPD (Q+ or Q-) and subjects with or without COPD diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria (G+ or G-). METHODS: From a previous population-based study 450 subjects were examined with spirometry and IOS and answered a questionnaire on respiratory symptoms and diseases. RESULTS: Seventy-seven subjects were Q+, of whom 34 also were G+. Q+/G- subjects (n = 43) reported respiratory symptoms more frequently (35-40% vs 8-14%) but had higher FEV(1) (100% vs 87%) than Q-/G+ subjects (n = 90), p < 0.05 for both comparisons. Q+ subjects had higher pulmonary resistance and lower pulmonary reactance than Q- subjects (p < 0.01 for all comparisons). The same pattern was seen both in G+ subjects ((Q+/Q-) R5 0.39/0.32, R5-R20 0.10/0.07, X5 0.13/0.09, AX 0.55/0.27, p < 0.05 for all) and G- subjects ((Q+/Q-) R5 0.35/0.29, R5-R20 0.08/0.06, X5 0.10/0.08, AX 0.31/0.19 p < 0.05 for all) except for R20 (adjusted for gender and age). CONCLUSIONS: Self-reported chronic bronchitis or emphysema or COPD was associated with higher pulmonary resistance and lower pulmonary reactance measured by IOS, both among subjects with and without COPD according to GOLD criteria. IOS may have the potential to detect pathology associated with COPD earlier than spirometry.


OBJECTIVES: To analyze the conditions of psychological dysfunction and positive mental health in patients with asthma and chronic bronchitis (CB), as compared to healthy individuals, and to identify the factors associated with these mental health indicators. METHODS: Cross-sectional study based on data obtained from the European Health Interview Survey for Spain (EHISS, 2009). We identified individuals with asthma and CB using a specific questionnaire. In order to
assess mental health, two indicators extracted from questionnaire SF-36 were used: psychological dysfunction and positive mental health status. RESULTS: Out of 19,598 subjects included in the study, 8.3% were classified as asthmatic and 7.4% as CB. Healthy individuals had significantly higher psychological dysfunction scores than those with asthma and CB. The same occurred with positive mental health. The variables independently associated with lower scores out of these variables were gender female, a greater number of chronic diseases and obesity. On the contrary, alcohol consumption and physical exercise were associated with a higher score in the aforementioned variables. CONCLUSIONS: Healthy individuals have significantly higher scores in psychological dysfunction and positive mental health than patients with asthma and CB. This suggests that their mental health is much better. The variables related with lower scores out of these variables, and therefore with worse mental health, are: being female, having a greater number of chronic diseases and obesity. On the contrary, alcohol consumption and the practicing of physical exercise are associated with a higher score in the aforementioned variables, thus indicating a greater degree of mental health


BACKGROUND: Gemifloxacin is a fluoroquinolone antibiotic with broad spectrum of antibacterial activity. The aim of the study was to evaluate the comparative effectiveness and safety of gemifloxacin for the treatment of patients with community-acquired pneumonia (CAP) or acute exacerbation of chronic bronchitis (AECB). METHODS: We performed a meta-analysis of randomized controlled trials (RCTs) comparing gemifloxacin with other approved antibiotics. The PubMed, EMBASE, Chinese Biomedical Literature Database and the Cochrane Central Register of Controlled Trials were searched, with no language restrictions. RESULTS: Ten RCTs, comparing gemifloxacin with other quinolones (in 5 RCTs) and beta-lactams and/or macrolides (in 5 RCTs), involving 3940 patients, were included in this meta-analysis. Overall, the treatment success was higher for gemifloxacin when compared with other antibiotics (odds ratio 1.39, 95% confidence interval 1.15 - 1.68 in intention-to-treat patients, and 1.33, 1.02 - 1.73 in clinically evaluable patients). There was no significant difference between the compared antibiotics regarding microbiological success (1.19, 0.84 - 1.68) or all-cause mortality (0.82, 0.41 - 1.63). The total drug related adverse events were similar for gemifloxacin when compared with other quinolones (0.89, 0.56 - 1.41), while lower when compared with beta-lactams and/or macrolides (0.71, 0.57 - 0.89). In subgroup analyses, administration of gemifloxacin was associated with fewer cases of diarrhoea and more rashes compared with other antibiotics (0.66, 0.48 - 0.91, and 2.36, 1.18 - 4.74, respectively). CONCLUSIONS: The available evidence suggests that gemifloxacin 320 mg oral daily is equivalent or superior to other approved antibiotics in effectiveness and safety for CAP and AECB. The development of rash represents potential limitation of gemifloxacin

(6) NACHMAN KE, PARKER JD. Exposures to fine particulate air pollution and respiratory outcomes in adults using two national datasets: a cross-sectional study. Environ Health. 2012, vol. 11, p.25

BACKGROUND: Relationships between chronic exposures to air pollution and respiratory health outcomes have yet to be clearly articulated for adults. Recent data from nationally representative surveys suggest increasing disparity by race/ethnicity regarding asthma-related morbidity and mortality. The objectives of this study are to evaluate the relationship between annual average ambient fine particulate matter (PM2.5) concentrations and respiratory outcomes for adults using modeled air pollution and health outcome data and to examine PM2.5 sensitivity across race/ethnicity. METHODS: Respondents from the 2002-2005 National Health Interview Survey
(NHIS) were linked to annual kriged PM2.5 data from the USEPA AirData system. Logistic regression was employed to investigate increases in ambient PM2.5 concentrations and self-reported prevalence of respiratory outcomes including asthma, sinusitis and chronic bronchitis. Models included health, behavioral, demographic and resource-related covariates. Stratified analyses were conducted by race/ethnicity. RESULTS: Of nearly 110,000 adult respondents, approximately 8,000 and 4,000 reported current asthma and recent attacks, respectively. Overall, odds ratios (OR) for current asthma (0.97 (95% Confidence Interval: 0.87-1.07)) and recent attacks (0.90 (0.78-1.03)) did not suggest an association with a 10 mug/m3 increase in PM2.5. Stratified analyses revealed significant associations for non-Hispanic blacks [OR = 1.73 (1.17-2.56) for current asthma and OR = 1.76 (1.07-2.91) for recent attacks] but not for Hispanics and non-Hispanic whites. Significant associations were observed overall (1.18 (1.08-1.30)) and in non-Hispanic whites (1.31 (1.18-1.46)) for sinusitis, but not for chronic bronchitis. CONCLUSIONS: Non-Hispanic blacks may be at increased sensitivity of asthma outcomes from PM2.5 exposure. Increased chronic PM2.5 exposures in adults may contribute to population sinusitis burdens


OBJECTIVE: To evaluate the efficacy and safety of roflumilast, approved by the Food and Drug Administration in February 2011 as a treatment to reduce the risk of chronic obstructive pulmonary disease (COPD) exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. DATA SOURCES: Literature was retrieved through MEDLINE (1977-December 2011), using the terms roflumilast and COPD. In addition, US government Web sites, including clinicaltrials.gov and fda.gov, were reviewed for pertinent information. Lastly, reference citations from publications identified were reviewed. STUDY SELECTION AND DATA EXTRACTION: All articles published in English identified from the data sources were evaluated. For the evaluation of clinical efficacy and safety, only Phase 3 studies were included. DATA SYNTHESIS: Limited treatment options are available for patients with moderate-to-severe COPD and repeated exacerbations. In 6 published Phase 3 trials to date, roflumilast 500 mug daily exhibited modest improvements in lung function, measured by pre- and postbronchodilator forced expiratory volume in 1 second, and reduced rates of moderate and severe exacerbations. Roflumilast was generally well tolerated, with diarrhea, nausea, and headache the most common adverse events seen in clinical trials, although it has also been associated with an increased risk of neuropsychiatric abnormalities and dose-limiting weight loss. The greatest benefit seen with roflumilast was among patients with moderate-to-severe COPD associated with chronic bronchitis along with a recent history of exacerbations. The benefits were demonstrated with monotherapy and in combination with long-acting beta(2)-agonists or anticholinergic agents. CONCLUSIONS: Despite its only modest benefits in improving lung function and reducing exacerbation rates, roflumilast serves as a safe and effective option in the treatment of COPD


BACKGROUND: Specific occupations are associated with adverse respiratory health. Inhalation exposures encountered in these jobs may place workers at risk of new-onset respiratory disease. METHODS: We analyzed data from 8,967 participants from the Atherosclerosis Risk in Communities (ARIC) study, a longitudinal cohort study. Participants included in this analysis were free of chronic cough and phlegm, wheezing, asthma, chronic bronchitis, emphysema and other chronic lung conditions at the baseline examination, when they were aged 45-64 years. Using data collected in the baseline and first follow-up examination, we evaluated associations between occupation and the three-year incidence of cough, phlegm, wheezing, and airway obstruction and
changes in forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) measured by spirometry. All associations were adjusted for age, cigarettes per day, race, smoking status, and study center. RESULTS: During the approximately three-year follow-up, the percentage of participants developing chronic cough was 3%; chronic phlegm, 3%; wheezing, 3%; and airway obstruction, defined as FEV1 < lower limit of normal (LLN) and FEV1/FVC < LLN, 2%. The average annual declines in FEV1 and FVC were 56 mL and 66 mL, respectively, among men and 40 mL and 52 mL, respectively, among women. Relative to a referent category of managerial and administrative support occupations, elevated risks of new-onset chronic cough and chronic phlegm were observed for mechanics and repairers (chronic cough: RR: 1.81, 95% CI: 1.02, 3.21; chronic phlegm: RR: 2.10, 95% CI: 1.23, 3.57) and cleaning and building service workers (chronic cough: RR: 1.85, 95% CI: 1.01, 3.37; chronic phlegm: RR: 2.28, 95% CI: 1.27, 4.08). Despite the elevated risk of new-onset symptoms, employment in cleaning and building services was associated with attenuated lung function decline, particularly among men, who averaged annual declines in FEV1 and FVC of 14 mL and 23 mL, respectively, less than the declines observed in the referent population. CONCLUSIONS: Employment in mechanic and repair jobs and cleaning and building service occupations are associated with increased incidence of respiratory symptoms. Specific occupations affect the respiratory health of adults without pre-existing respiratory health symptoms and conditions, though long-term health consequences of inhalation exposures in these jobs remain largely unexplored.


COPD is a heterogeneous disorder whose assessment is going to be increasingly multidimensional. Grading systems such as BODE (Body-Mass Index, Obstruction, Dyspnea, Exercise), mBODE (BODE modified in grading of walked distance), ADO (Age, Dyspnea, Obstruction) are proposed to assess COPD severity and outcome. Computed tomography (CT) is deemed to reflect COPD lung pathologic changes. We studied the relationship of multidimensional grading systems (MGS) with clinically determined COPD phenotypes and CT lung density. Seventy-two patients underwent clinical and chest x-ray evaluation, pulmonary function tests (PFT), 6-minute walking test (6MWT) to derive: predominant COPD clinical phenotype, BODE, mBODE, ADO. Inspiratory and expiratory CT was performed to calculate mean lung attenuation (MLA), relative area with density below-950 HU at inspiration (RAI(-950)), and below -910 HU at expiration (RAE(-910)). MGS, PFT, and CT data were compared between bronchial versus emphysematous COPD phenotype. MGS were correlated with CT data. The prediction of CT density by means of MGS was investigated by direct and stepwise multivariate regression. MGS did not differ in clinically determined COPD phenotypes. BODE was more closely related and better predicted CT findings than mBODE and ADO; the better predictive model was obtained for CT expiratory data; stepwise regression models of CT data did not include 6MWT distance; the dyspnea score MRC was included only to predict RA-950 and RA-910 which quantify emphysema extent. BODE reflect COPD severity better than other MGS, but not its clinical heterogeneity. 6MWT does not significantly increase BODE predictivity of CT lung density changes.


BACKGROUND: The risks of long term sequelae from childhood pneumonia have not been systematically assessed. The aims of this study were to: (i) estimate the risks of respiratory sequelae after pneumonia in children under five years; (ii) estimate the distribution of the different types of respiratory sequelae; and (iii) compare sequelae risk by hospitalisation status and pathogen. METHODS: We systematically reviewed published papers from 1970 to 2011. Standard global burden of disease categories (restrictive lung disease, obstructive lung disease,
bronchiectasis) were labelled as major sequelae. ‘Minor’ sequelae (chronic bronchitis, asthma, other abnormal pulmonary function, other respiratory disease), and multiple impairments were also included. Thirteen papers were selected for inclusion. Synthesis was by random effects meta-analysis and meta-regression. RESULTS: Risk of at least one major sequelae was 5.5% (95% confidence interval [95% CI] 2.8-8.3%) in non hospitalised children and 13.6% [6.2-21.1%]) in hospitalised children. Adenovirus pneumonia was associated with the highest sequelae risk (54.8% [39.2-70.5%]) but children hospitalised with no pathogen isolated also had high risk (17.6% [10.9-24.3%]). The most common type of major sequel was restrictive lung disease (5.4% [2.5-10.2%]). Potential confounders such as loss to follow up and median age at infection were not associated with sequelae risk in the final models. CONCLUSIONS: All children with pneumonia diagnosed by a health professional should be considered at risk of long term sequelae. Evaluation of childhood pneumonia interventions should include potential impact on long term respiratory sequelae.
17 with renal-cell cancer, 17 with ovarian cancer, 14 with pancreatic cancer, 7 with gastric cancer, and 4 with breast cancer—had received anti-PD-L1 antibody. The median duration of therapy was 12 weeks (range, 2 to 111). Grade 3 or 4 toxic effects that investigators considered to be related to treatment occurred in 9% of patients. Among patients with a response that could be evaluated, an objective response (a complete or partial response) was observed in 9 of 52 patients with melanoma, 2 of 17 with renal-cell cancer, 5 of 49 with non-small-cell lung cancer, and 1 of 17 with ovarian cancer. Responses lasted for 1 year or more in 8 of 16 patients with at least 1 year of follow-up. CONCLUSIONS: Antibody-mediated blockade of PD-L1 induced durable tumor regression (objective response rate of 6 to 17%) and prolonged stabilization of disease (rates of 12 to 41% at 24 weeks) in patients with advanced cancers, including non-small-cell lung cancer, melanoma, and renal-cell cancer. (Funded by Bristol-Myers Squibb and others; ClinicalTrials.gov number, NCT00729664.)


BACKGROUND: Blockade of programmed death 1 (PD-1), an inhibitory receptor expressed by T cells, can overcome immune resistance. We assessed the antitumor activity and safety of BMS-936558, an antibody that specifically blocks PD-1. METHODS: We enrolled patients with advanced melanoma, non-small-cell lung cancer, castration-resistant prostate cancer, or renal-cell or colorectal cancer to receive anti-PD-1 antibody at a dose of 0.1 to 10.0 mg per kilogram of body weight every 2 weeks. Response was assessed after each 8-week treatment cycle. Patients received up to 12 cycles until disease progression or a complete response occurred. RESULTS: A total of 296 patients received treatment through February 24, 2012. Grade 3 or 4 drug-related adverse events occurred in 14% of patients; there were three deaths from pulmonary toxicity. No maximum tolerated dose was defined. Adverse events consistent with immune-related causes were observed. Among 236 patients in whom response could be evaluated, objective responses (complete or partial responses) were observed in those with non-small-cell lung cancer, melanoma, or renal-cell cancer. Cumulative response rates (all doses) were 18% among patients with non-small-cell lung cancer (14 of 76 patients), 28% among patients with melanoma (26 of 94 patients), and 27% among patients with renal-cell cancer (9 of 33 patients). Responses were durable; 20 of 31 responses lasted 1 year or more in patients with 1 year or more of follow-up. To assess the role of intratumoral PD-1 ligand (PD-L1) expression in the modulation of the PD-1-PD-L1 pathway, immunohistochemical analysis was performed on pretreatment tumor specimens obtained from 42 patients. Of 17 patients with PD-L1-negative tumors, none had an objective response; 9 of 25 patients (36%) with PD-L1-positive tumors had an objective response (P=0.006). CONCLUSIONS: Anti-PD-1 antibody produced objective responses in approximately one in four to one in five patients with non-small-cell lung cancer, melanoma, or renal-cell cancer; the adverse-event profile does not appear to preclude its use. Preliminary data suggest a relationship between PD-L1 expression on tumor cells and objective response. (Funded by Bristol-Myers Squibb and others; ClinicalTrials.gov number, NCT00730639.)


(7) MAYOR S. Lung cancer teams pair up to review care processes and improve outcomes. BMJ. 2012, vol. 344, p.e2770

Genome-wide association studies have identified variants on chromosome 15q25.1 that increase the risks of both lung cancer and nicotine dependence and associated smoking behavior. However, there remains debate as to whether the association with lung cancer is direct or is mediated by pathways related to smoking behavior. Here, the authors apply a novel method for mediation analysis, allowing for gene-environment interaction, to a lung cancer case-control study (1992-2004) conducted at Massachusetts General Hospital using 2 single nucleotide polymorphisms, rs8034191 and rs1051730, on 15q25.1. The results are validated using data from 3 other lung cancer studies. Tests for additive interaction ($P = 2 \times 10^{-10}$ and $P = 1 \times 10^{-9}$) and multiplicative interaction ($P = 0.01$ and $P = 0.01$) were significant. Pooled analyses yielded a direct-effect odds ratio of 1.26 (95% confidence interval (CI): 1.19, 1.33; $P = 2 \times 10^{-15}$) for rs8034191 and an indirect-effect odds ratio of 1.01 (95% CI: 1.00, 1.01; $P = 0.09$); the proportion of increased risk mediated by smoking was 3.2%. For rs1051730, direct- and indirect-effect odds ratios were 1.26 (95% CI: 1.19, 1.33; $P = 1 \times 10^{-15}$) and 1.00 (95% CI: 0.99, 1.01; $P = 0.22$), respectively, with a proportion mediated of 2.3%. Adjustment for measurement error in smoking behavior allowing up to 75% measurement error increased the proportions mediated to 12.5% and 9.2%, respectively. These analyses indicate that the association of the variants with lung cancer operates primarily through other pathways.

CONTEXT: Unrecognized myocardial infarction (MI) is prognostically important. Electrocardiography (ECG) has limited sensitivity for detecting unrecognized MI (UMI). OBJECTIVE: Determine prevalence and mortality risk for UMI detected by cardiac magnetic resonance (CMR) imaging or ECG among older individuals. DESIGN, SETTING, AND PARTICIPANTS: ICELAND MI is a cohort substudy of the Age, Gene/Environment Susceptibility-Reykjavik Study (enrollment January 2004-January 2007) using ECG or CMR to detect UMI. From a community-dwelling cohort of older individuals in Iceland, data for 936 participants aged 67 to 93 years were analyzed, including 670 who were randomly selected and 266 with diabetes. MAIN OUTCOME MEASURES: Prevalence and mortality of MI through September 1, 2011. Results reported with 95% confidence limits and net reclassification improvement (NRI). RESULTS: Of 936 participants, 91 had recognized MI (RMI) (9.7%; 95% CI, 8% to 12%), and 157 had UMI detected by CMR (17%; 95% CI, 14% to 19%), which was more prevalent than the 46 UMI detected by ECG (5%; 95% CI, 4% to 6%; P < .001). Participants with diabetes (n = 337) had more UMI detected by CMR than by ECG (n = 72; 21%; 95% CI, 17% to 26%, vs n = 15; 4%; 95% CI, 2% to 7%; P < .001). Unrecognized MI by CMR was associated with atherosclerosis risk factors, coronary calcium, coronary revascularization, and peripheral vascular disease. Over a median of 6.4 years, 30 of 91 participants (33%; 95% CI, 23% to 43%) with RMI died, and 44 of 157 participants (28%; 95% CI, 21% to 35%) with UMI died, both higher rates than the 119 of 688 participants (17%; 95% CI, 15% to 20%) with no MI who died. Unrecognized MI by CMR improved risk stratification for mortality over RMI (NRI, 0.34; 95% CI, 0.16 to 0.53). Adjusting for age, sex, diabetes, and RMI, UMI by CMR remained associated with mortality (hazard ratio [HR], 1.45; 95% CI, 1.02 to 2.06, absolute risk increase [ARI], 8%) and significantly improved risk stratification for mortality (NRI, 0.16; 95% CI, 0.01 to 0.31), but UMI by ECG did not (HR, 0.88; 95% CI, 0.45 to 1.73; ARI, -2%; NRI, -0.05; 95% CI, -0.17 to 0.05). Compared with those with RMI, participants with UMI by CMR used cardiac medications such as statins less often (36%; 95% CI, 28% to 43%, or 56/157, vs 73%; 95% CI, 63% to 82%, or 66/91; P < .001). CONCLUSIONS: In a community-based cohort of older individuals, the prevalence of UMI by CMR was higher than the prevalence of RMI and was associated with increased mortality risk. In contrast, UMI by ECG prevalence was lower than that of RMI and was not associated with increased mortality risk. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT01322568


CONTEXT: Unrecognized myocardial infarction (MI) is prognostically important. Electrocardiography (ECG) has limited sensitivity for detecting unrecognized MI (UMI). OBJECTIVE: Determine prevalence and mortality risk for UMI detected by cardiac magnetic resonance (CMR) imaging or ECG among older individuals. DESIGN, SETTING, AND PARTICIPANTS: ICELAND MI is a cohort substudy of the Age, Gene/Environment Susceptibility-Reykjavik Study (enrollment January 2004-January 2007) using ECG or CMR to detect UMI. From a community-dwelling cohort of older individuals in Iceland, data for 936 participants aged 67 to 93 years were analyzed, including 670 who were randomly selected and 266 with diabetes. MAIN OUTCOME MEASURES: Prevalence and mortality of MI through September 1, 2011. Results reported with 95% confidence limits and net reclassification improvement (NRI). RESULTS: Of 936 participants, 91 had recognized MI (RMI) (9.7%; 95% CI, 8% to 12%), and 157 had UMI detected by CMR (17%; 95% CI, 14% to 19%), which was more prevalent than the 46 UMI detected by ECG (5%; 95% CI, 4% to 6%; P < .001). Participants with diabetes (n = 337) had more UMI detected by CMR than by ECG (n = 72; 21%; 95% CI, 17% to 26%, vs n = 15; 4%; 95% CI, 2% to 7%; P < .001). Unrecognized MI by CMR was associated with atherosclerosis risk factors, coronary calcium, coronary revascularization, and peripheral vascular disease. Over a median of 6.4 years, 30 of 91 participants (33%; 95% CI, 23% to 43%) with RMI died, and 44 of 157 participants (28%; 95% CI, 21% to 35%) with UMI died, both higher rates than the 119 of 688 participants (17%; 95% CI, 15% to 20%) with no MI who died. Unrecognized MI by CMR improved risk stratification for mortality over RMI (NRI, 0.34; 95% CI, 0.16 to 0.53). Adjusting for age, sex, diabetes, and RMI, UMI by CMR remained associated with mortality (hazard ratio [HR], 1.45; 95% CI, 1.02 to 2.06, absolute risk increase [ARI], 8%) and significantly improved risk stratification for mortality (NRI, 0.16; 95% CI, 0.01 to 0.31), but UMI by ECG did not (HR, 0.88; 95% CI, 0.45 to 1.73; ARI, -2%; NRI, -0.05; 95% CI, -0.17 to 0.05). Compared with those with RMI, participants with UMI by CMR used cardiac medications such as statins less often (36%; 95% CI, 28% to 43%, or 56/157, vs 73%; 95% CI, 63% to 82%, or 66/91; P < .001). CONCLUSIONS: In a community-based cohort of older individuals, the prevalence of UMI by CMR was higher than the prevalence of RMI and was associated with increased mortality risk. In contrast, UMI by ECG prevalence was lower than that of RMI and was not associated with increased mortality risk. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT01322568

CONTEXT: Pharmacodynamic studies have shown that persistently high platelet reactivity is common in patients with diabetes in spite of clopidogrel treatment. Clinical trials have not convincingly demonstrated that clopidogrel benefits patients with diabetes as much patients without diabetes. OBJECTIVES: To estimate the clinical effectiveness associated with clopidogrel treatment after myocardial infarction (MI) in patients with diabetes. DESIGN, SETTING, AND PATIENTS: By individual-level linkage of the Danish nationwide administrative registries between 2002-2009, patients who were hospitalized with incident MI and who had survived and not undergone coronary artery bypass surgery 30 days after discharge were followed up for as long as 1 year (maximally until December 31, 2009). Adjusted for age, sex, comorbidity, calendar year, concomitant pharmacotherapy, and invasive interventions, hazard ratios that were associated with clopidogrel in patients with and without diabetes were analyzed by Cox proportional-hazard models and propensity score-matched models. MAIN OUTCOME MEASURES: All-cause mortality, cardiovascular mortality, and a composite end point of recurrent MI and all-cause mortality. RESULTS: Of the 58,851 patients included in the study, 7247 (12%) had diabetes and 35,380 (60%) received clopidogrel. In total, 1790 patients (25%) with diabetes and 7931 patients (15%) without diabetes met the composite end point. Of these, 1225 (17%) with and 5377 (10%) without diabetes died. In total, 978 patients (80%) with and 4100 patients (76%) without diabetes died of events of cardiovascular origin. For patients with diabetes who were treated with clopidogrel, the unadjusted mortality rates (events/100 person-years) were 13.4 (95% CI, 12.8-14.0) vs 29.3 (95% CI, 28.3-30.4) for those not treated. For patients without diabetes who were treated with clopidogrel, the unadjusted mortality rates were 6.4 (95% CI, 6.3-6.6) vs 21.3 (95% CI, 21.0-21.7) for those not treated. However, among patients with diabetes vs those without diabetes, clopidogrel was associated with less effectiveness for all-cause mortality (HR, 0.89 [95% CI, 0.79-1.00] vs 0.75 [95% CI, 0.70-0.80]; P for interaction, .001) and for cardiovascular mortality (HR, 0.93 [95% CI, 0.81-1.06] vs 0.77 [95% CI, 0.72-0.83]; P for interaction, .01) but not for the composite end point (HR, 1.00 [95% CI, 0.91-1.10] vs 0.91 [95% CI, 0.87-0.96]; P for interaction, .08). Propensity score-matched models gave similar results. CONCLUSION: Among patients with diabetes compared with patients without diabetes, the use of conventional clopidogrel treatment after MI was associated with lower reduction in the risk of all-cause death and cardiovascular death.


BACKGROUND: Weight loss protects against type 2 diabetes but is hard to maintain with behavioral modification alone. In an analysis of data from a nonrandomized, prospective,
controlled study, we examined the effects of bariatric surgery on the prevention of type 2 diabetes. METHODS: In this analysis, we included 1658 patients who underwent bariatric surgery and 1771 obese matched controls (with matching performed on a group, rather than individual, level). None of the participants had diabetes at baseline. Patients in the bariatric-surgery cohort underwent banding (19%), vertical banded gastroplasty (69%), or gastric bypass (12%); nonrandomized, matched, prospective controls received usual care. Participants were 37 to 60 years of age, and the body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) was 34 or more in men and 38 or more in women. This analysis focused on the rate of incident type 2 diabetes, which was a prespecified secondary end point in the main study. At the time of this analysis (January 1, 2012), participants had been followed for up to 15 years. Despite matching, some baseline characteristics differed significantly between the groups; the baseline body weight was higher and risk factors were more pronounced in the bariatric-surgery group than in the control group. At 15 years, 36.2% of the original participants had dropped out of the study, and 30.9% had not yet reached the time for their 15-year follow-up examination. RESULTS: During the follow-up period, type 2 diabetes developed in 392 participants in the control group and in 110 in the bariatric-surgery group, corresponding to incidence rates of 28.4 cases per 1000 person-years and 6.8 cases per 1000 person-years, respectively (adjusted hazard ratio with bariatric surgery, 0.17; 95% confidence interval, 0.13 to 0.21; P<0.001). The effect of bariatric surgery was influenced by the presence or absence of impaired fasting glucose (P=0.002 for the interaction) but not by BMI (P=0.54). Sensitivity analyses, including end-point imputations, did not change the overall conclusions. The postoperative mortality was 0.2%, and 2.8% of patients who underwent bariatric surgery required reoperation within 90 days owing to complications. CONCLUSIONS: Bariatric surgery appears to be markedly more efficient than usual care in the prevention of type 2 diabetes in obese persons. (Funded by the Swedish Research Council and others; ClinicalTrials.gov number, NCT01479452.)


CONTEXT: Type 2 diabetes in normal-weight adults (body mass index [BMI] <25) is a representation of the metabolically obese normal-weight phenotype with unknown mortality consequences. OBJECTIVE: To test the association of weight status with mortality in adults with new-onset diabetes in order to minimize the influence of diabetes duration and voluntary weight loss on mortality. DESIGN, SETTING, AND PARTICIPANTS: Pooled analysis of 5 longitudinal cohort studies: Atherosclerosis Risk in Communities study, 1990-2006; Cardiovascular Health Study, 1992-2008; Coronary Artery Risk Development in Young Adults, 1987-2011; Framingham Offspring Study, 1979-2007; and Multi-Ethnic Study of Atherosclerosis, 2002-2011. A total of 2625 participants with incident diabetes contributed 27,125 person-years of follow-up. Included were men and women (age >40 years) who developed incident diabetes based on fasting glucose 126 mg/dL or greater or newly initiated diabetes medication and who had concurrent measurements of BMI. Participants were classified as normal weight if their BMI was 18.5 to 24.99 or overweight/obese if BMI was 25 or greater. MAIN OUTCOME MEASURES: Total, cardiovascular, and noncardiovascular mortality. RESULTS: The proportion of adults who were normal weight at the time of incident diabetes ranged from 9% to 21% (overall 12%). During follow-up, 449 participants died: 178 from cardiovascular causes and 253 from noncardiovascular causes (18 were not classified). The rates of total, cardiovascular, and noncardiovascular mortality were
higher in normal-weight participants (284.8, 99.8, and 198.1 per 10,000 person-years, respectively) than in overweight/obese participants (152.1, 67.8, and 87.9 per 10,000 person-years, respectively). After adjustment for demographic characteristics and blood pressure, lipid levels, waist circumference, and smoking status, hazard ratios comparing normal-weight participants with overweight/obese participants for total, cardiovascular, and noncardiovascular mortality were 2.08 (95% CI, 1.52-2.85), 1.52 (95% CI, 0.89-2.58), and 2.32 (95% CI, 1.55-3.48), respectively. CONCLUSION: Adults who were normal weight at the time of incident diabetes had higher mortality than adults who are overweight or obese


BACKGROUND: Strong evidence shows that physical inactivity increases the risk of many adverse health conditions, including major non-communicable diseases such as coronary heart disease, type 2 diabetes, and breast and colon cancers, and shortens life expectancy. Because much of the world's population is inactive, this link presents a major public health issue. We aimed to quantify the effect of physical inactivity on these major non-communicable diseases by estimating how much disease could be averted if inactive people were to become active and to estimate gain in life expectancy at the population level. METHODS: For our analysis of burden of disease, we calculated population attributable fractions (PAFs) associated with physical inactivity using conservative assumptions for each of the major non-communicable diseases, by country, to estimate how much disease could be averted if physical inactivity were eliminated. We used life-table analysis to estimate gains in life expectancy of the population. FINDINGS: Worldwide, we estimate that physical inactivity causes 6% (ranging from 3.2% in southeast Asia to 7.8% in the eastern Mediterranean region) of the burden of disease from coronary heart disease, 7% (3.9-9.6) of type 2 diabetes, 10% (5.6-14.1) of breast cancer, and 10% (5.7-13.8) of colon cancer. Inactivity causes 9% (range 5.1-12.5) of premature mortality, or more than 5.3 million of the 57 million deaths that occurred worldwide in 2008. If inactivity were not eliminated, but decreased instead by 10% or 25%, more than 533 000 and more than 1.3 million deaths, respectively, could be averted every year. We estimated that elimination of physical inactivity would increase the life expectancy of the world's population by 0.68 (range 0.41-0.95) years. INTERPRETATION: Physical inactivity has a major health effect worldwide. Decrease in or removal of this unhealthy behaviour could improve health substantially. FUNDING: None


Tuberculosis is a major threat to global health, infecting a third of the world’s population. In the United States, however, control of tuberculosis has been increasingly successful. Only 3.2% of the US population is estimated to have latent tuberculosis and there are only 11,000 cases annually of active disease. More than half the cases in this country occur in individuals born outside the United States. Human immunodeficiency virus coinfection is not a major factor in the United States, since only approximately 10% of cases are coinfected. Drug resistance is also uncommon in this country. Because the United States has more resources for the diagnosis, therapy, and public health control of tuberculosis than many regions of the world, and because many hospitals have more cases of clinically significant nontuberculous mycobacteria than tuberculosis, the management approaches to tuberculosis need to be quite different in this country than in other regions. The resurgence in interest in developing new tools and the investment in public health infrastructure will hopefully be sustained in the United States so that the effect of tuberculosis on the US population will continue to diminish, and these new tools and approaches can be adapted to both high and low prevalence areas to meet the global challenge.


BACKGROUND: Addition of a sulphonylurea to metformin improves glycaemic control in type 2 diabetes, but is associated with hypoglycaemia and weight gain. We aimed to compare a dipeptidyl peptidase-4 inhibitor (linagliptin) against a commonly used sulphonylurea (glimepiride).

METHODS: In this 2-year, parallel-group, non-inferiority double-blind trial, outpatients with type 2 diabetes and glycated haemoglobin A(1c) (HbA(1c)) 6.5-10.0% on stable metformin alone or with one additional oral antidiabetic drug (washed out during screening) were randomly assigned (1:1) by computer-generated random sequence via a voice or web response system to linagliptin (5 mg) or glimepiride (1-4 mg) orally once daily. Study investigators and participants were masked to treatment assignment. The primary endpoint was change in HbA(1c) from baseline to week 104. Analyses included all patients randomly assigned to treatment groups who received at least one dose of treatment, had a baseline HbA(1c) measurement, and had at least one on-treatment HbA(1c) measurement. This trial is registered at ClinicalTrials.gov, number NCT00622284.

FINDINGS: 777 patients were randomly assigned to linagliptin and 775 to glimepiride; 764 and 755 were included in analysis of the primary endpoint. Reductions in adjusted mean HbA(1c) (baseline 7.69% [SE 0.03] in both groups) were similar in the linagliptin (-0.16% [SE 0.03]) and glimepiride groups (-0.36% [0.03]; difference 0.20%, 97.5% CI 0.09-0.30), meeting the predefined non-inferiority criterion of 0.35%. Fewer participants had hypoglycaemia (58 [7%] of 776 vs 280 [36%] of 775 patients, p<0.0001) or severe hypoglycaemia (1 [<1%] vs 12 [2%]) with linagliptin compared with glimepiride. Linagliptin was associated with significantly fewer cardiovascular events (12 vs 26 patients; relative risk 0.46, 95% CI 0.23-0.91, p=0.0213). INTERPRETATION: The results of this long-term randomised active-controlled trial advance the clinical evidence and comparative effectiveness bases for treatment options available to patients with type 2 diabetes mellitus. The findings could improve decision making for clinical treatment when metformin alone is insufficient. FUNDING: Boehringer Ingelheim


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Obesity and type-2 diabetes have increased markedly over the past few decades, in parallel. One of the major links between these two disorders is chronic, low-grade inflammation. Prolonged nutrient excess promotes the accumulation and activation of leukocytes in visceral adipose tissue (VAT) and ultimately other tissues, leading to metabolic abnormalities such as insulin resistance, type-2 diabetes and fatty-liver disease. Although invasion of VAT by pro-inflammatory macrophages is considered to be a key event driving adipose-tissue inflammation and insulin resistance, little is known about the roles of other immune system cell types in these processes. A unique population of VAT-resident regulatory T (Treg) cells was recently implicated in control of the inflammatory state of adipose tissue and, thereby, insulin sensitivity. Here we identify peroxisome proliferator-activated receptor (PPAR)-gamma, the 'master regulator' of adipocyte differentiation, as a crucial molecular orchestrator of VAT Treg cell accumulation, phenotype and function. Unexpectedly, PPAR-gamma expression by VAT Treg cells was necessary for complete
restoration of insulin sensitivity in obese mice by the thiazolidinedione drug pioglitazone. These findings suggest a previously unknown cellular mechanism for this important class of thiazolidinedione drugs, and provide proof-of-principle that discrete populations of Treg cells with unique functions can be precisely targeted to therapeutic ends.

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BACKGROUND: The provision of sufficient basal insulin to normalize fasting plasma glucose levels may reduce cardiovascular events, but such a possibility has not been formally tested. METHODS: We randomly assigned 12,537 people (mean age, 63.5 years) with cardiovascular risk factors plus impaired fasting glucose, impaired glucose tolerance, or type 2 diabetes to receive insulin glargine (with a target fasting blood glucose level of </=95 mg per deciliter [5.3 mmol per liter]) or standard care and to receive n-3 fatty acids or placebo with the use of a 2-by-2 factorial design. The results of the comparison between insulin glargine and standard care are reported here. The coprimary outcomes were nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes and these events plus revascularization or hospitalization for heart failure. Microvascular outcomes, incident diabetes, hypoglycemia, weight, and cancers were also compared between groups. RESULTS: The median follow-up was 6.2 years (interquartile range, 5.8 to 6.7). Rates of incident cardiovascular outcomes were similar in the insulin glargine and standard-care groups: 2.94 and 2.85 per 100 person-years, respectively, for the first coprimary outcome (hazard ratio, 1.02; 95% confidence interval [CI], 0.94 to 1.11; P=0.63) and 5.52 and 5.28 per 100 person-years, respectively, for the second coprimary outcome (hazard ratio, 1.04; 95% CI, 0.97 to 1.11; P=0.27). New diabetes was diagnosed approximately 3 months after therapy was stopped among 30% versus 35% of 1456 participants without baseline diabetes (odds ratio, 0.80; 95% CI, 0.64 to 1.00; P=0.05). Rates of severe hypoglycemia were 1.00 versus 0.31 per 100 person-years. Median weight increased by 1.6 kg in the insulin-glargine group and fell by 0.5 kg in the standard-care group. There was no significant difference in cancers (hazard ratio, 1.00; 95% CI, 0.88 to 1.13; P=0.97). CONCLUSIONS: When used to target normal fasting plasma glucose levels for more than 6 years, insulin glargine had a neutral effect on cardiovascular outcomes and cancers. Although it reduced new-onset diabetes, insulin glargine also increased hypoglycemia and modestly increased weight. (Funded by Sanofi; ORIGIN ClinicalTrials.gov number, NCT00069784.)
BACKGROUND: The use of n-3 fatty acids may prevent cardiovascular events in patients with recent myocardial infarction or heart failure. Their effects in patients with (or at risk for) type 2 diabetes mellitus are unknown. METHODS: In this double-blind study with a 2-by-2 factorial design, we randomly assigned 12,536 patients who were at high risk for cardiovascular events and had impaired fasting glucose, impaired glucose tolerance, or diabetes to receive a 1-g capsule containing at least 900 mg (90% or more) of ethyl esters of n-3 fatty acids or placebo daily and to receive either insulin glargine or standard care. The primary outcome was death from cardiovascular causes. The results of the comparison between n-3 fatty acids and placebo are reported here. RESULTS: During a median follow up of 6.2 years, the incidence of the primary outcome was not significantly decreased among patients receiving n-3 fatty acids, as compared with those receiving placebo (574 patients [9.1%] vs. 581 patients [9.3%]; hazard ratio, 0.98; 95% confidence interval [CI], 0.87 to 1.10; P = 0.72). The use of n-3 fatty acids also had no significant effect on the rates of major vascular events (1034 patients [16.5%] vs. 1017 patients [16.3%]; hazard ratio, 1.01; 95% CI, 0.93 to 1.10; P = 0.81), death from any cause (951 [15.1%] vs. 964 [15.4%]; hazard ratio, 0.98; 95% CI, 0.89 to 1.07; P = 0.63), or death from arrhythmia (288 [4.6%] vs. 259 [4.1%]; hazard ratio, 1.10; 95% CI, 0.93 to 1.30; P = 0.26). Triglyceride levels were reduced by 14.5 mg per deciliter (0.16 mmol per liter) more among patients receiving n-3 fatty acids than among those receiving placebo (P < 0.001), without a significant effect on other lipids. Adverse effects were similar in the two groups. CONCLUSIONS: Daily supplementation with 1 g of n-3 fatty acids did not reduce the rate of cardiovascular events in patients at high risk for cardiovascular events. (Funded by Sanofi; ORIGIN ClinicalTrials.gov number, NCT00069784.)


OBJECTIVES: To assess the association between pre-diabetes and risk of stroke, and to evaluate whether this relation varies by diagnostic criteria for pre-diabetes. DESIGN: Systematic review and meta-analysis of prospective studies. DATA SOURCES: A search of Medline, Embase, and the Cochrane Library (1947 to 16 July 2011) was supplemented by manual searches of bibliographies of key retrieved articles and relevant reviews. SELECTION CRITERIA: Prospective cohort studies that reported multivariate adjusted relative risks and corresponding 95% confidence intervals for stroke with respect to baseline pre-diabetes status at baseline, risk estimates of stroke, study quality, and methods used to assess pre-diabetes and stroke. Relative risks were pooled using random effects models when appropriate. Associations were tested in subgroups representing different characteristics of participants and studies. Publication bias was evaluated with funnel plots. RESULTS: The search yielded 15 prospective cohort studies including 760,925 participants. In 8 studies analysing pre-diabetes defined as fasting glucose 100-125 mg/dL (5.6-6.9 mmol/L), the random effects summary estimate did not show an increased risk of stroke after adjustment for established cardiovascular risk factors (1.08, 95% confidence interval 0.94 to 1.23; P = 0.26). In 5 studies analysing pre-diabetes defined as fasting glucose 110-125 mg/dL (6.1-6.9 mmol/L), the random effects summary estimate showed an increased risk of stroke after adjustment for established cardiovascular risk factors (1.21, 1.02 to 1.44; P = 0.03). In 8 studies with information about impaired glucose tolerance or combined impaired glucose tolerance and impaired fasting glucose, the random effects summary estimate showed an increased risk of stroke after adjustment for established cardiovascular risk factors (1.26, 1.10 to


1.43; P < 0.001). When studies that might have enrolled patients with undiagnosed diabetes were excluded, only impaired glucose tolerance or a combination of impaired fasting glucose and impaired glucose tolerance independently raised the future risk of stroke (1.20, 1.07 to 1.35; P = 0.002). CONCLUSION: Pre-diabetes, defined as impaired glucose tolerance or a combination of impaired fasting glucose and impaired glucose tolerance, may be associated with a higher future risk of stroke, but the relative risks are modest and may reflect underlying confounding.

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OBJECTIVE: To determine if the use of pioglitazone is associated with an increased risk of incident bladder cancer in people with type 2 diabetes. DESIGN: Retrospective cohort study using a nested case-control analysis. SETTING: Over 600 general practices in the United Kingdom contributing to the general practice research database. PARTICIPANTS: The cohort consisted of people with type 2 diabetes who were newly treated with oral hypoglycaemic agents between 1 January 1988 and 31 December 2009. All incident cases of bladder cancer occurring during follow-up were identified and matched to up to 20 controls on year of birth, year of cohort entry, sex, and duration of follow-up. Exposure was defined as ever use of pioglitazone, along with measures of duration and cumulative dosage. MAIN OUTCOME MEASURE: Risk of incident bladder cancer associated with use of pioglitazone. RESULTS: The cohort included 115,727 new users of oral hypoglycaemic agents, with 470 patients diagnosed as having bladder cancer during follow-up (rate 89.4 per 100,000 person years). The 376 cases of bladder cancer that were diagnosed beyond one year of follow-up were matched to 6699 controls. Overall, ever use of pioglitazone was associated with an increased rate of bladder cancer (rate ratio 1.83, 95% confidence interval 1.10 to 3.05). The rate increased as a function of duration of use, with the highest rate observed in patients exposed for more than 24 months (1.99, 1.14 to 3.45) and in those with a cumulative dosage greater than 28,000 mg (2.54, 1.05 to 6.14). CONCLUSION: The use of pioglitazone is associated with an increased risk of incident bladder cancer among people with type 2 diabetes.

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The authors examined the independent and combined associations of physical activity and obesity with incident type 2 diabetes among 675,496 Korean men from the database of the National Health Insurance Corporation. During an average follow-up of 7.5 years (1996-2005), 52,995 men developed type 2 diabetes. Men with overweight, obese I, and obese II classifications had 1.47, 2.05, and 3.69 times higher risk of type 2 diabetes, respectively, compared with normal weight men, and men with low, medium, and high activity had 5%, 10%, and 9% lower risk of type 2 diabetes, respectively, compared with inactive men after adjustment for confounders and physical activity or body mass index for each other. Overweight and obesity were detrimental within all activity categories, and meeting the activity recommendations (medium and high activity) was beneficial at all body mass index levels. Meeting the activity recommendations appeared to attenuate some negative effects of overweight or obesity, and the increased risk of type 2 diabetes due to inactivity was lower in normal weight men. Both preventing overweight or obesity and increasing physical activity are important to reduce the global epidemic of type 2 diabetes, regardless of body weight and activity levels


Although feast and famine cycles illustrate that remodelling of adipose tissue in response to fluctuations in nutrient availability is essential for maintaining metabolic homeostasis, the underlying mechanisms remain poorly understood. Here we identify fibroblast growth factor 1 (FGF1) as a critical transducer in this process in mice, and link its regulation to the nuclear receptor PPARgamma (peroxisome proliferator activated receptor gamma), which is the adipocyte master regulator and the target of the thiazolidinedione class of insulin sensitizing drugs. FGF1 is the prototype of the 22-member FGF family of proteins and has been implicated in a range of physiological processes, including development, wound healing and cardiovascular changes. Surprisingly, FGF1 knockout mice display no significant phenotype under standard laboratory conditions. We show that FGF1 is highly induced in adipose tissue in response to a high-fat diet and that mice lacking FGF1 develop an aggressive diabetic phenotype coupled to aberrant adipose expansion when challenged with a high-fat diet. Further analysis of adipose depots in FGF1-deficient mice revealed multiple histopathologies in the vasculature network, an accentuated inflammatory response, aberrant adipocyte size distribution and ectopic expression of pancreatic lipases. On withdrawal of the high-fat diet, this inflamed adipose tissue fails to properly resolve, resulting in extensive fat necrosis. In terms of mechanisms, we show that adipose induction of FGF1 in the fed state is regulated by PPARgamma acting through an evolutionarily conserved promoter proximal PPAR response element within the FGF1 gene. The
discovery of a phenotype for the FGF1 knockout mouse establishes the PPARgamma-FGF1 axis as critical for maintaining metabolic homeostasis and insulin sensitization


Perfluorooctane sulfonate and perfluorooctanoic acid are perfluorinated compounds (PFCs) widely distributed in the environment. Previous studies of PFCs and birth weight are equivocal. The authors examined this association in the Norwegian Mother and Child Cohort Study (MoBa), using data from 901 women enrolled from 2003 to 2004 and selected for a prior case-based study of PFCs and subfecundity. Maternal plasma samples were obtained around 17 weeks of gestation. Outcomes included birth weight z scores, preterm birth, small for gestational age, and large for gestational age. The adjusted birth weight z scores were slightly lower among infants born to mothers in the highest quartiles of PFCs compared with infants born to mothers in the lowest quartiles: for perfluorooctane sulfonate, beta = -0.18 (95% confidence interval: -0.41, 0.05) and, for perfluorooctanoic acid, beta = -0.21 (95% confidence interval: -0.45, 0.04). No clear evidence of an association with small for gestational age or large for gestational age was observed. Perfluorooctane sulfonate and perfluorooctanoic acid were each associated with decreased adjusted odds of preterm birth, although the cell counts were small. Whether some of the associations suggested by these findings may be due to a noncausal pharmacokinetic mechanism remains unclear


OBJECTIVES: We investigated whether abused and neglected children are at risk for negative physical health outcomes in adulthood. METHODS: Using a prospective cohort design, we matched children (aged 0-11 years) with documented cases of physical and sexual abuse and neglect from a US Midwestern county during 1967 through 1971 with nonmaltreated children. Both groups completed a medical status examination (measured health outcomes and blood tests) and interview during 2003 through 2005 (mean age=41.2 years). RESULTS: After adjusting for age, gender, and race, child maltreatment predicted above normal hemoglobin, lower albumin levels, poor peak airflow, and vision problems in adulthood. Physical abuse predicted malnutrition, albumin, blood urea nitrogen, and hemoglobin A1C. Neglect predicted hemoglobin A1C, albumin, poor peak airflow, and oral health and vision problems. Additional controls for childhood socioeconomic status, adult socioeconomic status, unhealthy behaviors, smoking, and mental health problems play varying roles in attenuating or intensifying these relationships. CONCLUSIONS: Child abuse and neglect affect long-term health status-increasing risk for diabetes, lung disease, malnutrition, and vision problems-and support the need for early health care prevention

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BACKGROUND: In Switzerland, health policies are decided at the local level, but little is known regarding their impact on the screening and management of cardiovascular risk factors (CVRFs). We thus aimed at assessing geographical levels of CVRFs in Switzerland. METHODS: Swiss Health Survey for 2007 (N = 17,879). Seven administrative regions were defined: West (Leman), West-Central (Mittelland), Zurich, South (Ticino), North-West, East and Central Switzerland. Obesity, smoking, hypertension, dyslipidemia and diabetes prevalence, treatment and screening within the last 12 months were assessed by interview. RESULTS: After multivariate adjustment for age, gender, educational level, marital status and Swiss citizenship, no significant differences were found between regions regarding prevalence of obesity or current smoking. Similarly, no differences were found regarding hypertension screening and prevalence. Two thirds of subjects who had been told they had high blood pressure were treated, the lowest treatment rates being found in East Switzerland: odds-ratio and [95% confidence interval] 0.65 [0.50-0.85]. Screening for hypercholesterolemia was more frequently reported in French (Leman) and Italian (Ticino) speaking regions. Four out of ten participants who had been told they had high cholesterol levels were treated and the lowest treatment rates were found in German-speaking regions. Screening for diabetes was higher in Ticino (1.24 [1.09 - 1.42]). Six out of ten participants who had been told they had diabetes were treated, the lowest treatment rates were found for German-speaking regions. CONCLUSIONS: In Switzerland, cardiovascular risk factor screening and management differ between regions and these differences cannot be accounted for by differences in populations' characteristics. Management of most cardiovascular risk factors could be improved.


BACKGROUND: Sub-Saharan Africa faces a rapid spread of diabetes mellitus type 2 (DM2) but its potentially specific characteristics are inadequately defined. In this hospital-based study in Kumasi, Ghana, we aimed at characterizing clinical, anthropometric, socio-economic, nutritional and behavioural parameters of DM2 patients and at identifying associated factors. METHODS: Between August 2007 and June 2008, 1466 individuals were recruited from diabetes and hypertension clinics, outpatients, community, and hospital staff. Fasting plasma glucose (FPG), serum lipids and urinary albumin were measured. Physical examination, anthropometry, and interviews on medical history, socio-economic status (SES), physical activity and nutritional behaviour were performed. RESULTS: The majority of the 675 DM2 patients (mean FPG, 8.31 mmol/L) was female (75%) and aged 40-60 years (mean, 55 years). DM2 was known in 97% of patients, almost all were on medication. Many had hypertension (63%) and microalbuminuria (43%); diabetic complications occurred in 20%. Overweight (body mass index > 25 kg/m2), increased body fat (> 20% (male), > 33% (female)), and central adiposity (waist-to-hip ratio > 0.90 (male), > 0.85 (female)) were frequent occurring in 53%, 56%, and 75%, respectively. Triglycerides were increased (> = 1.695 mmol/L) in 31% and cholesterol (> = 5.17 mmol/L) in 65%. Illiteracy (46%) was high and SES indicators generally low. Factors independently associated with DM2 included a diabetes family history (adjusted odds ratio (aOR), 3.8; 95% confidence interval (95%CI), 2.6-5.5), abdominal adiposity (aOR, 2.6; 95%CI, 1.8-3.9), increased triglycerides (aOR, 1.8; 95%CI, 1.1-3.0), and also several indicators of low SES. CONCLUSIONS: In this study from urban Ghana, DM2 affects predominantly obese patients of rather low socio-economic status and frequently is accompanied by hypertension and hyperlipidaemia. Prevention and management need to account for a specific risk profile in this population.

BACKGROUND: Diabetes has reached epidemic proportions in the United States, particularly among minorities, and if improperly managed can lead to medical complications and death. Healthcare providers play vital roles in communicating standards of care, which include guidance on diabetes self-management. The background of the client may play a role in the patient-provider communication process. The aim of this study was to determine the association between medical advice and diabetes self care management behaviors for a nationally representative sample of adults with diabetes. Moreover, we sought to establish whether or not race/ethnicity was a modifier for reported medical advice received and diabetes self-management behaviors.

METHODS: We analyzed data from 654 adults aged 21 years and over with diagnosed diabetes [130 Mexican-Americans; 224 Black non-Hispanics; and, 300 White non-Hispanics] and an additional 161 with 'undiagnosed diabetes' [N = 815(171 MA, 281 BNH and 364 WNH)] who participated in the National Health and Nutrition Examination Survey (NHANES) 2007-2008. Logistic regression models were used to evaluate whether medical advice to engage in particular self-management behaviors (reduce fat or calories, increase physical activity or exercise, and control or lose weight) predicted actually engaging in the particular behavior and whether the impact of medical advice on engaging in the behavior differed by race/ethnicity. Additional analyses examined whether these relationships were maintained when other factors potentially related to engaging in diabetes self management such as participants’ diabetes education, sociodemographics and physical characteristics were controlled. Sample weights were used to account for the complex sample design. RESULTS: Although medical advice to the patient is considered a standard of care for diabetes, approximately one-third of the sample reported not receiving dietary, weight management, or physical activity self-management advice. Participants who reported being given medical advice for each specific diabetes self-management behaviors were 4-8 times more likely to report performing the corresponding behaviors, independent of race. These results supported the ecological model with certain caveats. CONCLUSIONS: Providing standard medical advice appears to lead to diabetes self-management behaviors as reported by adults across the United States. Moreover, it does not appear that race/ethnicity influenced reporting performance of the standard diabetes self-management behavior. Longitudinal studies evaluating patient-provider communication, medical advice and diabetes self-management behaviors are needed to clarify our findings.


Subjective social status has been shown to be inversely associated with multiple cardiovascular risk factors, independent of objective social status. However, few studies have examined this association among African Americans and the results have been mixed. Additionally, the influence of discrimination on this relationship has not been explored. Using baseline data (2000-2004) from the Jackson Heart Study, an African American cohort from the U.S. South (N=5301), we quantified the association of subjective social status with selected cardiovascular risk factors: depressive symptoms, perceived stress, waist circumference, insulin resistance and prevalence of diabetes. We contrasted the strength of the associations of these outcomes with subjective versus objective social status and examined whether perceived discrimination confounded or modified these associations. Subjective social status was measured using two 10-rung “ladders,” using the U.S. and the community as referent groups. Objective social status was measured using annual family income and years of schooling completed. Gender-specific multivariable linear and logistic regression models were fit to examine associations. Subjective and objective measures were weakly positively correlated. Independent of objective measures, subjective social status was significantly inversely associated with depressive symptoms (men and women) and insulin resistance (women). The associations of subjective social status with the outcomes were modest and generally similar to the objective measures. We did not find evidence that perceived racial
discrimination strongly confounded or modified the association of subjective social status with the outcomes. Subjective social status was related to depressive symptoms but not consistently to stress or metabolic risk factors in African Americans.


BACKGROUND: The relationship between presence of diabetes and adverse neighborhood and housing conditions and their effect on functional decline is unclear. We examined the association of adverse neighborhood (block face) and housing conditions with incidence of lower-body functional limitations among persons with and those without diabetes using a prospective population-based cohort study of 563 African Americans 49-65 years of age at their 2000-2001 baseline interviews. METHODS: Participants were randomly sampled African Americans living in the St. Louis area (response rate: 76%). Physician-diagnosed diabetes was self reported at baseline interview. Lower-body functional limitations were self reported based on the Nagi physical performance scale at baseline and the three-year follow-up interviews. The external appearance of the block the respondent lived on and five housing conditions were rated by study interviewers. All analyses were done using propensity score methods to control for confounders. RESULTS: 109 (19.4%) of subjects experienced incident lower-body functional limitations at three-year follow-up. In adjusted analysis, persons with diabetes who lived on block faces rated as fair-poor on each of the five conditions had higher odds (7.79 [95% confidence interval: 1.36-37.55] to 144.6 [95% confidence interval: 4.45-775.53]) of developing lower-body functional limitations than the referent group of persons without diabetes who lived on block faces rated as good-excellent. At least 80 percent of incident lower-body functional limitations was attributable to the interaction between block face conditions and diabetes status. CONCLUSIONS: Adverse neighborhood conditions appear to exacerbate the detrimental effects on lower-body functioning associated with diabetes.


BACKGROUND: An interaction between genetic susceptibility and environmental factors is thought to be involved in the aetiology of type 1 diabetes. The aim of this study was to investigate maternal and neonatal risk factors for type 1 diabetes in children under 15 years old in Grampian, Scotland. METHODS: A matched case-control study was conducted by record linkage. Cases (n = 361) were children born in Aberdeen Maternity Hospital from 1972 to 2002, inclusive, who developed type 1 diabetes, identified from the Scottish Study Group for the Care of Diabetes in the Young Register. Controls (n = 1083) were randomly selected from the Aberdeen Maternity Neonatal Databank, matched by year of birth. Exposure data were obtained from the Aberdeen Maternity Neonatal Databank. Conditional logistic regression was used to evaluate the association between various maternal and neonatal factors and the risk of type 1 diabetes. RESULTS: There was no evidence of statistically significant associations between type 1 diabetes and maternal age, maternal body mass index, previous abortions, pre-eclampsia, amniocentesis, maternal deprivation, use of syntocinon, mode of delivery, antepartum haemorrhage, baby's sex, gestational age at birth, birth order, birth weight, jaundice, phototherapy, breast feeding, admission to neonatal unit and Apgar score (P > 0.05). A significantly decreased risk of type 1
diabetes was observed in children whose mothers smoked at the booking appointment compared to those whose mothers did not, with an adjusted OR of 0.67, 95% CI (0.46, 0.99).

CONCLUSIONS: This case-control study found limited evidence of a reduced risk of the development of type 1 diabetes in children whose mothers smoked, compared to children whose mothers did not. No evidence was found of a significant association between other maternal and neonatal factors and childhood type 1 diabetes


BACKGROUND: There is strong evidence for the beneficial effects of physical activity in diabetes. There has been little research demonstrating a dose-response relationship between physical activity and self-rated health in diabetics. The aim of this study was to explore the dose-response association between leisure time physical activity and self-rated health among diabetics in Taiwan. METHODS: Data came from the 2001 Taiwan National Health Interview Survey (NHIS). Inclusion criteria were a physician confirmed diagnosis of diabetes mellitus and age 18 years and above (n = 797). Self-rated health was assessed by the question "In general, would you say that your health is excellent, very good, good, fair, or poor?" Individuals with a self perceived health status of good, very good, or excellent were considered to have positive health status. RESULTS: In the full model, the odds ratio (OR) for positive health was 2.51(95% CI = 1.53-4.13), 1.62(95% CI = 0.93-2.84), and 1.35(95% CI = 0.77-2.37), for those with a total weekly energy expenditure of > or = 1000 kcal, between 500 and 999 kcal, and between 1 and 499 kcal, respectively, compared to inactive individuals. Those with duration over 10 years (OR = 0.53, 95%CI = 0.30-0.94), heart disease (OR = 0.50, 95%CI = 0.30-0.85), and dyslipidemia (OR = 0.65, 95% CI = 0.43-0.98) were less likely to have positive health than their counterparts. After stratified participants by duration, those with a duration of diabetes < 6 years, the adjusted OR for positive health was 1.95(95% CI = 1.02-3.72), 1.22(95% CI = 0.59-2.52), and 1.19(95% CI = 0.58-2.41) for those with a total weekly energy expenditure of > or = 1000 kcal, between 500 and 999 kcal, and between 1 and 499 kcal, respectively, compared to inactive individuals. In participants with a duration of diabetes > or = 6 years, total energy expenditure showed a gradient effect on self-perceived positive health. The adjusted OR for positive health was 3.45(95% CI = 1.53-7.79), 2.77(95% CI = 1.11-6.92), and 1.90(95% CI = 0.73-4.94) for those with a total weekly energy expenditure of > or = 1000 kcal, between 500 and 999 kcal, and between 1 and 499 kcal, respectively, compared to inactive individuals. CONCLUSIONS: Our results highlight that regular leisure activity with an energy expenditure -- 500 kcal per week is associated with better self-rated health for those with longstanding diabetes
including electroconvulsive therapy. Several changes in treatment approaches are usually needed before patients achieve complete remission. Maintenance treatment and relapse-prevention planning (summarization of early warning signs for depression, maintenance treatments such as medications, and other strategies to reduce the risk of relapse [eg, regular physical activity or pleasant activities]) can reduce the risk of relapse. Collaborative programs, in which primary care clinicians work closely with mental health specialists following a measurement-based treatment-to-target approach, are significantly more effective than typical primary care treatment.

(2) KARP JF, WHYTE EM. Depression treatment for patients with complex conditions. JAMA. 2012 Sept. 5, vol. 308, n° 9, pp.860-861


CONTEXT: Depression is common in patients with cardiac disease, especially in patients with heart failure, and is associated with increased risk of adverse health outcomes. Some evidence suggests that aerobic exercise may reduce depressive symptoms, but to our knowledge the effects of exercise on depression in patients with heart failure have not been evaluated.

OBJECTIVE: To determine whether exercise training will result in greater improvements in depressive symptoms compared with usual care among patients with heart failure.

DESIGN, SETTING, AND PARTICIPANTS: Multicenter, randomized controlled trial involving 2322 stable patients treated for heart failure at 82 medical clinical centers in the United States, Canada, and France. Patients who had a left ventricular ejection fraction of 35% or lower, had New York Heart Association class I to IV heart failure, and had completed the Beck Depression Inventory II (BDI-II) score were randomized (1:1) between April 2003 and February 2007. Depressive scores ranged from 0 to 59; scores of 14 or higher are considered clinically significant.

INTERVENTIONS: Participants were randomized either to supervised aerobic exercise (goal of 90 min/wk for months 1-3 followed by home exercise with a goal of >/=120 min/wk for months 4-12) or to education and usual guideline-based heart failure care.

MAIN OUTCOME MEASURES: Composite of death or hospitalization due to any cause and scores on the BDI-II at months 3 and 12.

RESULTS: Over a median follow-up period of 30 months, 789 patients (68%) died or were hospitalized in the usual care group compared with 759 (66%) in the aerobic exercise group (hazard ratio [HR], 0.89; 95% CI, 0.81 to 0.99; P = .03). The median BDI-II score at study entry was 8, with 28% of the sample having BDI-II scores of 14 or higher. Compared with usual care, aerobic exercise resulted in lower mean BDI-II scores at 3 months (aerobic exercise, 8.95; 95% CI, 8.61 to 9.29 vs usual care, 9.70; 95% CI, 9.34 to 10.06; difference, -0.76; 95% CI,-1.22 to -0.29; P = .002) and at 12 months (aerobic exercise, 8.86; 95% CI, 8.67 to 9.24 vs usual care, 9.54; 95% CI, 9.15 to 9.92; difference, -0.68; 95% CI, -1.20 to -0.16; P = .01). CONCLUSIONS: Compared with guideline-based usual care, exercise training resulted in a modest reduction in depressive symptoms, although the clinical significance of this improvement is unknown.

TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00047437


Chronic stress is a strong diathesis for depression in humans and is used to generate animal models of depression. It commonly leads to several major symptoms of depression, including dysregulated feeding behaviour, anhedonia and behavioural despair. Although hypotheses defining the neural pathophysiology of depression have been proposed, the critical synaptic adaptations in key brain circuits that mediate stress-induced depressive symptoms remain poorly.
understood. Here we show that chronic stress in mice decreases the strength of excitatory synapses on D1 dopamine receptor-expressing nucleus accumbens medium spiny neurons owing to activation of the melanocortin 4 receptor. Stress-elicited increases in behavioural measurements of anhedonia, but not increases in measurements of behavioural despair, are prevented by blocking these melanocortin 4 receptor-mediated synaptic changes in vivo. These results establish that stress-elicited anhedonia requires a neuropeptide-triggered, cell-type-specific synaptic adaptation in the nucleus accumbens and that distinct circuit adaptations mediate other major symptoms of stress-elicited depression.


(6) DONNELLY L. Study's conclusion is misleading and ill considered. BMJ. 2012, vol. 345, p.e4494


(9) SHELDON T. Reserve antidepressants for cases of severe depression, Dutch doctors are told. BMJ. 2012, vol. 344, p.e4211


OBJECTIVES: We examined individual, friend or family, and community or tribe correlates of suicidality in a representative on-reserve sample of First Nations adolescents. METHODS: Data came from the 2002-2003 Manitoba First Nations Regional Longitudinal Health Survey of Youth. Interviews were conducted with adolescents aged 12 to 17 years (n=1125) from 23 First Nations communities in Manitoba. We used bivariate logistic regression analyses to examine the relationships between a range of factors and lifetime suicidality. We conducted sex-by-covariate interactions for each significant correlate at the bivariate level. A multivariate logistic regression analysis identified those correlates most strongly related to suicidality. RESULTS: We found several variables to be associated with an increased likelihood of suicidality in the multivariate model, including being female, depressed mood, abuse or fear of abuse, a hospital stay, and substance use (adjusted odds ratio range=2.43-11.73). Perceived community caring was protective against suicidality (adjusted odds ratio=0.93; 95% confidence interval=0.88, 0.97) in the same model. CONCLUSIONS: Results of this study may be important in informing First Nations and government policy related to the implementation of suicide prevention strategies in First Nations communities.


OBJECTIVE: To investigate the effectiveness of facilitated physical activity as an adjunctive treatment for adults with depression presenting in primary care. DESIGN: Pragmatic, multicentre, two arm parallel randomised controlled trial. SETTING: General practices in Bristol and Exeter. PARTICIPANTS: 361 adults aged 18-69 who had recently consulted their general practitioner with symptoms of depression. All those randomised had a diagnosis of an episode of depression as assessed by the clinical interview schedule-revised and a Beck depression inventory score of 14 or more. INTERVENTIONS: In addition to usual care, intervention participants were offered up to three face to face sessions and 10 telephone calls with a trained physical activity facilitator over eight months. The intervention was based on theory and aimed to provide individually tailored support and encouragement to engage in physical activity. MAIN OUTCOME MEASURES: The primary outcome was self reported symptoms of depression, assessed with the Beck depression inventory at four months post-randomisation. Secondary outcomes included use of antidepressants and physical activity at the four, eight, and 12 month follow-up points, and symptoms of depression at eight and 12 month follow-up. RESULTS: There was no evidence that participants offered the physical activity intervention reported improvement in mood by the four month follow-up point compared with those in the usual care group; adjusted between group difference in mean Beck depression inventory score -0.54 (95% confidence interval -3.06 to 1.99; P=0.68). Similarly, there was no evidence that the intervention group reported a change in mood by the eight and 12 month follow-up points. Nor was there evidence that the intervention reduced antidepressant use compared with usual care (adjusted odds ratio 0.63, 95% confidence interval 0.19 to 2.06; P=0.44) over the duration of the trial. However, participants allocated to the intervention group reported more physical activity during the follow-up period than those allocated to the usual care group (adjusted odds ratio 2.27, 95% confidence interval 1.32 to 3.89; P=0.003). CONCLUSIONS: The addition of a facilitated physical activity intervention to usual care did not improve depression outcome or reduce use of antidepressants compared with usual care alone. TRIAL REGISTRATION: Current Controlled Trials ISRCTN16900744

(13) MARCANTONIO ER. Postoperative delirium: a 76-year-old woman with delirium following surgery. JAMA. 2012 July 4, vol. 308, n° 1, pp.73-81

Delirium (acute confusion) complicates 15% to 50% of major operations in older adults and is associated with other major postoperative complications, prolonged length of stay, poor functional recovery, institutionalization, dementia, and death. Importantly, delirium may be predictable and preventable through proactive intervention. Yet clinicians fail to recognize and address postoperative delirium in up to 80% of cases. Using the case of Ms R, a 76-year-old woman who developed delirium first after colectomy with complications and again after routine surgery, the diagnosis, prevention, and treatment of delirium in the postoperative setting is reviewed. The risk of postoperative delirium can be quantified by the sum of predisposing and precipitating factors. Successful strategies for prevention and treatment of delirium include proactive multifactorial intervention targeted to reversible risk factors, limiting use of sedating medications (especially benzodiazepines), effective management of postoperative pain, and, perhaps, judicious use of antipsychotics


While observational studies have suggested that vitamin D deficiency increases risk of depression, few clinical trials have tested whether vitamin D supplementation affects the occurrence of depression symptoms. The authors evaluated the impact of daily supplementation with 400 IU of vitamin D(3) combined with 1,000 mg of elemental calcium on measures of
depression in a randomized, double-blinded US trial comprising 36,282 postmenopausal women. The Burnam scale and current use of antidepressant medication were used to assess depressive symptoms at randomization (1995-2000). Two years later, women again reported on their antidepressant use, and 2,263 completed a second Burnam scale. After 2 years, women randomized to receive vitamin D and calcium had an odds ratio for experiencing depressive symptoms (Burnam score >0.06) of 1.16 (95% confidence interval: 0.86, 1.56) compared with women in the placebo group. Supplementation was not associated with antidepressant use (odds ratio = 1.01, 95% confidence interval: 0.92, 1.12) or continuous depressive symptom score. Results stratified by baseline vitamin D and calcium intake, solar irradiance, and other factors were similar. The findings do not support a relation between supplementation with 400 IU/day of vitamin D(3) along with calcium and depression in older women. Additional trials testing higher doses of vitamin D are needed to determine whether this nutrient may help prevent or treat depression.


OBJECTIVES: We examined stress levels and other indicators of mental health in reservists and active-duty military personnel by deployment status. METHODS: We used data from the Department of Defense Health-Related Behaviors surveys, which collect comprehensive, population-based data for reserve and active-duty forces. Data were collected from 18,342 reservists and 16,146 active-duty personnel. RESULTS: Overall, with adjustment for sociodemographic and service differences, reservists reported similar or less work and family stress, depression, and anxiety symptoms than did active-duty personnel. However, reservists who had been deployed reported higher rates of suicidal ideation and attempts than did active-duty personnel who had been deployed and higher rates of post-traumatic stress disorder symptomatology than did any active-duty personnel and reservists who had not been deployed. The highest rates of suicidal ideation and attempts were among reservists who had served in theaters other than Iraq and Afghanistan. CONCLUSIONS: Our results suggest that deployment has a greater impact on reservists than on active-duty members, thus highlighting the urgent need for services addressing reservists’ unique postdeployment mental health issues. Also, deployment to any theater, not only Iraq or Afghanistan, represents unique threats to all service members’ mental well-being.


To investigate the relation between work environmental factors and the risk of major depressive disorder (MDD) over 1 year, the authors conducted a population-based longitudinal study of randomly selected employees in Alberta, Canada (January 2008 to November 2011). Participants without a current or lifetime diagnosis of MDD at baseline (n = 2,752) were followed for 1 year. MDD was assessed using the World Health Organization's Composite International Diagnostic Interview-Auto 2.1. The overall 1-year incidence of MDD was 3.6% (95% confidence interval: 2.8, 4.6); it was 2.9% (95% confidence interval: 1.9, 4.2) in men and 4.5% (95% confidence interval: 3.3, 6.2) in women. The relations between work environmental factors and MDD differed by sex. In men, high job strain increased the risk of MDD in those who worked 35-40 hours per week; job insecurity and family-to-work conflict were predictive of MDD. Women who worked 35-40 hours per week and reported job insecurity, a high effort-reward imbalance, and work-to-family conflict were at a higher risk of developing MDD. Job strain, effort-reward imbalance, job insecurity, and work-to-family conflicts are important risk factors for the onset of MDD and should be targets of
primary prevention. However, these work environmental factors appear to operate differently in men and in women


OBJECTIVES: We evaluated a quality improvement program with a pay-for-performance (P4P) incentive in a population-focused, integrated care program for safety-net patients in 29 community health clinics. METHODS: We used a quasi-experimental design with 1673 depressed adults before and 6304 adults after the implementation of the P4P program. Survival analyses examined the time to improvement in depression before and after implementation of the P4P program, with adjustments for patient characteristics and clustering by health care organization. RESULTS: Program participants had high levels of depression, other psychiatric and substance abuse problems, and social adversity. After implementation of the P4P incentive program, participants were more likely to experience timely follow-up, and the time to depression improvement was significantly reduced. The hazard ratio for achieving treatment response was 1.73 (95% confidence interval=1.39, 2.14) after the P4P program implementation compared with pre-program implementation. CONCLUSIONS: Although this quasi-experiment cannot prove that the P4P initiative directly caused improved patient outcomes, our analyses strongly suggest that when key quality indicators are tracked and a substantial portion of payment is tied to such quality indicators, the effectiveness of care for safety-net populations can be substantially improved


Depression is common among people living with HIV/AIDS and contributes to a wide range of worsened HIV-related outcomes, including AIDS-related mortality. Targeting modifiable causes of depression, either through primary or secondary prevention, may reduce suffering as well as improve HIV-related outcomes. Food insecurity is a pervasive source of uncertainty for those living in resource-limited settings, and cross-sectional studies have increasingly recognized it as a critical determinant of poor mental health. Using cohort data from 456 men and women living with HIV/AIDS initiating HIV antiretroviral therapy in rural Uganda, we sought to (a) estimate the association between food insecurity and depression symptom severity, (b) assess the extent to which social support may serve as a buffer against the adverse effects of food insecurity, and (c) determine whether the buffering effects are specific to certain types of social support. Quarterly data were collected by structured interviews and blood draws. The primary outcome was depression symptom severity, measured by a modified Hopkins Symptom Checklist for Depression. The primary explanatory variables were food insecurity, measured with the Household Food Insecurity Access Scale, and social support, measured with a modified version of the Functional Social Support Questionnaire. We found that food insecurity was associated with depression symptom severity among women but not men, and that social support buffered the impacts of food insecurity on depression. We also found that instrumental support had a greater buffering influence than emotional social support. Interventions aimed at improving food security and strengthening instrumental social support may have synergistic beneficial effects on both mental health and HIV outcomes among PLWHA in resource-limited settings

This study investigated the extent to which differences in the types of war trauma, economic pressure, religiosity and ideology accounted for variation in PTSD and psychiatric disorders among adolescents from Gaza Strip and South Lebanon. Participants were 600 adolescents aged 12-16 years. They were selected from the public school system in the highly war exposed areas. Questionnaires were administered in an interview format with adolescents at school by two trained psychologists. Results indicated that the various types of trauma had differential effects on the psychological status of adolescents in both countries. Economic pressure was more predictive of PTSD and psychological distress in adolescents from Gaza. Differences in religiosity and ideology did not account for similar variation in stress response among adolescents from Gaza and South Lebanon. While higher levels of religiosity evidenced the greatest levels of depression and anxiety in adolescents from Gaza, religiosity had an attenuated effect on adolescents from South Lebanon. Ideology was negatively associated with depression and anxiety in Gaza strip adolescents, whereas it did not play a role for adolescents from South Lebanon. The clinical and research implications of these conclusions are discussed.


Studies of individual differences in bereavement have revealed prototypical patterns of outcome. However, many of these studies were conducted prior to the advent of sophisticated contemporary data analytic techniques. For example, Bonanno et al. (2002) used rudimentary categorization procedures to identify unique trajectories of depression symptomatology from approximately 3 years prior to 4 years following conjugal loss in a representative sample of older American adults. In the current study, we revisited these same data using Latent Class Growth Analysis (LCGA) to derive trajectories and test predictors. LCGA is a technique well-suited for modeling empirically- and conceptually-derived heterogeneous longitudinal patterns while simultaneously modeling predictors of those longitudinal patterns. We uncovered four discrete trajectories similar in shape and proportion to the previous analyses: Resilience (characterized by little or no depression; 66.3%), Chronic Grief (characterized by depression following loss, alleviated by 4 years post-loss; 9.1%), Pre-existing Chronic Depression (ongoing high pre-through post-loss depression; 14.5%), and Depressed-Improved (characterized by high pre-loss depression that decreases following loss; 10.1%). Using this analytic strategy, we were able to examine multiple hypotheses about bereavement simultaneously. Health, financial stress, and emotional stability emerged as strong predictors of variability in depression only for some trajectories, indicating that depression levels do not have a common etiology across all the bereaved. As such, we find that identifying distinct patterns informs both the course and etiology of depression in response to bereavement.


BACKGROUND: Non-compliance with antidepressant treatment continues to be a complex problem in mental health care. In immigrant populations non-compliance is one of several barriers to adequate management of mental illness; some data suggest greater difficulties in adhering to pharmacological treatment in these groups and an increased risk of therapeutic failure. The aim of this study is to assess differences in the duration and compliance with antidepressant treatment among immigrants and natives in a Spanish health region. METHODS: Population-based (n = 206,603), retrospective cohort study including all subjects prescribed ADT between 2007 and 2009 and recorded in the national pharmacy claims database. Compliance was considered adequate when the duration was longer than 4 months and when patients withdrew more than 80% of the packs required. RESULTS: 5334 subjects (8.5% of them being immigrants) initiated...
ADT. Half of the immigrants abandoned treatment during the second month (median for natives = 3 months). Of the immigrants who continued, only 29.5% presented good compliance (compared with 38.8% in natives). The estimated risk of abandoning/end treatment in the immigrant group compared with the native group, adjusted for age and sex, was 1.28 (95%CI 1.16-1.42).

CONCLUSIONS: In the region under study, immigrants of all origins present higher percentages of early discontinuation of ADT and lower median treatment durations than the native population. Although this is a complex, multifactor situation, the finding of differences between natives and immigrants in the same region suggests the need to investigate the causes in greater depth and to introduce new strategies and interventions in this population group.


The influence of community-level indicators in understanding mental health has been of interest since the seminal work of Faris and Dunham (1939). The emergence of Geographic Information Systems (GIS), and concepts such as social capital and recovery add new tools and concepts for further explorations in this area. This correlational study uses an innovative GIS approach to examine the relative contribution of community indicators, such as crime, unemployment, social capital, and individual-level sociodemographic characteristics, such as gender, age, and experience of homelessness, to the well-being and recovery of 378 individuals diagnosed with either major depression or a schizophrenia-spectrum disorder residing in an urban environment in the Northeast United States. Results indicate that community-level indicators are only marginally correlated with well-being, including self-reported symptoms, quality of life, empowerment, and recovery. These associations are further reduced when considering individuals' sociodemographic characteristics, which appear to explain a greater amount of variability in well-being and recovery. Contrary to expectations, these results suggest that community indicators may not have a major impact on individuals who have already developed a significant psychiatric condition, at least in the domains studied, and that personal factors play a more significant role. These findings further advance our knowledge about the relationship between "place" and personal factors on mental health and wellness.


Given the increased access of antiretroviral therapy (ART) throughout the developing world, what was once a terminal illness is now a chronic disease for those receiving treatment. This requires a paradigmatic shift in service provision for those affected by HIV/AIDS in low-resource settings. Although there is a need for psychosocial support interventions for HIV-affected youth and their caregivers, to date there has been limited empirical evidence on the effectiveness of curriculum-based psychosocial support groups in HIV-affected families in low-income countries. Therefore, the purpose of this study is to examine the feasibility and assess the preliminary effectiveness of a psychosocial support group intervention for HIV-affected youth and their caregivers in central Haiti. The study was conducted at six Partners In Health-affiliated sites between February 2006 and September 2008 and included quantitative as well as qualitative methods. HIV-affected youth (n = 168) and their caregivers (n = 130) completed a baseline structured questionnaire prior to participation in a psychosocial support group intervention. Ninety-five percent of families completed the intervention and a follow-up questionnaire. Psychological symptoms, psychosocial functioning, social support, and HIV-related stigma at baseline were compared with outcomes one year later. Qualitative methods were also used to assess the participants' perspectives of the intervention. Comparing pre- and post-intervention assessment, youth affected by HIV experienced decreased psychological symptoms as well as improved psychosocial functioning.
and social support. Caregivers (95% HIV-positive) demonstrated a significant reduction in depressive symptoms, improved social support, and decreased HIV-related stigma. Although further study is needed to assess effectiveness in a randomized controlled trial, corroborative findings from qualitative data reflected reduced psychological distress, less social isolation and greater hope for the future for families affected by HIV/AIDS following the intervention.


A previous study suggested an increased risk of preeclampsia among women treated with selective serotonin reuptake inhibitors (SSRIs). Using population-based health-care utilization databases from British Columbia (1997-2006), the authors conducted a study of 69,448 pregnancies in women with depression. They compared risk of preeclampsia in women using SSRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs), or tricyclic antidepressants (TCAs) between gestational weeks 10 and 20 with risk in depressed women not using antidepressants. Among prepregnancy antidepressant users, the authors compared the risk in women who continued antidepressants between gestational weeks 10 and 24 with the risk in those who discontinued. Relative risks and 95% confidence intervals were estimated. The risk of preeclampsia in depressed women not treated with antidepressants (2.4%) was similar to that in women without depression (2.3%). Compared with women with untreated depression, women treated with SSRI, SNRI, and TCA monotherapy had adjusted relative risks of 1.22 (95% confidence interval (CI): 0.97, 1.54), 1.95 (95% CI: 1.25, 3.03), and 3.23 (95% CI: 1.87, 5.59), respectively. Within prepregnancy antidepressant users, the relative risk for preeclampsia among continuers compared with discontinuers was 1.32 (95% CI: 0.95, 1.84) for SSRI, 3.43 (95% CI: 1.77, 6.65) for SNRI, and 3.26 (95% CI: 1.04, 10.24) for TCA monotherapy. Study results suggest that women who use antidepressants during pregnancy, especially SNRIs and TCAs, have an elevated risk of preeclampsia. These associations may reflect drug effects or more severe depression.


Previous research has revealed a negative impact of orphanhood and HIV-related stigma on the psychological well-being of children affected by HIV/AIDS. Little is known about psychological protective factors that can mitigate the effect of orphanhood and HIV-related stigma on psychological well-being. This research examines the relationships among several risk and protective factors for depression symptoms using structural equation modeling. Cross-sectional data were collected from 755 AIDS orphans and 466 children of HIV-positive parents aged 6-18 years in 2006-2007 in rural central China. Participants reported their experiences of traumatic events, perceived HIV-related stigma, perceived social support, future orientation, trusting relationships with current caregivers, and depression symptoms. We found that the experience of traumatic events and HIV-related stigma had a direct contributory effect on depression among children affected by HIV/AIDS. Trusting relationships together with future orientation and perceived social support mediated the effects of traumatic events and HIV-related stigma on depression. The final model demonstrated a dynamic interplay among future orientation, perceived social support and trusting relationships. Trusting relationships was the most proximate protective factor for depression. Perceived social support and future orientation were positively related to trusting relationships. We conclude that perceived social support, trusting relationships, and future orientation offer multiple levels of protection that can mitigate the effect of traumatic events and HIV-related stigma on depression. Trusting relationships with caregivers provides the most immediate source of psychological support. Future prevention interventions seeking to...
improve psychological well-being among children affected by HIV/AIDS should attend to these factors


Marginalization and stigmatization heighten the vulnerability of sexual minorities to inequitable mental health outcomes. There is a dearth of information regarding stigma and mental health among men who have sex with men (MSM) in India. We adapted Meyer’s minority stress model to explore associations between stigma and depression among MSM in South India. The study objective was to examine the influence of sexual stigma, gender non-conformity stigma (GNS) and HIV-related stigma (HIV-S) on depression among MSM in South India. A cross-sectional survey was administered to MSM in urban (Chennai) (n=100) and semi-urban (Kumbakonam) (n=100) locations in Tamil Nadu. The majority of participants reported moderate/severe depression scores. Participants in Chennai reported significantly higher levels of GNS, social support and resilient coping, and lower levels of HIV-S and depression, than participants in Kumbakonam. Hierarchical block regression analyses were conducted to measure associations between independent (GNS, HIV-S), moderator (social support, resilient coping) and dependent (depression) variables. Sexual stigma was not included in regression analyses due to multicollinearity with GNS. The first regression analyses assessed associations between depression and stigma subtypes. In Chennai, perceived GNS was associated with depression; in Kumbakonam enacted/perceived GNS and vicarious HIV-S were associated with depression. In the moderation analyses, overall GNS and HIV-S scores (subtypes combined) accounted for a significant amount of variability in depression in both locations, although HIV-S was only a significant predictor in Kumbakonam. Social support and resilient coping were associated with lower depression but did not moderate the influence of HIV-S or GNS on depression. Differences in stigma, coping, social support and depression between locations highlight the salience of considering geographical context in stigma analyses. Associations between HIV-S and depression among HIV-negative MSM emphasize the significance of symbolic stigma. Findings may inform multi-level stigma reduction and health promotion interventions with MSM in South India


Subjective social status has been shown to be inversely associated with multiple cardiovascular risk factors, independent of objective social status. However, few studies have examined this association among African Americans and the results have been mixed. Additionally, the influence of discrimination on this relationship has not been explored. Using baseline data (2000-2004) from the Jackson Heart Study, an African American cohort from the U.S. South (N=5301), we quantified the association of subjective social status with selected cardiovascular risk factors: depressive symptoms, perceived stress, waist circumference, insulin resistance and prevalence of diabetes. We contrasted the strength of the associations of these outcomes with subjective versus objective social status and examined whether perceived discrimination confounded or modified these associations. Subjective social status was measured using two 10-rung “ladders,” using the U.S. and the community as referent groups. Objective social status was measured using annual family income and years of schooling completed. Gender-specific multivariable linear and logistic regression models were fit to examine associations. Subjective and objective measures were weakly positively correlated. Independent of objective measures, subjective social status was significantly inversely associated with depressive symptoms (men and women) and insulin
resistance (women). The associations of subjective social status with the outcomes were modest and generally similar to the objective measures. We did not find evidence that perceived racial discrimination strongly confounded or modified the association of subjective social status with the outcomes. Subjective social status was related to depressive symptoms but not consistently to stress or metabolic risk factors in African Americans.


BACKGROUND: Information on the health-related quality of life (HRQoL) of patients with genital warts (GW) in populations in mainland China is still limited. The aim of the study was to use a generic instrument to measure the impact of genital warts on HRQoL in men and women in this setting. METHODS: A multi-centre hospital-based cross-sectional study across 18 centers in China was conducted to interview patients using the European quality of life-5 dimension (EQ-5D) instrument; respondents' demographic and clinical data were also collected. RESULTS: A total of 1,358 GW patients (612 men, 746 women) were included in the analysis, with a mean age of 32.0 +/- 10.6 years. 56.4% of the patients reported some problems in the dimension of Anxiety/Depression (highest), followed by Pain/Discomfort (24.7%) and Mobility (3.5%). The overall visual analogue scale (VAS) score of the study population was found to be 65.2 +/- 22.0, and the EQ-5D index score was found to be 0.843 +/- 0.129 using Japanese preference weights (the Chinese preference was unavailable yet). Patients with lower VAS means and EQ-5D index scores were more often female, living in urban area, and suffering multiple GW (all p values < 0.05), but the values did not differ notably by age (p values > 0.05). CONCLUSIONS: The HRQoL of patients with GW was substantially lower, compared to a national representative general population in China (VAS = ~80); the findings of different subgroups are informative for future GW prevention and control efforts.


This U.S.A.-based study examined the quantitative and qualitative characteristics of sleep, as well as the role of sleep, in the association of stress with depression, fatigue, and health-related quality of life (H-QOL) among mothers with a low-birth-weight, preterm infant in the neonatal intensive care unit at early postpartum. Fifty-five first-time mothers kept a sleep diary and filled out a battery of questionnaires. The wrist actigraphy method was also applied to collect information on maternal sleep. We tested a path model, with sleep disturbance and depression mediating the effect of stress on health-related well-being. Results showed that the majority of the study participants were stressed, depressed, fatigued, and at risk for poor physical and mental health. Poor sleep quality as perceived by mothers was significantly associated with their stress, fatigue, and poor mental and physical H-QOL. A cascading effect was found in the path model where maternal stress contributed to poor sleep quality and depression, which in turn contributed to poor mental H-QOL. In addition, poor sleep quality was associated with fatigue, which in turn contributed to poor physical and mental H-QOL. The underlying neurobiological mechanisms through which sleep affects the stress-health relation are discussed. The implications of sleep for intervention and prevention are also addressed.

(30) UCHINO BN, BOWEN K, CARLISLE M, BIRMINGHAM W. Psychological pathways linking social support to health outcomes: a visit with the "ghosts" of research past, present, and future. Soc Sci Med. 2012 Apr., vol. 74, n° 7, pp.949-957

Contemporary models postulate the importance of psychological mechanisms linking perceived
and received social support to physical health outcomes. In this review, we examine studies that
directly tested the potential psychological mechanisms responsible for links between social
support and health-relevant physiological processes (1980s-2010). Inconsistent with existing
theoretical models, no evidence was found that psychological mechanisms such as depression,
perceived stress, and other affective processes are directly responsible for links between support
and health. We discuss the importance of considering statistical/design issues, emerging
conceptual perspectives, and limitations of our existing models for future research aimed at
elucidating the psychological mechanisms responsible for links between social support and
physical health outcomes

longitudinal association between n-3 fatty acid intake and depressive symptoms: results

Findings regarding the association between n-3 polyunsaturated fatty acid (PUFA) status and
depression are conflicting. Thus, the authors studied associations between PUFA intake and
depressive symptoms. In 1996, depressive symptoms were assessed in a subsample of
participants from the Supplementation with Antioxidant Vitamins and Minerals (SU.VI.MAX) Study
using the Center for Epidemiologic Studies Depression Scale (CES-D). In 2007-2009, information
on CES-D score, history of depression, and use of antidepressant medication was obtained.
Intakes of n-3 PUFAs were estimated from repeated 24-hour dietary records collected during
1994-1996. Subjects with depressive symptoms (cases) were identified using CES-D scores
greater than 15 and/or antidepressant use. Logistic regression analyses were used. Cross-
sectional (n = 2,744) and longitudinal (n = 1,235) associations between quartiles of PUFA intake
and depressive symptoms were estimated. In cross-sectional analyses, quartile of n-3 PUFA
intake was associated with lower odds of depressive symptoms (fourth quartile vs. first: odds ratio
= 0.74, 95% confidence interval: 0.58, 0.95; P for trend = 0.001). No association between PUFA
intake and incidence of depressive symptoms over 13 years was detected. This study provides
new insights into the PUFA-depression link. While no association between n-3 PUFA intake and
incidence of depressive symptoms was detected, an association was observed in cross-sectional
analyses, which may reflect unhealthy dietary patterns among subjects with depressive symptoms

(32) LINDLEY LL, WALSEMANN KM, CARTER JW, JR. The association of sexual orientation
102, n° 6, pp.1177-1185

OBJECTIVES: We examined associations among 3 dimensions of sexual orientation (identity,
behavior, and attraction) and key health-related indicators commonly studied among sexual
minority populations: depressive symptoms, perceived stress, smoking, binge drinking, and
victimization. METHODS: We analyzed data from the National Longitudinal Study of Adolescent
Health, Wave IV (2007-2008) when respondents were aged 24 to 32 years (n=14,412). We used
multivariate linear and logistic regressions to examine consistency of associations between sexual
orientation measures and health-related indicators. RESULTS: Strength of associations differed
by gender and sexual orientation measure. Among women, being attracted to both sexes,
identifying as "mostly straight" or "bisexual," and having mostly opposite-sex sexual partners was
associated with greater risk for all indicators. Among men, sexual attraction was unrelated to
health indicators. Men who were "mostly straight" were at greater risk for some, but not all,
indicators. Men who had sexual partners of the same-sex or both sexes were at lower risk for
binge drinking. CONCLUSIONS: Using all 3 dimensions of sexual orientation provides a more
complete picture of the association between sexual orientation and health among young adults
than does using any 1 dimension alone

BACKGROUND: Health professionals and organizations in developed countries adapt slowly to the increase of ethnically diverse populations attending health care centres. Several studies report that attention to immigrant mental health comes up with barriers in access, diagnosis and therapeutics, threatening equity. This study analyzes differences in exposure to antidepressant drugs between the immigrant and the native population of a Spanish health region. METHODS: Cross-sectional study of the dispensation of antidepressant drugs to the population aged 15 years or older attending the public primary health centres of a health region, 232,717 autochthonous and 33,361 immigrants, during 2008. Data were obtained from computerized medical records and pharmaceutical records of medications dispensed in pharmacies. Age, sex, country of origin, visits, date of entry in the regional health system, generic drugs and active ingredients were considered. Statistical analysis expressed the percentage of persons exposed to antidepressants stratified by age, gender, and country of origin and prevalence ratios of antidepressant exposition were calculated. RESULTS: Antidepressants were dispensed to 11% of native population and 2.6% of immigrants. Depending on age, native women were prescribed antidepressants between 1.9 and 2.7 times more than immigrant women, and native men 2.5 and 3.1 times more than their immigrant counterparts. Among immigrant females, the highest rate was found in the Latin Americans (6.6%) and the lowest in the sub-Saharan (1.4%). Among males, the highest use was also found in the Latin Americans (1.6%) and the lowest in the sub-Saharan (0.7%). The percentage of immigrants prescribed antidepressants increased significantly in relation to the number of years registered with the local health system. Significant differences were found for the new antidepressants, prescribed 8% more in the native population than in immigrants, both in men and in women. CONCLUSIONS: All the immigrants, regardless of the country of origin, had lower antidepressant consumption than the native population of the same age and sex. Latin American women presented the highest levels of consumption, and the sub-Saharan men the lowest. The prescription profiles also differed, since immigrants consumed more generics and fewer recently commercialized active ingredients


BACKGROUND: Recent evidence, both animal and human, suggests that modifiable factors during fetal and infant development predispose for cardiovascular disease in adult life and that they may become possible future targets for prevention. One of these factors is maternal psychosocial stress, but so far, few prospective studies have been able to investigate the longer-term effects of stress in detail, i.e. effects in childhood. Therefore, our general aim is to study whether prenatal maternal psychosocial stress is associated with an adverse cardio-metabolic risk profile in the child at age five. METHODS/DESIGN: Data are available from the Amsterdam Born Children and their Development (ABCD) study, a prospective birth cohort in the Netherlands. Between 2003-2004, 8,266 pregnant women filled out a questionnaire including instruments to determine anxiety (STAI), pregnancy related anxiety (PRAQ), depressive symptoms (CES-D), parenting stress (PDH scale) and work stress (Job Content Questionnaire). Outcome measures in the offspring (age 5-7) are currently collected. These include lipid profile, blood glucose, insulin sensitivity, body composition (body mass index, waist circumference and bioelectrical impedance analysis), autonomic nervous system activity (parasympathetic and sympathetic measures) and blood pressure. Potential mediators are maternal serum cortisol, gestational age and birth weight for gestational age (intrauterine growth restriction). Possible gender differences in programming are also studied. DISCUSSION: Main strengths of the proposed study are the longitudinal measurements during three important periods (pregnancy, infancy and childhood), the extensive
measurement of maternal psychosocial stress with validated questionnaires and the thorough measurement of the children's cardio-metabolic profile. The availability of several confounding factors will give us the opportunity to quantify the independent contribution of maternal stress during pregnancy to the cardio-metabolic risk profile of her offspring. Moreover, the mediating role of maternal cortisol, intrauterine growth, gestational age and potential gender differences can be explored extensively. If prenatal psychosocial stress is indeed found to be associated with the offspring's cardio-metabolic risk, these results support the statement that primary prevention of cardiovascular disease may start even before birth by reducing maternal stress during pregnancy.

Etudes sur le tabagisme


5. ROEHR B. California defeats tax increase on cigarettes to fund research. BMJ. 2012, vol. 344, p.e4112


BACKGROUND: The risk that a positive smoking history in lung donors could adversely affect survival of transplant recipients causes concern. Conversely, reduction of the donor pool by exclusion of donors with positive smoking histories could compromise survival of patients waiting to receive a transplant. We examined the consequences of donor smoking on post-transplantation survival, and the potential effect of not transplanting lungs from such donors. METHODS: We analysed the effect of donor smoking on 3 year survival after first adult lung transplantation from brain-dead donors done between July 1, 1999, and Dec 31, 2010, by Cox regression modelling of data from the UK Transplant Registry. We estimated the effect of acceptance of lungs from donors with positive smoking histories on survival and compared it with the effect of remaining on the waiting list for a potential transplant from a donor with a negative smoking history donor, by analysing all waiting-list registrations during the same period with a risk-adjusted sequentially stratified Cox regression model. FINDINGS: Of 1295 lung transplantations, 510 (39%) used lungs from donors with positive smoking histories. Recipients of such lungs had worse 3 year survival after transplantation than did those who received lungs from donors with negative smoking histories (unadjusted hazard ratio [HR] 1.46, 95% CI 1.20-1.78; adjusted HR 1.36, 1.11-1.67). Independent factors affecting survival were recipient's age, donor-recipient cytomegalovirus...
matching, donor-recipient height difference, donor's sex, and total ischaemic time. Of 2181 patients registered on the waiting list, 802 (37%) died or were removed from the list without receiving a transplant. Patients receiving lungs from donors with positive smoking histories had a lower unadjusted hazard of death after registration than did those who remained on the waiting list (0.79, 95% CI 0.70-0.91). Patients with septic or fibrotic lung disease registered in 1999-2003 had risk-adjusted hazards of 0.60 (95% CI 0.42-0.87) and 0.39 (0.28-0.55), respectively.

**INTERPRETATION:** In the UK, an organ selection policy that uses lungs from donors with positive smoking histories improves overall survival of patients registered for lung transplantation, and should be continued. Although lungs from such donors are associated with worse outcomes, the individual probability of survival is greater if they are accepted than if they are declined and the patient chooses to wait for a potential transplant from a donor with a negative smoking history. This situation should be fully explained to and discussed with patients who are accepted for lung transplantation. **FUNDING:** National Health Service Blood and Transplant


OBJECTIVES: We sought to present new data on smoking prevalence in 8 countries, analyze prevalence changes between 2001 and 2010, and examine trend variance by age, location, education level, and household economic status. METHODS: We conducted cross-sectional household surveys in 2010 in Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, and Ukraine. We compared smoking prevalence with a related 2001 study for the different countries and population subgroups, and also calculated the adjusted prevalence rate ratios of smoking. RESULTS: All-age 2010 smoking prevalence among men ranged from 39% (Moldova) to 59% (Armenia), and among women from 2% (Armenia) to 16% (Russia). There was a significantly lower smoking prevalence among men in 2010 compared with 2001 in Belarus, Kazakhstan, Kyrgyzstan, and Russia, but not for women in any country. For all countries combined, there was a significantly lower smoking prevalence in 2010 than in 2001 for men aged 18 to 39 years and men with a good or average economic situation. CONCLUSIONS: Smoking prevalence appears to have stabilized and may be declining in younger groups, but remains extremely high among men, especially those in lower socioeconomic groups


This study examines patterns of menthol and nonmenthol cigarette use from 2003 to 2005 in a cohort of smokers, aged 16 to 24 years in the National Youth Smoking Cessation Survey. At follow-up, 15.0% of baseline menthol smokers had switched to nonmentholated cigarettes; by contrast, 6.9% of baseline nonmenthol smokers had switched to mentholated cigarettes. Differences in switching patterns were evident by gender, race/ethnicity, parental education, and smoking frequency. These data support previous evidence that young smokers start with mentholated cigarettes and progress to nonmentholated cigarettes.
OBJECTIVES: We investigated the relationship between implementation of workplace smoking cessation support activities and employee smoking cessation. METHODS: In 2 cohort studies, participants were 6179 Finnish public-sector employees who self-reported as smokers at baseline in 2004 (study 1) or 2008 (study 2) and responded to follow-up surveys in 2008 (study 1; n=3298; response rate = 71%) or 2010 (study 2; n=2881; response rate=83%). Supervisors’ reports were used to assess workplace smoking cessation support activities. We conducted multilevel logistic regression analyses to examine changes in smoking status. RESULTS: After adjustment for sociodemographic characteristics, number of cigarettes smoked per day, work unit size, shift work, type of job contract, health status, and health behaviors, baseline smokers whose supervisors reported that the employing agency had offered pharmacological treatments or financial incentives were more likely than those in workplaces that did not offer such support to have quit smoking. In general, associations were stronger among moderate or heavy smokers (>= 10 cigarettes/day) than among light smokers (<10 cigarettes/day). CONCLUSIONS: Cessation activities offered by employers may encourage smokers, particularly moderate or heavy smokers, to quit smoking.


Although several studies have shown a lower risk of non-Hodgkin lymphoma (NHL) in alcohol drinkers compared with nondrinkers, the dose-response relation and potential differences between former and current drinking and across beverage types and subtypes are unclear. The authors examined associations of alcohol intake with risk of NHL in NHL subtypes in the Cancer Prevention Study II Nutrition Cohort, a prospective study of US men and women aged 50-74 years. Between 1992 and 2007, there were 1,991 incident NHL cases among 143,124 participants. Multivariable-adjusted relative risks and 95% confidence intervals were computed using Cox proportional hazards regression. Compared with nondrinkers, the relative risk of NHL associated with former drinking was 0.90 (95% confidence interval (CI): 0.75, 1.10); the relative risks associated with current intakes of <1, 1-2, and >2 drinks/day were 0.93 (95% CI: 0.83, 1.03), 0.91 (95% CI: 0.78, 1.06), and 0.78 (95% CI: 0.65, 0.93), respectively. Associations did not differ by sex (P-interaction = 0.45) or beverage type (P-difference = 0.22). Alcohol intake was more strongly associated with B-cell lymphoma (P-trend = 0.005) than with T-cell lymphoma (P-trend = 0.76), and associations were similar among B-cell lymphoma subtypes. In this prospective study, current heavy alcohol intake was associated with a reduced risk of NHL. Associations did not differ by beverage type and were slightly stronger for B-cell tumors than for T-cell tumors.


Pyloric stenosis occurs with a nearly 5-fold male predominance. To what extent this is due to environmental factors is unknown. In a cohort of all children born in Denmark, 1977-2008, the authors examined the association between pre- and perinatal exposures and pyloric stenosis and investigated whether these factors modified the male predominance. Information on pre- and perinatal factors and pyloric stenosis was obtained from national registers. Poisson regression models were used to estimate rate ratios. Among 1,925,313 children, 3,174 had surgery for pyloric stenosis. The authors found pyloric stenosis to be significantly associated with male sex,
age between 2 and 7 weeks, early study period, being first born, maternal smoking during pregnancy, preterm delivery, small weight for gestational age, cesarean section, and congenital malformations. Among cases, 2,595 were males and 579 were females. Lower male predominance was associated with age at diagnosis outside the peak ages, early study period, no maternal smoking during pregnancy, preterm delivery, and congenital malformations. The authors have previously found a strong familial aggregation of pyloric stenosis indicating a genetic influence. This study shows that environmental factors during and shortly after pregnancy also play a role and that several of these modify the strong male predominance.


BACKGROUND: Widening of socioeconomic status (SES) inequalities in smoking prevalence has occurred in several Western countries from the mid 1970's onwards. However, little is known about a widening of SES inequalities in smoking consumption, initiation and cessation.

METHODS: Repeated cross-sectional population surveys from 2001 to 2008 (n approximately 18,000 per year) were used to examine changes in smoking prevalence, smoking consumption (number of cigarettes per day), initiation ratios (ratio of ever smokers to all respondents), and quit ratios (ratio of former smokers to ever smokers) in the Netherlands. Education level and income level were used as indicators of SES and results were reported separately for men and women.

RESULTS: Lower educated respondents were significantly more likely to be smokers, smoked more cigarettes per day, had higher initiation ratios, and had lower quit ratios than higher educated respondents. Income inequalities were smaller than educational inequalities and were not all significant, but were in the same direction as educational inequalities. Among women, educational inequalities widened significantly between 2001 and 2008 for smoking prevalence, smoking initiation, and smoking cessation. Among low educated women, smoking prevalence remained stable between 2001 and 2008 because both the initiation and quit ratio increased significantly. Among moderate and high educated women, smoking prevalence decreased significantly because initiation ratios remained constant, while quit ratios increased significantly. Among men, educational inequalities widened significantly between 2001 and 2008 for smoking consumption only. CONCLUSIONS: While inequalities in smoking prevalence were stable among Dutch men, they increased among women, due to widening inequalities in both smoking cessation and initiation. Both components should be addressed in equity-oriented tobacco control policies.


Two previous studies suggest that cigarette smoking reduces acoustic neuroma risk; however, an association between use of snuff tobacco and acoustic neuroma has not been investigated previously. The authors conducted a case-control study in Sweden from 2002 to 2007, in which 451 cases and 710 population-based controls completed questionnaires. Cases and controls were matched on gender, region, and age within 5 years. The authors estimated odds ratios using conditional logistic regression analyses, adjusted for education and tobacco use (snuff use in the smoking analysis and smoking in the snuff analysis). The risk of acoustic neuroma was greatly reduced in male current smokers (odds ratio (OR) = 0.41, 95% confidence interval (CI): 0.23, 0.74) and moderately reduced in female current smokers (OR = 0.70, 95% CI: 0.40, 1.23). In contrast, current snuff use among males was not associated with risk of acoustic neuroma (OR = 0.94, 95% CI: 0.57, 1.55). The authors’ findings are consistent with previous reports of lower acoustic neuroma risk among current cigarette smokers than among never smokers. The absence
of an association between snuff use and acoustic neuroma suggests that some constituent of tobacco smoke other than nicotine may confer protection against acoustic neuroma.


OBJECTIVES: We investigated the associations between smoking and friend selection in the social networks of US adolescents. METHODS: We used a stochastic actor-based model to simultaneously test the effects of friendship networks on smoking and several ways that smoking can affect the friend selection process. Data are from 509 US high school students in the National Longitudinal Study of Adolescent Health, 1994-1996 (46.6% female, mean age at outset=15.4 years). RESULTS: Over time, adolescents' smoking became more similar to their friends. Smoking also affected who adolescents selected as friends; adolescents were more likely to select friends whose smoking level was similar to their own, and smoking enhanced popularity such that smokers were more likely to be named as friends than were nonsmokers, after controlling for other friend selection processes. CONCLUSIONS: Both friend selection and peer influence are associated with smoking frequency. Interventions to reduce adolescent smoking would benefit by focusing on selection and influence mechanisms.


The authors prospectively examined whether caffeine intake was associated with lower risk of Parkinson disease (PD) in both men and women among 304,980 participants in the National Institutes of Health-AARP Diet and Health Study and whether smoking affected this relation. Multivariate odds ratios and 95% confidence intervals were derived from logistic regression models. Higher caffeine intake as assessed in 1995-1996 was monotonically associated with lower PD risk (diagnosed in 2000-2006) in both men and women. After adjustment for age, race, and physical activity, the odds ratio comparing the highest quintile of caffeine intake with the lowest was 0.75 (95% confidence interval: 0.60, 0.94; P(trend) = 0.005) for men and 0.60 (95% confidence interval: 0.39, 0.91; P(trend) = 0.005) for women. Further adjustment for duration of smoking and analyses carried out among never smokers showed similar results. A joint analysis with smoking suggested that smoking and caffeine may act independently in relation to PD risk. Finally, the authors conducted a meta-analysis of prospective studies and confirmed that caffeine intake was inversely associated with PD risk in both men and women. These findings suggest no gender difference in the relation between caffeine and PD.


In this paper, we study the smoking behavior of students aged from 18 to 25 using four cross-section data sets collected in France from 1997 to 2006. We focus on the role played by student income and parental resources. We find that both the probability of smoking and the number of cigarettes smoked are positively correlated to family resources. Among students, only wages earned and transfers received from parents increase smoking participation. However, sensitivity to income remains weak since a rise of 1% in income of either the students or their parents leads to an increase in smoking prevalence of about 0.15-0.20%.

This study investigates two contagion mechanisms of peer influence based on direct communication (cohesion) versus comparison through peers who occupy similar network positions (structural equivalence) in the context of adolescents’ drinking alcohol and smoking. To date, the two contagion mechanisms have been considered observationally inseparable, but this study attempts to disentangle structural equivalence from cohesion as a contagion mechanism by examining the extent to which the transmission of drinking and smoking behaviors attenuates as a function of social distance (i.e., from immediate friends to indirectly connected peers). Using the U.S. Add Health data consisting of a nationally representative sample of American adolescents (Grades 7-12), this study measured peer risk-taking up to four steps away from the adolescent (friends of friends of friends of friends) using a network exposure model. Peer influence was tested using a logistic regression model of alcohol drinking and cigarette smoking. Results indicate that influence based on structural equivalence tended to be stronger than influence based on cohesion in general, and that the magnitude of the effect decreased up to three steps away from the adolescent (friends of friends of friends). Further analysis indicated that structural equivalence acted as a mechanism of contagion for drinking and cohesion acted as one for smoking. These results indicate that the two transmission mechanisms with differing network proximities can differentially affect drinking and smoking behaviors in American adolescents.


This article aims to help resolve the apparent paradox of producers of addictive goods who claim to be socially responsible while marketing a product clearly identified as harmful. It advances that reputation effects are crucial in this issue and that determining whether harm reduction practices are costly or profitable for the producers can help to assess the sincerity of their discourse. An analytical framework based on an epidemic model of addictive consumption that includes a deterrent effect of heavy use on initiation is developed. This framework enables us to establish a clear distinction between a simple responsible discourse and genuine harm reduction practices and, among harm reduction practices, between use reduction practices and micro harm reduction practices. Using simulations based on tobacco sales in France from 1950 to 2008, we explore the impact of three corresponding types of actions: communication on damage, restraining selling practices and development of safer products on total sales and on the social cost. We notably find that restraining selling practices toward light users, that is, preventing light users from escalating to heavy use, can be profitable for the producer, especially at early stages of the epidemic, but that such practices also contribute to increase the social cost. These results suggest that the existence of a deterrent effect of heavy use on the initiation of the consumption of an addictive good can shed new light on important issues, such as the motivations for corporate social responsibility and the definition of responsible actions in the particular case of harm reduction.


BACKGROUND: In Switzerland, health policies are decided at the local level, but little is known regarding their impact on the screening and management of cardiovascular risk factors (CVRFs). We thus aimed at assessing geographical levels of CVRFs in Switzerland. METHODS: Swiss

BACKGROUND: Behavioral risk factors are known to co-occur among youth, and to increase risks of chronic diseases morbidity and mortality later in life. However, little is known about determinants of multiple chronic disease behavioral risk factors, particularly among youth. Previous studies have been cross-sectional and carried out without a sound theoretical framework. METHODS: Using longitudinal data (n = 1135) from Cycle 4 (2000-2001), Cycle 5 (2002-2003) and Cycle 6 (2004-2005) of the National Longitudinal Survey of Children and Youth, a nationally representative sample of Canadian children who are followed biennially, the present study examines the influence of a set of conceptually-related individual/social distal variables (variables situated at an intermediate distance from behaviors), and individual/social ultimate variables (variables situated at an utmost distance from behaviors) on the rate of occurrence of multiple behavioral risk factors (physical inactivity, sedentary behavior, tobacco smoking, alcohol drinking, and high body mass index) in a sample of children aged 10-11 years at baseline.


Previous studies have associated youth's exposure to filmic images of smoking with real-life smoking acquisition; initial research in low- and middle-income countries confirms this relationship. The present study in Yunnan, southwest China sought answers to the following questions: How do young people in China make sense of smoking imagery they have seen in film? How are these perceptions shaped by the cultural and social context of images? How do these understandings relate to real-life tobacco use? A study with focus groups and grounded theory was conducted in 2010 and 2011 (Sept-Jan) with middle-school students ages 12 and 13 (n=68, focus groups=12, schools=6). Films and media literacy were important means through which knowledge about smoking was constructed and communicated. Film representations of smoking concurred with Chinese social behaviour (Confucian social networks, face-making, and the notion of society as a harmonious social unit), and were interpreted as congruent with real-life smoking. This pattern, in turn, was intertwined with perceived gender identities of smokers, gender-specific social behaviour, and willingness of girls to explore issues of gender equity. These findings lend new insights into interaction between smoking imagery in film and Chinese youth's smoking beliefs. Tobacco control programs in China should consider young people's interpretations of smoking and the ways they are nested in cultural and social milieu.
Multiple behavioral risk factors were assessed using a multiple risk factor score. All statistical analyses were performed using SAS, version 9.1, and SUDAAN, version 9.01. RESULTS: Multivariate longitudinal Poisson models showed that social distal variables including parental/peer smoking and peer drinking (Log-likelihood ratio (LLR) = 187.86, degrees of freedom (DF) = 8, p < .001), as well as individual distal variables including low self-esteem (LLR = 76.94, DF = 4, p < .001) increased the rate of occurrence of multiple behavioral risk factors. Individual ultimate variables including age, sex, and anxiety (LLR = 9.34, DF = 3, p < .05), as well as social ultimate variables including family socioeconomic status, and family structure (LLR = 10.93, DF = 5, p = .05) contributed minimally to the rate of co-occurrence of behavioral risk factors.

CONCLUSIONS: The results suggest targeting individual/social distal variables in prevention programs of multiple chronic disease behavioral risk factors among youth.


Using data from a study of high risk adolescents in Southern California, U.S.A. (N=851), this study examined synergy between social network measures of social integration and peer influence in relation to past month cigarette smoking. Using Hierarchical Linear Modeling, results indicated that being central in networks was significantly and positively related to past month cigarette smoking, across all study models. In addition, there is modest evidence that the number of reciprocated friendship ties was positively related to past month cigarette smoking. There is also some modest evidence that the relationship between having reciprocated friendships and past month cigarette smoking was moderated by a network peer influence process, smoking with those in youths' best friend networks. Findings indicate that being integrated within a social network context of peer influences favoring drug use relates to more smoking among these high risk youth.


BACKGROUND: Physical inactivity, unhealthy dietary habits, smoking and high alcohol consumption are recognized risk factors for cardiovascular disease and cancer. Web-based health risk assessments with tailored feedback seem promising in promoting a healthy lifestyle. This study evaluates the effectiveness of a web-based health risk assessment with individually-tailored feedback on lifestyle behaviour, conducted in a worksite setting. METHODS/DESIGN: The web-based health risk assessment starts with a questionnaire covering socio-demographic variables, family and personal medical history, lifestyle behaviour and psychological variables. Prognostic models are used to estimate individual cardiovascular risks. In case of high risk further biometric and laboratory evaluation is advised. All participants receive individually-tailored feedback on their responses to the health risk assessment questionnaire. The study uses a quasi-experimental design with a waiting list control group. Data are collected at baseline (T0) and after six months (T1). Within each company, clusters of employees are allocated to either the intervention or the control group. Primary outcome is lifestyle behaviour, expressed as the sum of five indicators namely physical activity, nutrition, smoking behaviour, alcohol consumption, and symptoms of burnout. Multilevel regression analysis will be used to answer the main research question and to correct for clustering effects. Baseline differences between the intervention and control group in the distribution of characteristics with a potential effect on lifestyle change will be taken into account in further analyses using propensity scores. DISCUSSION: This study will increase insight into the effectiveness of health risk assessments with tailored feedback and into conditions that may modify the effectiveness. This information can be used to design effective interventions for lifestyle behaviour change among employees. TRIAL REGISTRATION: Dutch Trial Register NTR8148

BACKGROUND: Public policy and clinical treatment in tobacco addiction in the UK has focused on cessation: an abrupt attempt to stop all cigarettes. However, recent evidence suggests that allowing more gradual withdrawal from tobacco or even permanent partial substitution by nicotine replacement therapy (NRT) could lead to net benefits to public health. No jurisdiction has introduced smoking reduction programmes in normal clinical care and the best methods for their implementation is uncertain. Community pharmacists offering smoking cessation services in the UK are ideally placed to implement reduction programmes. This pilot study aims therefore to examine the feasibility of implementing smoking reduction programme in pharmacies, and also to see if behavioural support and a longer treatment affect the success rate for cessation.

DESIGN AND METHODS: This is a 2 x 2 randomised factorial trial of behavioural support versus no support and short versus standard length reduction programme. The pharmacists will recruit 16 patients per pharmacy, 160 smokers altogether. Pharmacists will randomise each participant by sealed envelopes. In a standard supported programme, the pharmacist will give support for 34 weeks, inviting participants to set a treatment goal and providing advice on how to reduce cigarette use. Participants in the short programme will be given the same advice on how to reduce but will reduce smoking over four weeks. Participants in the no support arms will be given a leaflet that describes the reduction programmes in 4-week and 34-week format. All participants are encouraged to use of NRT to support the reduction. These processes will be measured by recording the number of recruited smokers; percentage of those who reduce and sustain their consumption to at least 50% of baseline value, and the proportion of people who attain 4 weeks abstinence and 6 months abstinence. Interviews will assess smokers' and pharmacists' views on the way the programme ran.

DISCUSSION: This is a pilot study to assess the feasibility of offering smoking reduction programme within pharmacies that offer naturalistic setting to show population benefit from these programmes. Findings from this trial will inform the development of evidence-based treatment for smokers who want to reduce and best approaches to engage reluctant quitters onto the programme.

TRIAL REGISTRATION: Current Controlled Trials ISRCTN 2010-019259-24


Since 1997, the Advisory Committee on Immunization Practices has recommended the 23-valent pneumococcal polysaccharide vaccine (PPSV23) for nonelderly adults with certain medical conditions. In 2008, the Committee added asthma and cigarette smoking to the list of indications for PPSV23 vaccination. Using data from the 2009 National Health Interview Survey, the authors assessed PPSV23 uptake in people with established and new indications. To identify factors independently associated with receiving PPSV23, they used multivariable logistic regression and predictive marginal analyses. In 2009, a total of 35.2 million adults 18-64 years of age (18.6%) had established PPSV23 indications; adding asthma and smoking to the list of indications increased the high-risk population to 71.6 million people (37.9%). Overall, 26.1% of people with established indications for PPSV23 and 17.4% of people with any indication (those previously established, as well as asthma and smoking) had received the vaccine; overall coverage among persons 50-64 years of age was significantly higher than that among persons 18-49 years of age (34.6% vs. 16.7%; P < 0.001) and for all specific indications except cancer. For persons who had asthma or who smoked but had no other indications, rates of coverage were 12.3% and 8.5%, respectively. In persons who had established indications, being older, white, and unemployed and having more physician visits, a prior hospitalization, a regular physician, and health insurance were independently associated with PPSV23 receipt. PPSV23 uptake varies substantially by age
and indication but remains low overall, with approximately 59 million unvaccinated high-risk working-age adults. Effective strategies to increase pneumococcal vaccination coverage among at-risk groups are needed.


Some researchers suggest that the effect of smoking on health depends on socioeconomic status; while others purport that the effect of smoking on health is similar across all social groups. This question of the interaction between smoking and socioeconomic status is important to an improved understanding of the role of smoking in the social gradient in mortality and morbidity. For this purpose, we examined whether educational level modifies the association between smoking and mortality. Information on smoking by age, gender and educational level was extracted from the Belgian Health Interview Surveys of 1997 and 2001. The mortality follow up of the survey respondents was reported until December 2010. A Poisson regression was used to estimate the hazard ratio of mortality for heavy smokers, light smokers, and former smokers compared with never smokers by educational level controlling for age and other confounders. Among men, we found lower hazard ratios in the lowest educational category compared with the intermediate and high-educated categories. For instance, for heavy smokers, the hazard ratios were 2.59 (1.18-5.70) for those with low levels of education, 4.03 (2.59-6.26) for those with intermediate levels of education and 3.78 (1.52-9.43) for the highly educated. However, the interaction between smoking and education was not statistically significant. For women, the hazard ratios were not significant for any educational category except for heavy smokers with intermediate levels of education. Also here the interaction was not statistically significant. Our results support the hypothesis that educational attainment does not substantially influence the association between smoking and mortality.


Despite reportedly having less tobacco exposure compared with whites, African Americans account for a disproportionate number of smoking-related deaths. The purpose of this study was to compare the prospective associations between smoking and cardiovascular risk in whites and African Americans. Smoking status was obtained on 14,200 participants from the Atherosclerosis Risk in Communities Study. Incidence of cardiovascular disease (CVD) was ascertained from 1987 through 2007. Adjusted Cox proportional hazard models were used to estimate the CVD incidence associated with smoking behavior. Over 17 years' follow-up, there were 2,777 cardiovascular events. In men, compared with never smoking, current smoking was independently associated with 67% (95% confidence interval (CI): 43, 95) and 72% (95% CI: 30, 126) greater risk of CVD in whites and African Americans, respectively. Early age at smoking initiation was independently associated with increased risk among all participants irrespective of race. Smoking cessation during follow-up was equally beneficial in both whites and African Americans. African Americans who smoke incur a similar level of cardiovascular risk as white smokers and would derive the same benefits from quitting as whites.

Graphic warning labels and plain cigarette packaging are two initiatives developed to increase quit behaviour among smokers. Although a little is known about how adolescents interpret graphic warning labels, very few studies have examined how plain cigarette packaging would affect adolescents' perceptions of cigarette smoking and smoking behaviour. We explored how teens interpret and respond to graphic warning labels and the plain packaging of cigarettes, to assess the potential these strategies may offer in deterring smoking initiation. Twelve focus group interviews with a sample of 80 14-16 year old students from a diverse range of schools in Auckland, New Zealand were undertaken between June and August 2009. Textual analysis revealed that graphic warning labels may influence adolescents by reiterating a negative image of smokers. Graphic warning on a plain cigarette pack increased the attention paid to graphic warning labels and the overall perceptions of harm caused by cigarette smoking, and reduced the social appeal of cigarette smoking. This research offers evidence on how adolescents are appraising and interpreting graphic warning labels, and explores how dominant appraisals may affect the role graphic warning labels play in preventing smoking. Not only would plain cigarette packaging enhance the salience and impact of graphic warning labels, but it would potentially bolster the overall message that cigarette smoking is harmful. In the context of a comprehensive tobacco control programme, graphic warning labels on plain cigarette packaging present an explicit message about the risks (to health and image) associated with cigarette smoking.


This paper aims to examine the relationship between parental socio-economic status (SES) and adolescent substance use. The central question posed in the title is approached in two stages. First, theoretical and empirical research in this area is reviewed. Second, data from an ongoing longitudinal study of young people in England (the Peterborough Adolescent and Young Adult Development Study—PADS+) are used to highlight the nature of this relationship in one city. Results from discrete-time event history analyses show that when examining what predicts initiation of substance use, familial and demographic factors emerge as important predictors, but SES does not appear to be relevant. The concluding discussion focuses on whether support is found for hypotheses derived from the existing literature and implications for future research.


Previous studies have not shown a survival advantage for smoking reduction. The authors assessed survival and life expectancy according to changes in smoking intensity in a cohort of Israeli working men. Baseline smokers recruited in 1963 were reassessed in 1965 (n = 4,633; mean age, 51 years) and followed up prospectively for mortality through 2005. Smoking intensity at both time points was self-reported and categorized as none, 1-10, 11-20, and >/=21 cigarettes per day. Change between smoking categories was noted, and participants were classified as increased (8%), maintained (65%), reduced (17%), or quit (10%) smoking. During a median follow-up of 26 (quartiles 1-3: 16-35) years, 87% of participants died. Changes in intensity were associated with survival. In multivariable-adjusted models, the hazard ratios for mortality were 1.14 (95% confidence interval (CI): 0.99, 1.32) among increasers, 0.85 (95% CI: 0.77, 0.95) among reducers, and 0.78 (95% CI: 0.69, 0.89) among quitters, compared with maintainers. Inversely, the adjusted odds ratios of surviving to age 80 years were 0.77 (95% CI: 0.60, 0.98), 1.22 (95% CI: 1.01, 1.47), and 1.33 (95% CI: 1.07, 1.66), respectively. The survival benefit associated with smoking reduction was mostly evident among heavy smokers and for...
cardiovascular disease mortality. These results suggest that decreasing smoking intensity should be considered as a risk-reduction strategy for heavy smokers who cannot quit abruptly


Genome-wide association studies have identified variants on chromosome 15q25.1 that increase the risks of both lung cancer and nicotine dependence and associated smoking behavior. However, there remains debate as to whether the association with lung cancer is direct or is mediated by pathways related to smoking behavior. Here, the authors apply a novel method for mediation analysis, allowing for gene-environment interaction, to a lung cancer case-control study (1992-2004) conducted at Massachusetts General Hospital using 2 single nucleotide polymorphisms, rs8034191 and rs1051730, on 15q25.1. The results are validated using data from 3 other lung cancer studies. Tests for additive interaction (P = 2 x 10(-10) and P = 1 x 10(-9)) and multiplicative interaction (P = 0.01 and P = 0.01) were significant. Pooled analyses yielded a direct-effect odds ratio of 1.26 (95% confidence interval (CI): 1.19, 1.33; P = 2 x 10(-15)) for rs8034191 and an indirect-effect odds ratio of 1.01 (95% CI: 1.00, 1.01; P = 0.09); the proportion of increased risk mediated by smoking was 3.2%. For rs1051730, direct- and indirect-effect odds ratios were 1.26 (95% CI: 1.19, 1.33; P = 1 x 10(-15)) and 1.00 (95% CI: 0.99, 1.01; P = 0.22), respectively, with a proportion mediated of 2.3%. Adjustment for measurement error in smoking behavior allowing up to 75% measurement error increased the proportions mediated to 12.5% and 9.2%, respectively. These analyses indicate that the association of the variants with lung cancer operates primarily through other pathways


BACKGROUND: Variation in the complement factor H gene (CFH) is associated with risk of late age-related macular degeneration (AMD). Previous studies have been case-control studies in populations of European ancestry with little differentiation in AMD subtype, and insufficient power to confirm or refute effect modification by smoking. METHODS: To precisely quantify the association of the single nucleotide polymorphism (SNP rs1061170, *Y402H*) with risk of AMD among studies with differing study designs, participant ancestry and AMD grade and to investigate effect modification by smoking, we report two unpublished genetic association studies (n = 2759) combined with data from 24 published studies (26 studies, 26,494 individuals, including 14,174 cases of AMD) of European ancestry, 10 of which provided individual-level data used to test gene-smoking interaction; and 16 published studies from non-Europeans ancestry. RESULTS: In individuals of European ancestry, there was a significant association between Y402H and late-AMD with a per-allele odds ratio (OR) of 2.27 [95% confidence interval (CI) 2.10-2.45; P = 1.1 x 10(-161)]. There was no evidence of effect modification by smoking (P = 0.75). The frequency of Y402H varied by ancestral origin and the association with AMD in non-Europeans was less clear, limited by paucity of studies. CONCLUSION: The Y402H variant confers a 2-fold higher risk of late-AMD per copy in individuals of European descent. This was stable to stratification by study design and AMD classification and not modified by smoking. The lack of association in non-Europeans requires further verification. These findings are of direct relevance for disease prediction. New research is needed to ascertain if differences in circulating levels, expression or activity of factor H protein explain the genetic association

OBJECTIVES: We examined temporal and regional trends in the prevalence of health lifestyles in the United States. METHODS: We used 1994 to 2007 data from the Behavioral Risk Factor Surveillance System to assess 4 healthy lifestyle characteristics: having a healthy weight, not smoking, consuming fruits and vegetables, and engaging in physical activity. The concurrent presence of all 4 characteristics was defined as a healthy overall lifestyle. We used logistic regression to assess temporal and regional trends. RESULTS: The percentages of individuals who did not smoke (4% increase) and had a healthy weight (10% decrease) showed the strongest temporal changes from 1994 to 2007. There was little change in fruit and vegetable consumption or physical activity. The prevalence of healthy lifestyles increased minimally over time and varied modestly across regions; in 2007, percentages were higher in the Northeast (6%) and West (6%) than in the South (4%) and Midwest (4%). CONCLUSIONS: Because of the large increases in overweight and the declines in smoking, there was little net change in the prevalence of healthy lifestyles. Despite regional differences, the prevalence of healthy lifestyles across the United States remains very low


OBJECTIVES: We examined interrelationships among the 3 dimensions of sexual orientation-self-identity, sexual attraction, and sexual experience-and their associations with substance use among adolescents and young adults. METHODS: To estimate total and net associations of sexual identity, attraction, and experience with use of tobacco, drugs, and alcohol, we applied logistic regression to cross-sectional data from the National Survey of Family Growth Cycle 6. RESULTS: We found a lack of concordance among the different dimensions of sexual orientation. More youths reported same-gender sexual attraction and same-gender sexual experiences than identified as lesbian, gay, or bisexual. Estimates of substance use prevalence differed significantly by gender and across dimensions of sexual orientation. Sexual experience was the most consistent predictor of substance use. Women and men with no sexual experience had the lowest odds of all forms of substance use; those reporting sexual experience with partners of both genders had the highest odds. CONCLUSIONS: Our findings indicate that sexual identity was less strongly associated with substance use than sexual experience and attraction were, pointing to the need for more nuanced indicators of sexual orientation in public health studies


OBJECTIVES: We examined associations among 3 dimensions of sexual orientation (identity, behavior, and attraction) and key health-related indicators commonly studied among sexual minority populations: depressive symptoms, perceived stress, smoking, binge drinking, and victimization. METHODS: We analyzed data from the National Longitudinal Study of Adolescent Health, Wave IV (2007-2008) when respondents were aged 24 to 32 years (n=14,412). We used multivariate linear and logistic regressions to examine consistency of associations between sexual orientation measures and health-related indicators. RESULTS: Strength of associations differed by gender and sexual orientation measure. Among women, being attracted to both sexes, identifying as "mostly straight" or "bisexual," and having mostly opposite-sex sexual partners was associated with greater risk for all indicators. Among men, sexual attraction was unrelated to health indicators. Men who were "mostly straight" were at greater risk for some, but not all, indicators. Men who had sexual partners of the same-sex or both sexes were at lower risk for binge drinking. CONCLUSIONS: Using all 3 dimensions of sexual orientation provides a more
complete picture of the association between sexual orientation and health among young adults than does using any 1 dimension alone


BACKGROUND: Estimates of global DNA methylation from repetitive DNA elements, such as Alu and LINE-1, have been increasingly used in epidemiological investigations because of their relative low-cost, high-throughput and quantitative results. Nevertheless, determinants of these methylation measures in healthy individuals are still largely unknown. The aim of this study was to examine whether age, gender, smoking habits, alcohol drinking and body mass index (BMI) are associated with Alu or LINE-1 methylation levels in blood leucocyte DNA of healthy individuals.

METHODS: Individual data from five studies including a total of 1465 healthy subjects were combined. DNA methylation was quantified by PCR-pyrosequencing. RESULTS: Age (β = -0.011% of 5-methyl-cytosine (%5 mC)/year, 95% confidence interval (CI) -0.020 to -0.001%5 mC/year) and alcohol drinking (β = -0.214, 95% CI -0.415 to -0.013) were inversely associated with Alu methylation. Compared with females, males had lower Alu methylation (β = -0.385, 95% CI -0.665 to -0.104) and higher LINE-1 methylation (β = 0.796, 95% CI 0.261 to 1.330). No associations were found with smoking or BMI. Percent neutrophils and lymphocytes in blood counts exhibited a positive (β = 0.036, 95% CI 0.010 to 0.061) and negative (β = -0.038, 95% CI -0.065 to -0.012) association with LINE-1 methylation, respectively. CONCLUSIONS: Global methylation measures in blood DNA vary in relation with certain host and lifestyle characteristics, including age, gender, alcohol drinking and white blood cell counts. These findings need to be considered in designing epidemiological investigations aimed at identifying associations between DNA methylation and health outcomes.


BACKGROUND: An interaction between genetic susceptibility and environmental factors is thought to be involved in the aetiology of type 1 diabetes. The aim of this study was to investigate maternal and neonatal risk factors for type 1 diabetes in children under 15 years old in Grampian, Scotland. METHODS: A matched case-control study was conducted by record linkage. Cases (n = 361) were children born in Aberdeen Maternity Hospital from 1972 to 2002, inclusive, who developed type 1 diabetes, identified from the Scottish Study Group for the Care of Diabetes in the Young Register. Controls (n = 1083) were randomly selected from the Aberdeen Maternity Neonatal Databank, matched by year of birth. Exposure data were obtained from the Aberdeen Maternity Neonatal Databank. Conditional logistic regression was used to evaluate the association between various maternal and neonatal factors and the risk of type 1 diabetes. RESULTS: There was no evidence of statistically significant associations between type 1 diabetes and maternal age, maternal body mass index, previous abortions, pre-eclampsia, amniocentesis, maternal deprivation, use of syntocinon, mode of delivery, antepartum haemorrhage, baby's sex, gestational age at birth, birth order, birth weight, jaundice, phototherapy, breast feeding, admission to neonatal unit and Apgar score (P > 0.05). A significantly decreased risk of type 1 diabetes was observed in children whose mothers smoked at the booking appointment compared to those whose mothers did not, with an adjusted OR of 0.67, 95% CI (0.46, 0.99). CONCLUSIONS: This case-control study found limited evidence of a reduced risk of the development of type 1 diabetes in children whose mothers smoked, compared to children whose mothers did not. No evidence was found of a significant association between other maternal and neonatal factors and childhood type 1 diabetes.

BACKGROUND: Radon is the second risk factor for lung cancer after tobacco consumption and therefore it is necessary to know the burden of disease due to its exposure. The objective of this study is to estimate radon-attributable lung cancer mortality in Galicia, a high emission area located at the Northwest Spain. METHODS: A prevalence-based attribution method was applied. Prevalence of tobacco use and radon exposure were obtained from a previously published study of the same area. Attributable mortality was calculated for each of six possible risk categories, based on radon exposure and smoking status. Two scenarios were used, with 37 Bq/m3 and 148 Bq/m3 as the respective radon exposure thresholds. As the observed mortality we used lung cancer mortality for 2001 from the Galician mortality registry. RESULTS: Mortality exclusively attributable to radon exposure ranged from 3% to 5% for both exposure thresholds, respectively. Attributable mortality to combined exposure to radon and smoking stood at around 22% for exposures above 148 Bq/m3. Applying the United States Environmental Protection Agency (EPA) action level, radon has a role in 25% of all lung cancers. CONCLUSIONS: Although the estimates have been derived from a study with a relatively limited sample size, these results highlight the importance of radon exposure as a cause of lung cancer and its effect in terms of disease burden. Radon mitigation activities in the study area must therefore be enforced.

(42) KOH HK, SEBELIUS KG. Ending the tobacco epidemic. JAMA. 2012 Aug. 22, vol. 308, n° 8, pp.767-768


BACKGROUND: Cessation of smoking reduces morbidity and mortality related to tobacco smoking. It is essential to explore the intention of individuals to quit smoking to design effective interventions. The objective of this study was to assess cigarette smokers' intention to quit smoking in Dire Dawa town using the Transtheoretical model. METHODS: From February 15 to 19, 2009, we conducted a community based cross-sectional study among 384 current cigarette smokers in Dire Dawa town east Ethiopia. Data was collected by trained personnel using a pretested structured questionnaire. The data was analyzed using SPSS version 16.0. RESULTS: Two hundred and nineteen (57%) smokers in the study area had the intention to quit cigarette smoking within the next six months and all the process of change had an increasing trend across the stages. Based on the Fragestrom test of nicotine dependence of cigarette, 35 (9.1%), 69 (18%) and 48(12.5%) were very high, high and medium dependent on nicotine respectively. For the majority 247(64.3%) of the respondents, the mean score of cons of smoking outweighs the pros score (negative decisional balance). Only 66(17.2%) had high self efficacy not to smoke in places and situations that can aggravate smoking. CONCLUSIONS: Majority of the smokers had the intention to quit smoking. All the process of change had an increasing trend across the stages. Those who had no intention to quit smoking had high level of dependence on nicotine and low self efficacy. The pros of smoking were decreasing while the cons were increasing across the stages. Stage based interventions should be done to move the smokers from their current stage to an advanced stages of quitting cigarette smoking.
In estimates of illness severity from the spring wave of the 2009 influenza A (H1N1) pandemic, reported case fatality proportions were less than 0.05%. In prior pandemics, subsequent waves of illness were associated with higher mortality. The authors evaluated the burden of the pandemic H1N1 (pH1N1) outbreak in metropolitan Atlanta, Georgia, in the fall of 2009, when increased influenza activity heralded the second wave of the pandemic in the United States. Using data from a community survey, existing surveillance systems, public health laboratories, and local hospitals, they estimated numbers of pH1N1-associated illnesses, emergency department (ED) visits, hospitalizations, intensive care unit (ICU) admissions, and deaths occurring in metropolitan Atlanta during the period August 16, 2009-September 26, 2009. The authors estimated 132,140 pediatric and 132,110 adult symptomatic cases of pH1N1 in metropolitan Atlanta during the investigation time frame. Among children, these cases were associated with 4,560 ED visits, 190 hospitalizations, 51 ICU admissions, and 4 deaths. Among adults, they were associated with 1,130 ED visits, 590 hospitalizations, 140 ICU admissions, and 63 deaths. The combined symptomatic case hospitalization proportion, case ICU admission proportion, and case fatality proportion were 0.281%, 0.069%, and 0.024%, respectively. Influenza burden can be estimated using existing data and local surveys. The increased severity reported for subsequent waves in past pandemics was not evident in this investigation. Nevertheless, the second pH1N1 pandemic wave led to substantial numbers of ED visits, hospitalizations, and deaths in metropolitan Atlanta.

References:

The rapid spread of the new influenza virus A(H1N1)v in young age groups in 2009 has been partly attributed to a high transmission intensity in schools. However, detailed characterization of the spread of influenza in school populations has been difficult to obtain, simply because it is very hard to identify who infected whom in a large outbreak. Data collected in large outbreak investigations typically miss many transmission events, and some reported transmission events will be incorrect. Here the authors present robust likelihood-based methods that can be used to analyze outbreak data while explicitly accounting for both missing data and erroneous data. They apply this method to a school-based outbreak of pandemic influenza A(H1N1)v that occurred in London, United Kingdom, in April 2009. The authors show that the generation interval in this school-based population was 2.20 days and that the reproduction number declined coincident with school closure, from 1.33 secondary cases per primary case to 0.43 secondary cases per primary case. These results provide quantitative evidence for the change in influenza transmission that is to be expected from school closure.
CONTEXT: In fall 2009 in Quebec, Canada, an immunization campaign was launched against the 2009 influenza A(H1N1) pandemic strain, mostly using an AS03 adjuvant vaccine. By the end of the year, 57% of the 7.8 million residents had been vaccinated. OBJECTIVE: To assess the risk of Guillain-Barre syndrome (GBS) following pandemic influenza vaccine administration. DESIGN: Population-based cohort study with follow-up over the 6-month period October 2009 through March 2010. The investigation was ordered by the chief medical officer of health in accordance with the Quebec Public Health Act. SETTING: All acute care hospitals and neurology clinics in Quebec. POPULATION: Suspected and confirmed GBS cases reported by physicians, mostly neurologists, during active surveillance or identified in the provincial hospital summary discharge database. Medical records were reviewed and cases classified according to Brighton Collaboration definitions (categorized as level 1, 2, or 3, corresponding to criteria of decreasing certainty in diagnosis). Immunization status was verified and denominators were estimated from the provincial immunization registry (4.4 million vaccinated) and census data (total target population aged >/=6 months, 7.8 million), with a total of 3,623,046 person-years of observation. MAIN OUTCOME MEASURES: Relative and attributable risks were calculated using a Poisson model and the self-controlled case-series method. RESULTS: Over a 6-month period, 83 confirmed GBS cases were identified, including 71 Brighton level 1 through 3 cases. Twenty-five confirmed cases had been vaccinated against 2009 influenza A(H1N1) 8 or fewer weeks before disease onset, with most (19/25) vaccinated 4 or fewer weeks before onset. In the Poisson model, the age- and sex-adjusted relative risk was 1.80 (95% CI, 1.12-2.87) for all confirmed cases during the 8-week postvaccination period and was 2.75 (95% CI, 1.63-4.62) during the 4-week postvaccination period. Using the self-controlled case-series method, relative risk estimates during the 4-week postvaccination period were 3.02 (95% CI, 1.64-5.56) for all confirmed cases (n = 42) and 2.33 (95% CI, 1.19-4.57) for Brighton level 1 through 3 cases (n = 36). The number of GBS cases attributable to vaccination was approximately 2 per 1 million doses. There was no indication of an excess risk in persons younger than 50 years. CONCLUSIONS: In Quebec, the 2009 influenza A(H1N1) vaccine was associated with a small but significant risk of GBS. It is likely that the benefits of immunization outweigh the risks.

CONTEXT: Assessment of the fetal safety of vaccination against influenza A(H1N1)pdm09 in pregnancy has been limited. OBJECTIVE: To investigate whether exposure to an adjuvanted influenza A(H1N1)pdm09 vaccine during pregnancy was associated with increased risk of adverse fetal outcomes. DESIGN, SETTING, AND PARTICIPANTS: Registry-based cohort study based on all liveborn singleton infants in Denmark, delivered between November 2, 2009, and September 30, 2010. In propensity score-matched analyses, we estimated prevalence odds ratios (PORs) of adverse fetal outcomes, comparing infants exposed and unexposed to an AS03-adjuvanted influenza A(H1N1)pdm09 vaccine during pregnancy. MAIN OUTCOME MEASURES: Major birth defects, preterm birth, and small size for gestational age. RESULTS: From a cohort of 53,432 infants (6989 [13.1%] exposed to the influenza A[H1N1]pdm09 vaccine during pregnancy [345 in the first trimester and 6644 in the second or third trimester]), 660 (330 exposed) were included in propensity score-matched analyses of adverse fetal outcomes associated with first-
trimester exposure. For analysis of small size for gestational age after second- or third-trimester exposure, 13,284 (6642 exposed) were included; for analyses of preterm birth, 12,909 (6543 exposed) were included. A major birth defect was diagnosed in 18 of 330 infants (5.5%) exposed to the vaccine in the first trimester, compared with 15 of 330 unexposed infants (4.5%) (POR, 1.21; 95% CI, 0.60-2.45). Preterm birth occurred in 31 of 330 infants (9.4%) exposed in the first trimester, compared with 24 of 330 unexposed infants (7.3%) (POR, 1.32; 95% CI, 0.76-2.31), and in 302 of 6543 infants (4.6%) with second- or third-trimester exposure, compared with 295 of 6366 unexposed infants (4.6%) (POR, 1.00; 95% CI, 0.84-1.17). Small size for gestational age was observed in 25 of 330 infants (7.6%) with first-trimester exposure compared with 31 of 330 unexposed infants (9.4%) (POR, 0.79; 95% CI, 0.46-1.37), and in 641 of 6642 infants (9.7%) with second- or third-trimester exposure, compared with 657 of 6642 unexposed infants (9.9%) (POR, 0.97; 95% CI, 0.87-1.09). CONCLUSIONS: In this Danish cohort, exposure to an adjuvanted influenza A(H1N1)pdm09 vaccine during pregnancy was not associated with a significantly increased risk of major birth defects, preterm birth, or fetal growth restriction


Influenza A virus (IAV) infection leads to variable and imperfectly understood pathogenicity. We report that segment 3 of the virus contains a second open reading frame ("X-ORF"), accessed via ribosomal frameshifting. The frameshift product, termed PA-X, comprises the endonuclease domain of the viral PA protein with a C-terminal domain encoded by the X-ORF and functions to repress cellular gene expression. PA-X also modulates IAV virulence in a mouse infection model, acting to decrease pathogenicity. Loss of PA-X expression leads to changes in the kinetics of the global host response, which notably includes increases in inflammatory, apoptotic, and T lymphocyte-signaling pathways. Thus, we have identified a previously unknown IAV protein that modulates the host response to infection, a finding with important implications for understanding IAV pathogenesis


Highly pathogenic avian H5N1 influenza A viruses occasionally infect humans, but currently do not transmit efficiently among humans. The viral haemagglutinin (HA) protein is a known host-range determinant as it mediates virus binding to host-specific cellular receptors. Here we assess the molecular changes in HA that would allow a virus possessing subtype H5 HA to be transmissible among mammals. We identified a reassortant H5 HA/H1N1 virus-comprising H5 HA (from an H5N1 virus) with four mutations and the remaining seven gene segments from a 2009 pandemic H1N1 virus-that was capable of droplet transmission in a ferret model. The transmissible H5 reassortant virus preferentially recognized human-type receptors, replicated efficiently in ferrets, caused lung lesions and weight loss, but was not highly pathogenic and did not cause mortality. These results indicate that H5 HA can convert to an HA that supports efficient viral transmission in mammals; however, we do not know whether the four mutations in the H5 HA identified here would render a wholly avian H5N1 virus transmissible. The genetic origin of the remaining seven viral gene segments may also critically contribute to transmissibility in mammals. Nevertheless, as H5N1 viruses continue to evolve and infect humans, receptor-binding variants of H5N1 viruses with pandemic potential, including avian-human reassortant viruses as tested here, may emerge. Our findings emphasize the need to prepare for potential pandemics caused by influenza viruses possessing H5 HA, and will help individuals conducting surveillance in regions with circulating H5N1 viruses to recognize key residues that predict the pandemic potential of
isolates, which will inform the development, production and distribution of effective countermeasures


Objectives. We estimated and compared total costs and costs per dose administered for 2 influenza A 2009 monovalent vaccine campaigns in New York City: an elementary school-located campaign targeting enrolled children aged 4 years and older, and a community-based points-of-dispensing campaign for anyone aged 4 years and older. Methods. We determined costs from invoices or we estimated costs. We obtained vaccination data from the Citywide Immunization Registry and reports from the community points of dispensing. Results. The school campaign delivered approximately 202,089 vaccines for $17.9 million and $88 per dose. The community campaign could have delivered 49,986 vaccines for $7.6 million and $151 per dose. Conclusions. The school campaign delivered vaccines at a lower cost per dose than did the community campaign. Had demand been higher, both campaigns may have delivered vaccine at lower, more comparable cost per dose.


An increased risk of Guillain-Barre syndrome (GBS) following administration of the 1976 swine influenza vaccine led to a heightened focus on GBS when monovalent vaccines against a novel influenza A (H1N1) virus of swine origin were introduced in 2009. GBS cases following receipt of monovalent inactivated (MIV) and seasonal trivalent inactivated (TIV) influenza vaccines in the Vaccine Safety Datalink Project in 2009-2010 were identified in electronic data and confirmed by medical record review. Within 1-42 days following vaccination, 9 cases were confirmed in MIV recipients (1.48 million doses), and 8 cases were confirmed in TIV-only recipients who did not also receive MIV during 2009-2010 (1.72 million doses). Five cases following MIV and 1 case following TIV-only had an antecedent respiratory infection, a known GBS risk factor; furthermore, unlike TIV, MIV administration was concurrent with heightened influenza activity. In a self-controlled risk interval analysis comparing GBS onset within 1-42 days following MIV with GBS onset 43-127 days following TIV, the risk difference was 5.0 cases per million doses (95% confidence interval: 0.5, 9.5). No statistically significant increased GBS risk was found within 1-42 days following TIV-only vaccination versus 43-84 days following vaccination (risk difference = 1.1 cases per million doses, 95% confidence interval: -3.1, 5.4). Further evaluation to assess GBS risk following both vaccination and respiratory infection is warranted.

Because of widespread distribution of the influenza A (H1N1) 2009 monovalent vaccine (pH1N1 vaccine) and the prior association between Guillain-Barre syndrome (GBS) and the 1976 H1N1 influenza vaccine, enhanced surveillance was implemented to estimate the magnitude of any increased GBS risk following administration of pH1N1 vaccine. The authors conducted active, population-based surveillance for incident cases of GBS among 45 million persons residing at 10 Emerging Infections Program sites during October 2009-May 2010; GBS was defined according to published criteria. The authors determined medical and vaccine history for GBS cases through medical record review and patient interviews. The authors used vaccine coverage data to estimate person-time exposed and unexposed to pH1N1 vaccine and calculated age- and sex-adjusted rate ratios comparing GBS incidence in these groups, as well as age- and sex-adjusted numbers of excess GBS cases. The authors received 411 reports of confirmed or probable GBS. The rate of GBS immediately following pH1N1 vaccination was 57% higher than in person-time unexposed to vaccine (adjusted rate ratio = 1.57, 95% confidence interval: 1.02, 2.21), corresponding to 0.74 excess GBS cases per million pH1N1 vaccine doses (95% confidence interval: 0.04, 1.56). This excess risk was much smaller than that observed during the 1976 vaccine campaign and was comparable to some previous seasonal influenza vaccine risk assessments.

(14) NELSON KE. Invited commentary: Influenza vaccine and Guillain-Barre syndrome--is there a risk? Am J Epidemiol. 2012 June 1, vol. 175, n° 11, pp.1129-1132

After a new reassortant swine influenza A H1N1 virus caused outbreaks in Mexico and the United States in 2009, a vaccine was prepared from this virus to immunize the entire US population. Surveillance for Guillain-Barre syndrome (GBS) after receipt of this vaccine was carried out in 3 populations: the Vaccine Safety Datalink Project, the 10 Centers for Disease Control and Prevention Emerging Infections Program sites, and a network of large insurance companies. These studies found a small increase of approximately 1 case of GBS per million vaccinees above the baseline rate, which is similar to that observed after administration of seasonal influenza vaccines over the past several years. Enhanced surveillance for GBS was conducted in 2009-2010 because of the experience in 1976 of 362 GBS cases occurring during the 6 weeks after influenza vaccination of 45 million persons, an 8.8-fold increase over background rates. The 1976 mass immunization had been conducted to prevent an influenza epidemic from another swine influenza A H1N1 recombinant virus. It can be concluded from these recent studies that influenza vaccination overall is of public health benefit, helping to reduce mortality and prevent the thousands of deaths that occur from annual seasonal influenza outbreaks, despite the possibility of a small increased risk of GBS associated with influenza vaccines.


The Post-Licensure Rapid Immunization Safety Monitoring (PRISM) system is a cohort-based active surveillance network initiated by the US Department of Health and Human Services to supplement preexisting and other vaccine safety monitoring systems in tracking the safety of monovalent pandemic 2009 H1N1 influenza vaccine in the United States during 2009-2010. PRISM investigators conducted retrospective analysis to determine whether 2009 H1N1 vaccination was associated with increased risk of any of 14 prespecified outcomes. Five health insurance and associated companies with 38 million members and 9 state/city immunization registries contributed records on more than 2.6 million doses of 2009 H1N1 vaccine. Data on outcomes came from insurance claims. Complementary designs (self-controlled risk interval, case-centered, and current-vs.-historical comparison) were used to optimize control for confounding and statistical power. The self-controlled risk interval analysis of chart-confirmed
Guillain-Barre syndrome found an elevated but not statistically significant incidence rate ratio following receipt of inactivated 2009 H1N1 vaccine (incidence rate ratio = 2.50, 95% confidence interval: 0.42, 15.0) and no cases following live attenuated 2009 H1N1 vaccine. The study did not control for infection prior to Guillain-Barre syndrome, which may have been a confounder. The risks of other health outcomes of interest were generally not significantly elevated after 2009 H1N1 vaccination.


OBJECTIVES: We evaluated the relationship between maternal H1N1 vaccination and fetal and neonatal outcomes among singleton births during the 2009-2010 H1N1 pandemic. METHODS: We used a population-based perinatal database in Ontario, Canada, to examine preterm birth (PTB), small-for-gestational-age (SGA) births, 5-minute Apgar score below 7, and fetal death via multivariable regression. We compared outcomes between women who did and did not receive an H1N1 vaccination during pregnancy. RESULTS: Of the 55,570 mothers with a singleton birth, 23,340 (42.0%) received an H1N1 vaccination during pregnancy. Vaccinated mothers were less likely to have an SGA infant based on the 10th (adjusted risk ratio [RR]=0.90; 95% confidence interval [CI]=0.85, 0.96) and 3rd (adjusted RR=0.81; 95% CI=0.72, 0.92) growth percentiles; PTB at less than 32 weeks' gestation (adjusted RR=0.73; 95% CI=0.58, 0.91) and fetal death (adjusted RR=0.66; 95% CI=0.47, 0.91) were also less likely among these women. CONCLUSIONS: Our results suggest that second- or third-trimester H1N1 vaccination was associated with improved fetal and neonatal outcomes during the recent pandemic. Our findings need to be confirmed in future studies with designs that can better overcome concerns regarding biased estimates of vaccine efficacy.


BACKGROUND: Surveillance of severe acute respiratory infections (SARI) in sentinel hospitals is recommended to estimate the burden of severe influenza-cases. Therefore, we monitored patients admitted with respiratory infections (RI) in 9 Berlin hospitals from 7.12.2009 to 12.12.2010 according to different case definitions (CD) and determined the proportion of cases with influenza A(H1N1)pdm09 (pH1N1). We compared the sensitivity and specificity of CD for capturing pandemic pH1N1 cases. METHODS: We established an RI-surveillance restricted to adults aged <=65 years within the framework of a pH1N1 vaccine effectiveness study, which required active identification of RI-cases. The hospital information-system was screened daily for newly admitted RI-patients. Nasopharyngeal swabs from consenting patients were tested by PCR for influenza-virus subtypes. Four clinical CD were compared in terms of capturing pH1N1-positives among hospitalized RI-patients by applying sensitivity and specificity analyses. The broadest case definition (CD1) was used for inclusion of RI-cases; the narrowest case definition (CD4) was identical to the SARI case definition recommended by ECDC/WHO. RESULTS: Over the study period, we identified 1,025 RI-cases, of which 283 (28%) met the ECDC/WHO SARI case definition. The percentage of SARI-cases among internal medicine admissions decreased from 3.2% (calendar-week 50-2009) to 0.2% (week 25-2010). Of 354 patients tested by PCR, 20 (6%) were pH1N1-positive. Two case definitions narrower than CD1 but -in contrast to

Prospective community-based studies have provided fundamental insights into the epidemiology of influenza in temperate regions, but few comparable studies have been undertaken in the tropics. The authors conducted prospective influenza surveillance and intermittent seroprevalence surveys in a household-based cohort in Vietnam between December 2007 and April 2010, resulting in 1,793 person-seasons of influenza surveillance. Age- and sex-standardized estimates of the risk of acquiring any influenza infection per season in persons 5 years of age or older were 21.1% (95% confidence interval: 17.4, 24.7) in season 1, 26.4% (95% confidence interval: 22.6, 30.2) in season 2, and 17.0% (95% confidence interval: 13.6, 20.4) in season 3. Some individuals experienced multiple episodes of infection with different influenza types/subtypes in the same season (n = 27) or reinfection with the same subtype in different seasons (n = 22). The highest risk of influenza infection was in persons 5-9 years old, in whom the risk of influenza infection per season was 41.8%. Although the highest infection risk was in school-aged children, there were important heterogeneities in the age of infection by subtype and season. These heterogeneities could influence the impact of school closure and childhood vaccination on influenza transmission in tropical areas, such as Vietnam


BACKGROUND: In Quebec, the influenza A (H1N1) pandemic was managed using a top-down style that left many involved players with critical views and frustrations. We aimed to describe physicians’ perceptions--infectious diseases specialists/medical microbiologists (IDMM) and public health/preventive medicine specialists (PHPMS)--in regards to issues encountered with the pandemics management at the physician level and highlight suggested improvements for future healthcare emergencies. METHODS: In April 2010, Quebec IDMM and PHPMS physicians were invited to anonymously complete a web-based learning needs assessment. The survey included both open-ended and multiple-choice questions. Descriptive statistics were used to report on the frequency distribution of multiple choice responses whereas thematic content analysis was used to analyse qualitative data generated from the survey and help understand respondents’ experience and perceptions with the pandemics. RESULTS: Of the 102 respondents, 85.3% reported difficulties or frustrations in their practice during the pandemic. The thematic analysis revealed two core themes describing the problems experienced in the pandemic management: coordination and resource-related difficulties. Coordination issues included communication, clinical practice guidelines, decision-making, roles and responsibilities, epidemiological investigation, and public health expert advisory committees. Resources issues included laboratory resources, patient management, and vaccination process. CONCLUSION: Together, the quantitative and qualitative data suggest a need for improved coordination, a better definition of roles and responsibilities, increased use of information technologies, merged communications, and transparency in the decisional process. Increased flexibility and less contradiction in clinical practice guidelines from different sources and increased laboratory/clinical capacity were felt critical to the proper management of infectious disease emergencies


Reported data sets on infection of volunteers challenged with wild-type influenza A virus at graded doses are few. Alternatively, we aimed at developing a dose-response assessment for this virus based on the data sets for its live attenuated reassortants. Eleven data sets for live attenuated reassortants that were fit to beta-Poisson and exponential dose-response models. Dose-response
relationships for those reassortants were characterized by pooling analysis of the data sets with respect to virus subtype (H1N1 or H3N2), attenuation method (cold-adapted or avian-human gene reassortment), and human age (adults or children). Furthermore, by comparing the above data sets to a limited number of reported data sets for wild-type virus, we quantified the degree of attenuation of wild-type virus with gene reassortment and estimated its infectivity. As a result, dose-response relationships of all reassortants were best described by a beta-Poisson model. Virus subtype and human age were significant factors determining the dose-response relationship, whereas attenuation method affected only the relationship of H1N1 virus infection to adults. The data sets for H3N2 wild-type virus could be pooled with those for its reassortants on the assumption that the gene reassortment attenuates wild-type virus by at least 63 times and most likely 1,070 times. Considering this most likely degree of attenuation, 10% infectious dose of H3N2 wild-type virus for adults was estimated at 18 TCID50 (95% CI = 8.8-35 TCID50). The infectivity of wild-type H1N1 virus remains unknown as the data set pooling was unsuccessful.


Global nuclear proliferation, bioterrorism, and emerging infections have challenged national capacities to achieve and maintain global security. Over the last century, emerging infectious disease threats resulted in the development of the preliminary versions of the International Health Regulations (IHR) of the World Health Organization (WHO). The current HR(2005) contain major differences compared to earlier versions, including: substantial shifts from containment at the border to containment at the source of the event; shifts from a rather small disease list (smallpox, plague, cholera, and yellow fever) required to be reported, to all public health threats; and shifts from preset measures to tailored responses with more flexibility to deal with the local situations on the ground. The new IHR(2005) call for accountability. They also call for strengthened national capacity for surveillance and control; prevention, alert, and response to international public health emergencies beyond the traditional short list of required reporting; global partnership and collaboration; and human rights, obligations, accountability, and procedures of monitoring. Under these evolved regulations, as well as other measures, such as the Revolving Fund for vaccine procurement of the Pan American Health Organization (PAHO), global health security could be maintained in the response to urban yellow fever in Paraguay in 2008 and the influenza (H1N1) pandemic of 2009-2010.


India has made appreciable progress and continues to demonstrate a strong commitment for establishing and operating a disease surveillance programme responsive to the requirements of the International Health Regulations (IHR[2005]). Within five years of its launch, India has effectively used modern information and communication technology for collection, storage, transmission and management of data related to disease surveillance and effective response. Terrestrial and/or satellite based linkages are being established within all states, districts, state-run medical colleges, infectious disease hospitals, and public health laboratories. This network enables speedy data transfer, video conferencing, training and e-learning for outbreaks and programme monitoring. A 24x7 call centre is in operation to receive disease alerts. To complement these efforts, a media scanning and verification cell functions to receive reports of early warning signals. During the 2009 H1N1 outbreak, the usefulness of the information and communication technology (ICT) network was well appreciated. India is using ICT as part of its Integrated Disease Surveillance Project (IDSP) to help overcome the challenges in further expansion in hard-to-reach populations, to increase the involvement of the private sector, and to increase the use of other modes of communication like e-mail and voicemail.

BACKGROUND: Having been overwhelmed by the complexity of the response needed for the severe acute respiratory syndrome (SARS) epidemic, public health professionals in the small island state of Barbados put various measures in place to improve its response in the event of a pandemic

METHODS: Data for this study was collected using Barbados’ National Influenza Surveillance System, which was revitalized in 2007. It is comprised of ten sentinel sites which send weekly notifications of acute respiratory illness (ARI) and severe acute respiratory illness (SARI) to the Office of the National Epidemiologist. During the 2009 H1N1 pandemic, meetings of the National Pandemic Planning Committee and the Technical Command Committee were convened. The pharmaceutical and non-pharmaceutical interventions (NPIs) implemented as a result of these meetings form the basis of the results presented in this paper. RESULTS: On June 3, 2009, Barbados reported its first case of 2009 H1N1. From June until October 2009, there were 155 laboratory confirmed cases of 2009 H1N1, with one additional case occurring in January 2010. For the outbreak period (June-October 2009), the surveillance team received reports of 2,483 ARI cases, compared to 412 cases for the same period in 2008. The total hospitalization rate due to SARIs for the year 2009 was 90.1 per 100,000 people, as compared to 7.3 per 100,000 people for 2008. Barbados’ pandemic response was characterized by a strong surveillance system combining active and passive surveillance, good risk communication strategy, a strengthened public and private sector partnership, and effective regional and international collaborations. Community restriction strategies such as school and workplace closures and cancellation of group events were not utilized as public health measures to delay the spread of the virus. Some health care facilities struggled with providing adequate isolation facilities.

CONCLUSIONS: The number of confirmed cases was small but the significant surge in ARI and SARI cases indicate that the impact of the virus on the island was moderate. As a result of 2009 H1N1, virological surveillance has improved significantly and local, regional and international partnerships have been strengthened.

Maladie d’Alzheimer


http://www.ncbi.nlm.nih.gov/pubmed/22859199


The prevalence of dementia in the Western world in people over the age of 60 has been estimated to be greater than 5%, about two-thirds of which are due to Alzheimer's disease. The age-specific prevalence of Alzheimer's disease nearly doubles every 5 years after age 65, leading to a prevalence of greater than 25% in those over the age of 90 (ref. 3). Here, to search for low-frequency variants in the amyloid-beta precursor protein (APP) gene with a significant effect on the risk of Alzheimer's disease, we studied coding variants in APP in a set of whole-genome sequence data from 1,795 Icelanders. We found a coding mutation (A673T) in the APP gene that protects against Alzheimer's disease and cognitive decline in the elderly without Alzheimer's disease. This substitution is adjacent to the aspartyl protease beta-site in APP, and results in an approximately 40% reduction in the formation of amyloidogenic peptides in vitro. The strong protective effect of the A673T substitution against Alzheimer's disease provides proof of principle for the hypothesis that reducing the beta-cleavage of APP may protect against the disease. Furthermore, as the A673T allele also protects against cognitive decline in the elderly without Alzheimer's disease, the two may be mediated through the same or similar mechanisms.


BACKGROUND: The order and magnitude of pathologic processes in Alzheimer's disease are not well understood, partly because the disease develops over many years. Autosomal dominant Alzheimer's disease has a predictable age at onset and provides an opportunity to determine the sequence and magnitude of pathologic changes that culminate in symptomatic disease.

METHODS: In this prospective, longitudinal study, we analyzed data from 128 participants who underwent baseline clinical and cognitive assessments, brain imaging, and cerebrospinal fluid (CSF) and blood tests. We used the participant's age at baseline assessment and the parent's age at the onset of symptoms of Alzheimer's disease to calculate the estimated years from expected symptom onset (age of the participant minus parent's age at symptom onset). We conducted cross-sectional analyses of baseline data in relation to estimated years from expected symptom onset in order to determine the relative order and magnitude of pathophysiological changes. RESULTS: Concentrations of amyloid-beta (Abeta)(42) in the CSF appeared to decline 25 years before expected symptom onset. Abeta deposition, as measured by positron-emission tomography with the use of Pittsburgh compound B, was detected 15 years before expected symptom onset. Increased concentrations of tau protein in the CSF and an increase in brain atrophy were detected 15 years before expected symptom onset. Cerebral hypometabolism and impaired episodic memory were observed 10 years before expected symptom onset.
cognitive impairment, as measured by the Mini-Mental State Examination and the Clinical Dementia Rating scale, was detected 5 years before expected symptom onset, and patients met diagnostic criteria for dementia at an average of 3 years after expected symptom onset.

CONCLUSIONS: We found that autosomal dominant Alzheimer’s disease was associated with a series of pathophysiological changes over decades in CSF biochemical markers of Alzheimer’s disease, brain amyloid deposition, and brain metabolism as well as progressive cognitive impairment. Our results require confirmation with the use of longitudinal data and may not apply to patients with sporadic Alzheimer’s disease. ( Funded by the National Institute on Aging and others; DIAN ClinicalTrials.gov number, NCT00869817.)


Extracellular plaques of amyloid-beta and intraneuronal neurofibrillary tangles made from tau are the histopathological signatures of Alzheimer’s disease. Plaques comprise amyloid-beta fibrils that assemble from monomeric and oligomeric intermediates, and are prognostic indicators of Alzheimer’s disease. Despite the importance of plaques to Alzheimer’s disease, oligomers are considered to be the principal toxic forms of amyloid-beta. Interestingly, many adverse responses to amyloid-beta, such as cytotoxicity, microtubule loss, impaired memory and learning, and neuritic degeneration, are greatly amplified by tau expression. Amino-terminally truncated, pyroglutamylated (pE) forms of amyloid-beta are strongly associated with Alzheimer’s disease, are more toxic than amyloid-beta, residues 1-42 (Abeta(1-42)) and Abeta(1-40), and have been proposed as initiators of Alzheimer’s disease pathogenesis. Here we report a mechanism by which pE-Abeta may trigger Alzheimer’s disease. Abeta(3(pE)-42) co-oligomerizes with excess Abeta(1-42) to form metastable low-n oligomers (LNOs) that are structurally distinct and far more cytotoxic to cultured neurons than comparable LNOs made from Abeta(1-42) alone. Tau is required for cytotoxicity, and LNOs comprising 5% Abeta(3(pE)-42) plus 95% Abeta(1-42) (5% pE-Abeta) seed new cytotoxic LNOs through multiple serial dilutions into Abeta(1-42) monomers in the absence of additional Abeta(3(pE)-42). LNOs isolated from human Alzheimer’s disease brain contained Abeta(3(pE)-42), and enhanced Abeta(3(pE)-42) formation in mice triggered neuron loss and gliosis at 3 months, but not in a tau-null background. We conclude that Abeta(3(pE)-42) confers tau-dependent neuronal death and causes template-induced misfolding of Abeta(1-42) into structurally distinct LNOs that propagate by a prion-like mechanism. Our results raise the possibility that Abeta(3(pE)-42) acts similarly at a primary step in Alzheimer’s disease pathogenesis


BACKGROUND: Lacunar infarcts are a frequent type of stroke caused mainly by cerebral small-vessel disease. The effectiveness of antiplatelet therapy for secondary prevention has not been defined. METHODS: We conducted a double-blind, multicenter trial involving 3020 patients with recent symptomatic lacunar infarcts identified by magnetic resonance imaging. Patients were randomly assigned to receive 75 mg of clopidogrel or placebo daily; patients in both groups received 325 mg of aspirin daily. The primary outcome was any recurrent stroke, including ischemic stroke and intracranial hemorrhage. RESULTS: The participants had a mean age of 63 years, and 63% were men. After a mean follow-up of 3.4 years, the risk of recurrent stroke was not significantly reduced with aspirin and clopidogrel (dual antiplatelet therapy) (125 strokes; rate, 2.5% per year) as compared with aspirin alone (138 strokes, 2.7% per year) (hazard ratio, 0.92; 95% confidence interval [CI], 0.72 to 1.16), nor was the risk of recurrent ischemic stroke (hazard ratio, 0.82; 95% CI, 0.63 to 1.09) or disabling or fatal stroke (hazard ratio, 1.06; 95% CI, 0.69 to 1.64). The risk of major hemorrhage was almost doubled with dual antiplatelet therapy (105 hemorrhages, 2.1% per year) as compared with aspirin alone (56, 1.1% per year) (hazard ratio, 1.97; 95% CI, 1.41 to 2.71; P<0.001). Among classifiable recurrent ischemic strokes, 71% (133 of 187) were lacunar strokes. All-cause mortality was increased among patients assigned to receive dual antiplatelet therapy (77 deaths in the group receiving aspirin alone vs. 113 in the group receiving dual antiplatelet therapy) (hazard ratio, 1.52; 95% CI, 1.14 to 2.04; P=0.004); this difference was not accounted for by fatal hemorrhages (9 in the group receiving dual antiplatelet therapy vs. 4 in the group receiving aspirin alone). CONCLUSIONS: Among patients with recent lacunar strokes, the addition of clopidogrel to aspirin did not significantly reduce the risk of recurrent stroke and did significantly increase the risk of bleeding and death. (Funded by the National Institute of Neurological Disorders and Stroke and others; SPS3 ClinicalTrials.gov number, NCT00059306.)


CONTEXT: The evidence that measurement of the common carotid intima-media thickness (CIMT) improves the risk scores in prediction of the absolute risk of cardiovascular events is inconsistent. OBJECTIVE: To determine whether common CIMT has added value in 10-year risk prediction of first-time myocardial infarctions or strokes, above that of the Framingham Risk Score. DATA SOURCES: Relevant studies were identified through literature searches of databases (PubMed from 1950 to June 2012 and EMBASE from 1980 to June 2012) and expert opinion. STUDY SELECTION: Studies were included if participants were drawn from the general population, common CIMT was measured at baseline, and individuals were followed up for first-
time myocardial infarction or stroke. DATA EXTRACTION: Individual data were combined into 1 data set and an individual participant data meta-analysis was performed on individuals without existing cardiovascular disease. RESULTS: We included 14 population-based cohorts contributing data for 45,828 individuals. During a median follow-up of 11 years, 4007 first-time myocardial infarctions or strokes occurred. We first refitted the risk factors of the Framingham Risk Score and then extended the model with common CIMT measurements to estimate the absolute 10-year risks to develop a first-time myocardial infarction or stroke in both models. The C statistic of both models was similar (0.757; 95% CI, 0.749-0.764; and 0.759; 95% CI, 0.752-0.766). The net reclassification improvement with the addition of common CIMT was small (0.8%; 95% CI, 0.1%-1.6%). In those at intermediate risk, the net reclassification improvement was 3.6% in all individuals (95% CI, 2.7%-4.6%) and no differences between men and women. CONCLUSION: The addition of common CIMT measurements to the Framingham Risk Score was associated with small improvement in 10-year risk prediction of first-time myocardial infarction or stroke, but this improvement is unlikely to be of clinical importance.


BACKGROUND: Both atrial fibrillation and chronic kidney disease increase the risk of stroke and systemic thromboembolism. However, these risks, and the effects of antithrombotic treatment, have not been thoroughly investigated in patients with both conditions. METHODS: Using Danish national registries, we identified all patients discharged from the hospital with a diagnosis of nonvalvular atrial fibrillation between 1997 and 2008. The risk of stroke or systemic thromboembolism and bleeding associated with non-end-stage chronic kidney disease and with end-stage chronic kidney disease (i.e., disease requiring renal-replacement therapy) was estimated with the use of time-dependent Cox regression analyses. In addition, the effects of treatment with warfarin, aspirin, or both in patients with chronic kidney disease were compared with the effects in patients with no renal disease. RESULTS: Of 132,372 patients included in the analysis, 3587 (2.7%) had non-end-stage chronic kidney disease and 901 (0.7%) required renal-replacement therapy at the time of inclusion. As compared with patients who did not have renal disease, patients with non-end-stage chronic kidney disease had an increased risk of stroke or systemic thromboembolism (hazard ratio, 1.49; 95% confidence interval [CI], 1.38 to 1.59; P<0.001), as did those requiring renal-replacement therapy (hazard ratio, 1.83; 95% CI, 1.57 to 2.14; P<0.001); this risk was significantly decreased for both groups of patients with warfarin but not with aspirin. The risk of bleeding was also increased among patients who had non-end-stage chronic kidney disease or required renal-replacement therapy and was further increased with warfarin, aspirin, or both. CONCLUSIONS: Chronic kidney disease was associated with an increased risk of stroke or systemic thromboembolism and bleeding among patients with atrial fibrillation. Warfarin treatment was associated with a decreased risk of stroke or systemic thromboembolism among patients with chronic kidney disease, whereas warfarin and aspirin were associated with an increased risk of bleeding. (Funded by the Lundbeck Foundation.)


CONTEXT: The safety and durability of endoscopic vein graft harvest in coronary artery bypass graft (CABG) surgery has recently been called into question. OBJECTIVE: To compare the long-term outcomes of endoscopic vs open vein-graft harvesting for Medicare patients undergoing CABG surgery in the United States. DESIGN, SETTING, AND PATIENTS: An observational study of 235,394 Medicare patients undergoing isolated CABG surgery between 2003 and 2008 at 934 surgical centers participating in the Society of Thoracic Surgeons (STS) national database. The STS records were linked to Medicare files to allow longitudinal assessment (median 3-year follow-up) through December 31, 2008. MAIN OUTCOME MEASURES: All-cause mortality. Secondary outcome measures included wound complications and the composite of death, myocardial infarction, and revascularization. RESULTS: Based on Medicare Part B coding, 52% of patients received endoscopic vein-graft harvesting during CABG surgery. After propensity score adjustment for clinical characteristics, there were no significant differences between long-term mortality rates (13.2% [12,429 events] vs 13.4% [13,096 events]) and the composite of death, myocardial infarction, and revascularization (19.5% [18,419 events] vs 19.7% [19,232 events]). Time-to-event analysis for those patients receiving endoscopic vs open vein-graft harvesting revealed adjusted hazard ratios [HRs] of 1.00 (95% CI, 0.97-1.04) for mortality and 1.00 (95% CI, 0.98-1.05) for the composite outcome. Endoscopic vein-graft harvesting was associated with lower harvest site wound complications relative to open vein-graft harvesting (3.0% [3654/122,899 events] vs 3.6% [4047/112,495 events]; adjusted HR, 0.83; 95% CI, 0.77-0.89; P < .001). CONCLUSION: Among patients undergoing CABG surgery, the use of endoscopic vein-graft harvesting compared with open vein-graft harvesting was not associated with increased mortality


BACKGROUND: Strong evidence shows that physical inactivity increases the risk of many adverse health conditions, including major non-communicable diseases such as coronary heart disease, type 2 diabetes, and breast and colon cancers, and shortens life expectancy. Because much of the world's population is inactive, this link presents a major public health issue. We aimed to quantify the effect of physical inactivity on these major non-communicable diseases by estimating how much disease could be averted if inactive people were to become active and to estimate gain in life expectancy at the population level. METHODS: For our analysis of burden of disease, we calculated population attributable fractions (PAFs) associated with physical inactivity using conservative assumptions for each of the major non-communicable diseases, by country, to estimate how much disease could be averted if physical inactivity were eliminated. We used life-table analysis to estimate gains in life expectancy of the population. FINDINGS: Worldwide, we estimate that physical inactivity causes 6% (ranging from 3.2% in southeast Asia to 7.8% in the eastern Mediterranean region) of the burden of disease from coronary heart disease, 7% (3.9-9.6) of type 2 diabetes, 10% (5.6-14.1) of breast cancer, and 10% (5.7-13.8) of colon cancer. Inactivity causes 9% (range 5.1-12.5) of premature mortality, or more than 5.3 million of the 57 million deaths that occurred worldwide in 2008. If inactivity were not eliminated, but decreased instead by 10% or 25%, more than 533 000 and more than 1.3 million deaths, respectively, could be averted every year. We estimated that elimination of physical inactivity would increase the life expectancy of the world's population by 0.68 (range 0.41-0.95) years. INTERPRETATION: Physical inactivity has a major health effect worldwide. Decrease in or removal of this unhealthy behaviour could improve health substantially. FUNDING: None


BACKGROUND: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis is a severe condition encompassing two major syndromes: granulomatosis with polyangiitis (formerly known as Wegener's granulomatosis) and microscopic polyangiitis. Its cause is unknown, and there is debate about whether it is a single disease entity and what role ANCA plays in its pathogenesis. We investigated its genetic basis. METHODS: A genomewide association study was performed in a discovery cohort of 1233 U.K. patients with ANCA-associated vasculitis and 5884 controls and was replicated in 1454 Northern European case patients and 1666 controls. Quality control, population stratification, and statistical analyses were performed according to standard criteria. RESULTS: We found both major-histocompatibility-complex (MHC) and non-MHC associations with ANCA-associated vasculitis and also that granulomatosis with polyangiitis and microscopic polyangiitis were genetically distinct. The strongest genetic associations were with the antigenic specificity of ANCA, not with the clinical syndrome. Anti-proteinase 3 ANCA was associated with
HLA-DP and the genes encoding alpha(1)-antitrypsin (SERPINA1) and proteinase 3 (PRTN3) (P=6.2x10(-89), P=5.6x10(-12), and P=2.6x10(-7), respectively). Anti-myeloperoxidase ANCA was associated with HLA-DQ (P=2.1x10(-8)). CONCLUSIONS: This study confirms that the pathogenesis of ANCA-associated vasculitis has a genetic component, shows genetic distinctions between granulomatosis with polyangiitis and microscopic polyangiitis that are associated with ANCA specificity, and suggests that the response against the autoantigen proteinase 3 is a central pathogenic feature of proteinase 3 ANCA-associated vasculitis. These data provide preliminary support for the concept that proteinase 3 ANCA-associated vasculitis and myeloperoxidase ANCA-associated vasculitis are distinct autoimmune syndromes. (Funded by the British Heart Foundation and others.)


CONTEXT: There is increasing interest in reporting risk-standardized outcomes for Medicare beneficiaries hospitalized with acute ischemic stroke, but whether it is necessary to include adjustment for initial stroke severity has not been well studied. OBJECTIVE: To evaluate the degree to which hospital outcome ratings and potential eligibility for financial incentives are altered after including initial stroke severity in a claims-based risk model for hospital 30-day mortality for acute ischemic stroke. DESIGN, SETTING, AND PATIENTS: Data were analyzed from 782 Get With The Guidelines-Stroke participating hospitals on 127,950 fee-for-service Medicare beneficiaries with ischemic stroke who had a score documented for the National Institutes of Health Stroke Scale (NIHSS, a 15-item neurological examination scale with scores from 0 to 42, with higher scores indicating more severe stroke) between April 2003 and December 2009. Performance of claims-based hospital mortality risk models with and without inclusion of NIHSS scores for 30-day mortality was evaluated and hospital rankings from both models were compared. MAIN OUTCOMES MEASURES: Model discrimination, hospital 30-day mortality outcome rankings, and value-based purchasing financial incentive categories. RESULTS: Across the study population, the mean (SD) NIHSS score was 8.23 (8.11) (median, 5; interquartile range, 2-12). There were 18,186 deaths (14.5%) within the first 30 days, including 7430 deaths (5.8%) during the index hospitalization. The hospital mortality model with NIHSS scores had significantly better discrimination than the model without (C statistic, 0.864; 95% CI, 0.861-0.867, vs 0.772; 95% CI, 0.769-0.776; P < .001). Among hospitals ranked in the top 20% or bottom 20% of performers by the claims model without NIHSS scores, 26.3% were ranked differently by the model with NIHSS. Of hospitals initially classified as having "worse than expected" mortality, 57.7% were reclassified to "as expected" by the model with NIHSS scores. The net reclassification improvement (93.1%; 95% CI, 91.6%-94.6%; P < .001) and integrated discrimination improvement (15.0%; 95% CI, 14.6%-15.3%; P < .001) indexes both demonstrated significant enhancement of model performance after the addition of NIHSS. Explained variance and model calibration was also improved with the addition of NIHSS scores. CONCLUSION: Adding stroke severity as measured by the NIHSS to a hospital 30-day risk model based on claims data for Medicare beneficiaries with acute ischemic stroke was associated with considerably improved model discrimination and change in mortality performance rankings for a substantial portion of hospitals


CONTEXT: Ischemia/reperfusion injury remains an important cause of morbidity and mortality after coronary artery bypass graft (CABG) surgery. In a meta-analysis of randomized controlled trials, perioperative and postoperative infusion of acadesine, a first-in-class adenosine-regulating agent, was associated with a reduction in early cardiac death, myocardial infarction, and combined adverse cardiac outcomes in participants undergoing on-pump CABG surgery.

OBJECTIVE: To assess the efficacy and safety of acadesine administered in the perioperative period in reducing all-cause mortality, nonfatal stroke, and severe left ventricular dysfunction (SLVD) through 28 days. DESIGN, SETTING, AND PARTICIPANTS: The Reduction in Cardiovascular Events by Acadesine in Patients Undergoing CABG (RED-CABG) trial, a randomized, double-blind, placebo-controlled, parallel-group evaluation of intermediate- to high-risk patients (median age, 66 years) undergoing nonemergency, on-pump CABG surgery at 300 sites in 7 countries. Enrollment occurred from May 6, 2009, to July 30, 2010. INTERVENTIONS: Eligible participants were randomized 1:1 to receive acadesine (0.1 mg/kg per minute for 7 hours) or placebo (both also added to cardioplegic solutions) beginning just before anesthesia induction. MAIN OUTCOME MEASURE: Composite of all-cause mortality, nonfatal stroke, or need for mechanical support for SLVD during and following CABG surgery through postoperative day 28. RESULTS: Because results of a prespecified futility analysis indicated a very low likelihood of a statistically significant efficacious outcome, the trial was stopped after 3080 of the originally projected 7500 study participants were randomized. The primary outcome occurred in 75 of 1493 participants (5.0%) in the placebo group and 76 of 1493 (5.1%) in the acadesine group (odds ratio, 1.01 [95% CI, 0.73-1.41]). There were no differences in key secondary end points measured. CONCLUSION: In this population of intermediate- to high-risk patients undergoing CABG surgery, acadesine did not reduce the composite of all-cause mortality, nonfatal stroke, or SLVD. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00872001


BACKGROUND: Thrombolysis with intravenous alteplase is the only approved treatment for acute ischaemic stroke. After alteplase-induced recanalisation, reocclusion occurs in 14-34% of patients, probably because of platelet activation. Early administration of antiplatelet therapy after alteplase could reduce the risk of reocclusion and improve outcome. We compared the effects of early addition of intravenous aspirin to alteplase with standard alteplase without aspirin.

METHODS: In this multicentre, randomised, open-label trial with blind-endpoint assessment, patients with acute ischaemic stroke treated with alteplase were randomly assigned to 300 mg intravenous aspirin within 90 min after start of alteplase treatment or to no additional treatment. In both groups, oral antiplatelet therapy was started 24 h after alteplase treatment. The primary endpoint was favourable outcome, defined as a score of 0-2 on the modified Rankin scale at 3 months. This trial is registered with the Netherlands Trial Register (NTR822). FINDINGS: Between July 29, 2008, and April 20, 2011, 642 patients (322 patients aspirin, 320 patients standard treatment) of the targeted 800 patients were enrolled. At that time, the trial was terminated prematurely because of an excess of symptomatic intracranial haemorrhage (SICH) and no evidence of benefit in the aspirin group. At 3 months, 174 (54.0%) patients in the aspirin group versus 183 (57.2%) patients in the standard treatment group had a favourable outcome (absolute difference -3.2%, 95% CI -10.8 to 4.2; crude relative risk 0.94, 0.82 to 1.09, p=0.42). Adjusted odds ratio was 0.91 (95% CI 0.66-1.26, p=0.58). SICH occurred more often in the aspirin group (14 [4.3%] patients) than in the standard treatment group (five [1.6%]; absolute difference 2.8%, 95% CI 0.2-5.4; p=0.04). SICH was more often the cause of poor outcome in the aspirin group compared with the standard treatment group (11 vs 1, p=0.008). INTERPRETATION: Early administration of intravenous aspirin in patients with acute ischaemic stroke treated with alteplase does not improve outcome at 3 months and increases the risk of SICH. The results of this trial do not support a change of the current guidelines, which advise to start antiplatelet therapy 24 h after alteplase.

FUNDING: The Dutch Heart Foundation


BACKGROUND: The natural history of unruptured cerebral aneurysms has not been clearly defined. METHODS: From January 2001 through April 2004, we enrolled patients with newly identified, unruptured cerebral aneurysms in Japan. Information on the rupture of aneurysms, deaths, and the results of periodic follow-up examinations were recorded. We included 5720 patients 20 years of age or older (mean age, 62.5 years; 68% women) who had saccular aneurysms that were 3 mm or more in the largest dimension and who initially presented with no more than a slight disability. RESULTS: Of the 6697 aneurysms studied, 91% were discovered incidentally. Most aneurysms were in the middle cerebral arteries (36%) and the internal carotid
arteries (34%). The mean (+/−SD) size of the aneurysms was 5.7+/−3.6 mm. During a follow-up period that included 11,660 aneurysm-years, ruptures were documented in 111 patients, with an annual rate of rupture of 0.95% (95% confidence interval [CI], 0.79 to 1.15). The risk of rupture increased with increasing size of the aneurysm. With aneurysms that were 3 to 4 mm in size as the reference, the hazard ratios for size categories were as follows: 5 to 6 mm, 1.13 (95% CI, 0.58 to 2.22); 7 to 9 mm, 3.35 (95% CI, 1.87 to 6.00); 10 to 24 mm, 9.09 (95% CI, 5.25 to 15.74); and 25 mm or larger, 76.26 (95% CI, 32.76 to 177.54). As compared with aneurysms in the middle cerebral arteries, those in the posterior and anterior communicating arteries were more likely to rupture (hazard ratio, 1.90 [95% CI, 1.12 to 3.21] and 2.02 [95% CI, 1.13 to 3.58], respectively). Aneurysms with a daughter sac (an irregular protrusion of the wall of the aneurysm) were also more likely to rupture (hazard ratio, 1.63; 95% CI, 1.08 to 2.48). CONCLUSIONS: This study showed that the natural course of unruptured cerebral aneurysms varies according to the size, location, and shape of the aneurysm. (Fundied by the Ministry of Health, Labor, and Welfare in Japan and others; UCAS Japan UMIN-CTR number, C000000418.)

(37) ALBERTS MJ. Cerebral hemorrhage, warfarin, and intravenous tPA: the real risk is not treating. JAMA. 2012 June 27, vol. 307, n° 24, pp.2637-2639


CONTEXT: Intravenous tissue plasminogen activator (tPA) is known to improve outcomes in ischemic stroke; however, patients receiving long-term chronic warfarin therapy may face an increased risk for intracranial hemorrhage when treated with tPA. Although current guidelines endorse administering intravenous tPA to warfarin-treated patients if their international normalized ratio (INR) is 1.7 or lower, there are few data on safety of intravenous tPA in warfarin-treated patients in clinical practice. OBJECTIVES: To determine the risk of symptomatic intracranial hemorrhage (sICH) among patients with ischemic stroke treated with intravenous tPA who were receiving warfarin vs those who were not and to determine this risk as a function of INR. DESIGN, SETTING, AND PATIENTS: Observational study, using data from the American Heart Association Get With The Guidelines-Stroke Registry, of 23,437 patients with ischemic stroke and with INR of 1.7 or lower, treated with intravenous tPA in 1203 registry hospitals from April 2009 through June 2011. MAIN OUTCOME MEASURE: Symptomatic intracranial hemorrhage. Secondary end points include life-threatening/serious systemic hemorrhage, any tPA complications, and in-hospital mortality. RESULTS: Overall, 1802 (7.7%) patients with stroke treated with tPA were receiving warfarin (median INR, 1.20; interquartile range [IQR], 1.07-1.40). Warfarin-treated patients were older, had more comorbid conditions, and had more severe strokes. The unadjusted sICH rate in warfarin-treated patients was higher than in non-warfarin-treated patients (5.7% vs 4.6%, P < .001), but these differences were not significantly different after adjustment for baseline clinical factors (adjusted odds ratio [OR], 1.01 [95% CI, 0.82-1.25]). Similarly, there were no significant differences between warfarin-treated and non-warfarin-treated patients for serious systemic hemorrhage (0.9% vs 0.9%; adjusted OR, 0.78 [95% CI, 0.49-1.24]), any tPA complications (10.6% vs 8.4%; adjusted OR, 1.09 [95% CI, 0.93-1.29]), or in-hospital mortality (11.4% vs 7.9%; adjusted OR, 0.94 [95% CI, 0.79-1.13]). Among warfarin-treated patients with INRs of 1.7 or lower, the degree of anticoagulation was not statistically significantly associated with sICH risk (adjusted OR, 1.10 per 0.1-unit increase in INR [95% CI, 1.00-1.20]; P = .06). CONCLUSION: Among patients with ischemic stroke, the use of intravenous tPA among warfarin-treated patients
(INR \leq 1.7) was not associated with increased sICH risk compared with non-warfarin-treated patients


OBJECTIVE: To investigate whether an internet based, nurse led vascular risk factor management programme promoting self management on top of usual care is more effective than usual care alone in reducing vascular risk factors in patients with clinically manifest vascular disease. DESIGN: Prospective randomised controlled trial. SETTING: Multicentre trial in secondary and tertiary healthcare setting. PARTICIPANTS: 330 patients with a recent clinical manifestation of atherosclerosis in the coronary, cerebral, or peripheral arteries and with at least two treatable risk factors not at goal. INTERVENTION: Personalised website with an overview and actual status of patients’ risk factors and mail communication via the website with a nurse practitioner for 12 months; the intervention combined self management support, monitoring of disease control, and drug treatment. MAIN OUTCOME MEASURES: The primary endpoint was the relative change in Framingham heart risk score after 1 year. Secondary endpoints were absolute changes in the levels of risk factors and the differences between groups in the change in proportion of patients reaching treatment goals for each risk factor. RESULTS: Participants' mean age was 59.9 (SD 8.4) years, and most patients (n=246; 75%) were male. After 1 year, the relative change in Framingham heart risk score of the intervention group compared with the usual care group was -14% (95% confidence interval -25% to -2%). At baseline, the Framingham heart risk score was higher in the intervention group than in the usual care group (16.1 (SD 10.6) v 14.0 (10.5)), so the outcome was adjusted for the separate variables of the Framingham heart risk score and for the baseline Framingham heart risk score. This produced a relative change of -12% (-22% to -3%) in Framingham heart risk score for the intervention group compared with the usual care group adjusted for the separate variables of the score and -8% (-18% to 2%) adjusted for the baseline score. Of the individual risk factors, a difference between groups was observed in low density lipoprotein cholesterol (-0.3, -0.5 to -0.1, mmol/L) and smoking (-7.7%, -14.9% to -0.4%). Some other risk factors tended to improve (body mass index, triglycerides, systolic blood pressure, renal function) or tended to worsen (glucose concentration, albuminuria). CONCLUSION: An internet based, nurse led treatment programme on top of usual care for vascular risk factors had a small effect on lowering vascular risk and on lowering of some vascular risk factors in patients with vascular disease. TRIAL REGISTRATION: Clinical trials NCT00785031


OBJECTIVES: To develop prediction models that better estimate the pretest probability of coronary artery disease in low prevalence populations. DESIGN: Retrospective pooled analysis of individual patient data. SETTING: 18 hospitals in Europe and the United States. PARTICIPANTS: Patients with stable chest pain without evidence for previous coronary artery disease, if they were referred for computed tomography (CT) based coronary angiography or catheter based coronary angiography (indicated as low and high prevalence settings, respectively). MAIN OUTCOME MEASURES: Obstructive coronary artery disease (\geq 50% diameter stenosis in at least one vessel found on catheter based coronary angiography). Multiple
imputation accounted for missing predictors and outcomes, exploiting strong correlation between the two angiography procedures. Predictive models included a basic model (age, sex, symptoms, and setting), clinical model (basic model factors and diabetes, hypertension, dyslipidaemia, and smoking), and extended model (clinical model factors and use of the CT based coronary calcium score). We assessed discrimination (c statistic), calibration, and continuous net reclassification improvement by cross validation for the four largest low prevalence datasets separately and the smaller remaining low prevalence datasets combined. RESULTS: We included 5677 patients (3283 men, 2394 women), of whom 1634 had obstructive coronary artery disease found on catheter based coronary angiography. All potential predictors were significantly associated with the presence of disease in univariable and multivariable analyses. The clinical model improved the prediction, compared with the basic model (cross validated c statistic improvement from 0.77 to 0.79, net reclassification improvement 35%); the coronary calcium score in the extended model was a major predictor (0.79 to 0.88, 102%). Calibration for low prevalence datasets was satisfactory. CONCLUSIONS: Updated prediction models including age, sex, symptoms, and cardiovascular risk factors allow for accurate estimation of the pretest probability of coronary artery disease in low prevalence populations. Addition of coronary calcium scores to the prediction models improves the estimates


BACKGROUND: Citicoline is approved in some countries for the treatment of acute ischaemic stroke. The drug has shown some evidence of efficacy in a pooled analysis. We sought to confirm the efficacy of citicoline in a larger trial. METHODS: We undertook a randomised, placebo-controlled, sequential trial in patients with moderate-to-severe acute ischaemic stroke admitted at university hospitals in Germany, Portugal, and Spain. Using a centralised minimisation process, patients were randomly assigned in a 1:1 ratio to receive citicoline or placebo within 24 h after the onset of symptoms (1000 mg every 12 h intravenously during the first 3 days and orally thereafter for a total of 6 weeks [2x500 mg oral tablets given every 12 h]). All study participants were masked. The primary outcome was recovery at 90 days measured by a global test combining three measures of success: National Institutes of Health Stroke Scale </=1, modified Rankin score </=1, and Barthel Index >/=95. Safety endpoints included symptomatic intracranial haemorrhage in patients treated with recombinant tissue plasminogen activator, neurological deterioration, and mortality. This trial is registered, NCT00331890. RESULTS: 2298 patients were enrolled into the study from Nov 26, 2006, to Oct 27, 2011. 37 centres in Spain, 11 in Portugal, and 11 in Germany recruited patients. Of the 2298 patients who gave informed consent and underwent randomisation, 1148 were assigned to citicoline and 1150 to placebo. The trial was stopped for futility at the third interim analysis on the basis of complete data from 2078 patients. The final randomised analysis was based on data for 2298 patients: 1148 in citicoline group and 1150 in placebo group. Global recovery was similar in both groups (odds ratio 1.03, 95% CI 0.86-1.25; p=0.364). No significant differences were reported in the safety variables nor in the rate of adverse events. INTERPRETATION: Under the circumstances of the ICTUS trial, citicoline is not efficacious in the treatment of moderate-to-severe acute ischaemic stroke. FUNDING: Ferrer Grupo


OBJECTIVES: To assess the association between pre-diabetes and risk of stroke, and to evaluate whether this relation varies by diagnostic criteria for pre-diabetes. DESIGN: Systematic review and meta-analysis of prospective studies. DATA SOURCES: A search of Medline, Embase, and the Cochrane Library (1947 to 16 July 2011) was supplemented by manual searches of bibliographies of key retrieved articles and relevant reviews. SELECTION CRITERIA: Prospective cohort studies that reported multivariate adjusted relative risks and corresponding 95% confidence intervals for stroke with respect to baseline pre-diabetes were included. DATA EXTRACTION: Two independent reviewers extracted data on pre-diabetes status at baseline, risk estimates of stroke, study quality, and methods used to assess pre-diabetes and stroke. Relative risks were pooled using random effects models when appropriate. Associations were tested in subgroups representing different characteristics of participants and studies. Publication bias was evaluated with funnel plots. RESULTS: The search yielded 15 prospective cohort studies including 760,925 participants. In 8 studies analysing pre-diabetes defined as fasting glucose 100-125 mg/dL (5.6-6.9 mmol/L), the random effects summary estimate did not show an increased risk of stroke after adjustment for established cardiovascular risk factors (1.08, 95% confidence interval 0.94 to 1.23; P = 0.26). In 5 studies analysing pre-diabetes defined as fasting glucose 110-125 mg/dL (6.1-6.9 mmol/L), the random effects summary estimate showed an increased risk of stroke after adjustment for established cardiovascular risk factors (1.21, 1.02 to 1.44; P = 0.03). In 8 studies with information about impaired glucose tolerance or combined impaired glucose tolerance and impaired fasting glucose, the random effects summary estimate showed an increased risk of stroke after adjustment for established cardiovascular risk factors (1.26, 1.10 to 1.43; P < 0.001). When studies that might have enrolled patients with undiagnosed diabetes were excluded, only impaired glucose tolerance or a combination of impaired fasting glucose and impaired glucose tolerance independently raised the future risk of stroke (1.20, 1.07 to 1.35; P = 0.002). CONCLUSION: Pre-diabetes, defined as impaired glucose tolerance or a combination of impaired fasting glucose and impaired glucose tolerance, may be associated with a higher future risk of stroke, but the relative risks are modest and may reflect underlying confounding

(48) TREADWELL JR. Pre-diabetes as a contributor to stroke. BMJ. 2012, vol. 344, p.e3285

(49) DELAMOTHE T. From rags to riches: the atrial fibrillation story. BMJ. 2012, vol. 344, p.e3871


OBJECTIVE: To determine whether women with atrial fibrillation have a higher risk of stroke than men. DESIGN: Nationwide retrospective cohort study. SETTING: Patients with a diagnosis of atrial fibrillation in the Swedish hospital discharge register between 1 July 2005 and 31 December
2008. Information about drug treatment taken from the Swedish drug register. PARTICIPANTS: 100,802 patients with atrial fibrillation at any Swedish hospital or hospital affiliated outpatient clinic with a total follow-up of 139,504 years at risk (median 1.2 years). We excluded patients with warfarin at baseline, mitral stenosis, previous valvular surgery, or who died within 14 days from baseline. MAIN OUTCOME MEASURE: Incidence of ischaemic stroke. RESULTS: Ischaemic strokes were more common in women than in men (6.2% v 4.2% per year, P<0.0001). The univariable hazard ratio for women compared with men was 1.47 (95% confidence 1.40 to 1.54), indicating a 47% higher incidence of ischaemic stroke in women than in men. Stratification according to the CHADS(2) scheme showed increased stroke rates for women in all strata. After multivariable adjustment for 35 cofactors for stroke, an increased risk of stroke in women remained (1.18, 1.12 to 1.24). Among patients with "lone atrial fibrillation" (age <65 years and no vascular disease), the annual stroke rate tended to be higher in women than in men, although this difference was not significant (0.7% v 0.5%, P=0.09). When low risk patients with CHADS(2) scores of 0-1 were stratified according to their CHA(2)DS(2)-VASc scores, women did not have higher stroke incidence than men at CHA(2)DS(2)-VASc scores of 2 or less. CONCLUSION: Women with atrial fibrillation have a moderately increased risk of stroke compared with men, and thus, female sex should be considered when making decisions about anticoagulation treatment. However, women younger than 65 years and without other risk factors have a low risk for stroke, and do not need anticoagulant treatment.


BACKGROUND: Magnesium sulphate is a neuroprotective agent that might improve outcome after aneurysmal subarachnoid haemorrhage by reducing the occurrence or improving the outcome of delayed cerebral ischaemia. We did a trial to test whether magnesium therapy improves outcome after aneurysmal subarachnoid haemorrhage. METHODS: We did this phase 3 randomised, placebo-controlled trial in eight centres in Europe and South America. We randomly assigned (with computer-generated random numbers, with permuted blocks of four, stratified by centre) patients aged 18 years or older with an aneurysmal pattern of subarachnoid haemorrhage on brain imaging who were admitted to hospital within 4 days of haemorrhage, to receive intravenous magnesium sulphate, 64 mmol/day, or placebo. We excluded patients with renal failure or bodyweight lower than 50 kg. Patients, treating physicians, and investigators assessing outcomes and analysing data were masked to the allocation. The primary outcome was poor outcome-defined as a score of 4-5 on the modified Rankin Scale-3 months after subarachnoid haemorrhage, or death. We analysed results by intention to treat. We also updated a previous meta-analysis of trials of magnesium treatment for aneurysmal subarachnoid haemorrhage. This study is registered with controlled-trials.com (ISRCTN 68742385) and the EU Clinical Trials Register (EudraCT 2006-003523-36). FINDINGS: 1204 patients were enrolled, one of whom had his treatment allocation lost. 606 patients were assigned to the magnesium group (two lost to follow-up), 597 to the placebo (one lost to follow-up). 158 patients (26.2%) had poor outcome in the magnesium group compared with 151 (25.3%) in the placebo group (risk ratio [RR] 1.03, 95% CI 0.85-1.25). Our updated meta-analysis of seven randomised trials involving 2047 patients shows that magnesium is not superior to placebo for reduction of poor outcome after aneurysmal subarachnoid haemorrhage (RR 0.96, 95% CI 0.86-1.08). INTERPRETATION: Intravenous magnesium sulphate does not improve clinical outcome after aneurysmal subarachnoid haemorrhage, therefore routine administration of magnesium cannot be recommended. FUNDING: Netherlands Heart Foundation, UK Medical Research Council
BACKGROUND: Thrombolysis is of net benefit in patients with acute ischaemic stroke, who are younger than 80 years of age and are treated within 4.5 h of onset. The third International Stroke Trial (IST-3) sought to determine whether a wider range of patients might benefit up to 6 h from stroke onset. METHODS: In this international, multicentre, randomised, open-treatment trial, patients were allocated to 0.9 mg/kg intravenous recombinant tissue plasminogen activator (rt-PA) or to control. The primary analysis was of the proportion of patients alive and independent, as defined by an Oxford Handicap Score (OHS) of 0-2 at 6 months. The study is registered, ISRCTN25765518. FINDINGS: 3035 patients were enrolled by 156 hospitals in 12 countries. All of these patients were included in the analyses (1515 in the rt-PA group vs 1520 in the control group), of whom 1617 (53%) were older than 80 years of age. At 6 months, 554 (37%) patients in the rt-PA group versus 534 (35%) in the control group were alive and independent (OHS 0-2; adjusted odds ratio [OR] 1.13, 95% CI 0.95-1.35, p=0.181; a non-significant absolute increase of 14/1000, 95% CI -20 to 48). An ordinal analysis showed a significant shift in OHS scores; common OR 1.27 (95% CI 1.10-1.47, p=0.001). Fatal or non-fatal symptomatic intracranial haemorrhage within 7 days occurred in 104 (7%) patients in the rt-PA group versus 16 (1%) in the control group (adjusted OR 6.94, 95% CI 4.07-11.8; absolute excess 58/1000, 95% CI 44-72). More deaths occurred within 7 days in the rt-PA group (163 [11%]) than in the control group (107 [7%], adjusted OR 1.60, 95% CI 1.22-2.08, p=0.001; absolute increase 37/1000, 95% CI 17-57), but between 7 days and 6 months there were fewer deaths in the rt-PA group than in the control group, so that by 6 months, similar numbers, in total, had died (408 [27%] in the rt-PA group vs 407 [27%] in the control group). INTERPRETATION: For the types of patient recruited in IST-3, despite the early hazards, thrombolysis within 6 h improved functional outcome. Benefit did not seem to be diminished in elderly patients. FUNDING: UK Medical Research Council, Health Foundation UK, Stroke Association UK, Research Council of Norway, Arbetsmarknadens Partners Forsakringsbolag (AFA) Insurances Sweden, Swedish Heart Lung Fund, The Foundation of Marianne and Marcus Wallenberg, Polish Ministry of Science and Education, the Australian Heart Foundation, Australian National Health and Medical Research Council (NHMRC), Swiss National Research Foundation, Swiss Heart Foundation, Assessorato alla Sanita, Regione dell'Umbria, Italy, and Danube University


BACKGROUND: Recombinant tissue plasminogen activator (rt-PA, alteplase) improved functional outcome in patients treated soon after acute ischaemic stroke in randomised trials, but licensing is restrictive and use varies widely. The IST-3 trial adds substantial new data. We therefore assessed all the evidence from randomised trials for rt-PA in acute ischaemic stroke in an updated systematic review and meta-analysis. METHODS: We searched for randomised trials of intravenous rt-PA versus control given within 6 h of onset of acute ischaemic stroke up to March 30, 2012. We estimated summary odds ratios (ORs) and 95% CI in the primary analysis for prespecified outcomes within 7 days and at the final follow-up of all patients treated up to 6 h after stroke. FINDINGS: In up to 12 trials (7012 patients), rt-PA given within 6 h of stroke significantly increased the odds of being alive and independent (modified Rankin Scale, mRS 0-2) at final follow-up (1611/3483 [46.3%] vs 1434/3404 [42.1%], OR 1.17, 95% CI 1.06-1.29; p=0.001), absolute increase of 42 (19-66) per 1000 people treated, and favourable outcome (mRS 0-1) absolute increase of 55 (95% CI 33-77) per 1000. The benefit of rt-PA was greatest in patients treated within 3 h (mRS 0-2, 365/896 [40.7%] vs 280/883 [31.7%], 1.53, 1.26-1.86, p<0.0001),
absolute benefit of 90 (46-135) per 1000 people treated, and mRS 0-1 (283/896 [31.6%] vs 202/883 [22.9%], 1.61, 1.30-1.90; p=0.0001), absolute benefit 87 (46-128) per 1000 treated. Numbers of deaths within 7 days were increased (250/2807 [8.9%] vs 174/2728 [6.4%], 1.44, 1.18-1.76; p=0.0003), but by final follow-up the excess was no longer significant (679/3548 [19.1%] vs 640/3464 [18.5%], 1.06, 0.94-1.20; p=0.33). Symptomatic intracranial haemorrhage (272/3548 [7.7%] vs 63/3463 [1.8%], 3.72, 2.98-4.64; p<0.0001) accounted for most of the early excess deaths. Patients older than 80 years achieved similar benefit to those aged 80 years or younger, particularly when treated early. INTERPRETATION: The evidence indicates that intravenous rt-PA increased the proportion of patients who were alive with favourable outcome and alive and independent at final follow-up. The data strengthen previous evidence to treat patients as early as possible after acute ischaemic stroke, although some patients might benefit up to 6 h after stroke. FUNDING: UK Medical Research Council, Stroke Association, University of Edinburgh, National Health Service Health Technology Assessment Programme, Swedish Heart-Lung Fund, AFA Insurances Stockholm (Arbetsmarknadsens Partners Forsakringsbolag), Karolinska Institute, Marianne and Marcus Wallenberg Foundation, Research Council of Norway, Oslo University Hospital


OBJECTIVE: To assess the effect of tranexamic acid on blood transfusion, thromboembolic events, and mortality in surgical patients. DESIGN: Systematic review and meta-analysis. DATA SOURCES: Cochrane central register of controlled trials, Medline, and Embase, from inception to September 2011, the World Health Organization International Clinical Trials Registry Platform, and the reference lists of relevant articles. STUDY SELECTION: Randomised controlled trials comparing tranexamic acid with no tranexamic acid or placebo in surgical patients. Outcome measures of interest were the number of patients receiving a blood transfusion; the number of patients with a thromboembolic event (myocardial infarction, stroke, deep vein thrombosis, and pulmonary embolism); and the number of deaths. Trials were included irrespective of language or publication status. RESULTS: 129 trials, totalling 10,488 patients, carried out between 1972 and 2011 were included. Tranexamic acid reduced the probability of receiving a blood transfusion by a third (risk ratio 0.62, 95% confidence interval 0.58 to 0.65; P<0.001). This effect remained when the analysis was restricted to trials using adequate allocation concealment (0.68, 0.62 to 0.74; P<0.001). 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) was uncertain. Fewer deaths occurred in the tranexamic acid group (0.61, 0.38 to 0.98; P = 0.04), although when the analysis was restricted to trials using adequate concealment there was considerable uncertainty (0.67, 0.33 to 1.34; P = 0.25). Cumulative meta-analysis showed that reliable evidence that tranexamic acid reduces the need for transfusion has been available for over 10 years. CONCLUSIONS: Strong evidence that tranexamic acid reduces blood transfusion in surgery has been available for many years. Further trials on the effect of tranexamic acid on blood transfusion are unlikely to add useful new information. However, the effect of tranexamic acid on thromboembolic events and mortality remains uncertain. Surgical patients should be made aware of this evidence so that they can make an informed choice.

(60) DANDONA L, PRASAD J. Strengthening primary healthcare in India. BMJ. 2012, vol. 344, p.e3410


OBJECTIVE: To analyse the effect of task oriented circuit training compared with usual physiotherapy in terms of self reported walking competency for patients with stroke discharged from a rehabilitation centre to their own home. DESIGN: Randomised controlled trial with follow-up to 24 weeks. SETTING: Multicentre trial in nine outpatient rehabilitation centres in the Netherlands PARTICIPANTS: Patients with stroke who were able to walk a minimum of 10 m without physical assistance and were discharged from inpatient rehabilitation to an outpatient rehabilitation clinic. Patients were randomly allocated to circuit training or usual physiotherapy, after stratification by rehabilitation centre, with an online randomisation procedure. INTERVENTION: Patients in the intervention group received circuit training in 90 minute sessions twice a week for 12 weeks. The training included eight different workstations in a gym and was intended to improve performance in tasks relating to walking competency. The control group received usual outpatient physiotherapy. MAIN OUTCOME MEASURES: The primary outcome was the mobility domain of the stroke impact scale (SIS, version 3.0). Secondary outcomes were standing balance, self reported abilities, gait speed, walking distance, stair climbing, instrumental activities of daily living, fatigue, anxiety, and depression. Differences between groups were analysed according to the intention to treat principle. All outcomes were assessed by blinded observers in a repeated measurement design lasting 24 weeks. RESULTS: 126 patients were included in the circuit training group and 124 in the usual care group (control), with data from 125 and 117, respectively, available for analysis. One patient from the circuit training group and seven from the control group dropped out. Circuit training was a safe intervention, and no serious adverse events were reported. There were no significant differences between groups for the stroke impact scale mobility domain (beta=0.05 (SE 0.68), P=0.943) at 12 weeks. Circuit training was associated with significantly higher scores in terms of gait speed (0.09 m/s (SE 0.02), P<0.001), walking distance (20.0 m (SE 7.4), P=0.007), and modified stairs test (-1.6 s (SE 0.7), P=0.015). There were no significant differences between groups for the other secondary outcomes, except for the leisure domain of the Nottingham extended activities of daily living and the memory and thinking domain of the stroke impact scale. With the exception of gait speed (-0.04 m/s (SE 0.02), P=0.040), there were no significant differences between groups at follow-up. CONCLUSION: Task oriented circuit training can safely replace usual physiotherapy for patients with stroke who are discharged from inpatient rehabilitation to the community and need further training in gait and gait related activities as an outpatient. TRIAL REGISTRATION: Dutch Trial Register (NTR1534)


Primary CNS vasculitis is an uncommon disorder of unknown cause that is restricted to brain and
spinal cord. The median age of onset is 50 years. The neurological manifestations are diverse, but generally consist of headache, altered cognition, focal weakness, or stroke. Serological markers of inflammation are usually normal. Cerebrospinal fluid is abnormal in about 80-90% of patients. Diagnosis is unlikely in the presence of a normal MRI of the brain. Biopsy of CNS tissue showing vasculitis is the only definitive test; however, angiography has often been used for diagnosis even though it has only moderate sensitivity and specificity. The size of the affected vessels varies and determines outcome and response to treatment. Early recognition is important because treatment with corticosteroids with or without cytotoxic drugs can often prevent serious outcomes. The differential diagnosis includes reversible cerebral vasoconstriction syndromes and secondary cerebral vasculitis


BACKGROUND: Carotid intima-media thickness (cIMT) is related to the risk of cardiovascular events in the general population. An association between changes in cIMT and cardiovascular risk is frequently assumed but has rarely been reported. Our aim was to test this association.

METHODS: We identified general population studies that assessed cIMT at least twice and followed up participants for myocardial infarction, stroke, or death. The study teams collaborated in an individual participant data meta-analysis. Excluding individuals with previous myocardial infarction or stroke, we assessed the association between cIMT progression and the risk of cardiovascular events (myocardial infarction, stroke, vascular death, or a combination of these) for each study with Cox regression. The log hazard ratios (HRs) per SD difference were pooled by random effects meta-analysis.

FINDINGS: Of 21 eligible studies, 16 with 36,984 participants were included. During a mean follow-up of 7.0 years, 1519 myocardial infarctions, 1339 strokes, and 2028 combined endpoints (myocardial infarction, stroke, vascular death) occurred. Yearly cIMT progression was derived from two ultrasound visits 2-7 years (median 4 years) apart. For mean common carotid artery intima-media thickness progression, the overall HR of the combined endpoint was 0.97 (95% CI 0.94-1.00) when adjusted for age, sex, and mean common carotid artery intima-media thickness, and 0.98 (0.95-1.01) when also adjusted for vascular risk factors.

Although we detected no associations with cIMT progression in sensitivity analyses, the mean cIMT of the two ultrasound scans was positively and robustly associated with cardiovascular risk (HR for the combined endpoint 1.16, 95% CI 1.10-1.22, adjusted for age, sex, mean common carotid artery intima-media thickness progression, and vascular risk factors). In three studies including 3439 participants who had four ultrasound scans, cIMT progression did not correlate between occasions (reproducibility correlations between r=-0.06 and r=-0.02).

INTERPRETATION: The association between cIMT progression assessed from two ultrasound scans and cardiovascular risk in the general population remains unproven. No conclusion can be derived for the use of cIMT progression as a surrogate in clinical trials. FUNDING: Deutsche Forschungsgemeinschaft


BACKGROUND: Understanding the signs and symptoms of heart attacks and strokes are important not only in saving lives, but also in preserving quality of life. Findings from recent research have yielded that the prevalence of cardiovascular disease risk factors are higher in rural populations, suggesting that adults living in rural locales may be at higher risk for heart attack and/or stroke. Knowledge of heart attack and stroke symptomology as well as calling 911 for a suspected heart attack or stroke are essential first steps in seeking care. This study sought to
examine the knowledge of heart attack and stroke symptoms among rural adults in comparison to non-rural adults living in the U.S. METHODS: Using multivariate techniques, a cross-sectional analysis of an amalgamated multi-year Behavioral Risk Factor Surveillance Survey (BRFSS) database was performed. The dependent variable for this analysis was low heart attack and stroke knowledge score. The covariates for the analysis were: age, sex, race/ethnicity, annual household income, attained education, health insurance status, having a health care provider (HCP), timing of last routine medical check-up, medical care deferment because of cost, self-defined health status and geographic locale. RESULTS: The weighted n for this study overall was 103,262,115 U.S. adults > =18 years of age. Approximately 22.0% of these respondents were U.S. adults living in rural locales. Logistic regression analysis revealed that those U.S. adults who had low composite heart attack and stroke knowledge scores were more likely to be rural (OR=1.218 95%CI 1.216-1.219) rather than non-rural residents. Furthermore, those with low scores were more likely to be: male (OR=1.353 95%CI 1.352-1.354), >65 years of age (OR=1.369 95%CI 1.368-1.371), African American (OR=1.892 95%CI 1.889-1.894), not educated beyond high school (OR=1.400 95%CI 1.399-1.402), uninsured (OR=1.308 95%CI 1.3-6-1.310), without a HCP (OR=1.216 95%CI 1.215-1.218), and living in a household with an annual income of < $50,000 (OR=1.429 95%CI 1.428-1.431). CONCLUSIONS: Analysis identified clear disparities between the knowledge levels U.S. adults have regarding heart attack and stroke symptoms. These disparities should guide educational endeavors focusing on improving knowledge of heart attack and stroke symptoms.


BACKGROUND: Conflicting results have been recently reported evaluating the relationship between pneumococcal vaccination and the risk of thrombotic vascular events. This study assessed the clinical effectiveness of the 23-valent polysaccharide pneumococcal vaccine (PPV23) against acute myocardial infarction and ischaemic stroke in older adults. METHODS: Population-based prospective cohort study conducted from December 1, 2008 until November 30, 2009, including all individuals >= 60 years-old assigned to nine Primary Care Centres in Tarragona, Spain (N = 27,204 individuals). Primary outcomes were hospitalisation for acute myocardial infarction and/or ischaemic stroke. All cases were validated by checking clinical records. The association between pneumococcal vaccination and the risk of each outcome was evaluated by Multivariable Cox proportional-hazard models (adjusted by age, sex, influenza vaccine status, presence of comorbidities and cardiovascular risk factors). RESULTS: Cohort members were followed for a total of 26,444 person-years, of which 34% were for vaccinated subjects. Overall incidence rates (per 1000 person-years) were 4.9 for myocardial infarction and 4.6 for ischaemic stroke. In the multivariable analysis, vaccination was associated with a marginally significant 35% lower risk of stroke (hazard ratio [HR]: 0.65; 95% confidence interval [CI]: 0.42-0.99; p = 0.046). We found no evidence for an association between pneumococcal vaccination and reduced risk of myocardial infarction (HR: 0.83; 95% CI: 0.56-1.22; p = 0.347). CONCLUSIONS: Our data supports a benefit of PPV23 against ischaemic stroke among the general population over 60 years, suggesting a possible protective role of pneumococcal vaccination against some acute thrombotic events.

(67) BOZORGMANESH M. Added predictive ability of the information on job strain beyond the standard Framingham risk score. Int J Epidemiol. 2012 Feb., vol. 41, n° 1, pp.322-324

BACKGROUND: Physical activity (PA) is inversely associated with mortality in the general population. We wanted to quantify the association of self-reported PA with mortality from all causes, ischaemic heart disease (IHD) and stroke, and compare it with other known risk factors in different age segments. METHODS: The Bergen Clinical Blood Pressure Survey examined a sample of 6811 Norwegian men and women in 1965-71 with follow-up until 2005-07. Cox proportional hazard regression ratio (HR) and population attributable fraction (PAF) were calculated for the old (>65), middle-aged (45-64) and young adults (22-44), respectively. We minimized confounding and bias by progressive comprehensive adjustments and subgroup-analyses (excluding early follow-up deaths, participants with self-reported disease and participants with changes in their PA-level prior baseline due to disease). RESULTS: The HR [95% confidence interval (CI)] associated with a high PA-level was 0.63(0.56-0.71), 0.66(0.52-0.83) and 0.66(0.47-0.93) for mortality from all causes, IHD and stroke, respectively (reference: no participation in any of the listed activities, adjusted for age and gender). PAF (95% CI) of no/low activity (reference: any activity) was consistent across all age groups, varying from 7.3% (3.4-11.4) in the young adults to 9.1% (3.6-15.3) in the old. PAF of smoking and high s-cholesterol declined with increasing age [smoking from 19.9% (15.3-24.7) to 1.5% (-1.3 to 6.2) and s-cholesterol from 11.5% (5.6-17.5) to -9.5% (-18.1 to -0.7)], whereas PAF of hypertension increased from 5.3% (2.1-9.1) to 18.9% (8.3-28.4). CONCLUSION: The relative importance of traditional risk factors varies between the age groups, but physical activity is a major health promoting factor across all age segments and should be encouraged particularly in an ageing population.


BACKGROUND: As the incidence of stroke has increased, its impact on society has increased accordingly, while it continues to have a major impact on the individual. New strategies to further improve the quality, efficiency and logistics of stroke services are necessary. Early discharge from hospital to a nursing home with an adequate rehabilitation programme could help to optimise integrated care for stroke patients. The objective is to describe the design of a non-randomised comparative study evaluating early admission to a nursing home, with multidisciplinary assessment, for stroke patients. The study is comprised of an effect evaluation, an economic evaluation and a process evaluation. METHODS/DESIGN: The design involves a non-randomised comparative trial for two groups. Participants are followed for 6 months from the time of stroke. The intervention consists of a redesigned care pathway for stroke patients. In this care pathway, patients are discharged from hospital to a nursing home within 5 days, in comparison with 12 days in the usual situation. In the nursing home a structured assessment takes place, aimed at planning adequate rehabilitation. People in the control group receive the usual care. The main outcome measures of the effect evaluation are quality of life and daily functioning. In addition, an economic evaluation will be performed from a societal perspective. A process evaluation will be carried out to evaluate the feasibility of the intervention as well as the experiences and opinions of patients and professionals. DISCUSSION: The results of this study will provide information about the cost effectiveness of the intervention and its effects on clinical outcomes and quality of life. Relevant strengths and weaknesses of the study are addressed in this article. TRIAL REGISTRATION: Current Controlled Trails ISRCTN58135104


BACKGROUND: Observational studies have suggested a complex relationship between alcohol...
consumption and stroke, dependent on sex, type of stroke and outcome (morbidity vs. mortality). We undertook a systematic review and a meta-analysis of studies assessing the association between levels of average alcohol consumption and relative risks of ischemic and hemorrhagic strokes separately by sex and outcome. This meta-analysis is the first to explicitly separate morbidity and mortality of alcohol-attributable stroke and thus has implications for public health and prevention. METHODS: Using Medical Subject Headings (alcohol drinking, ethanol, cerebrovascular accident, cerebrovascular disorders, and intracranial embolism and thrombosis and the key word stroke), a literature search of MEDLINE, EMBASE, CINAHL, CABS, WHOList, SIGLE, ETOH, and Web of Science databases between 1980 to June 2009 was performed followed by manual searches of bibliographies of key retrieved articles. From twenty-six observational studies (cohort or case-control) with ischemic or hemorrhagic strokes the relative risk or odds ratios or hazard ratios of stroke associated with alcohol consumption were reported; alcohol consumption was quantified; and life time abstention (manually estimated where data for current abstainers were given) was used as the reference group. Two reviewers independently extracted the information on study design, participant characteristics, level of alcohol consumption, stroke outcome, control for potential confounding factors, risk estimates and key criteria of study quality using a standardized protocol. RESULTS: The dose-response relationship for hemorrhagic stroke had monotonically increasing risk for increasing consumption, whereas ischemic stroke showed a curvilinear relationship, with a protective effect of alcohol for low to moderate consumption, and increased risk for higher exposure. For more than 3 drinks on average/day, in general women had higher risks than men, and the risks for mortality were higher compared to the risks for morbidity. CONCLUSIONS: These results indicate that heavy alcohol consumption increases the relative risk of any stroke while light or moderate alcohol consumption may be protective against ischemic stroke. Preventive measures that should be initiated are discussed.


CONTEXT: Anecdotal reports suggest bariatric surgery may increase the risk of alcohol use disorder (AUD), but prospective data are lacking. OBJECTIVE: To determine the prevalence of preoperative and postoperative AUD, and independent predictors of postoperative AUD. DESIGN, SETTING, AND PARTICIPANTS: A prospective cohort study (Longitudinal Assessment of Bariatric Surgery-2) of adults who underwent bariatric surgery at 10 US hospitals. Of 2458 participants, 1945 (78.8% female; 87.0% white; median age, 47 years; median body mass index, 45.8) completed preoperative and postoperative (at 1 year and/or 2 years) assessments between 2006 and 2011. MAIN OUTCOME MEASURE: Past year AUD symptoms determined with the Alcohol Use Disorders Identification Test (indication of alcohol-related harm, alcohol dependence...
BACKGROUND: Hazardous drinking among adolescents is a major public health concern. The purpose of this study was to examine the prevalence of binge drinking/alcohol consumption and its association with different types of friendship networks, gender and socioeconomic status among students in Belo Horizonte, Minas Gerais, Brazil. METHODS: We conducted a cross-sectional study on a representative random sample of 891 adolescents (41% male, aged 15-19 years) from public and private schools in 2009. Information on friendship networks and binge drinking was collected using two validated self-administered questionnaires: the Integrated Questionnaire for the Measurement of Social Capital and the first 3 items in the Alcohol Use Disorders Identification Test (AUDIT C). We used the area-based Social Vulnerability Index (SVI), mother and father’s educational background, and the type of school to assess socioeconomic status. The chi-squared test was used to examine the associations between sample characteristics or the type of friends and binge drinking (p-values <0.05 were considered

RESULTS: The prevalence of AUD symptoms did not significantly differ from 1 year before to 1 year after bariatric surgery (7.6% vs 7.3%; P = 0.98), but was significantly higher in the second postoperative year (9.6%; P = 0.01). The following preoperative variables were independently related to an increased odds of AUD after bariatric surgery: male sex (adjusted odds ratio [AOR], 2.14 [95% CI, 1.51-3.01]; P < 0.001), younger age (age per 10 years younger with preoperative AUD: AOR, 1.31 [95% CI, 1.03-1.68]; P = 0.03; age per 10 years younger without preoperative AUD: AOR, 1.95 [95% CI, 1.65-2.30]; P < 0.001), smoking (AOR, 2.58 [95% CI, 1.19-5.58]; P = 0.02), regular alcohol consumption (>2 drinks/week: AOR, 6.37 [95% CI, 4.17-9.72]; P < 0.001), AUD (eg, at age 45, AOR, 11.14 [95% CI, 7.71-16.10]; P < 0.001), recreational drug use (AOR, 2.38 [95% CI, 1.37-4.14]; P = 0.01), lower sense of belonging (12-item Interpersonal Support Evaluation List score per 1 point lower: AOR, 1.09 [95% CI, 1.04-1.15]; P = 0.01), and undergoing a Roux-en-Y gastric bypass procedure (AOR, 2.07 [95% CI, 1.40-3.08]; P < 0.001; reference category: laparoscopic adjustable gastric band procedure). CONCLUSION: In this cohort, the prevalence of AUD was greater in the second postoperative year than the year prior to surgery or in the first postoperative year and was associated with male sex and younger age, numerous preoperative variables (smoking, regular alcohol consumption, AUD, recreational drug use, and lower interpersonal support) and undergoing a Roux-en-Y gastric bypass procedure.
statistically significant). Ordinal logistic regression was used to estimate the association between binge drinking and the independent variables. RESULTS: A total of 321 (36%) adolescents reported binge drinking (5 or more drinks in one occasion), and among them, 233 (26.2%) adolescents reported binge drinking less than monthly to monthly, and 88 (9.9%) weekly to daily. Binge drinking was associated with being male (OR = 1.52, 95% CI 1.01-2.28) and with living in a low vulnerability area (having the best housing conditions, schooling, income, jobs, legal assistance and health) (OR = 1.66, 95% CI 1.05-2.62). Students who reported that their closest friends were from school (as opposed to friends from church) had an increased risk of binge drinking (OR = 3.55, 95% CI 1.91-5.87). In analyses stratified by gender, the association was significant only among the female students. CONCLUSIONS: The prevalence of binge drinking was high in this sample of Brazilian adolescents, and gender, low social vulnerability and friendship network were associated with binge drinking (6)


OBJECTIVES: We examined associations among 3 dimensions of sexual orientation (identity, behavior, and attraction) and key health-related indicators commonly studied among sexual minority populations: depressive symptoms, perceived stress, smoking, binge drinking, and victimization. METHODS: We analyzed data from the National Longitudinal Study of Adolescent Health, Wave IV (2007-2008) when respondents were aged 24 to 32 years (n=14,412). We used multivariate linear and logistic regressions to examine consistency of associations between sexual orientation measures and health-related indicators. RESULTS: Strength of associations differed by gender and sexual orientation measure. Among women, being attracted to both sexes, identifying as "mostly straight" or "bisexual," and having mostly opposite-sex sexual partners was associated with greater risk for all indicators. Among men, sexual attraction was unrelated to health indicators. Men who were "mostly straight" were at greater risk for some, but not all, indicators. Men who had sexual partners of the same-sex or both sexes were at lower risk for binge drinking. CONCLUSIONS: Using all 3 dimensions of sexual orientation provides a more complete picture of the association between sexual orientation and health among young adults than does using any 1 dimension alone
genotyping quality control in 227 samples from Africa, Asia and Oceania provides genome-wide estimates of allele frequency distribution, population structure and linkage disequilibrium. By comparing the genetic diversity of individual infections with that of the local parasite population, we derive a metric of within-host diversity that is related to the level of inbreeding in the population. An open-access web application has been established for the exploration of regional differences in allele frequency and of highly differentiated loci in the P. falciparum genome.


BACKGROUND: In order to achieve universal health coverage, the government of Anambra State, southeast Nigeria has distributed free Long-lasting Insecticide treated Nets (LLINs) to the general population and delivered free Artemisinin-based Combination Therapy (ACT) to pregnant women and children less than 5 years. However, the levels of coverage with LLINS and ACTs is not clear, especially coverage of different socio-economic status (SES) population groups. This study was carried out to determine the level of coverage and access to LLINs and ACTs amongst different SES groups. METHODS: A questionnaire was used to collect data from randomly selected households in 19 local government areas of the State. Selected households had a pregnant woman and/or a child less than 5 years. The lot quality assurance sampling (LQAS) methodology was used in sampling. The questionnaire explored the availability and utilization of LLINs and ACTs from 2394 households. An asset-based SES index was used to examine the level of access of LLINS and ACTs to different SES quintiles. RESULTS: It was found that 80.5% of the households had an LLIN and 64.4% of the households stated that they actually used the nets the previous night. The findings showed that 42.3% of pregnant women who had fever within the past month received ACTs, while 37.5% of children<5 years old who had malaria in the past month had received ACTs. There was equity in ownership of nets for the range 1-5 nets per household. No significant SES difference was found in use of ACTs for treatment of malaria in children under five years old and in pregnant women. CONCLUSIONS: The free distribution of LLINs and ACTs increased household coverage of both malaria control interventions and bridged the equity gap in access to them among the most vulnerable groups.


In response to widespread overuse of antimalarial drugs, the World Health Organisation changed guidelines in 2010 to restrict the use of antimalarials to parasitologically confirmed malaria cases. Malaria rapid diagnostic tests (RDTs) have been presented as a means to realize the new guidelines, and National Malaria Control Programmes, including that of Cameroon, are developing plans to introduce the tests to replace microscopy or clinical diagnosis at public health facilities.
across the country. We aimed to understand how malaria tests and antimalarial drugs are currently used as part of social interactions between health workers and patients at public and mission health facilities in Yaounde and Bamenda and surrounding districts in the Northwest region of Cameroon. In May to June 2010, we held 17 focus group discussions with 146 health workers involved in clinical care from 49 health facilities. Clinicians enacted malaria as a ‘juggling’ exercise, involving attention to pathophysiology of the patient as well as their desires and medical reputations, utilising tests and medicines for their therapeutic effects as symbols in the process of care. Parasites were rarely mentioned in describing diagnostic decisions. These enactments of malaria contrast with evidence-based guidelines emanating from WHO, which assume the parasite is the central driver of practice. If RDTs are to be taken up in practice, public health practitioners need to pay careful attention to the values and priorities of health workers and patients if they are to work with them to improve diagnosis and treatment of febrile illnesses.


BACKGROUND: The adverse impact of Plasmodium vivax on child health beyond acute febrile illness is poorly studied. The effect of vivax malaria on child growth was evaluated and compared with diarrhoeal disease and non-specific fever. METHODS: Using data from a 43-month longitudinal cohort of children 0-72 months of age (n = 442) in the Peruvian Amazon, ponderal and linear growth velocities over 2-, 4- and 6-month periods were examined using longitudinal models and related to the incidence of disease during the same period. RESULTS: An episode of vivax malaria led to 138.6 g (95% confidence interval (CI) 81.9-195.4), 108.6 g (62.8-153.2) and 61 g (20.9-101.1) less weight gain over 2-, 4- and 6-month intervals, respectively. These deficits were larger than both diarrhoea (21.9, 17.2 and 13.8 g less weight gain, respectively) and fever (39.0, 30.3 and 25.6 g less weight gain, respectively). An incident episode of vivax also led to 0.070 cm (0.004-0.137) and 0.083 cm (0.015-0.151) less linear growth over 4 and 6 months, respectively, which were also larger than deficits from diarrhoea (0.029 and 0.028 cm, respectively) and fever (not associated with linear growth deficits). Despite the larger effect of P. vivax incident episodes on growth of a particular child, diarrhoeal disease had a larger cumulative impact on growth deficits as diarrhoeal incidence rates in this community were >10-fold higher than vivax malaria. CONCLUSIONS: Disease control measures for vivax malaria and diarrhoeal disease have the potential to improve the growth of children in endemic areas.
obese matched controls (with matching performed on a group, rather than individual, level). None of the participants had diabetes at baseline. Patients in the bariatric-surgery cohort underwent banding (19%), vertical banded gastroplasty (69%), or gastric bypass (12%); nonrandomized, matched, prospective controls received usual care. Participants were 37 to 60 years of age, and the body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) was 34 or more in men and 38 or more in women. This analysis focused on the rate of incident type 2 diabetes, which was a prespecified secondary end point in the main study. At the time of this analysis (January 1, 2012), participants had been followed for up to 15 years. Despite matching, some baseline characteristics differed significantly between the groups; the baseline body weight was higher and risk factors were more pronounced in the bariatric-surgery group than in the control group. At 15 years, 36.2% of the original participants had dropped out of the study, and 30.9% had not yet reached the time for their 15-year follow-up examination. RESULTS: During the follow-up period, type 2 diabetes developed in 392 participants in the control group and in 110 in the bariatric-surgery group, corresponding to incidence rates of 28.4 cases per 1000 person-years and 6.8 cases per 1000 person-years, respectively (adjusted hazard ratio with bariatric surgery, 0.17; 95% confidence interval, 0.13 to 0.21; P<0.001). The effect of bariatric surgery was influenced by the presence or absence of impaired fasting glucose (P=0.002 for the interaction) but not by BMI (P=0.54). Sensitivity analyses, including end-point imputations, did not change the overall conclusions. The postoperative mortality was 0.2%, and 2.8% of patients who underwent bariatric surgery required reoperation within 90 days owing to complications. CONCLUSIONS: Bariatric surgery appears to be markedly more efficient than usual care in the prevention of type 2 diabetes in obese persons. (Funded by the Swedish Research Council and others; ClinicalTrials.gov number, NCT01479452.)


CONTEXT: Type 2 diabetes in normal-weight adults (body mass index [BMI] <25) is a representation of the metabolically obese normal-weight phenotype with unknown mortality consequences. OBJECTIVE: To test the association of weight status with mortality in adults with new-onset diabetes in order to minimize the influence of diabetes duration and voluntary weight loss on mortality. DESIGN, SETTING, AND PARTICIPANTS: Pooled analysis of 5 longitudinal cohort studies: Atherosclerosis Risk in Communities study, 1990-2006; Cardiovascular Health Study, 1992-2008; Coronary Artery Risk Development in Young Adults, 1987-2011; Framingham Offspring Study, 1979-2007; and Multi-Ethnic Study of Atherosclerosis, 2002-2011. A total of 2625 participants with incident diabetes contributed 27,125 person-years of follow-up. Included were men and women (age >40 years) who developed incident diabetes based on fasting glucose 126 mg/dL or greater or newly initiated diabetes medication and who had concurrent measurements of BMI. Participants were classified as normal weight if their BMI was 18.5 to 24.99 or overweight/obese if BMI was 25 or greater. MAIN OUTCOME MEASURES: Total, cardiovascular, and noncardiovascular mortality. RESULTS: The proportion of adults who were normal weight at the time of incident diabetes ranged from 9% to 21% (overall 12%). During follow-up, 449 participants died: 178 from cardiovascular causes and 253 from noncardiovascular causes (18 were not classified). The rates of total, cardiovascular, and noncardiovascular mortality were higher in normal-weight participants (284.8, 99.8, and 198.1 per 10,000 person-years, respectively) than in overweight/obese participants (152.1, 67.8, and 87.9 per 10,000 person-years, respectively). After adjustment for demographic characteristics and blood pressure, lipid levels, waist circumference, and smoking status, hazard ratios comparing normal-weight participants with overweight/obese participants for total, cardiovascular, and noncardiovascular
mortality were 2.08 (95% CI, 1.52-2.85), 1.52 (95% CI, 0.89-2.58), and 2.32 (95% CI, 1.55-3.48), respectively. CONCLUSION: Adults who were normal weight at the time of incident diabetes had higher mortality than adults who are overweight or obese.


(12) AFDHAL NH. Management of nonalcoholic fatty liver disease: a 60-year-old man with probable nonalcoholic fatty liver disease: weight reduction, liver biopsy, or both? JAMA. 2012 Aug. 8, vol. 308, n° 6, pp.608-616

Nonalcoholic fatty liver disease (NAFLD) is one of the most common hepatic disorders in the United States, but uncertainty remains as to the optimal way to manage it. Using the case of Mr T, a 60-year-old man with obesity, diabetes mellitus, and increased serum transaminase levels, an evidence-based approach to diagnosis and treatment is discussed. Diagnosis of NAFLD is based on patient clinical profile and risk factors for metabolic syndrome, the exclusion of other liver diseases, radiologic imaging and sometimes biopsy. At this point in Mr T's disease, the most important step is differentiation between simple steatosis and nonalcoholic steatohepatitis (NASH). Simple steatosis has a benign natural history, but NASH is progressive and may lead to cirrhosis, liver failure, and liver cancer. An evidence-based approach to treatment is limited by lack of large randomized trials, particularly of combinations of therapies, but weight loss, exercise, and medical therapies targeted at the mechanism of liver injury in NASH are recommended. Improved noninvasive diagnostic tests, a clearer understanding of the natural history of NAFLD, and large, well-designed clinical trials are needed.

CONTEXT: Reduced energy expenditure following weight loss is thought to contribute to weight gain. However, the effect of dietary composition on energy expenditure during weight-loss maintenance has not been studied. OBJECTIVE: To examine the effects of 3 diets differing widely in macronutrient composition and glycemic load on energy expenditure following weight loss.

DESIGN, SETTING, AND PARTICIPANTS: A controlled 3-way crossover design involving 21 overweight and obese young adults conducted at Children's Hospital Boston and Brigham and Women's Hospital, Boston, Massachusetts, between June 16, 2006, and June 21, 2010, with recruitment by newspaper advertisements and postings. INTERVENTION: After achieving 10% to 15% weight loss while consuming a run-in diet, participants consumed an isocaloric low-fat diet (60% of energy from carbohydrate, 20% from fat, 20% from protein; high glycemic load), low-glycemic index diet (40% from carbohydrate, 40% from fat, and 20% from protein; moderate glycemic load), and very low-carbohydrate diet (10% from carbohydrate, 60% from fat, and 30% from protein; low glycemic load) in random order, each for 4 weeks. MAIN OUTCOME MEASURES: Primary outcome was resting energy expenditure (REE), with secondary outcomes of total energy expenditure (TEE), hormone levels, and metabolic syndrome components.

RESULTS: Compared with the pre-weight-loss baseline, the decrease in REE was greatest with the low-fat diet (mean [95% CI], -205 [-265 to -144] kcal/d), intermediate with the low-glycemic index diet (-166 [-227 to -106] kcal/d), and least with the very low-carbohydrate diet (-138 [-198 to -77] kcal/d; overall P = .03; P for trend by glycemic load = .009). The decrease in TEE showed a similar pattern (mean [95% CI], -423 [-606 to -239] kcal/d; -297 [-479 to -115] kcal/d; and -97 [-281 to 86] kcal/d, respectively; overall P = .003; P for trend by glycemic load <.001). Hormone levels and metabolic syndrome components also varied during weight maintenance by diet (leptin, P < .001; 24-hour urinary cortisol, P = .005; indexes of peripheral [P = .02] and hepatic [P = .03] insulin sensitivity; high-density lipoprotein [HDL] cholesterol, P < .001; non-HDL cholesterol, P < .001; triglycerides, P < .001; plasminogen activator inhibitor 1, P for trend = .04; and C-reactive protein, P for trend = .05), but no consistent favorable pattern emerged. CONCLUSION: Among overweight and obese young adults compared with pre-weight-loss energy expenditure, isocaloric feeding following 10% to 15% weight loss resulted in decreases in REE and TEE that were greatest with the low-fat diet, intermediate with the low-glycemic index diet, and least with the very low-carbohydrate diet. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00315354


CONTEXT: Given the obesity epidemic, effective but resource-efficient weight loss treatments are needed. Stepped-treatment approaches customize interventions based on milestone completion and can be more effective while costing less to administer than conventional treatment approaches. OBJECTIVE: To determine whether a stepped-care weight loss intervention (STEP) compared with a standard behavioral weight loss intervention (SBWI) would result in greater weight loss. DESIGN, SETTING, AND PARTICIPANTS: A randomized clinical trial of 363 overweight and obese adults (body mass index: 25-<40; age: 18-55 years, 33% nonwhite, and 83% female) who were randomized to SBWI (n = 165) or STEP (n = 198) at 2 universities affiliated with academic medical centers in the United States (Step-Up Study). Participants were enrolled between May 2008 and February 2010 and data collection was completed by September 2010. 

**References**


2011. INTERVENTIONS: All participants were placed on a low-calorie diet, prescribed increases in physical activity, and attended group counseling sessions ranging from weekly to monthly during an 18-month period. The SBWI group was assigned to a fixed program. Counseling frequency, type, and weight loss strategies could be modified every 3 months for the STEP group in response to observed weight loss as it related to weight loss goals. MAIN OUTCOME MEASURE: Mean change in weight over 18 months. Additional outcomes included resting heart rate and blood pressure, waist circumference, body composition, fitness, physical activity, dietary intake, and cost of the program. RESULTS: Of the 363 participants randomized, 260 (71.6%) provided a measure of mean change in weight over 18 months. The 18-month intervention resulted in weight decreasing from 93.1 kg (95% CI, 91.0 to 95.2 kg) to 85.6 kg (95% CI, 83.4 to 87.7 kg) (P < .001) in the SBWI group and from 92.7 kg (95% CI, 90.8 to 94.6 kg) to 86.4 kg (95% CI, 84.5 to 88.4 kg) in the STEP group (P < .001). The percentage change in weight from baseline to 18 months was -8.1% (95% CI, -9.4% to -6.9%) in the SBWI group (P < .001) compared with -6.9% (95% CI, -8.0% to -5.8%) in the STEP group (P < .001). Although the between-group difference in 18-month weight loss was not statistically different (-1.3 kg [95% CI, -2.8 to 0.2 kg]; P = .09), there was a significant group x time interaction effect (P = .03). The cost per participant was $1357 (95% CI, $1272 to $1442) for the SBWI group vs $785 (95% CI, $739 to $830) for the STEP group (P < .001). Both groups had significant and comparable improvements in resting heart rate, blood pressure level, and fitness. CONCLUSIONS: Among overweight and obese adults, the use of SBWI resulted in a greater mean weight loss than STEP over 18 months. Compared with SBWI, STEP resulted in clinically meaningful weight loss that cost less to implement. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00714168


OBJECTIVE: To study the long term consequences of low carbohydrate diets, generally characterised by concomitant increases in protein intake, on cardiovascular health. DESIGN: Prospective cohort study. SETTING: Uppsala, Sweden. PARTICIPANTS: From a random population sample, 43,396 Swedish women, aged 30-49 years at baseline, completed an extensive dietary questionnaire and were followed-up for an average of 15.7 years. MAIN OUTCOME MEASURES: Association of incident cardiovascular diseases (ascertained by linkage with nationwide registries), overall and by diagnostic category, with decreasing carbohydrate intake (in tenths), increasing protein intake (in tenths), and an additive combination of these variables (low carbohydrate-high protein score, from 2 to 20), adjusted for intake of energy, intake of saturated and unsaturated fat, and several non-dietary variables. RESULTS: A one tenth decrease in carbohydrate intake or increase in protein intake or a 2 unit increase in the low carbohydrate-high protein score were all statistically significantly associated with increasing incidence of cardiovascular disease overall (n=1270)--incidence rate ratio estimates 1.04 (95% confidence interval 1.00 to 1.08), 1.04 (1.02 to 1.06), and 1.05 (1.02 to 1.08). No heterogeneity existed in the association of any of these scores with the five studied cardiovascular outcomes: ischaemic heart disease (n=703), ischaemic stroke (n=294), haemorrhagic stroke (n=70), subarachnoid haemorrhage (n=121), and peripheral arterial disease (n=82). CONCLUSIONS: Low carbohydrate-high protein diets, used on a regular basis and without consideration of the nature of carbohydrates or the source of proteins, are associated with increased risk of cardiovascular disease

(18) RUDOLF M. Prevention of obesity through home visiting up to the age of 2 years. BMJ. 2012, vol. 344, p.e3931

OBJECTIVE: To assess the effectiveness of a home based early intervention on children's body mass index (BMI) at age 2. DESIGN: Randomised controlled trial. SETTING: The Healthy Beginnings Trial was conducted in socially and economically disadvantaged areas of Sydney, Australia, during 2007-10. PARTICIPANTS: 667 first time mothers and their infants. INTERVENTION: Eight home visits from specially trained community nurses delivering a staged home based intervention, one in the antenatal period, and seven at 1, 3, 5, 9, 12, 18 and 24 months after birth. Timing of the visits was designed to coincide with early childhood developmental milestones. MAIN OUTCOME MEASURES: The primary outcome was children's BMI (the healthy BMI ranges for children aged 2 are 14.12-18.41 for boys and 13.90-18.02 for girls). Secondary outcomes included infant feeding practices and TV viewing time when children were aged 2, according to a modified research protocol. The data collectors and data entry staff were blinded to treatment allocation, but the participating mothers were not blinded. RESULTS: 497 mothers and their children (75%) completed the trial. An intention to treat analysis in all 667 participants recruited, and multiple imputation of BMI for the 170 lost to follow-up and the 14 missing, showed that mean BMI was significantly lower in the intervention group (16.53) than in the control group (16.82), with a difference of 0.29 (95% confidence interval -0.55 to -0.02; P=0.04). CONCLUSIONS: The home based early intervention delivered by trained community nurses was effective in reducing mean BMI for children at age 2. TRIAL REGISTRATION: Australian Clinical Trial Registry No 12607000168459


Obesity and type-2 diabetes have increased markedly over the past few decades, in parallel. One of the major links between these two disorders is chronic, low-grade inflammation. Prolonged nutrient excess promotes the accumulation and activation of leukocytes in visceral adipose tissue (VAT) and ultimately other tissues, leading to metabolic abnormalities such as insulin resistance, type-2 diabetes and fatty-liver disease. Although invasion of VAT by pro-inflammatory macrophages is considered to be a key event driving adipose-tissue inflammation and insulin resistance, little is known about the roles of other immune system cell types in these processes. A unique population of VAT-resident regulatory T (Treg) cells was recently implicated in control of the inflammatory state of adipose tissue and, thereby, insulin sensitivity. Here we identify peroxisome proliferator-activated receptor (PPAR)-gamma, the ‘master regulator’ of adipocyte differentiation, as a crucial molecular orchestrator of VAT Treg cell accumulation, phenotype and function. Unexpectedly, PPAR-gamma expression by VAT Treg cells was necessary for complete restoration of insulin sensitivity in obese mice by the thiazolidinedione drug pioglitazone. These findings suggest a previously unknown cellular mechanism for this important class of thiazolidinedione drugs, and provide proof-of-principle that discrete populations of Treg cells with unique functions can be precisely targeted to therapeutic ends

(21) MAYOR S. Increasing global obesity to US level equates to an extra half a billion people in food energy demand. BMJ. 2012, vol. 344, p.e4255


CONTEXT: Anecdotal reports suggest bariatric surgery may increase the risk of alcohol use disorder (AUD), but prospective data are lacking. OBJECTIVE: To determine the prevalence of preoperative and postoperative AUD, and independent predictors of postoperative AUD. DESIGN, SETTING, AND PARTICIPANTS: A prospective cohort study (Longitudinal Assessment of Bariatric Surgery-2) of adults who underwent bariatric surgery at 10 US hospitals. Of 2458 participants, 1945 (78.8% female; 87.0% white; median age, 47 years; median body mass index, 45.8) completed preoperative and postoperative (at 1 year and/or 2 years) assessments between 2006 and 2011. MAIN OUTCOME MEASURE: Past year AUD symptoms determined with the Alcohol Use Disorders Identification Test (indication of alcohol-related harm, alcohol dependence symptoms, or score >/=8). RESULTS: The prevalence of AUD symptoms did not significantly differ from 1 year before to 1 year after bariatric surgery (7.6% vs 7.3%; P = .98), but was significantly higher in the second postoperative year (9.6%; P = .01). The following preoperative variables were independently related to an increased odds of AUD after bariatric surgery: male sex (adjusted odds ratio [AOR], 2.14 [95% CI, 1.51-3.01]; P < .001), younger age (age per 10 years younger with preoperative AUD: AOR, 1.31 [95% CI, 1.03-1.68]; P = .03; age per 10 years younger without preoperative AUD: AOR, 1.95 [95% CI, 1.65-2.30], P < .001), smoking (AOR, 2.58 [95% CI, 1.19-5.58]; P = .02), regular alcohol consumption (>2 drinks/week: AOR, 6.37 [95% CI, 4.17-9.72]; P < .001), AUD (eg, at age 45, AOR, 11.14 [95% CI, 7.71-16.10]; P < .001), recreational drug use (AOR, 2.38 [95% CI, 1.37-4.14]; P = .01), lower sense of belonging (12-item Interpersonal Support Evaluation List score per 1 point lower: AOR, 1.09 [95% CI, 1.04-1.15]; P = .01), and undergoing a Roux-en-Y gastric bypass procedure (AOR, 2.07 [95% CI, 1.40-3.08]; P < .001; reference category: laparoscopic adjustable gastric band procedure). CONCLUSION: In this cohort, the prevalence of AUD was greater in the second postoperative year than the year prior to surgery or in the first postoperative year and was associated with male sex and younger age, numerous preoperative variables (smoking, regular alcohol consumption, AUD, recreational drug use, and lower interpersonal support) and undergoing a Roux-en-Y gastric bypass procedure.


KERMODE-SCOTT B. Canadian MPs dismiss findings that food policies are leading to hunger and obesity. BMJ. 2012, vol. 344, p.e3550


OBJECTIVE: To evaluate the effects of dietary and lifestyle interventions in pregnancy on maternal and fetal weight and to quantify the effects of these interventions on obstetric outcomes.

DESIGN: Systematic review and meta-analysis. DATA SOURCES: Major databases from inception to January 2012 without language restrictions. STUDY SELECTION: Randomised controlled trials that evaluated any dietary or lifestyle interventions with potential to influence maternal weight during pregnancy and outcomes of pregnancy. DATA SYNTHESIS: Results summarised as relative risks for dichotomous data and mean differences for continuous data. RESULTS: We identified 44 relevant randomised controlled trials (7278 women) evaluating three categories of interventions: diet, physical activity, and a mixed approach. Overall, there was a 1.42 kg reduction (95% confidence interval 0.95 to 1.89 kg) in gestational weight gain with any intervention compared with control. With all interventions combined, there were no significant differences in birth weight (mean difference -50 g, -100 to 0 g) and 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 between the groups, though by itself physical activity was associated with reduced birth weight (mean difference -60 g, -120 to -10 g). Interventions were associated with a reduced the 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. Dietary intervention resulted in the largest reduction in maternal gestational weight gain (3.84 kg, 2.45 to 5.22 kg), with improved pregnancy outcomes compared with other interventions. The overall evidence rating was low to very low for important outcomes such as pre-eclampsia, gestational diabetes, gestational hypertension, and preterm delivery. CONCLUSIONS: Dietary and lifestyle interventions in pregnancy can reduce maternal gestational weight gain and improve outcomes for both mother and baby. Among the interventions, those based on diet are the most effective and are associated with reductions in maternal gestational weight gain and improved obstetric outcomes.


Childhood asthma, a growing health concern, has been associated with low birth weight and elevated body mass index. This study tested the hypothesis that overweight and obese adolescents with a history of low birth weight are at even greater risk of developing asthma. A cohort of 75,871 junior high school students was screened for asthma during 1995-1996 in Taiwan. Birth weight and estimated gestational age were obtained from the birth registry. Logistic regression and simple regression analyses were adjusted for confounding variables. Asthma was more prevalent in those with birth weights below 3,000 g and higher adolescent body mass indexes. Furthermore, those with both characteristics were consistently most likely to have asthma. Whether the asthma diagnosis among low-birth-weight subjects was assigned by physicians or medical questionnaire, the risks were elevated for both overweight (physician diagnosis: odds ratio = 1.41; medical questionnaire: odds ratio = 1.25) and obese (physician diagnosis: odds ratio = 1.38; medical questionnaire: odds ratio = 1.47) boys as well as overweight (physician diagnosis: odds ratio = 1.63; medical questionnaire: odds ratio = 1.30) and obese (physician diagnosis: odds ratio = 1.44; medical questionnaire: odds ratio = 1.32) girls (P < 0.05). Low birth weight predisposes one to develop asthma, and excess body mass amplifies the risk. A sex difference was observed. This study suggests that prenatal care and nutritional counseling could reduce asthma prevalence.

The authors examined the independent and combined associations of physical activity and obesity with incident type 2 diabetes among 675,496 Korean men from the database of the National Health Insurance Corporation. During an average follow-up of 7.5 years (1996-2005), 52,995 men developed type 2 diabetes. Men with overweight, obese I, and obese II classifications had 1.47, 2.05, and 3.69 times higher risk of type 2 diabetes, respectively, compared with normal weight men, and men with low, medium, and high activity had 5%, 10%, and 9% lower risk of type 2 diabetes, respectively, compared with inactive men after adjustment for confounders and physical activity or body mass index for each other. Overweight and obesity were detrimental within all activity categories, and meeting the activity recommendations (medium and high activity) was beneficial at all body mass index levels. Meeting the activity recommendations appeared to attenuate some negative effects of overweight or obesity, and the increased risk of type 2 diabetes due to inactivity was lower in normal weight men. Both preventing overweight or obesity and increasing physical activity are important to reduce the global epidemic of type 2 diabetes, regardless of body weight and activity levels.


Because of the strong correlations among neighborhoods’ characteristics, it is not clear whether the associations of specific environmental exposures (e.g., densities of physical features and services) with obesity can be disentangled. Using data from the RECORD (Residential Environment and Coronary Heart Disease) Cohort Study (Paris, France, 2007-2008), the authors investigated whether neighborhood characteristics related to the sociodemographic, physical, service-related, and social-interactional environments were associated with body mass index and waist circumference. The authors developed an original neighborhood characteristic-matching technique (analyses within pairs of participants similarly exposed to an environmental variable) to assess whether or not these associations could be disentangled. After adjustment for individual/neighborhood socioeconomic variables, body mass index/waist circumference was negatively associated with characteristics of the physical/service environments reflecting higher densities (e.g., proportion of built surface, densities of shops selling fruits/vegetables, and restaurants). Multiple adjustment models and the neighborhood characteristic-matching technique were unable to identify which of these neighborhood variables were driving the associations because of high correlations between the environmental variables. Overall, beyond the socioeconomic environment, the physical and service environments may be associated with weight status, but it is difficult to disentangle the effects of strongly correlated environmental dimensions, even if they imply different causal mechanisms and interventions.


Despite efforts to combat increasing rates of childhood obesity, the problem is worsening. Safe Routes to School (SRTS), an international movement motivated by the childhood obesity epidemic, seeks to increase the number of children actively commuting (walking or biking) to school by funding projects that remove barriers preventing them from doing so. We summarize the evaluation of the first phase of an ongoing SRTS program in California and discuss ways to enhance data collection.


There are concerns that prenatal exposure to endocrine-disrupting chemicals increases children's risk of obesity. African-American and Hispanic children born in the Bronx or Northern Manhattan, New York (1998-2006), whose mothers underwent personal air monitoring for polycyclic aromatic hydrocarbon (PAH) exposure during pregnancy, were followed up to ages 5 (n = 422) and 7 (n = 341) years. At age 5 years, 21% of the children were obese, as were 25% of those followed to age 7 years. After adjustment for child's sex, age at measurement, ethnicity, and birth weight and maternal receipt of public assistance and prepregnancy obesity, higher prenatal PAH exposures were significantly associated with higher childhood body size. In adjusted analyses, compared with children of mothers in the lowest tertile of PAH exposure, children of mothers in the highest exposure tertile had a 0.39-unit higher body mass index z score (95% confidence interval (CI): 0.08, 0.70) and a relative risk of 1.79 (95% CI: 1.09, 2.96) for obesity at age 5 years, and they had a 0.30-unit higher body mass index z score (95% CI: 0.01, 0.59), a 1.93-unit higher percentage of body fat (95% CI: 0.33, 3.54), and a relative risk of 2.26 (95% CI: 1.28, 4.00) for obesity at age 7 years. The data indicate that prenatal exposure to PAHs is associated with obesity in childhood.


We explored the extent to which economic contextual factors moderated the association of Supplemental Nutrition Assistance Program (SNAP) participation with body mass index (BMI) among low-income adults whose family income (adjusted for family size) is less than 130% of the federal poverty guideline. We drew on individual-level data from the Panel Study of Income Dynamics in the United States, including three waves of data in 1999, 2001, and 2003. Economic contextual data were drawn from the American Chamber of Commerce Researchers Association for food prices and Dun & Bradstreet for food outlet measures. In addition to cross-sectional estimation, a longitudinal individual fixed effects model was used to control for permanent unobserved individual heterogeneity. Our study found a statistically significant joint moderating effect of the economic contextual factors in longitudinal individual fixed effects model for both women (BMI only) and men (both BMI and obesity). For both women and men, SNAP participants' BMI was statistically significantly lower if they faced increased numbers of available supermarkets/grocery stores in the longitudinal model. A simulated 20% reduction in the price of fruits and vegetables resulted in a larger decrease in BMI among SNAP participants than non-participants for women and men, whereas a simulated 20% increase in the availability of supermarkets and grocery stores resulted in a statistically significant difference in the change in BMI by SNAP participation for women but not for men. Policies related to economic contextual factors, such as subsidies for fruits and vegetables or those that would improve access to supermarkets and grocery stores may enhance the relationship between SNAP participation and body mass outcomes among food assistance program participants.
BACKGROUND: In Switzerland, health policies are decided at the local level, but little is known regarding their impact on the screening and management of cardiovascular risk factors (CVRFs). We thus aimed at assessing geographical levels of CVRFs in Switzerland. METHODS: Swiss Health Survey for 2007 (N = 17,879). Seven administrative regions were defined: West (Leman), West-Central (Mittelland), Zurich, South (Ticino), North-West, East and Central Switzerland. Obesity, smoking, hypertension, dyslipidemia and diabetes prevalence, treatment and screening within the last 12 months were assessed by interview. RESULTS: After multivariate adjustment for age, gender, educational level, marital status and Swiss citizenship, no significant differences were found between regions regarding prevalence of obesity or current smoking. Similarly, no differences were found regarding hypertension screening and prevalence. Two thirds of subjects who had been told they had high blood pressure were treated, the lowest treatment rates being found in East Switzerland: odds-ratio and [95% confidence interval] 0.65 [0.50-0.85]. Screening for hypercholesterolemia was more frequently reported in French (Leman) and Italian (Ticino) speaking regions. Four out of ten participants who had been told they had high cholesterol levels were treated and the lowest treatment rates were found in German-speaking regions. Screening for diabetes was higher in Ticino (1.24 [1.09 - 1.42]). Six out of ten participants who had been told they had diabetes were treated, the lowest treatment rates were found for German-speaking regions. CONCLUSIONS: In Switzerland, cardiovascular risk factor screening and management differ between regions and these differences cannot be accounted for by differences in populations’ characteristics. Management of most cardiovascular risk factors could be improved.


News media coverage can affect how Americans view health policy issues. While previous research has investigated the text content of news media coverage of obesity, these studies have tended to ignore the photographs and other images that accompany obesity-related news coverage. Images can convey important messages about which groups in society are more or less affected by a health problem, and, in turn, shape public understanding about the social epidemiology of that condition. In this study, we analyzed the images of overweight and obese individuals in Time and Newsweek coverage over a 25-year period (1984-2009), and compared these depictions, which we characterize as representing the “news media epidemiology” of obesity, to data describing the true national prevalence of obesity within key populations of interest over this period. Data collected included descriptive features of news stories and accompanying images, and demographic characteristics of individuals portrayed in images. Over the 25-year period, we found that news magazines increasingly depicted non-whites as overweight and obese, and showed overweight and obese individuals less often performing stereotypical behaviors. Even with increasing representation of non-whites over time, news magazines still underrepresented African Americans and Latinos. In addition, the elderly were starkly underrepresented in images of the overweight and obese compared to actual prevalence rates. Research in other policy arenas has linked media depictions of the populations affected by social problems with public support for policies to combat them. Further research is needed to understand how news media depictions can affect public stigma toward overweight and obese individuals and public support for obesity prevention efforts.

BACKGROUND: Sub-Saharan Africa faces a rapid spread of diabetes mellitus type 2 (DM2) but its potentially specific characteristics are inadequately defined. In this hospital-based study in Kumasi, Ghana, we aimed at characterizing clinical, anthropometric, socio-economic, nutritional and behavioural parameters of DM2 patients and at identifying associated factors. METHODS: Between August 2007 and June 2008, 1466 individuals were recruited from diabetes and hypertension clinics, outpatients, community, and hospital staff. Fasting plasma glucose (FPG), serum lipids and urinary albumin were measured. Physical examination, anthropometry, and interviews on medical history, socio-economic status (SES), physical activity and nutritional behaviour were performed. RESULTS: The majority of the 675 DM2 patients (mean FPG, 8.31 mmol/L) was female (75%) and aged 40-60 years (mean, 55 years). DM2 was known in 97% of patients, almost all were on medication. Many had hypertension (63%) and microalbuminuria (43%); diabetic complications occurred in 20%. Overweight (body mass index > 25 kg/m2), increased body fat (> 20% (male), > 33% (female)), and central adiposity (waist-to-hip ratio > 0.90 (male), > 0.85 (female)) were frequent occurring in 53%, 56%, and 75%, respectively. Triglycerides were increased (> = 1.695 mmol/L) in 31% and cholesterol (> = 5.17 mmol/L) in 65%. Illiteracy (46%) was high and SES indicators generally low. Factors independently associated with DM2 included a diabetes family history (adjusted odds ratio (aOR), 3.8; 95% confidence interval (95%CI), 2.6-5.5), abdominal adiposity (aOR, 2.6; 95%CI, 1.8-3.9), increased triglycerides (aOR, 1.8; 95%CI, 1.1-3.0), and also several indicators of low SES. CONCLUSIONS: In this study from urban Ghana, DM2 affects predominantly obese patients of rather low socio-economic status and frequently is accompanied by hypertension and hyperlipidaemia. Prevention and management need to account for a specific risk profile in this population.


BACKGROUND: Objectively measured physical activity is low in British children, and declines as childhood progresses. Observational studies suggest that dog-walking might be a useful approach to physical activity promotion in children and adults, but there are no published public health interventions based on dog-walking with children. The Children, Parents, and Pets Exercising Together Study aims to develop and evaluate a theory-driven, generalisable, family-based, dog-walking intervention for 9-11 year olds. METHODS/DESIGN: The Children, Parents, and Pets Exercising Together Study is an exploratory, assessor-blinded, randomised controlled trial as defined in the UK MRC Framework on the development and evaluation of complex interventions in public health. The trial will follow CONSORT guidance. Approximately 40 dog-owning families will be allocated randomly in a ratio of 1.5:1 to receive a simple behavioural intervention lasting for 10 weeks or to a ‘waiting list’ control group. The primary outcome is change in objectively measured child physical activity using Actigraph accelerometer. Secondary outcomes in the child, included in part to shape a future more definitive randomised controlled trial, are: total time spent sedentary and patterning of sedentary behaviour (Actigraph accelerometer); body composition and bone health from dual energy x-ray absorptiometry; body weight, height and BMI; and finally, health-related quality of life using the PedsQL. Secondary outcomes in parents and dogs are: changes in body weight; changes in Actigraph accelerometer measured physical activity and sedentary behaviour. Process evaluation will consist of assessment of simultaneous child, parent, and dog accelerometer data and brief interviews with participating families. DISCUSSION: The Children, Parents, and Pets Exercising Together trial should be the first randomised controlled study to establish and evaluate an intervention aimed at dog-based physical activity promotion in families. It should advance our understanding of whether and how to use pet dogs to promote physical activity and/or to reduce sedentary behaviour in children and adults. The trial is intended to lead to a subsequent more definitive randomised controlled trial, and the work should inform future dog-based public health interventions such as secondary prevention interventions in children or adults. TRIAL REGISTRATION NUMBER: ISRCTN85939423
In hemodialysis patients, lower body mass index and weight loss have been associated with higher mortality rates, a phenomenon sometimes called the obesity paradox. This apparent paradox might be explained by loss of muscle mass. The authors thus examined the relation to mortality of changes in dry weight and changes in serum creatinine levels (a muscle-mass surrogate) in a cohort of 121,762 hemodialysis patients who were followed for up to 5 years (2001-2006). In addition to conventional regression analyses, the authors conducted a ranking analysis of joint effects in which the sums and differences of the percentiles of change for the 2 measures in each patient were used as the regressors. Concordant with previous body mass index observations, lower body mass, lower muscle mass, weight loss, and serum creatinine decline were associated with higher death rates. Among patients with a discordant change, persons whose weight declined but whose serum creatinine levels increased had lower death rates than did those whose weight increased but whose serum creatinine level declined. A decline in serum creatinine appeared to be a stronger predictor of mortality than did weight loss. Assuming residual selection bias and confounding were not large, the present results suggest that a considerable proportion of the obesity paradox in dialysis patients might be explained by the amount of decline in muscle mass.

OBJECTIVES: Our purpose was to investigate the processes involved in, and outcomes of, implementing 3 new state-level, school-oriented childhood obesity policies enacted between 2004 and 2007. METHODS: We followed policy implementation in 8 high schools in Mississippi and Tennessee. We collected data between 2006 and 2009 from interviews with policymakers, administrators, teachers, and students; observations of school-based activities; and documents. RESULTS: Significant barriers to the effective implementation of obesity-related policies emerged. These most notably include a value system that prioritizes performances in standardized tests over physical education (PE) and a varsity sport system that negatively influences opportunities for PE. These and other factors, such as resource constraints and the overloading of school administrators with new policies, mitigate against the implementation of policies designed to promote improvements in student health through PE. CONCLUSIONS: Policies designed to address health and social problems in high-school settings face significant barriers to effective implementation. To have a broad impact, obesity-related policies must be tied to mainstream educational initiatives that both incentivize, and hold accountable, the school-level actors responsible for their implementation.

BACKGROUND: Increasing prevalences of overweight and obesity in children are known problems in industrialized countries. Early prevention is important as overweight and obesity persist over time and are related with health problems later in adulthood. "Komm mit in das gesunde Boot - Grundschule" is a school-based program to promote a healthier lifestyle. Main goals of the intervention are to increase physical activity, decrease the consumption of sugar-
sweetened beverages, and to decrease time spent sedentary by promoting active choices for healthy lifestyle. The program to date is distributed by 34 project delivery consultants in the state of Baden-Wurttemberg and is currently implemented in 427 primary schools. The efficacy of this large scale intervention is examined via the Baden-Wurttemberg Study. METHODS/DESIGN: The Baden-Wurttemberg Study is a prospective, stratified, cluster-randomized, and longitudinal study with two groups (intervention group and control group). Measurements were taken at the beginning of the academic years 2010/2011 and 2011/2012. Efficacy of the intervention is being assessed using three main outcomes: changes in waist circumference, skinfold thickness and 6 minutes run. Stratified cluster-randomization (according to class grade level) was performed for primary schools; pupils, teachers/principals, and parents were investigated. An approximately balanced number of classes in intervention group and control group could be reached by stratified randomization and was maintained at follow-up. DISCUSSION: At present, "Komm mit in das Gesunde Boot - Grundschule" is the largest school-based health promotion program in Germany. Comparative objective main outcomes are used for the evaluation of efficacy. Simulations showed sufficient power with the existing sample size. Therefore, the results will show whether the promotion of a healthier lifestyle in primary school children is possible using a relatively low effort within a school-based program involving children, teachers and parents. The research team anticipates that not only efficacy will be proven in this study but also expects many other positive effects of the program. TRIAL REGISTRATION: German Clinical Trials Register (DRKS), DRKS-ID: DRKS00000494


In recent years, research and public policy attention has increasingly focused on understanding whether modifiable aspects of the local food environment - the types and composition of food outlets families have proximate access to - are drivers of and potential solutions to the problem of childhood obesity in the United States. Given that much of the earlier published research has documented greater concentrations of fast-food outlets alongside limited access to large grocery stores in neighborhoods with higher shares of racial/ethnic minority groups and residents living in poverty, differences in retail food contexts may indeed exacerbate notable child obesity disparities along socioeconomic and racial/ethnic lines. This paper examines whether the lack of access to more healthy food retailers and/or the greater availability of "unhealthy" food purveyors in residential neighborhoods explains children's risk of excessive weight gain, and whether differential food availability explains obesity disparities. I do so by analyzing a national survey of U.S. children followed over elementary school (Early Childhood Longitudinal Study - Kindergarten Cohort) who are linked to detailed, longitudinal food availability measures from a comprehensive business establishment database (the National Establishment Time Series). I find that children who live in residentially poor and minority neighborhoods are indeed more likely to have greater access to fast-food outlets and convenience stores. However, these neighborhoods also have greater access to other food establishments that have not been linked to increased obesity risk, including large-scale grocery stores. When examined in a multi-level modeling framework, differential exposure to food outlets does not independently explain weight gain over time in this sample of elementary school-aged children. Variation in residential food outlet availability also does not explain socioeconomic and racial/ethnic differences. It may thus be important to reconsider whether food access is, in all settings, a salient factor in understanding obesity risk among young children


Studies of individual countries suggest that socioeconomic status (SES) and weight are positively associated in lower-income countries but negatively associated in higher-income countries.
However, this reversal in the direction of the SES-weight relationship and arguments about the underlying causes of the reversal need to be tested with comparable data for a large and diverse set of nations. This study systematically tests the reversal hypothesis using individual- and aggregate-level data for 67 nations representing all regions of the world. In support of the hypothesis, we find not only that the body mass index, being overweight, and being obese rise with national product but also that the associations of SES with these outcomes shift from positive to negative. These findings fit arguments about how health-related, SES-based resources, costs, and values differ across levels of economic development. Although economic and social development can improve health, it can also lead to increasing obesity and widening SES disparities in obesity.


Experimental studies suggest that vitamin D modulates the activity of adipocytes. The authors examined baseline serum 25-hydroxyvitamin D (25(OH)D) level in relation to prevalent and cumulative incident obesity in Norway. A cohort of 25,616 adults aged 19-55 years participated in both the second and third surveys of the Nord-Trondelag Health Study (HUNT 2 (1995-1997) and HUNT 3 (2006-2008)). Serum 25(OH)D levels measured at baseline and anthropometric measurements taken at both baseline and follow-up were available for a random sample of 2,460 subjects. Overall, 40% of the 2,460 subjects had a serum 25(OH)D level less than 50.0 nmol/L, and 37% had a level of 50.0-74.9 nmol/L. The prevalence and cumulative incidence of obesity, defined as body mass index (weight (kg)/height (m)(2)) >/=30, were 12% and 15%, respectively. Lower serum 25(OH)D level was associated with a higher prevalence of obesity. In the 2,165 subjects with baseline BMI less than 30, a serum 25(OH)D level less than 50.0 nmol/L was associated with a significantly increased odds ratio for incident obesity during follow-up (adjusted odds ratio = 1.73, 95% confidence interval: 1.24, 2.41). When prevalent and incident obesity were classified according to waist circumference (>88 cm for women, >/=102 cm for men), similar results were obtained. In addition to prevalent obesity, a serum 25(OH)D level less than 50.0 nmol/L was significantly associated with new-onset obesity in adults.


BACKGROUND: In southern and eastern Mediterranean countries, changes in lifestyle and the increasing prevalence of excess weight in childhood are risk factors for high blood pressure (BP) during adolescence and adulthood. The aim of this study was to evaluate the BP status of Tunisian adolescents and to identify associated factors. METHODS: A cross-sectional study in 2005, based on a national, stratified, random cluster sample of 1294 boys and 1576 girls aged 15-19 surveyed in home visits. The socio-economic and behavioral characteristics of the adolescents were recorded. Overweight/obesity were assessed by Body Mass Index (BMI) from measured height and weight (WHO, 2007), abdominal obesity by waist circumference (WC). BP was measured twice during the same visit. Elevated BP was systolic (SBP) or diastolic blood pressure (DBP) >/= 90th of the international reference or >/= 120/80 mm Hg for 15-17 y., and SBP/DBP >/= 120/80 mm Hg for 18-19 y.; hypertension was SBP/DBP >/= 95th for 15-17 y. and >/= 140/90 mm Hg for 18-19 y. Adjusted associations were assessed by logistic regression. RESULTS: The prevalence of elevated BP was 35.1%(32.9-37.4): higher among boys (46.1% vs. 33.3%; P < 0.0001); 4.7%(3.8-5.9) of adolescents had hypertension. Associations adjusted for all covariates showed independent relationships with BMI and WC: - obesity vs. no excess weight increased elevated BP (boys OR = 2.1[1.0-4.2], girls OR = 2.3[1.3-3.9]) and hypertension (boys OR = 3.5[1.4-8.9], girls OR = 5.4[2.2-13.4]), - abdominal obesity (WC) was also associated with
elevated BP in both genders (for boys: 2nd vs. 1st tertile OR = 1.7[1.3-2.3], 3rd vs.1st tertile OR = 2.8[1.9-4.2]; for girls: 2nd vs. 1st tertile OR = 1.6[1.2-2.1], 3rd vs.1st tertile OR = 2.1[1.5-3.0]) but only among boys for hypertension. Associations with other covariates were weaker: for boys, hypertension increased somewhat with sedentary lifestyle, while elevated BP was slightly more prevalent among urban girls and those not attending school. CONCLUSION: Within the limits of BP measurement on one visit only, these results suggest that Tunisian adolescents of both genders are likely not spared from early elevated BP. Though further assessment is likely needed, the strong association with overweight/obesity observed suggests that interventions aimed at changing lifestyles to reduce this main risk factor may also be appropriate for the prevention of elevated BP.


Weight cycling has been associated with an increased risk of death in some studies, but few studies differentiated weight cycling initiated by intentional weight loss from that initiated by illness. The association of weight cycling with death was examined among 55,983 men and 66,655 women in the Cancer Prevention Study II Nutrition Cohort from 1992 to 2008. A weight cycle was defined as an intentional loss of 10 or more pounds (>4.5 kg) followed by regain of that weight, and the lifetime number of weight cycles was reported on a questionnaire administered at enrollment in 1992. A total of 15,138 men and 10,087 women died during follow-up, which ended in 2008. Hazard ratios and 95% confidence intervals were estimated using Cox proportional hazards regression models. When the models were adjusted for age only, weight cycling was positively associated with mortality (P for trend < 0.0001). However, after adjustment for body mass index and other risk factors, low numbers of weight cycles (1-4 cycles) were associated with slightly lower mortality rates (hazard ratio (HR) = 0.93, 95% confidence interval (CI): 0.89, 0.97 in men and HR = 0.93, 95% CI: 0.89, 0.98 in women), whereas high numbers of weight cycles (>20 cycles) were not associated with mortality (HR = 1.03, 95% CI: 0.89, 1.19 in men and HR = 0.99, 95% CI: 0.88, 1.12 in women). These results do not support an increased risk of mortality associated with weight cycling.


BACKGROUND: Creating school environments that support student physical activity (PA) is a key recommendation of policy-makers to increase youth PA. Given males are more active than females at all ages, it has been suggested that investigating gender differences in the features of the environment that associate with PA may help to inform gender-focused PA interventions and reduce the gender disparity in PA. The purpose of this cross-sectional study was to explore gender differences in the association between factors of the school environment and students' time spent in PA. METHODS: Among a sample of 10781 female and 10973 male students in grades 9 to 12 from 76 secondary schools in Ontario, Canada, student- and school-level survey PA data were collected and supplemented with GIS-derived measures of the built environment within 1-km buffers of the 76 schools. RESULTS: Findings from the present study revealed significant differences in the time male and female students spent in PA as well as in some of the school- and student-level factors associated with PA. Results of the gender-specific multilevel analyses indicate schools should consider providing an alternate room for PA, especially for providing flexibility activities directed at female students. Schools should also consider offering daily physical education programming to male students in senior grades and providing PA promotion initiatives targeting obese male students. CONCLUSIONS: Although most variation in male and female students' time spent in PA lies between students within schools, there is...
sufficient between-school variation to be of interest to practitioners and policy-makers. More research investigating gender differentials in environment factors associated with youth PA are warranted.


BACKGROUND: Higher waist circumference and lower hip circumference are both associated with increased cardiovascular disease (CVD) risk, despite being directly correlated. The real effects of visceral obesity may therefore be underestimated when hip circumference is not fully taken into account. We hypothesized that adding waist and hip circumference to traditional risk factors would significantly improve CVD risk prediction. METHODS: In a population-based survey among South Asian and African Mauritians (n = 7978), 1241 deaths occurred during 15 years of follow-up. In a model that included variables used in previous CVD risk calculations (a Framingham-type model), the association between waist circumference and mortality was examined before and after adjustment for hip circumference. The percentage with an increase in estimated 10-year cumulative mortality of >25% and a decrease of >20% after waist and hip circumference were added to the model was calculated. RESULTS: Waist circumference was strongly related to mortality only after adjustment for hip circumference and vice versa. Adding waist and hip circumference to a Framingham-type model increased estimated 10-year cumulative CVD mortality by >25% for 23.7% of those who died and 15.7% of those censored. Cumulative mortality decreased by >20% for 4.5% of those who died and 14.8% of those censored. CONCLUSIONS: The effect of central obesity on mortality risk is seriously underestimated without adjustment for hip circumference. Adding waist and hip circumference to a Framingham-type model for CVD mortality substantially increased predictive power. Both may be important inclusions in CVD risk prediction models.


This paper investigates one explanation for the consistent observation of a strong, negative correlation in the United States between income and obesity among women, but not men. We argue that a key factor is the gendered expectation that mothers are responsible for feeding their children. When income is limited and households face food shortages, we predict that an enactment of these gendered norms places mothers at greater risk for obesity relative to child-free women and all men. We adopt an indirect approach to study these complex dynamics using data on men and women of childrearing age and who are household heads or partners in the 1999-2003 waves of the Panel Study of Income Dynamics (PSID). We find support for our prediction: Food insecure mothers are more likely than child-free men and women and food insecure fathers to be overweight or obese and to gain more weight over four years. The risks are greater for single mothers relative to mothers in married or cohabiting relationships. Supplemental models demonstrate that this pattern cannot be attributed to post-pregnancy biological changes that predispose mothers to weight gain or an evolutionary bias toward biological children. Further, results are unchanged with the inclusion of physical activity, smoking, drinking, receipt of food stamps, or Women, Infants and Children (WIC) nutritional program participation. Obesity, thus, offers a physical expression of the vulnerabilities that arise from the intersection of gendered childcare expectations and poverty.

OBJECTIVES: We examined temporal and regional trends in the prevalence of health lifestyles in the United States. METHODS: We used 1994 to 2007 data from the Behavioral Risk Factor Surveillance System to assess 4 healthy lifestyle characteristics: having a healthy weight, not smoking, consuming fruits and vegetables, and engaging in physical activity. The concurrent presence of all 4 characteristics was defined as a healthy overall lifestyle. We used logistic regression to assess temporal and regional trends. RESULTS: The percentages of individuals who did not smoke (4% increase) and had a healthy weight (10% decrease) showed the strongest temporal changes from 1994 to 2007. There was little change in fruit and vegetable consumption or physical activity. The prevalence of healthy lifestyles increased minimally over time and varied modestly across regions; in 2007, percentages were higher in the Northeast (6%) and West (6%) than in the South (4%) and Midwest (4%). CONCLUSIONS: Because of the large increases in overweight and the declines in smoking, there was little net change in the prevalence of healthy lifestyles. Despite regional differences, the prevalence of healthy lifestyles across the United States remains very low.


This study has three primary goals that make an important contribution to the literature on body weight and childbearing experiences among United States' women. It sheds light on the physiological and social nature of this relationship by examining whether the consequences of early adult weight for lifetime childbearing are shaped by historical social context, women's social characteristics, and their ability to marry. We analyze data from two female cohorts who participated in the National Longitudinal Study of Youth (NLSY79). Cohort 1 entered early adulthood before the U.S. obesity prevalence increased. Cohort 2 entered early adulthood after the obesity prevalence increased. We find that early adult weight is negatively related to the childbearing trajectories and marital status of Cohort 1 but not Cohort 2. Failing to account for race/ethnicity and women's educational background as confounders masks some of these associations, which are evident for both White and Black women. Our results suggest that the health consequences of body weight do not fully drive its impact on childbearing. Rather, the lifetime fertility consequences of early adult weight are malleable, involve social processes, and are dependent on social context.


BACKGROUND: Childhood obesity is high on the policy agenda of wealthier nations, and many interventions have been developed to address it. This work describes an overview of schemes for obese and overweight children and young people in England, and the 'mapping' approach we used. METHODS: Our search strategy, inclusion criteria and coding frame had to be suitable for describing a potentially large number of schemes within a short timeframe. Data were collected from key informants, scheme publicity and reports, and via a web-survey. To be included, schemes had to be based in England, follow a structured programme lasting at least two weeks, promote healthy weight, and be delivered exclusively to overweight and/or obese children and young people (age range 4-18). Data were entered into a coding frame recording similar information for each scheme, including any underpinning research evidence, evaluation or monitoring reports. Priority questions were identified in consultation with colleagues from the Department of Health and the Cross Government Obesity Unit. RESULTS: Fifty-one schemes were identified. Some operated in multiple areas, and by using estimates of the number of schemes provided by multi-site scheme leads, we found that between 314 and 375 local
programmes were running at any time. Uncertainty is largely due to the largest scheme provider undergoing rapid expansion at the time of the mapping exercise and therefore able to provide only an estimate of the number of programmes running. Many schemes were similar in their approach, had been recently established and were following NICE guidelines on interventions to promote healthy weight. Rigorous evaluation was rare. CONCLUSIONS: Our methods enabled us to produce a rapid overview of service activity across a wide geographic area and a range of organisations and sectors. In order to develop the evidence base for childhood obesity interventions, rigorous evaluation of these schemes is required. This overview can serve as a starting point for evaluations of interventions to address obesity. More generally, a rapid and systematic approach of this type is transferable to other types of service activity in health and social care, and may be a tool to inform public health planning.


BACKGROUND: We are a society that is fixated on the health consequences of 'being fat'. Public health agencies play an important role in 'alerting' people about the risks that obesity poses both to individuals and to the broader society. Quantitative studies suggest people comprehend the physical health risks involved but underestimate their own risk because they do not recognise that they are obese. METHODS: This qualitative study seeks to expand on existing research by exploring obese individuals' perceptions of public health messages about risk, how they apply these messages to themselves and how their personal and social contexts and experiences may influence these perceptions. The study uses in depth interviews with a community sample of 142 obese individuals. A constant comparative method was employed to analyse the data. RESULTS: Personal and contextual factors influenced the ways in which individuals interpreted and applied public health messages, including their own health and wellbeing and perceptions of stigma. Individuals felt that messages were overly focused on the physical rather than emotional health consequences of obesity. Many described feeling stigmatised and blamed by the simplicity of messages and the lack of realistic solutions. Participants described the need for messages that convey the risks associated with obesity while minimising possible stigmatisation of obese individuals. This included ensuring that messages recognise the complexity of obesity and focus on encouraging healthy behaviours for individuals of all sizes. CONCLUSION: This study is the first step in exploring the ways in which we understand how public health messages about obesity resonate with obese individuals in Australia. However, much more research--both qualitative and quantitative--is needed to enhance understanding of the impact of obesity messages on individuals.


BACKGROUND: Kids--'Go for your life' (K-GFYL) is an award-based health promotion program being implemented across Victoria, Australia. The program aims to reduce the risk of childhood obesity by improving the socio-cultural, policy and physical environments in children's care and educational settings. Membership of the K-GFYL program is open to all primary and pre-schools and early childhood services across the State. Once in the program, member schools and services are centrally supported to undertake the health promotion (intervention) activities. Once the K-GFYL program 'criteria' are reached the school/service is assessed and 'awarded'. This paper describes the design of the evaluation of the statewide K-GFYL intervention program.
METHODS/DESIGN: The evaluation is mixed method and cross sectional and aims to: 1) Determine if K-GFYL award status is associated with more health promoting environments in schools/services compared to those who are members only; 2) Determine if children attending K-
GFYL award schools/services have higher levels of healthy eating and physical activity-related behaviors compared to those who are members only; 3) Examine the barriers to implementing and achieving the K-GFYL award; and 4) Determine the economic cost of implementing K-GFYL in primary schools. Parent surveys will capture information about the home environment and child dietary and physical activity-related behaviors. Environmental questionnaires in early childhood settings and schools will capture information on the physical activity and nutrition environment and current health promotion activities. Lunchbox surveys and a set of open-ended questions for kindergarten parents will provide additional data. Resource use associated with the intervention activities will be collected from primary schools for cost analysis. DISCUSSION: The K-GFYL award program is a community-wide intervention that requires a comprehensive, multi-level evaluation. The evaluation design is constrained by the lack of a non-K-GFYL control group, short time frames and delayed funding of this large scale evaluation across all intervention settings. However, despite this, the evaluation will generate valuable evidence about the utility of a community-wide environmental approach to preventing childhood obesity which will inform future public health policies and health promotion programs internationally. TRIAL REGISTRATION: ACTRN12609001075279

(60) SMITH DM, WHITWORTH M, SIBLEY C, TAYLOR W, et al. The design of a community lifestyle programme to improve the physical and psychological well-being of pregnant women with a BMI of 30 kg/m2 or more. BMC Public Health. 2010, vol. 10, p.284

BACKGROUND: Obesity is a global public health issue. Having a BMI of 30 kg/m2 or more (classifying a person as obese) at the start of pregnancy is a significant risk factor for maternal and fetal morbidity. There is a dearth of evidence to inform suitable interventions to support pregnant women with a BMI of 30 kg/m2 or more. Here we describe a study protocol to test the feasibility of a variety of potential healthy lifestyle interventions for pregnant women with a BMI of 30 kg/m2 or more in a community based programme. METHODS/DESIGN: Four hundred women will be approached to attend a 10-week community lifestyle programme. The programme will be provided as a supplement to standard antenatal care. The programme is multi-faceted, aimed at equipping participants with the skills and knowledge needed to adopt healthy behaviours. The social (cognitive) learning theory will be used as a tool to encourage behaviour change, the behaviour change techniques are underpinned by five theoretical components; self-efficacy, outcome expectancies, goal setting, feedback and positive reinforcement. The main outcomes are pregnancy weight gain and caesarean section rate. Other important outcomes include clinical outcomes (e.g., birth weight) and psychological outcomes (e.g., well-being). Secondary outcomes include women's experience of pregnancy and health care services, amount of physical activity, food intake and the suitability of the intervention components. A prospective study using quantitative and qualitative methods will inform the feasibility of implementing the community lifestyle programme with pregnant women with a BMI of 30 kg/m2 or more. Mixed methods of data collection will be used, including diaries, focus groups/interviews, pedometers, validated and specifically designed questionnaires, a programme register, weight gain during pregnancy and perinatal outcome data. DISCUSSION: Findings from this current feasibility study will inform future interventions and NHS services and add to the evidence-base by providing information about the experiences of pregnant women with a BMI of 30 kg/m2 or more undertaking a community lifestyle programme. The study will lead on to a randomised control trial of a suitable intervention to improve the pregnancy outcomes of this target group.


BACKGROUND: There is an urgent need for more carefully developed public health measures in order to curb the obesity epidemic among youth. The overall aim of the “EuropeaN Energy
balance Research to prevent excessive weight Gain among Youth” (ENERGY)-project is the development and formative evaluation of a theory-informed and evidence-based multi-component school-based and family-involved intervention program ready to be implemented and evaluated for effectiveness across Europe. This program aims at promoting the adoption or continuation of health behaviors that contribute to a healthy energy balance among school-aged children. Earlier studies have indicated that school and family environments are key determinants of energy-balance behaviors in schoolchildren. Schools are an important setting for health promotion in this age group, but school-based interventions mostly fail to target and involve the family environment.

METHODS: Led by a multidisciplinary team of researchers from eleven European countries and supported by a team of Australian experts, the ENERGY-project is informed by the Environmental Research Framework for Weight gain Prevention, and comprises a comprehensive epidemiological analysis including 1) systematic reviews of the literature, 2) secondary analyses of existing data, 3) focus group research, and 4) a cross European school-based survey.

RESULTS AND DISCUSSION: The theoretical framework and the epidemiological analysis will subsequently inform stepwise intervention development targeting the most relevant energy balance-related behaviors and their personal, family-environmental and school-environmental determinants applying the Intervention Mapping protocol. The intervention scheme will undergo formative and pilot evaluation in five countries. The results of ENERGY will be disseminated among key stakeholders including researchers, policy makers and the general population.

CONCLUSIONS: The ENERGY-project is an international, multidisciplinary effort to develop and test an evidence-based and theory-informed intervention program for obesity prevention among school-aged children.

SIDA


Despite antiretroviral therapy, proviral latency of human immunodeficiency virus type 1 (HIV-1) remains a principal obstacle to curing the infection. Inducing the expression of latent genomes within resting CD4(+) T cells is the primary strategy to clear this reservoir. Although histone deacetylase inhibitors such as suberoylanilide hydroxamic acid (also known as vorinostat, VOR) can disrupt HIV-1 latency in vitro, the utility of this approach has never been directly proven in a translational clinical study of HIV-infected patients. Here we isolated the circulating resting CD4(+) T cells of patients in whom viraemia was fully suppressed by antiretroviral therapy, and directly studied the effect of VOR on this latent reservoir. In each of eight patients, a single dose of VOR...
increased both biomarkers of cellular acetylation, and simultaneously induced an increase in HIV RNA expression in resting CD4(+) cells (mean increase, 4.8-fold). This demonstrates that a molecular mechanism known to enforce HIV latency can be therapeutically targeted in humans, provides proof-of-concept for histone deacetylase inhibitors as a therapeutic class, and defines a precise approach to test novel strategies to attack and eradicate latent HIV infection directly.


Epidemics of HIV in men who have sex with men (MSM) continue to expand in most countries. We sought to understand the epidemiological drivers of the global epidemic in MSM and why it continues unabated. We did a comprehensive review of available data for HIV prevalence, incidence, risk factors, and the molecular epidemiology of HIV in MSM from 2007 to 2011, and modelled the dynamics of HIV transmission with an agent-based simulation. Our findings show that the high probability of transmission per act through receptive anal intercourse has a central role in explaining the disproportionate disease burden in MSM. HIV can be transmitted through large MSM networks at great speed. Molecular epidemiological data show substantial clustering of HIV infections in MSM networks, and higher rates of dual-variant and multiple-variant HIV infection in MSM than in heterosexual people in the same populations. Prevention strategies that lower biological transmission and acquisition risks, such as approaches based on antiretrovirals, offer promise for controlling the expanding epidemic in MSM, but their potential effectiveness is limited by structural factors that contribute to low health-seeking behaviours in populations of MSM in many parts of the world.


BACKGROUND: Progressive immune dysfunction and the acquired immunodeficiency syndrome (AIDS) develop in most persons with untreated infection with human immunodeficiency virus type 1 (HIV-1) but in only approximately 20 to 30% of persons infected with HIV type 2 (HIV-2); among persons infected with both types, the natural history of disease progression is poorly understood.

METHODS: We analyzed data from 223 participants who were infected with HIV-1 after enrollment (with either HIV-1 infection alone or HIV-1 and HIV-2 infection) in a cohort with a long follow-up duration (approximately 20 years), according to whether HIV-2 infection occurred first, the time to the development of AIDS (time to AIDS), CD4+ and CD8+ T-cell counts, and measures of viral evolution.

RESULTS: The median time to AIDS was 104 months (95% confidence interval [CI], 75 to 133) in participants with dual infection and 68 months (95% CI, 60 to 76) in participants infected with HIV-1 only (P=0.003). CD4+ T-cell levels were higher and CD8+ T-cell levels increased at a lower rate among participants with dual infection, reflecting slower disease progression. Participants with dual infection with HIV-2 infection preceding HIV-1 infection had the longest time to AIDS and highest levels of CD4+ T-cell counts. HIV-1 genetic diversity was significantly lower in participants with dual infection than in those with HIV-1 infection alone at similar time points after infection.

CONCLUSIONS: Our results suggest that HIV-1 disease progression is inhibited by concomitant HIV-2 infection and that dual infection is associated with slower disease progression. The slower rate of disease progression was most evident in participants with dual infection in whom HIV-2 infection preceded HIV-1 infection. These findings could have implications for the development of HIV-1 vaccines and therapeutics. (Funded by the Swedish International Development Cooperation Agency-Swedish Agency for Research Cooperation with Developing Countries and others.)


Certain human pathogens avoid elimination by our immune system by rapidly mutating the surface protein sites targeted by antibody responses, and consequently they tend to be problematic for vaccine development. The behavior described is prominent for a subset of viruses-the highly antigenically diverse viruses—which include HIV, influenza, and hepatitis C viruses. However, these viruses do harbor highly conserved exposed sites, usually associated with function, which can be targeted by broadly neutralizing antibodies. Until recently, not many such antibodies were known, but advances in the field have enabled increasing numbers to be identified. Molecular characterizations of the antibodies and, most importantly, of the sites of vulnerability that they recognize give hope for the discovery of new vaccines and drugs.


BACKGROUND: Preexposure prophylaxis with antiretroviral drugs has been effective in the prevention of human immunodeficiency virus (HIV) infection in some trials but not in others. METHODS: In this randomized, double-blind, placebo-controlled trial, we assigned 2120 HIV-negative women in Kenya, South Africa, and Tanzania to receive either a combination of tenofovir disoproxil fumarate and emtricitabine (TDF-FTC) or placebo once daily. The primary objective was to assess the effectiveness of TDF-FTC in preventing HIV acquisition and to evaluate safety. RESULTS: HIV infections occurred in 33 women in the TDF-FTC group (incidence rate, 4.7 per 100 person-years) and in 35 in the placebo group (incidence rate, 5.0 per 100 person-years), for an estimated hazard ratio in the TDF-FTC group of 0.94 (95% confidence interval, 0.59 to 1.52; P=0.81). The proportions of women with nausea, vomiting, or elevated alanine aminotransferase levels were significantly higher in the TDF-FTC group (P=0.04, P<0.001, and P=0.03, respectively). Rates of drug discontinuation because of hepatic or renal abnormalities were higher in the TDF-FTC group (4.7%) than in the placebo group (3.0%, P=0.051). Less than 40% of the HIV-uninfected women in the TDF-FTC group had evidence of recent pill use at visits that were matched to the HIV-infection window for women with seroconversion. The study was stopped early, on April 18, 2011, because of lack of efficacy. CONCLUSIONS: Prophylaxis with TDF-FTC did not significantly reduce the rate of HIV infection and was associated with increased rates of side effects, as compared with placebo. Despite substantial counseling efforts, drug adherence appeared to be low. (Supported by the U.S. Agency for International Development and others; FEM-PreP ClinicalTrials.gov number, NCT00625404.)


BACKGROUND: Preexposure prophylaxis with antiretroviral agents has been shown to reduce the transmission of human immunodeficiency virus (HIV) among men who have sex with men; however, the efficacy among heterosexuals is uncertain. METHODS: We randomly assigned HIV-seronegative men and women to receive either tenofovir disoproxil fumarate and emtricitabine (TDF-FTC) or matching placebo once daily. Monthly study visits were scheduled, and participants received a comprehensive package of prevention services, including HIV testing, counseling on
adherence to medication, management of sexually transmitted infections, monitoring for adverse events, and individualized counseling on risk reduction; bone mineral density testing was performed semiannually in a subgroup of participants. RESULTS: A total of 1219 men and women underwent randomization (45.7% women) and were followed for 1563 person-years (median, 1.1 years; maximum, 3.7 years). Because of low retention and logistic limitations, we concluded the study early and followed enrolled participants through an orderly study closure rather than expanding enrollment. The TDF-FTC group had higher rates of nausea (18.5% vs. 7.1%, P<0.001), vomiting (11.3% vs. 7.1%, P=0.008), and dizziness (15.1% vs. 11.0%, P=0.03) than the placebo group, but the rates of serious adverse events were similar (P=0.90). Participants who received TDF-FTC, as compared with those who received placebo, had a significant decline in bone mineral density. K65R, M184V, and A62V resistance mutations developed in 1 participant in the TDF-FTC group who had had an unrecognized acute HIV infection at enrollment. In a modified intention-to-treat analysis that included the 33 participants who became infected during the study (9 in the TDF-FTC group and 24 in the placebo group; 1.2 and 3.1 infections per 100 person-years, respectively), the efficacy of TDF-FTC was 62.2% (95% confidence interval, 21.5 to 83.4; P=0.03). CONCLUSIONS: Daily TDF-FTC prophylaxis prevented HIV infection in sexually active heterosexual adults. The long-term safety of daily TDF-FTC prophylaxis, including the effect on bone mineral density, remains unknown. (Fundied by the Centers for Disease Control and Prevention and the National Institutes of Health; TDF2 ClinicalTrials.gov number, NCT00448669.)


BACKGROUND: Antiretroviral preexposure prophylaxis is a promising approach for preventing human immunodeficiency virus type 1 (HIV-1) infection in heterosexual populations. METHODS: We conducted a randomized trial of oral antiretroviral therapy for use as preexposure prophylaxis among HIV-1-serodiscordant heterosexual couples from Kenya and Uganda. The HIV-1-seronegative partner in each couple was randomly assigned to one of three study regimen—one daily tenofovir (TDF), combination tenofovir-emtricitabine (TDF-FTC), or matching placebo—and followed monthly for up to 36 months. At enrollment, the HIV-1-seropositive participants were not eligible for antiretroviral therapy, according to national guidelines. All couples received standard HIV-1 treatment and prevention services. RESULTS: We enrolled 4758 couples, of whom 4747 underwent randomization (45.7% women) and were followed for 1563 person-years; maximum, 3.7 years). Because of low retention and logistic limitations, we concluded the study early and followed enrolled participants through an orderly study closure rather than expanding enrollment. The TDF-FTC group had higher rates of nausea (18.5% vs. 7.1%, P<0.001), vomiting (11.3% vs. 7.1%, P=0.008), and dizziness (15.1% vs. 11.0%, P=0.03) than the placebo group, but the rates of serious adverse events were similar (P=0.90). Participants who received TDF-FTC, as compared with those who received placebo, had a significant decline in bone mineral density. K65R, M184V, and A62V resistance mutations developed in 1 participant in the TDF-FTC group who had had an unrecognized acute HIV infection at enrollment. In a modified intention-to-treat analysis that included the 33 participants who became infected during the study (9 in the TDF-FTC group and 24 in the placebo group; 1.2 and 3.1 infections per 100 person-years, respectively), the efficacy of TDF-FTC was 62.2% (95% confidence interval, 21.5 to 83.4; P=0.03). CONCLUSIONS: Daily TDF-FTC prophylaxis prevented HIV infection in sexually active heterosexual adults. The long-term safety of daily TDF-FTC prophylaxis, including the effect on bone mineral density, remains unknown. (Fundied by the Centers for Disease Control and Prevention and the National Institutes of Health; TDF2 ClinicalTrials.gov number, NCT00448669.)

BACKGROUND: The integrase inhibitor elvitegravir (EVG) has been co-formulated with the CYP3A4 inhibitor cobicistat (COBI), emtricitabine (FTC), and tenofovir disoproxil fumarate (TDF) in a single tablet given once daily. We compared the efficacy and safety of EVG/COBI/FTC/TDF with standard of care-co-formulated efavirenz (EFV)/FTC/TDF as initial treatment for HIV infection. METHODS: In this phase 3 trial, treatment-naive patients from outpatient clinics in North America were randomly assigned by computer-generated allocation sequence with a block size of four in a 1:1 ratio to receive EVG/COBI/FTC/TDF or EFV/FTC/TDF, once daily, plus matching placebo. Patients and study staff involved in giving study treatment, assessing outcomes, and collecting and analysing data were masked to treatment allocation. Eligibility criteria included screening HIV RNA concentration of 5000 copies per mL or more, and susceptibility to efavirenz, emtricitabine, and tenofovir. The primary endpoint was HIV RNA concentration of fewer than 50 copies per mL at week 48. The study is registered with ClinicalTrials.gov, number NCT01095796.

FINDINGS: 700 patients were randomly assigned and treated (348 with EVG/COBI/FTC/TDF, 352 with EFV/FTC/TDF). EVG/COBI/FTC/TDF was non-inferior to EFV/FTC/TDF; 305/348 (87.6%) versus 296/352 (84.1%) of patients had HIV RNA concentrations of fewer than 50 copies per mL at week 48 (difference 3.6%, 95% CI -1.6% to 8.8%). Proportions of patients discontinuing drugs for adverse events did not differ substantially (13/348 in the EVG/COBI/FTC/TDF group vs 18/352 in the EFV/FTC/TDF group). Nausea was more common with EVG/COBI/FTC/TDF than with EFV/FTC/TDF (72/348 vs 48/352) and dizziness (23/348 vs 86/352), abnormal dreams (53/348 vs 95/352), insomnia (30/348 vs 49/352), and rash (22/348 vs 43/352) were less common. Serum creatinine concentration increased more by week 48 in the EVG/COBI/FTC/TDF group than in the EFV/FTC/TDF group (median 13 mumol/L, IQR 5 to 20 vs 1 mumol/L, -6 to 8; p<0.001).

INTERPRETATION: If regulatory approval is given, EVG/COBI/FTC/TDF would be the only single-tablet, once-daily, integrase-inhibitor-based regimen for initial treatment of HIV infection.

FUNDING: Gilead Sciences


BACKGROUND: The HIV integrase strand transfer inhibitor elvitegravir (EVG) has been co-formulated with the CYP3A4 inhibitor cobicistat (COBI), emtricitabine (FTC), and tenofovir disoproxil fumarate (TDF) into a once-daily, single tablet. We compared EVG/COBI/FTC/TDF with a ritonavir-boosted (RTV) protease inhibitor regimen of atazanavir (ATV)/RTV+FTC/TDF as initial therapy for HIV-1 infection. METHODS: This phase 3, non-inferiority study enrolled treatment-naive patients with an HIV-1 RNA concentration of 5000 copies per mL or more and susceptibility to atazanavir, emtricitabine, and tenofovir. Patients were randomly assigned (1:1) to receive EVG/COBI/FTC/TDF or ATV/RTV+FTC/TDF plus matching placebos, administered once daily. Randomisation was by computer-generated random sequence, accessed via an interactive telephone and web response system. Patients, and investigators and study staff who gave treatments, assessed outcomes, or analysed data were masked to the assignment. The primary endpoint was HIV RNA concentration of 50 copies per mL or less after 48 weeks (according to the US FDA snapshot algorithm), with a 12% non-inferiority margin. This trial is registered with ClinicalTrials.gov, number NCT01106586.

FINDINGS: 1017 patients were screened, 715 were enrolled, and 708 were treated (353 with EVG/COBI/FTC/TDF and 355 with ATV/RTV+FTC/TDF). EVG/COBI/FTC/TDF was non-inferior to ATV/RTV+FTC/TDF for the primary outcome (316 patients [89.5%] vs 308 patients [86.8%], adjusted difference 3.0%, 95% CI 1.9% to 7.8%). Both regimens had favourable safety and tolerability; 13 (3.7%) versus 18 (5.1%) patients discontinued treatment because of adverse events. Fewer patients receiving EVG/COBI/FTC/TDF had abnormal results in liver function tests than did those receiving ATV/RTV+FTC/TDF and had smaller median increases in fasting triglyceride concentration (90 mumol/L vs 260 mumol/L,

p=0.006). Small median increases in serum creatinine concentration with accompanying decreases in estimated glomerular filtration rate occurred in both study groups by week 2; they generally stabilised by week 8 and did not change up to week 48 (median change 11 mumol/L vs 7 mumol/L). INTERPRETATION: If regulatory approval is given, EVG/Cobi/FTC/TDF would be the first integrase-inhibitor-based regimen given once daily and the only one formulated as a single tablet for initial HIV treatment. FUNDING: Gilead Sciences


BACKGROUND: In resource-limited settings where no safe alternative to breastfeeding exists, WHO recommends that antiretroviral prophylaxis be given to either HIV-infected mothers or infants throughout breastfeeding. We assessed the effect of 28 weeks of maternal or infant antiretroviral prophylaxis on postnatal HIV infection at 48 weeks. METHODS: The Breastfeeding, Antiretrovirals, and Nutrition (BAN) Study was undertaken in Lilongwe, Malawi, between April 21, 2004, and Jan 28, 2010. 2369 HIV-infected breastfeeding mothers with a CD4 count of 250 cells per µL or more and their newborn babies were randomly assigned with a variable-block design to one of three, 28-week regimens: maternal triple antiretroviral (n=849); daily infant nevirapine (n=852); or control (n=680). Patients and local clinical staff were not masked to treatment allocation, but other study investigators were. All mothers and infants received one dose of nevirapine (mother 200 mg; infant 2 mg/kg) and 7 days of zidovudine (mother 300 mg; infants 2 mg/kg) and lamivudine (mothers 150 mg; infants 4 mg/kg) twice a day. Mothers were advised to wean between 24 weeks and 28 weeks after birth. The primary endpoint was HIV infection by 48 weeks in infants who were not infected at 2 weeks and in all infants randomised with censoring at loss to follow-up. This trial is registered with ClinicalTrials.gov, number NCT00164736. FINDINGS: 676 mother-infant pairs completed follow-up to 48 weeks or reached an endpoint in the maternal-antiretroviral group, 680 in the infant-nevirapine group, and 542 in the control group. By 32 weeks post partum, 96% of women in the intervention groups and 88% of those in the control group reported no breastfeeding since their 28-week visit. 30 infants in the maternal-antiretroviral group, 25 in the infant-nevirapine group, 38 in the control group became HIV infected between 2 weeks and 48 weeks of life; 28 (30%) infections occurred after 28 weeks (nine in maternal-antiretroviral, 13 in infant-nevirapine, and six in control groups). The cumulative risk of HIV-1 transmission by 48 weeks was significantly higher in the control group (7%, 95% CI 5-9) than in the maternal-antiretroviral (4%, 3-6; p=0.0273) or the infant-nevirapine (4%, 2-5; p=0.0027) groups. The rate of serious adverse events in infants was significantly higher during 29-48 weeks than during the intervention phase (1.1 [95% CI 1.0-1.2] vs 0.7 [0.7-0.8] per 100 person-weeks; p<0.0001), with increased risk of diarrhoea, malaria, growth faltering, tuberculosis, and death. Nine women died between 2 weeks and 48 weeks post partum (one in maternal-antiretroviral group, two in infant-nevirapine group, six in control group). INTERPRETATION: In resource-limited settings where no suitable alternative to breastfeeding is available, antiretroviral prophylaxis given to mothers or infants might decrease HIV transmission.
Weaning at 6 months might increase infant morbidity. FUNDING: US Centers for Disease Control and Prevention


OBJECTIVES: We examined the effectiveness of risk reduction counseling and the role of on-site HIV testing in drug treatment. METHODS: Between January and May 2009, we randomized 1281 HIV-negative (or status unknown) adults who reported no past-year HIV testing to (1) referral for off-site HIV testing, (2) HIV risk-reduction counseling with on-site rapid HIV testing, or (3) verbal information about testing only with on-site rapid HIV testing. RESULTS: We defined 2 primary self-reported outcomes a priori: receipt of HIV test results and unprotected anal or vaginal intercourse episodes at 6-month follow-up. The combined on-site rapid testing participants received more HIV test results than off-site testing referral participants (P<.001; Mantel-Haenszel risk ratio=4.52; 97.5% confidence interval [CI]=3.57, 5.72). At 6 months, there were no significant differences in unprotected intercourse episodes between the combined on-site testing arms and the referral arm (P=.39; incidence rate ratio [IRR]=1.04; 97.5% CI=0.95, 1.14) or the 2 on-site testing arms (P=.81; IRR=1.03; 97.5% CI=0.84, 1.26). CONCLUSIONS: This study demonstrated on-site rapid HIV testing's value in drug treatment centers and found no additional benefit from HIV sexual risk-reduction counseling.


OBJECTIVES: We examined the efforts of the US network of AIDS Education and Training Centers (AETCs) to increase HIV testing capacity across a variety of clinical settings. METHODS: We used quantitative process data from 8 regional AETCs for July 1, 2008, to June 30, 2009, and qualitative program descriptions to demonstrate how AETC education helped providers integrate HIV testing into routine clinical care with the goals of early diagnosis and treatment. RESULTS: Compared with other AETC training, HIV testing training was longer and used a broader variety of strategies to educate more providers per training. During education, providers were able to understand their primary care responsibility to address public health concerns through HIV testing. CONCLUSIONS: AETC efforts illustrate how integration of the principles of primary care and public health can be promoted through professional training.


This article analyses the causes of HIV stigmatisation in Burkina Faso as perceived by people living with HIV/AIDS (PLHIV) and people working in AIDS-related Community Based Organisations (CBOs). Stigmatisation continues to be a pressing issue when dealing with HIV/AIDS in Sub-Saharan Africa. The article is based on direct observation of HIV-related practices within 20 CBOs in Burkina Faso, as well as semi-structured interviews or focus group discussions with 72 PLHIV and 90 professionals and volunteers working in CBOs. PLHIV were chosen by convenience sampling among the persons who accessed CBO services and were interviewed about their life quality and experience relating to HIV. Professionals and volunteers were interviewed about their strategies, their achievements, and the problems they encountered. The research was conducted in the course of three months fieldwork between September and November 2009. Our principal findings show, firstly, that moral or social stigmatisation does not in
any simple way derive from fear, ignorance or inaccurate beliefs but that it is also established and continually reinforced by official campaigns addressing HIV/AIDS. Secondly, we show that stigmatisation is a socially complex and ambiguous process. Based on these empirical findings we conclude that HIV/AIDS need no longer be approached in AIDS intervention as a sexually acquired and fatal disease. When reliable access to antiretroviral drugs is in place, AIDS becomes a chronic condition with which one can live for many years, and this makes it easier to address HIV and moral or social stigmatisation by downplaying the current focus upon sexuality and morality

Tuberculosis is a major threat to global health, infecting a third of the world's population. In the United States, however, control of tuberculosis has been increasingly successful. Only 3.2% of the US population is estimated to have latent tuberculosis and there are only 11,000 cases annually of active disease. More than half the cases in this country occur in individuals born outside the United States. Human immunodeficiency virus coinfection is not a major factor in the United States, since only approximately 10% of cases are coinfected. Drug resistance is also uncommon in this country. Because the United States has more resources for the diagnosis, therapy, and public health control of tuberculosis than many regions of the world, and because many hospitals have more cases of clinically significant nontuberculous mycobacteria than tuberculosis, the management approaches to tuberculosis need to be quite different in this country than in other regions. The resurgence in interest in developing new tools and the investment in public health infrastructure will hopefully be sustained in the United States so that the effect of tuberculosis on the US population will continue to diminish, and these new tools and approaches can be adapted to both high and low prevalence areas to meet the global challenge.


Mitigation of the tuberculosis (TB) and HIV syndemic is undermined by critical clinical, operational and social challenges of which the social aspects have been least explored. This paper examines the lived experience of TB disease and HIV from the perspective of affected individuals to analyze how they may think about their dual illness; how they understand their illness with TB in relation to HIV, and vice versa; and how they characterize their (stigmatized) experiences in the context of their perceptions and identities. From February-August 2009, qualitative, semi-structured interviews were conducted with 40 adults with HIV and TB disease at three ambulatory clinics in KwaZulu-Natal, South Africa. Subjective meanings of illness experience were analyzed using modified grounded-theory. Emergent themes on illness perception and disclosure revealed how patients constructed dichotomous identities associated with TB and HIV through social constructs of moral susceptibility and (im)permanence. Each identity was associated with relatively disparate degrees of stigma as a product of labeling, negative stereotyping and discrimination. HIV bore the least desirable identity and invoked the greatest stigma. However, the confluence of the two epidemics rendered TB symbolic and symptomatic of HIV, and enhanced the visibility of AIDS. Dual illness thus introduced a paradox to patients’ identity constructions, and produced a unique, overlapping double stigma. This facilitated new forms of stigma against TB, and aggravated existing stigma against HIV. It also conferred visibility to some forms of extra-pulmonary TB. Patients managed their double stigmas through novel forms of information sharing that relied on segregating their dual illness identities. Patients deflected the dominant stigma of HIV through concurrent processes of HIV ‘othering’ - their symbolic distancing from persons affected by HIV, and ‘covering’ - their selective disclosure of illness (and identity associated) with TB over that of HIV. Findings call for greater consideration to the complex role of stigma in the delivery of TB/HIV healthcare.


BACKGROUND: Early and accurate diagnosis of pulmonary tuberculosis (TB) is critical for successful TB control. To assist in the diagnosis of smear-negative pulmonary TB, the World Health Organisation (WHO) recommends the use of a diagnostic algorithm. Our study evaluated the implementation of the national tuberculosis programme’s diagnostic algorithm in routine health care settings in Jogjakarta, Indonesia. The diagnostic algorithm is based on the WHO TB diagnostic algorithm, which had already been implemented in the health facilities. METHODS: We prospectively documented the diagnostic work-up of all new tuberculosis suspects until a diagnosis was reached. We used clinical audit forms to record each step chronologically. Data on the patient’s gender, age, symptoms, examinations (types, dates, and results), and final diagnosis were collected. RESULTS: Information was recorded for 754 TB suspects; 43.5% of whom were lost during the diagnostic work-up in health centres, 0% in lung clinics. Among the TB suspects who completed diagnostic work-ups, 51.1% and 100.0% were diagnosed without following the national TB diagnostic algorithm in health centres and lung clinics, respectively. However, the work-up in the health centres and lung clinics generally conformed to international standards for tuberculosis care (ISTC). Diagnostic delays were significantly longer in health centres compared to lung clinics. CONCLUSIONS: The high rate of patients lost in health centres needs to be addressed through the implementation of TB suspect tracing and better programme supervision. The national TB algorithm needs to be revised and differentiated according to the level of care.

BACKGROUND: India's Revised National Tuberculosis Control Programme (RNTCP) is deemed highly successful in terms of detection and cure rates. However, some patients experience delays in accessing diagnosis and treatment. Patients falling between the 96th and 100th percentiles for these access indicators are often ignored as atypical 'outliers' when assessing programme performance. They may, however, provide clues to understanding why some patients never reach the programme. This paper examines the underlying vulnerabilities of patients with extreme values for delays in accessing the RNTCP in Mumbai city, India. METHODS: We conducted a cross-sectional study with 266 new sputum positive patients registered with the RNTCP in Mumbai. Patients were classified as 'outliers' if patient, provider and system delays were beyond the 95th percentile for the respective variable. Case profiles of 'outliers' for patient, provider and system delays were examined and compared with the rest of the sample to identify key factors responsible for delays. RESULTS: Forty-two patients were 'outliers' on one or more of the delay variables. All 'outliers' had a significantly lower per capita income than the remaining sample. The lack of economic resources was compounded by social, structural and environmental vulnerabilities. Longer patient delays were related to patients' perception of symptoms as non-serious. Provider delays were incurred as a result of private providers' failure to respond to tuberculosis in a timely manner. Diagnostic and treatment delays were minimal, however, analysis of the 'outliers' revealed the importance of social support in enabling access to the programme. CONCLUSION: A proxy for those who fail to reach the programme, these case profiles highlight unique vulnerabilities that need innovative approaches by the RNTCP. The focus on 'outliers' provides a less resource- and time-intensive alternative to community-based studies for understanding the barriers to reaching public health programmes.


BACKGROUND: Current tuberculosis (TB) reporting protocols are insufficient to achieve the goals established by the Stop TB partnership. Some countries have recommended implementation of active case finding program. We assessed the effect of Cough Officer Screening (an active screening system) on the rate of TB detection and health care system delays over the course of four years. METHODS: Patients who were hospitalized at the Changhua Christian Hospital (Changhua, Taiwan) were enrolled from September 2004 to July 2006 (Stage I) and August 2006 to August 2008 (Stage II). Stage II was implemented after a Plan-Do-Check-Act (PDCA) cycle analysis indicated that we should exclude ICU and paediatric patients. RESULTS: In Stage I, our COS system alerted physicians to 19,836 patients, and 7,998 were examined. 184 of these 7,998 patients (2.3%) had TB. Among these 184 patients, 142 (77.2%) were examined for TB before COS alarming and 42 were diagnosed after COS alarming. In Stage II, a total of 11,323 patients were alerted by the COS system. Among them, 6,221 patients were examined by physicians, and 125 of these patients (2.0%) had TB. Among these 125 patients, 113 (90.4%) were examined for TB before COS alarming and 12 were diagnosed after COS alarming. The median time from COS alarm to clinical action was significantly less (p = 0.041) for Stage I (1 day; range: 0-16 days) than for Stage II (2 days; range: 0-10 days). CONCLUSION: Our COS system improves detection of TB by reducing the delay from infection to diagnosis. Modifications of scope may be needed to improve cost-effectiveness.