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Ce bulletin de veille est une publication mensuelle qui recueille les publications scientifiques autour des pathologies suivantes :

- 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
- SIDA
- Tuberculose

La recherche documentaire est effectuée dans la base de données Medline et porte sur les 12 titres de revues suivants :

- 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

Des rapports officiels et institutionnels en ligne sont également signalés en fin de bulletin.
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**Articles scientifiques**

### Bronchite chronique obstructive


Medical examination covered 41 workers with long length of service in coal and mining industry, diagnosed as having "Chronic obstructive dust bronchitis", who received a complex of therapeutic and prophylactic measures including traditional broncholytic therapy, physical therapy and exercise therapy. 20 patients of main group received additional complex "Vobenzyme + Vitrum + herbal tea + aeration". Efficiency of medical rehabilitation was assessed through external respiration parameters--maximal effect was seen among the main group members (reliable increase of forced vital capacity, peak flow and maximal flow at 25% forced vital capacity)

(2) OTCZYK DC, CLANCY RL, CRIPPS AW. *Haemophilus influenzae and smoking-related obstructive airways disease*. Int J Chron Obstruct Pulmon Dis. 2011, vol. 6, pp.345-351  

**BACKGROUND:** Intralumenal bacteria play a critical role in the pathogenesis of acute infective episodes and airway inflammation. Antigens from colonizing bacteria such as nontypeable Haemophilus influenzae (NTHi) may contribute to chronic lung disease through an immediate hypersensitivity response. The objective of this study was to determine the presence of specific NTHi-IgE antibodies in subjects with chronic bronchitis (CB) and COPD who had smoked.  
**METHODS:** Serum, sputum, and saliva samples were collected from subjects with CB and moderate-severe COPD and healthy aged-matched controls. Total IgE and specific NTHi IgE were measured by enzyme linked immunosorbent assay. Throat swabs were examined for the presence of NTHi.  
**RESULTS:** THE RESULTS DEMONSTRATE THAT: i) specific NTHi IgE antibodies occur at a low level in healthy subjects; ii) those with both CB and moderate-severe COPD have elevated specific NTHi IgE antibody compared with healthy controls, with higher levels in those with most severe disease; iii) IgE levels are greater in those with moderate-severe COPD than in those with CB. They demonstrate specific NTHi IgE antibody is regularly found at higher than normal levels in COPD.  
**CONCLUSION:** The detection of IgE antibody to colonizing bacteria in all subjects with CB or moderate-severe COPD identifies a possible mechanism of bronchospasm in these subjects amenable to specific intervention therapy


Human metapneumovirus infections are increasingly recognized among adult patients and the aim of this report is to present a series of 4 cases admitted during the winter of 2010. All were detected by direct fluorescence anti-bodies assay of respiratory samples and all were female patients with an age range of 79 to 95 years, including two bedridden cases, one with dementia and three with chronic obstructive pulmonary disease. One patient presented with parainfluenza 3 virus coinfection. Patients presented with pneumonia in 3 cases (interstitial pattern in 2 and lobar consolidation in the other) or acute exacerbation of chronic bronchitis in the remaining case. Symptoms were present for 3 to 7 days before admission and 3 have wheezing. All had hypoxemic or global respiratory failure and lymphopenia (< 1.000/mm(3)). Hospitalization lasted for 5 to 20 days, marked in the 3 cases that survived by prolonged bronchial obstructive manifestations. Two cases required non invasive mechanical ventilation. Human metapneumovirus infections can decompensate elderly patients with chronic respiratory diseases
generating hospital admission and a prolonged morbidity marked by obstructive manifestations and sometimes can become into death

(4) FOREY BA, THORNTON AJ, LEE PN. Systematic review with meta-analysis of the epidemiological evidence relating smoking to COPD, chronic bronchitis and emphysema. BMC Pulm Med. 2011, vol. 11, p.36  

BACKGROUND: Smoking is a known cause of the outcomes COPD, chronic bronchitis (CB) and emphysema, but no previous systematic review exists. We summarize evidence for various smoking indices. METHODS: Based on MEDLINE searches and other sources we obtained papers published to 2006 describing epidemiological studies relating incidence or prevalence of these outcomes to smoking. Studies in children or adolescents, or in populations at high respiratory disease risk or with co-existing diseases were excluded. Study-specific data were extracted on design, exposures and outcomes considered, and confounder adjustment. For each outcome RR/ORs and 95% CIs were extracted for ever, current and ex smoking and various dose response indices, and meta-analyses and meta-regressions conducted to determine how relationships were modified by various study and RR characteristics. RESULTS: Of 218 studies identified, 133 provide data for COPD, 101 for CB and 28 for emphysema. RR estimates are markedly heterogeneous. Based on random-effects meta-analyses of most-adjusted RR/ORs, estimates are elevated for ever smoking (COPD 2.89, CI 2.63-3.17, n = 129 RRs; CB 2.69, 2.50-2.90, n = 114; emphysema 4.51, 3.38-6.02, n = 28), current smoking (COPD 3.51, 3.08-3.99; CB 3.41, 3.13-3.72; emphysema 4.87, 2.83-8.41) and ex smoking (COPD 2.35, 2.11-2.63; CB 1.63, 1.50-1.78; emphysema 3.52, 2.51-4.94). For COPD, RR's are higher for males, for studies conducted in North America, for cigarette smoking rather than any product smoking, and where the unexposed base is never smoking any product, and are markedly lower when asthma is included in the COPD definition. Variations by sex, continent, smoking product and unexposed group are in the same direction for CB, but less clearly demonstrated. For all outcomes RR's are higher when based on mortality, and for COPD are markedly lower when based on lung function. For all outcomes, risk increases with amount smoked and pack-years. Limited data show risk decreases with increasing starting age for COPD and CB and with increasing quitting duration for COPD. No clear relationship is seen with duration of smoking. CONCLUSIONS: The results confirm and quantify the causal relationships with smoking


Management of feline chronic lower airway disease focuses on controlling clinical signs and decreasing airway inflammation. This retrospective study evaluated the correlation between the resolution of clinical signs in cats with lower airway disease receiving oral glucocorticoids with the resolution of inflammation based on bronchoalveolar lavage fluid (BALF) cytology. Ten cats diagnosed with lower airway disease based on characteristic clinical signs and inflammatory BALF cytology received oral glucocorticoids for at least 3 weeks. They were required to have resolution of clinical signs and BALF collected while asymptomatic and still receiving glucocorticoids. Cats received prednisolone or prednisone (average dose of 1.8+/-0.2mg/kg daily) for 35.7+/-5.5 days. Three cats had resolution of clinical signs and lacked inflammatory BALF cytology; seven had persistent inflammatory BALF cytology despite resolution of clinical signs. Given that subclinical inflammation during high-dose glucocorticoid treatment was common, current recommendations to taper therapy based on resolution of clinical signs should be re-evaluated
BACKGROUND: Chronic bronchitis (CB) in patients with COPD is associated with an accelerated lung function decline and an increased risk of respiratory infections. Despite its clinical significance, the chronic bronchitic phenotype in COPD remains poorly defined. METHODS: We analyzed data from subjects enrolled in the Genetic Epidemiology of COPD (COPDGene) Study. A total of 1,061 subjects with GOLD (Global Initiative for Chronic Obstructive Lung Disease) stage II to IV were divided into two groups: CB (CB+) if subjects noted chronic cough and phlegm production for >/= 3 mo/y for 2 consecutive years, and no CB (CB-) if they did not. RESULTS: There were 290 and 771 subjects in the CB+ and CB- groups, respectively. Despite similar lung function, the CB+ group was younger (62.8 +/- 8.4 vs 64.6 +/- 8.4 years, P = .002), smoked more (57 +/- 30 vs 52 +/- 25 pack-years, P = .006), and had more current smokers (48% vs 27%, P < .0001). A greater percentage of the CB+ group reported nasal and ocular symptoms, wheezing, and nocturnal awakenings secondary to cough and dyspnea. History of exacerbations was higher in the CB+ group (1.21 +/- 1.62 vs 0.63 +/- 1.12 per patient, P = .027), and more patients in the CB+ group reported a history of severe exacerbations (26.6% vs 20.0%, P = .024). There was no difference in percent emphysema or percent gas trapping, but the CB+ group had a higher mean percent segmental airway wall area (63.2% +/- 2.9% vs 62.6% +/- 3.1%, P = .013). CONCLUSIONS: CB in patients with COPD is associated with worse respiratory symptoms and higher risk of exacerbations. This group may need more directed therapy targeting chronic mucus production and smoking cessation not only to improve symptoms but also to reduce risk, improve quality of life, and improve outcomes. Trial registry: ClinicalTrials.gov; No.: NCT00608764; URL: www.clinicaltrials.gov

Non-asthmatic eosinophilic bronchitis (NAEB) is characterized by chronic cough and sputum eosinophilia without bronchial hyperresponsiveness. The aim of the present study is to determine whether increased levels of PGE(2) from NAEB sputum supernatants play a protective role in airway inflammation and muscular hyperplasia. Twenty-one patients with NAEB, 15 asthmatic patients, and 12 healthy subjects were studied. An up-regulated PGE(2) enzymatic pathway was observed in bronchial biopsies from patients with NAEB as compared with samples from asthmatic patients. Also, EP2 and EP4 receptor expression was increased in these samples. BSMC proliferation was inhibited to a greater extent in NAEB sputum supernatants than in those taken from asthmatic subjects and healthy controls. This inhibition was mostly due to PGE(2) levels, a fact which was confirmed by employing synthetic EP2 and EP4 agonist and antagonist receptors. These findings suggest that PGE(2) inhibits BSMC proliferation entailing a reduction of smooth muscle hyperplasia and thus protecting against the onset of airflow obstruction.

BACKGROUND: Nonasthmatic eosinophilic bronchitis (NAEB) and cough variant asthma (CVA) are common causes of chronic cough. Both are characterized by eosinophilic inflammation in the airways. However, airway hyperresponsiveness, which is a characteristic feature of CVA, is not observed in NAEB. We hypothesized that endogenous bronchodilator S-nitrosothiol (SNO) levels are different between patients with NAEB and CVA. METHODS: SNO concentrations in sputum supernatant were measured using a commercially available kit in 20 NAEB and 21 CVA patients. RESULTS: The mean sputum eosinophil counts and exhaled nitric oxide values were similar in patients with NAEB (12.4 +/- 2.3%, 80.6 +/- 8.1 ppb) and CVA (15.3 +/- 3.7%, 97.7 +/- 9.2 ppb). By contrast, SNO levels in the airway lining fluid of NAEB patients were substantially higher than
those of CVA patients (87.1 +/- 9.8 vs. 46.8 +/- 4.8 muM; p < 0.05). CONCLUSIONS: SNOs may be an important factor in determining the development of airway hyperresponsiveness in the presence of eosinophilic inflammation.


BACKGROUND: Occupational and environmental factors may be a cause of nonasthmatic eosinophilic bronchitis (NAEB). The diagnosis of occupational NAEB requires evidence of sputum eosinophilia. Nevertheless, a minority of patients are not able to produce suitable sputum specimens. METHODS: This case report describes a 25-year-old woman, working as a hairdresser since the age of 20 years and handling ammonium persulfate, who came under our observation for work-related rhinitis and cough. RESULTS: A specific inhalation challenge with ammonium persulfate elicited dry cough, without any significant change in forced expiratory volume in 1 s (FEV(1)). Sputum induction was unsuccessful both pre- and after specific inhalation challenge. Fractional exhaled nitric oxide (FeNO) values significantly increased after specific inhalation challenge, suggesting a diagnosis of occupational NAEB due to ammonium persulfate. CONCLUSIONS: From this observation we suggest that FeNO measurement should be added to the investigation of work-related cough during specific inhalation challenge, and may be considered as an alternative to induced sputum to evaluate bronchial inflammation when sputum collection is unavailable or unsuccessful.


(7) TORJESEN I. Death rates from lung cancer surgery have almost halved over 10 years. BMJ. 2011, vol. 343, p.d7055


http://dx.doi.org/10.1056/NEJMp1110117

http://dx.doi.org/10.1001/jama.2011.1591

CONTEXT: The effect on mortality of screening for lung cancer with modern chest radiographs is unknown. OBJECTIVE: To evaluate the effect on mortality of screening for lung cancer using radiographs in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial. DESIGN, SETTING, AND PARTICIPANTS: Randomized controlled trial that involved 154,901 participants aged 55 through 74 years, 77,445 of whom were assigned to annual screenings and 77,456 to usual care at 1 of 10 screening centers across the United States between November 1993 and July 2001. The data from a subset of eligible participants for the National Lung Screening Trial (NLST), which compared chest radiograph with spiral computed tomographic (CT) screening, were analyzed. INTERVENTION: Participants in the intervention group were offered annual posteroanterior view chest radiograph for 4 years. Diagnostic follow-up of positive screening results was determined by participants and their health care practitioners. Participants in the usual care group were offered no interventions and received their usual medical care. All diagnosed cancers, deaths, and causes of death were ascertained through the earlier of 13 years of follow-up or until December 31, 2009. MAIN OUTCOME MEASURES: Mortality from lung cancer. Secondary outcomes included lung cancer incidence, complications associated with diagnostic procedures, and all-cause mortality. RESULTS: Screening adherence was 86.6% at baseline and 79% to 84% at years 1 through 3; the rate of screening use in the usual care group was 11%. Cumulative lung cancer incidence rates through 13 years of follow-up were 20.1 per 10,000 person-years in the intervention group and 19.2 per 10,000 person-years in the usual care group (rate ratio [RR]; 1.05, 95% CI, 0.98-1.12). A total of 1213 lung cancer deaths were observed in the intervention group compared with 1230 in usual care group through 13 years (mortality RR, 0.99; 95% CI, 0.87-1.22). Stage and histology were similar between the 2 groups. The RR of mortality for the subset of participants eligible for the NLST, over the same 6-year follow-up period, was 0.94 (95% CI, 0.81-1.10). CONCLUSION: Annual screening with chest radiograph did not reduce lung cancer mortality compared with usual care. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00002540

http://dx.doi.org/10.1001/jama.2011.1609

(12) BERGWITZ C, COLLINS MT, KAMATH RS, ROSENBERG AE. Case records of the Massachusetts General Hospital. Case 33-2011. A 56-year-old man with
http://dx.doi.org/10.1001/jama.2011.1531

CONTEXT: Smoking is a major risk factor for both cancer and chronic obstructive pulmonary disease (COPD). Computed tomography (CT)-based lung cancer screening may provide an opportunity to detect additional individuals with COPD at an early stage. OBJECTIVE: To determine whether low-dose lung cancer screening CT scans can be used to identify participants with COPD. DESIGN, SETTING, AND PATIENTS: Single-center prospective cross-sectional study within an ongoing lung cancer screening trial. Prebronchodilator pulmonary function testing with inspiratory and expiratory CT on the same day was obtained from 1140 male participants between July 2007 and September 2008. Computed tomographic emphysema was defined as percentage of voxels less than -950 Hounsfield units (HU), and CT air trapping was defined as the expiratory:inspiratory ratio of mean lung density. Chronic obstructive pulmonary disease was defined as the ratio of forced expiratory volume in the first second to forced vital capacity (FEV(1)/FVC) of less than 70%. Logistic regression was used to develop a diagnostic prediction model for airflow limitation. MAIN OUTCOME MEASURES: Diagnostic accuracy of COPD diagnosis using pulmonary function tests as the reference standard. RESULTS: Four hundred thirty-seven participants (38%) had COPD according to lung function testing. A diagnostic model with CT emphysema, CT air trapping, body mass index, pack-years, and smoking status corrected for overoptimism (internal validation) yielded an area under the receiver operating characteristic curve of 0.83 (95% CI, 0.81-0.86). Using the point of optimal accuracy, the model identified 274 participants with COPD with 85 false positives, a sensitivity of 63% (95% CI, 58%-67%), specificity of 88% (95% CI, 85%-90%), positive predictive value of 76% (95% CI, 72%-81%); and negative predictive value of 79% (95% CI, 76%-82%). The diagnostic model showed an area under the receiver operating characteristic curve of 0.87 (95% CI, 0.86-0.88) for participants with symptoms and 0.78 (95% CI, 0.76-0.80) for those without symptoms. CONCLUSION: Among men who are current and former heavy smokers, low-dose inspiratory and expiratory CT scans obtained for lung cancer screening can identify participants with COPD, with a sensitivity of 63% and a specificity of 88%

http://dx.doi.org/10.1056/NEJMcpc1013930


http://dx.doi.org/10.1093/aje/kwr210

Prospective associations between quantity and frequency of alcohol consumption and cancer-specific mortality were studied using a nationally representative sample with pooled data from the 1988, 1990, 1991, and 1997-2004 administrations of the National Health Interview Survey (n = 323,354). By 2006, 8,362 participants had died of cancer. Cox proportional hazards regression was used to estimate relative risks. Among current alcohol drinkers, for all-site cancer mortality, higher-quantity drinking (>/= 3 drinks on drinking days vs. 1 drink on drinking days) was associated with increased risk among men (relative risk (RR) = 1.24, 95% confidence interval (CI):
1.09, 1.41; P for linear trend = 0.001); higher-frequency drinking (>/= 3 days/week vs. <1 day/week) was associated with increased risk among women (RR = 1.32, 95% CI: 1.13, 1.55; P-trend < 0.001). Lung cancer mortality results were similar, but among never smokers, results were null. For colorectal cancer mortality, higher-quantity drinking was associated with increased risk among women (RR = 1.93, 95% CI: 1.17, 3.18; P-trend = 0.03) and tended to be associated with increased risk of breast cancer (RR = 1.44, 95% CI: 0.96, 2.17; P-trend = 0.06). Epidemiologic studies of alcohol and cancer mortality should consider the independent effects of quantity and frequency


BACKGROUND: Platinum-based doublet chemotherapy is recommended to treat advanced non-small-cell lung cancer (NSCLC) in fit, non-elderly adults, but monotherapy is recommended for patients older than 70 years. We compared a carboplatin and paclitaxel doublet chemotherapy regimen with monotherapy in elderly patients with advanced NSCLC. METHODS: In this multicentre, open-label, phase 3, randomised trial we recruited patients aged 70-89 years with locally advanced or metastatic NSCLC and WHO performance status scores of 0-2. Patients received either four cycles (3 weeks on treatment, 1 week off treatment) of carboplatin (on day 1) plus paclitaxel (on days 1, 8, and 15) or five cycles (2 weeks on treatment, 1 week off treatment) of vinorelbine or gemcitabine monotherapy. Randomisation was done centrally with the minimisation method. The primary endpoint was overall survival, and analysis was done by intention to treat. This trial is registered, number NCT00298415. FINDINGS: 451 patients were enrolled. 226 were randomly assigned monotherapy and 225 doublet chemotherapy. Median age was 77 years and median follow-up was 30.3 months (range 8.6-45.2). Median overall survival was 10.3 months for doublet chemotherapy and 6.2 months for monotherapy (hazard ratio 0.64, 95% CI 0.52-0.78; p<0.0001); 1-year survival was 44.5% (95% CI 37.9-50.9) and 25.4% (19.9-31.3), respectively. Toxic effects were more frequent in the doublet chemotherapy group than in the monotherapy group (most frequent, decreased neutrophil count (108 [48.4%] vs 28 [12.4%]; asthenia 23 [10.3%] vs 13 [5.8%]). INTERPRETATION: Despite increased toxic effects, platinum-based doublet chemotherapy was associated with survival benefits compared with vinorelbine or gemcitabine monotherapy in elderly patients with NSCLC. We feel that the current treatment
paradigm for these patients should be reconsidered. FUNDING: Intergroupe Francophone de Cancerologie Thoracique, Institut National du Cancer


http://dx.doi.org/10.1016/S0140-6736(10)62101-0

In the decade since the last Lancet Seminar on lung cancer there have been advances in many aspects of the classification, diagnosis, and treatment of non-small-cell lung cancer (NSCLC). An international panel of experts has been brought together to focus on changes in the epidemiology and pathological classification of NSCLC, the role of CT screening and other techniques that could allow earlier diagnosis and more effective treatment of the disease, and the recently introduced seventh edition of the TNM classification and its relation to other prognostic factors such as biological markers. We also describe advances in treatment that have seen the introduction of a new generation of chemotherapy agents, a proven advantage to adjuvant chemotherapy after complete resection for specific stage groups, new techniques for the planning and administration of radiotherapy, and new surgical approaches to assess and reduce the risks of surgical treatment

http://dx.doi.org/10.1016/S0140-6736(11)60165-7

The incidence and mortality of small-cell lung cancer worldwide make this disease a notable health-care issue. Diagnosis relies on histology, with the use of immunohistochemical studies to confirm difficult cases. Typical patients are men older than 70 years who are current or past heavy smokers and who have pulmonary and cardiovascular comorbidities. Patients often present with rapid-onset symptoms due to local intrathoracic tumour growth, extrapulmonary distant spread, paraneoplastic syndromes, or a combination of these features. Staging aims ultimately to define disease as metastatic or non-metastatic. Combination chemotherapy, generally platinum-based plus etoposide or irinotecan, is the mainstream first-line treatment for metastatic small-cell lung cancer. For non-metastatic disease, evidence supports early concurrent thoracic radiotherapy. Prophylactic cranial irradiation should be considered for patients with or without metastases whose disease does not progress after induction chemotherapy and radiotherapy. Despite high initial response rates, most patients eventually relapse. Except for topotecan, few treatment options then remain. Signalling pathways have been identified that might yield new drug targets

http://dx.doi.org/10.1093/ije/dyr037

http://dx.doi.org/10.1093/ije/dyr011

BACKGROUND: In many developed countries, immigrants live longer—that is, have lower death rates at most or all ages-than native-born residents. This article tests whether different levels of smoking-related mortality can explain part of the ‘healthy immigrant effect’ in the USA, as well as part of the related ‘Hispanic paradox’: the tendency for US Hispanics to outlive non-Hispanic Whites. METHODS: With data from vital statistics and the national census, we calculate lung cancer death rates in 2000 for four US subpopulations: foreign-born, native-born, Hispanic and non-Hispanic White. We then use three different methods—the Peto-Lopez method, the Preston-
Glei-Wilmoth method and a novel method developed in this article to generate three alternative estimates of smoking-related mortality for each of the four subpopulations, extrapolating from lung cancer death rates. We then measure the contribution of smoking-related mortality to disparities in all-cause mortality. RESULTS: Taking estimates from any of the three methods, we find that smoking explains >50% of the difference in life expectancy at 50 years between foreign- and native-born men, and >70% of the difference between foreign- and native-born women; smoking explains >75% of the difference in life expectancy at 50 years between US Hispanic and non-Hispanic White men, and close to 75% of the Hispanic advantage among women.

CONCLUSIONS: Low smoking-related mortality was the main reason for immigrants' and Hispanics' longevity advantage in the USA in 2000.


Given that new protocols for assessing asbestos-related cancer risk have recently been published, questions arise concerning how they compare to the "IRIS" protocol currently used by regulators. The newest protocols incorporate findings from 20 additional years of literature. Thus, differences between the IRIS and newer Berman and Crump protocols are examined to evaluate whether these protocols can be reconciled. Risks estimated by applying these protocols to real exposure data from both laboratory and field studies are also compared to assess the relative health protectiveness of each protocol. The reliability of risks estimated using the two protocols are compared by evaluating the degree with which each potentially reproduces the known epidemiology study risks. Results indicate that the IRIS and Berman and Crump protocols can be reconciled; while environment-specific variation within fiber type is apparently due primarily to size effects (not addressed by IRIS), the 10-fold (average) difference between amphibole asbestos risks estimated using each protocol is attributable to an arbitrary selection of the lowest of available mesothelioma potency factors in the IRIS protocol. Thus, the IRIS protocol may substantially underestimate risk when exposure is primarily to amphibole asbestos. Moreover, while the Berman and Crump protocol is more reliable than the IRIS protocol overall (especially for predicting amphibole risk), evidence is presented suggesting a new fiber-size-related adjustment to the Berman and Crump protocol may ultimately succeed in reconciling the entire epidemiology database. However, additional data need to be developed before the performance of the adjusted protocol can be fully validated.


BACKGROUND: Emissions from household coal combustion associated with cooking and heating are an important public health issue, particularly in China where hundreds of millions of people are exposed. Although coal emissions are a known human carcinogen, there is still uncertainty about the level of risk for lung and other cancers. METHODS: We performed a meta-analysis on 25 case-control studies (10,142 cases and 13,416 controls) to summarize the association between household coal use and lung cancer risk, and to explore the effect modification of this association by geographical location. RESULTS: Using random-effects models, household coal use was found to be associated with lung cancer risk among all studies throughout the world [odds ratio (OR) = 2.15; 95% confidence interval (CI) = 1.61-2.89, N(studies) = 25], and particularly among those studies that carried out in mainland China and Taiwan (OR = 2.27; 95% CI = 1.65-3.12, N(studies) = 20). Stratification by regions of mainland China and Taiwan found a variation in effects across the regions, with south/southeastern China (OR = 3.27; 95% CI = 1.27-8.42, N(studies) = 3) and southwestern China (OR = 2.98; 95% CI = 1.18-7.53, N(studies) = 3) experiencing the highest risk. The elevated risk associated with coal use throughout Asia was also observed when stratifying studies by gender, smoking status, sample size, design (population vs hospital case-control) and publication language. No significant publication bias was found (p(Begg's) = 0.15).
CONCLUSIONS: Our results provide evidence that although the carcinogenic effect of coal use varies by location, coals from many locations exhibit elevated lung cancer risks

http://dx.doi.org/10.1093/ije/dyp353

Dengue

http://dx.doi.org/10.1126/science.1213798

(2) WATTS G. Bacterium blocks transmission of dengue by mosquitoes. BMJ. 2011, vol. 343, p.d5545

http://dx.doi.org/10.1038/nature10356

Genetic manipulations of insect populations for pest control have been advocated for some time, but there are few cases where manipulated individuals have been released in the field and no cases where they have successfully invaded target populations. Population transformation using the intracellular bacterium Wolbachia is particularly attractive because this maternally-inherited agent provides a powerful mechanism to invade natural populations through cytoplasmic incompatibility. When Wolbachia are introduced into mosquitoes, they interfere with pathogen transmission and influence key life history traits such as lifespan. Here we describe how the wMel Wolbachia infection, introduced into the dengue vector Aedes aegypti from Drosophila melanogaster, successfully invaded two natural A. aegypti populations in Australia, reaching near-fixation in a few months following releases of wMel-infected A. aegypti adults. Models with plausible parameter values indicate that Wolbachia-infected mosquitoes suffered relatively small fitness costs, leading to an unstable equilibrium frequency <30% that must be exceeded for invasion. These findings demonstrate that Wolbachia-based strategies can be deployed as a practical approach to dengue suppression with potential for area-wide implementation

http://dx.doi.org/10.1038/nature10355

Dengue fever is the most important mosquito-borne viral disease of humans with more than 50 million cases estimated annually in more than 100 countries. Disturbingly, the geographic range of dengue is currently expanding and the severity of outbreaks is increasing. Control options for dengue are very limited and currently focus on reducing population abundance of the major mosquito vector, Aedes aegypti. These strategies are failing to reduce dengue incidence in tropical communities and there is an urgent need for effective alternatives. It has been proposed that endosymbiotic bacterial Wolbachia infections of insects might be used in novel strategies for dengue control. For example, the wMelPop-CLA Wolbachia strain reduces the lifespan of adult A. aegypti mosquitoes in stably transinfected lines. This life-shortening phenotype was predicted to reduce the potential for dengue transmission. The recent discovery that several Wolbachia infections, including wMelPop-CLA, can also directly influence the susceptibility of insects to infection with a range of insect and human pathogens has markedly changed the potential for Wolbachia infections to control human diseases. Here we describe the successful transinfection of
A. aegypti with the avirulent wMel strain of Wolbachia, which induces the reproductive phenotype cytoplasmic incompatibility with minimal apparent fitness costs and high maternal transmission, providing optimal phenotypic effects for invasion. Under semi-field conditions, the wMel strain increased from an initial starting frequency of 0.65 to near fixation within a few generations, invading A. aegypti populations at an accelerated rate relative to trials with the wMelPop-CLA strain. We also show that wMel and wMelPop-CLA strains block transmission of dengue serotype 2 (DENV-2) in A. aegypti, forming the basis of a practical approach to dengue suppression


BACKGROUND: Many factors have been associated with circulation of the dengue fever virus and vector, although the dynamics of transmission are not yet fully understood. The aim of this work is to estimate the spatial distribution of the risk of dengue fever in an area of continuous dengue occurrence. METHODS: This is a spatial population-based case-control study that analyzed 538 cases and 727 controls in one district of the municipality of Campinas, Sao Paulo, Brazil, from 2006-2007, considering socio-demographic, ecological, case severity, and household infestation variables. Information was collected by in-home interviews and inspection of living conditions in and around the homes studied. Cases were classified as mild or severe according to clinical data, and they were compared with controls through a multinomial logistic model. A generalized additive model was used in order to include space in a non-parametric fashion with cubic smoothing splines. RESULTS: Variables associated with increased incidence of all dengue cases in the multiple binomial regression model were: higher larval density (odds ratio (OR) = 2.3 (95%CI: 2.0-2.7)), reports of mosquito bites during the day (OR = 1.8 (95%CI: 1.4-2.4)), the practice of water storage at home (OR = 2.5 (95%CI: 1.4, 4.3)), low frequency of garbage collection (OR = 2.6 (95%CI: 1.6-4.5)) and lack of basic sanitation (OR = 2.9 (95%CI: 1.8-4.9)). Staying at home during the day was protective against the disease (OR = 0.5 (95%CI: 0.3-0.6)). When cases were analyzed by categories (mild and severe) in the multinomial model, age and number of breeding sites more than 10 were significant only for the occurrence of severe cases (OR = 0.97, (95%CI: 0.96-0.99) and OR = 2.1 (95%CI: 1.2-3.5), respectively. Spatial distribution of risks of mild and severe dengue fever differed from each other in the 2006/2007 epidemic, in the study area. CONCLUSIONS: Age and presence of more than 10 breeding sites were significant only for severe cases. Other predictors of mild and severe cases were similar in the multiple models. The analyses of multinomial models and spatial distribution maps of dengue fever probabilities suggest an area-specific epidemic with varying clinical and demographic characteristics
sample (Kawasaki formula). We used restricted cubic spline plots to describe the association between sodium and potassium excretion and CV events and mortality, and to identify reference categories for sodium and potassium excretion. We used Cox proportional hazards multivariable models to determine the association of urinary sodium and potassium with CV events and mortality. MAIN OUTCOME MEASURES: CV death, myocardial infarction (MI), stroke, and hospitalization for congestive heart failure (CHF). RESULTS: At baseline, the mean (SD) estimated 24-hour excretion for sodium was 4.77 g (1.61); and for potassium was 2.19 g (0.57). After a median follow-up of 56 months, the composite outcome occurred in 4729 (16.4%) participants, including 2057 CV deaths, 1412 with MI, 1282 with stroke, and 1213 with hospitalization for CHF. Compared with the reference group with estimated baseline sodium excretion of 4 to 5.99 g per day (n = 14,156; 63.6% participants with CV death, 4.6% with MI, 4.2% with stroke, and 3.8% admitted to hospital with CHF), higher baseline sodium excretion was associated with an increased risk of CV death (9.7% for 7-8 g/day; hazard ratio [HR], 1.53; 95% CI, 1.26-1.86; and 11.2% for >8 g/day; HR, 1.66; 95% CI, 1.31-2.10), MI (6.8%; HR, 1.48; 95% CI, 1.11-1.98 for >8 g/day), stroke (6.6%; HR, 1.48; 95% CI, 1.09-2.01 for >8 g/day), and hospitalization for CHF (6.5%; HR, 1.51; 1.12-2.05 for >8 g/day). Lower sodium excretion was associated with an increased risk of CV death (8.6%; HR, 1.19; 95% CI, 1.02-1.39 for 2-2.99 g/day; 10.6%; HR, 1.37; 95% CI, 1.09-1.73 for <2 g/day), and hospitalization for CHF (5.2%; HR, 1.23; 95% CI, 1.01-1.49 for 2-2.99 g/day) on multivariable analysis. Compared with an estimated potassium excretion of less than 1.5 g per day (n = 2194; 6.2% with stroke), higher potassium excretion was associated with a reduced risk of CV death (8.6%; HR, 0.77; 95% CI, 0.63-0.94) for 1.5-1.99 g/day; 4.3% [HR, 0.73; 95% CI, 0.59-0.90] for 2-2.49 g/day; 3.9% [HR, 0.71; 95% CI, 0.56-0.91] for 2.5-3 g/day; and 3.5% [HR, 0.68; 95% CI, 0.49-0.92] for >3 g/day) on multivariable analysis. CONCLUSIONS: The association between estimated sodium excretion and CV events and mortality was J-shaped. Compared with baseline sodium excretion of 4 to 5.99 g per day, sodium excretion of greater than 7 g per day was associated with an increased risk of all CV events, and a sodium excretion of less than 3 g per day was associated with increased risk of CV mortality and hospitalization for CHF. Higher estimated potassium excretion was associated with a reduced risk of stroke.

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CONTEXT: Few studies have examined the association between the number of coronary heart disease risk factors and outcomes of acute myocardial infarction in community practice. OBJECTIVE: To determine the association between the number of coronary heart disease risk factors in patients with first myocardial infarction and hospital mortality. DESIGN: Observational study from the National Registry of Myocardial Infarction, 1994-2006. PATIENTS: We examined the presence and absence of 5 major traditional coronary heart disease risk factors (hypertension, smoking, dyslipidemia, diabetes, and family history of coronary heart disease) and hospital mortality among 542,008 patients with first myocardial infarction and without prior cardiovascular disease. MAIN OUTCOME MEASURE: All-cause in-hospital mortality. RESULTS: A majority (85.6%) of patients who presented with initial myocardial infarction had at least 1 of the 5 coronary heart disease risk factors, and 14.4% had none of the 5 risk factors. Age varied inversely with the number of coronary heart disease risk factors, from a mean age of 71.5 years with 0 risk factors to 56.7 years with 5 risk factors (P for trend < .001). The total number of in-hospital deaths for all causes was 50,788. Unadjusted in-hospital mortality rates were 14.9%, 10.9%, 7.9%, 5.3%, 4.2%, and 3.6% for patients with 0, 1, 2, 3, 4, and 5 risk factors, respectively. After adjusting for age and other clinical factors, there was an inverse association between the number of coronary heart disease risk factors and hospital mortality adjusted odds ratio (1.54; 95% CI, 1.23-1.94) among individuals with 0 vs 5 risk factors. This association was consistent among several age strata and important patient subgroups. CONCLUSION: Among patients with incident acute myocardial infarction without prior cardiovascular disease, in-hospital mortality was inversely related to the number of coronary heart disease risk factors.
   [http://dx.doi.org/10.1056/NEJMcibr1109442](http://dx.doi.org/10.1056/NEJMcibr1109442)

   [http://dx.doi.org/10.1056/NEJMoa1010112](http://dx.doi.org/10.1056/NEJMoa1010112)

**BACKGROUND:** Obesity in childhood is associated with increased cardiovascular risk. It is uncertain whether this risk is attenuated in persons who are overweight or obese as children but not obese as adults. **METHODS:** We analyzed data from four prospective cohort studies that measured childhood and adult body-mass index (BMI, the weight in kilograms divided by the square of the height in meters). The mean length of follow-up was 23 years. To define high adiposity status, international age-specific and sex-specific BMI cutoff points for overweight and obesity were used for children, and a BMI cutoff point of 30 was used for adults. **RESULTS:** Data were available for 6328 subjects. Subjects with consistently high adiposity status from childhood to adulthood, as compared with persons who had a normal BMI as children and were nonobese as adults, had an increased risk of type 2 diabetes (relative risk, 5.4; 95% confidence interval [CI], 3.4 to 8.5), hypertension (relative risk, 2.7; 95% CI, 2.2 to 3.3), elevated low-density lipoprotein cholesterol levels (relative risk, 1.8; 95% CI, 1.4 to 2.3), reduced high-density lipoprotein cholesterol levels (relative risk, 2.1; 95% CI, 1.8 to 2.5), elevated triglyceride levels (relative risk, 3.0; 95% CI, 2.4 to 3.8), and carotid-artery atherosclerosis (increased intima-media thickness of the carotid artery) (relative risk, 1.7; 95% CI, 1.4 to 2.2) (P ≤ 0.002 for all comparisons). Persons who were overweight or obese during childhood but were nonobese as adults had risks of the outcomes that were similar to those of persons who had a normal BMI consistently from childhood to adulthood (P>0.20 for all comparisons). **CONCLUSIONS:** Overweight or obese children who were obese as adults had increased risks of type 2 diabetes, hypertension, dyslipidemia, and carotid-artery atherosclerosis. The risks of these outcomes among overweight or obese children who became nonobese by adulthood were similar to those among persons who were never obese. (Funded by the Academy of Finland and others.)

   [http://dx.doi.org/10.1056/NEJMc11110239#SA4](http://dx.doi.org/10.1056/NEJMc11110239#SA4)

   [http://dx.doi.org/10.1056/NEJMc11110239#SA3](http://dx.doi.org/10.1056/NEJMc11110239#SA3)

   [http://dx.doi.org/10.1056/NEJMc11110239#SA2](http://dx.doi.org/10.1056/NEJMc11110239#SA2)

   [http://dx.doi.org/10.1056/NEJMc11110239#SA1](http://dx.doi.org/10.1056/NEJMc11110239#SA1)

   [http://dx.doi.org/10.1056/NEJMsa1011785](http://dx.doi.org/10.1056/NEJMsa1011785)

**BACKGROUND:** In the Medicare Modernization Act of 2003, Congress required the Centers for
Medicare and Medicaid Services to test the commercial disease-management model in the Medicare fee-for-service program. METHODS: The Medicare Health Support Pilot Program was a large, randomized study of eight commercial programs for disease management that used nurse-based call centers. We randomly assigned patients with heart failure, diabetes, or both to the intervention or to usual care (control) and compared them with the use of a difference-in-differences method to evaluate the effects of the commercial programs on the quality of clinical care, acute care utilization, and Medicare expenditures for Medicare fee-for-service beneficiaries. RESULTS: The study included 242,417 patients (163,107 in the intervention group and 79,310 in the control group). The eight commercial disease-management programs did not reduce hospital admissions or emergency room visits, as compared with usual care. We observed only 14 significant improvements in process-of-care measures out of 40 comparisons. These modest improvements came at substantial cost to the Medicare program in fees paid to the disease-management companies ($400 million), with no demonstrable savings in Medicare expenditures.

CONCLUSIONS: In this large study, commercial disease-management programs using nurse-based call centers achieved only modest improvements in quality-of-care measures, with no demonstrable reduction in the utilization of acute care or the costs of care.

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http://dx.doi.org/10.1056/NEJMct0908432

http://dx.doi.org/10.1056/NEJMsa1103216

BACKGROUND: The question of whether neighborhood environment contributes directly to the development of obesity and diabetes remains unresolved. The study reported on here uses data from a social experiment to assess the association of randomly assigned variation in neighborhood conditions with obesity and diabetes. METHODS: From 1994 through 1998, the Department of Housing and Urban Development (HUD) randomly assigned 4498 women with children living in public housing in high-poverty urban census tracts (in which >/=40% of residents had incomes below the federal poverty threshold) to one of three groups: 1788 were assigned to
receive housing vouchers, which were redeemable only if they moved to a low-poverty census tract (where <10% of residents were poor), and counseling on moving; 1312 were assigned to receive unrestricted, traditional vouchers, with no special counseling on moving; and 1398 were assigned to a control group that was offered neither of these opportunities. From 2008 through 2010, as part of a long-term follow-up survey, we measured data indicating health outcomes, including height, weight, and level of glycated hemoglobin (HbA1c)). RESULTS: As part of our long-term survey, we obtained data on body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) for 84.2% of participants and data on glycated hemoglobin level for 71.3% of participants. Response rates were similar across randomized groups. The prevalences of a BMI of 35 or more, a BMI of 40 or more, and a glycated hemoglobin level of 6.5% or more were lower in the group receiving the low-poverty vouchers than in the control group, with an absolute difference of 4.61 percentage points (95% confidence interval [CI], -8.54 to -0.69), 3.38 percentage points (95% CI, -6.39 to -0.36), and 4.31 percentage points (95% CI, -7.82 to -0.80), respectively. The differences between the group receiving traditional vouchers and the control group were not significant. CONCLUSIONS: The opportunity to move from a neighborhood with a high level of poverty to one with a lower level of poverty was associated with modest but potentially important reductions in the prevalence of extreme obesity and diabetes. The mechanisms underlying these associations remain unclear but warrant further investigation, given their potential to guide the design of community-level interventions intended to improve health. (Funded by HUD and others.)

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Although advances in immunosuppression, tissue typing, surgery, and medical management have made transplantation a routine and preferred treatment for patients with irreversible renal failure, successful transplant recipients have a greatly increased risk of premature mortality because of cardiovascular disease and malignancy compared with the general population. Conventional cardiovascular risk factors such as hyperlipidaemia, hypertension, and diabetes are common in transplant recipients, partly because of the effects of immunosuppressive drugs, and are associated with adverse outcomes. However, the natural history of cardiovascular disease in such recipients differs from that in the general population, and only statin therapy has been studied in a large-scale interventional trial. Thus, the management of this disease and the balance between management of conventional risk factors and modification of immunosuppression is complex.


OBJECTIVE: To study the risk of adverse pregnancy outcomes in women with polycystic ovary syndrome, taking into account maternal characteristics and assisted reproductive technology. DESIGN: Population based cohort study. SETTING: Singleton births registered in the Swedish medical birth register between 1995 and 2007. PARTICIPANTS: By linkage with the Swedish patient register, 3787 births among women with a diagnosis of polycystic ovary syndrome and 1,191,336 births among women without such a diagnosis. MAIN OUTCOME MEASURES: Risk of adverse pregnancy outcomes (gestational diabetes, pre-eclampsia, preterm birth, stillbirth, neonatal death, low Apgar score (<7 at five minutes), meconium aspiration, large for gestational age, macrosomia, small for gestational age), adjusted for maternal characteristics (body mass index, age), socioeconomic factors (educational level, and cohabitating with infant's father), and assisted reproductive technology. RESULTS: Women with polycystic ovary syndrome were more often obese and more commonly used assisted reproductive technology than women without such a diagnosis (60.6% v 34.8% and 13.7% v 1.5%). Polycystic ovary syndrome was strongly associated with pre-eclampsia (adjusted odds ratio 1.45, 95% confidence interval 1.24 to 1.69) and very preterm birth (2.21, 1.69 to 2.90) and the risk of gestational diabetes was more than doubled (2.32, 1.88 to 2.88). Infants born to mothers with polycystic ovary syndrome were more
prone to be large for gestational age (1.39, 1.19 to 1.62) and were at increased risk of meconium aspiration (2.02, 1.13 to 3.61) and having a low Apgar score (<7) at five minutes (1.41, 1.09 to 1.83). CONCLUSIONS: Women with polycystic ovary syndrome are at increased risk of adverse pregnancy and birth outcomes that cannot be explained by assisted reproductive technology. These women may need increased surveillance during pregnancy and parturition.


OBJECTIVE: To examine the risk of neurological and autoimmune disorders of special interest in people vaccinated against pandemic influenza A (H1N1) with Pandemrix (GlaxoSmithKline, Middlesex, UK) compared with unvaccinated people over 8-10 months. DESIGN: Retrospective cohort study linking individualised data on pandemic vaccinations to an inpatient and specialist database on healthcare utilisation in Stockholm county for follow-up during and after the pandemic period. SETTING: Stockholm county, Sweden. Population All people registered in Stockholm county on 1 October 2009 and who had lived in this region since 1 January 1998; 1,024,019 were vaccinated against H1N1 and 921,005 remained unvaccinated. MAIN OUTCOME MEASURES: Neurological and autoimmune diagnoses according to the European Medicines Agency strategy for monitoring of adverse events of special interest defined using ICD-10 codes for Guillain-Barre syndrome, Bell's palsy, multiple sclerosis, polyneuropathy, anaesthesia or hypoaesthesia, paraesthesia, narcolepsy (added), and autoimmune conditions such as rheumatoid arthritis, inflammatory bowel disease, and type 1 diabetes; and short term mortality according to vaccination status. RESULTS: Excess risks among vaccinated compared with unvaccinated people were of low magnitude for Bell's palsy (hazard ratio 1.25, 95% confidence interval 1.06 to 1.48) and paraesthesia (1.11, 1.00 to 1.23) after adjustment for age, sex, socioeconomic status, and healthcare utilisation. Risks for Guillain-Barre syndrome, multiple sclerosis, type 1 diabetes, and rheumatoid arthritis remained unchanged. The risks of paraesthesia and inflammatory bowel disease among those vaccinated in the early phase (within 45 days from 1 October 2009) of the vaccination campaign were significantly increased; the risk being increased within the first six weeks after vaccination. Those vaccinated in the early phase were at a slightly reduced risk of death than those who were unvaccinated (0.94, 0.91 to 0.98), whereas those vaccinated in the late phase had an overall reduced mortality (0.68, 0.64 to 0.71). These associations could be real or explained, partly or entirely, by residual confounding. CONCLUSIONS: Results for the safety of Pandemrix over 8-10 months of follow-up were reassuring -notably, no change in the risk for Guillain-Barre syndrome, multiple sclerosis, type 1 diabetes, or rheumatoid arthritis. Relative risks were significantly increased for Bell's palsy, paraesthesia, and inflammatory bowel disease after vaccination, predominantly in the early phase of the vaccination campaign. Small numbers of children and adolescents with narcolepsy precluded any meaningful conclusions.

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Determining the signalling pathways that direct tissue expansion is a principal goal of regenerative biology. Vigorous pancreatic beta-cell replication in juvenile mice and humans declines with age, and elucidating the basis for this decay may reveal strategies for inducing beta-cell expansion, a long-sought goal for diabetes therapy. Here we show that platelet-derived growth factor receptor (Pdgfr) signalling controls age-dependent beta-cell proliferation in mouse and human pancreatic islets. With age, declining beta-cell Pdgfr levels were accompanied by reductions in beta-cell enhancer of zeste homologue 2 (Ezh2) levels and beta-cell replication. Conditional inactivation of the Pdgfra gene in beta-cells accelerated these changes, preventing mouse neonatal beta-cell expansion and adult beta-cell regeneration. Targeted human PDGFR-alpha activation in mouse beta-cells stimulated Erk1/2 phosphorylation, leading to Ezh2-dependent expansion of adult beta-cells. Adult human islets lack PDGF signalling competence, but exposure of juvenile human islets...
to PDGF-AA stimulated beta-cell proliferation. The discovery of a conserved pathway controlling age-dependent beta-cell proliferation indicates new strategies for beta-cell expansion

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http://dx.doi.org/10.1001/jama.2011.1438


OBJECTIVE: To determine the prevalence of financial conflicts of interest among members of panels producing clinical practice guidelines on screening, treatment, or both for hyperlipidaemia or diabetes. DESIGN: Cross sectional study. SETTING: Relevant guidelines published by national organisations in the United States and Canada between 2000 and 2010. PARTICIPANTS: Members of guideline panels. MAIN OUTCOME MEASURES: Prevalence of financial conflicts of interest among members of guideline panels and chairs of panels. RESULTS: Fourteen guidelines met our search criteria, of which five had no accompanying declaration of conflicts of interest by panel members. 288 panel members had participated in the guideline development process. Among the 288 panel members, 138 (48%) reported conflicts of interest at the time of the publication of the guideline and 150 (52%) either stated that they had no such conflicts or did not have an opportunity to declare any. Among 73 panellists who formally declared no conflicts, 8 (11%) were found to have one or more. Twelve of the 14 guideline panels evaluated identified chairs, among whom six had financial conflicts of interest. Overall, 150 (52%) panel members had conflicts, of which 138 were declared and 12 were undeclared. Panel members from government sponsored guidelines were less likely to have conflicts of interest compared with guidelines sponsored by non-government sources (15/92 (16%) v 135/196 (69%); P<0.001). CONCLUSIONS: The prevalence of financial conflicts of interest and their under-reporting by members of panels producing clinical practice guidelines on hyperlipidaemia or diabetes was high, and a relatively high proportion of guidelines did not have public disclosure of conflicts of interest. Organisations that produce guidelines should minimise conflicts of interest among panel members to ensure the credibility and evidence based nature of the guidelines’ content

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http://dx.doi.org/10.1126/science.333.6049.1561


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OBJECTIVE: To examine short and long term time trends in mortality among patients with early onset (age 0-14 years) and late onset (15-29 years) type 1 diabetes and causes of deaths over time. DESIGN: Population based nationwide cohort study. SETTING: Finland. PARTICIPANTS: All Finnish patients diagnosed as having type 1 diabetes below age 30 years between 1970 and 1999 (n = 17,306). MAIN OUTCOME MEASURES: Crude mortality, standardised mortality ratios, time trends, and cumulative mortality. RESULTS: A total of 1338 deaths occurred during 370,733 person years of follow-up, giving an all cause mortality rate of 361/100,000 person years. The standardised mortality ratio was 3.6 in the early onset cohort and 2.8 in the late onset cohort. Women had higher standardised mortality ratios than did men in both cohorts (5.5 v 3.0 in the early onset cohort; 3.6 v 2.6 in the late onset cohort). The standardised mortality ratio at 20 years' duration of diabetes in the early onset cohort decreased from 3.5 in the patients diagnosed in 1970-4 to 1.9 in those diagnosed in 1985-9. In contrast, the standardised mortality ratio in the late onset cohort increased from 1.4 in those diagnosed in 1970-4 to 2.9 in those diagnosed in 1985-9. Mortality due to chronic complications of diabetes decreased with time in the early onset cohort but not in the late onset cohort. Mortality due to alcohol related and drug related causes increased in the late onset cohort and accounted for 39% of the deaths during the first 20 years of diabetes. Accordingly, mortality due to acute diabetic complications increased significantly in the late onset cohort. CONCLUSION: Survival of people with early onset type 1 diabetes has improved over time, whereas survival of people with late onset type 1 diabetes has deteriorated since the 1980s. Alcohol has become an important cause of death in patients with type 1 diabetes, and the proportion of deaths caused by acute complications of diabetes has increased in patients with late onset type 1 diabetes

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http://dx.doi.org/10.1038/nature10354

Genome-wide association studies (GWAS) have identified many risk loci for complex diseases, but effect sizes are typically small and information on the underlying biological processes is often lacking. Associations with metabolic traits as functional intermediates can overcome these problems and potentially inform individualized therapy. Here we report a comprehensive analysis of genotype-dependent metabolic phenotypes using a GWAS with non-targeted metabolomics. We identified 37 genetic loci associated with blood metabolite concentrations, of which 25 show effect sizes that are unusually high for GWAS and account for 10-60% differences in metabolite levels per allele copy. Our associations provide new functional insights for many disease-related associations that have been reported in previous studies, including those for cardiovascular and kidney disorders, type 2 diabetes, cancer, gout, venous thromboembolism and Crohn's disease. The study advances our knowledge of the genetic basis of metabolic individuality in humans and generates many new hypotheses for biomedical and pharmaceutical research.

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BACKGROUND: Available studies have shown few quality-related advantages of electronic health records (EHRs) over traditional paper records. We compared achievement of and improvement in quality standards for diabetes at practices using EHRs with those at practices using paper records. All practices, including many safety-net primary care practices, belonged to a regional quality collaborative and publicly reported performance. METHODS: We used generalized estimating equations to calculate the percentage-point difference between EHR-based and paper-based practices with respect to achievement of composite standards for diabetes care (including four component standards) and outcomes (five standards), after adjusting for covariates and accounting for clustering. In addition to insurance type (Medicare, commercial, Medicaid, or uninsured), patient-level covariates included race or ethnic group (white, black, Hispanic, or other), age, sex, estimated household income, and level of education. Analyses were conducted separately for the overall sample and for safety-net practices. RESULTS: From July 2009 through June 2010, data were reported for 27,207 adults with diabetes seen at 46 practices; safety-net practices accounted for 38% of patients. After adjustment for covariates, achievement of composite standards for diabetes care was 35.1 percentage points higher at EHR sites than at paper-based sites (P<0.001), and achievement of composite standards for outcomes was 15.2 percentage points higher (P=0.005). EHR sites were associated with higher achievement on eight of nine component standards. Such sites were also associated with greater improvement in care (a difference of 10.2 percentage points in annual improvement, P<0.001) and outcomes (a difference of 4.1 percentage points in annual improvement, P=0.02). Across all insurance types, EHR sites were associated with significantly higher achievement of care and outcome standards and greater improvement in diabetes care. Results confined to safety-net practices were similar. CONCLUSIONS: These findings support the premise that federal policies encouraging the meaningful use of EHRs may improve the quality of care across insurance types.

OBJECTIVE: To evaluate the association of chocolate consumption with the risk of developing cardiometabolic disorders. DESIGN: Systematic review and meta-analysis of randomised controlled trials and observational studies. DATA SOURCES: Medline, Embase, Cochrane Library, PubMed, CINAHL, IPA, Web of Science, Scopus, Pascal, reference lists of relevant studies to October 2010, and email contact with authors. STUDY SELECTION: Randomised trials and cohort, case-control, and cross sectional studies carried out in human adults, in which the association between chocolate consumption and the risk of outcomes related to cardiometabolic disorders were reported. DATA EXTRACTION: Data were extracted by two independent investigators, and a consensus was reached with the involvement of a third. The primary outcome was cardiometabolic disorders, including cardiovascular disease (coronary heart disease and stroke), diabetes, and metabolic syndrome. A meta-analysis assessed the risk of developing cardiometabolic disorders by comparing the highest and lowest level of chocolate consumption. RESULTS: From 4576 references seven studies met the inclusion criteria (including 114,009 participants). None of the studies was a randomised trial, six were cohort studies, and one a cross sectional study. Large variation was observed between these seven studies for measurement of chocolate consumption, methods, and outcomes evaluated. Five of the seven studies reported a beneficial association between higher levels of chocolate consumption and the risk of cardiometabolic disorders. The highest levels of chocolate consumption were associated with a 37% reduction in cardiovascular disease (relative risk 0.63 (95% confidence interval 0.44 to 0.90)) and a 29% reduction in stroke compared with the lowest levels. CONCLUSIONS: Based on observational evidence, levels of chocolate consumption seem to be associated with a substantial reduction in the risk of cardiometabolic disorders. Further experimental studies are required to confirm a potentially beneficial effect of chocolate consumption.

Rising prevalence of obesity is a worldwide health concern because excess weight gain within populations forecasts an increased burden from several diseases, most notably cardiovascular diseases, diabetes, and cancers. In this report, we used a simulation model to project the probable health and economic consequences in the next two decades from a continued rise in obesity in two ageing populations--the USA and the UK. These trends project 65 million more obese adults in the USA and 11 million more obese adults in the UK by 2030, consequently accruing an additional 6-8.5 million cases of diabetes, 5.7-7.3 million cases of heart disease and stroke, 492,000-669,000 additional cases of cancer, and 26-55 million quality-adjusted life years forgone for USA and UK combined. The combined medical costs associated with treatment of these preventable diseases are estimated to increase by $48-66 billion/year in the USA and by pound1.9-2 billion/year in the UK by 2030. Hence, effective policies to promote healthier weight also have economic benefits.


We surveyed state diabetes programs to determine whether they develop and disseminate diabetes guidelines. We found they largely disseminate clinical practice guidelines developed from subspecialty organizations, do not prioritize among the many recommendations contained in diabetes guidelines, and have not adapted guidelines to focus on population rather than individual health. An opportunity exists for state diabetes control programs to better align guidelines with public health goals.


BACKGROUND: Type 2 diabetes is an important preventable disease and a growing public health problem. Based on information provided by clinical trials, we know that Type 2 diabetes can be prevented or delayed by lifestyle intervention. In view of translating the findings of diabetes prevention research into real-life it is necessary to carry out community-based evaluations so as to learn about the feasibility and effectiveness of locally designed and implemented programmes. The aim of this project was to assess the effectiveness of an active real-life primary care strategy in high-risk individuals for developing diabetes, and then evaluate its efficiency.

METHODS/DESIGN: Cost-Effectiveness analysis of the DE-PLAN (Diabetes in Europe - Prevention using Lifestyle, physical Activity and Nutritional intervention) project when applied to a Mediterranean population in Catalonia (DE-PLAN-CAT). Multicenter, longitudinal cohort assessment (4 years) conducted in 18 primary health-care centres (Catalan Health Institute). Individuals without diabetes aged 45-75 years were screened using the Finnish Diabetes Risk Score - FINDR.


Health literacy is the degree to which individuals have the capacity to obtain, process, and understand health information, skills, and services needed to make informed health decisions and take informed actions. Narratives from Mr J, a 76-year-old man with multiple medical problems and limited health literacy, and his physician exhibit some of the difficulties experienced by patients with limited health literacy. Clinicians can help patients with limited health literacy by removing unneeded complexity in their treatment regimens and in the health care system and by using teach-back methods to assess and improve understanding. Rather than a selective screening approach for limited health literacy, a patient-based universal precaution approach for confirming patient comprehension of critical self-care activities helps ensure that all patients have their health literacy needs identified.


OBJECTIVE: To determine all cause mortality and deaths from cardiovascular events related to intensive glucose lowering treatment in people with type 2 diabetes. DESIGN: Meta-analysis of randomised controlled trials. DATA SOURCES: Medline, Embase, and the Cochrane database of

systematic reviews. STUDY SELECTION: Randomised controlled trials that assessed the effect of intensive glucose lowering treatment on cardiovascular events and microvascular complications in adults (≥ 18 years) with type 2 diabetes. DATA EXTRACTION: Primary end points were all cause mortality and death from cardiovascular causes. Secondary end points were severe hypoglycaemia and macrovascular and microvascular events. Synthesis of results Results are reported as risk ratios with 99% confidence intervals. Statistical heterogeneity between trials was assessed with chi(2), tau(2), and I(2) statistics. A fixed effect model was used to assess the effect on the outcomes of intensive glucose lowering versus standard treatment. The quality of clinical trials was assessed by the Jadad score. RESULTS: 13 studies were included. Of 34,533 patients, 18,315 received intensive glucose lowering treatment and 16,218 standard treatment. Intensive treatment did not significantly affect all cause mortality (risk ratio 1.04, 99% confidence interval 0.91 to 1.19) or cardiovascular death (1.11, 0.86 to 1.43). Intensive therapy was, however, associated with reductions in the risk of non-fatal myocardial infarction (0.85, 0.74 to 0.96, P<0.001), and microalbuminuria (0.90, 0.85 to 0.96, P<0.001) but a more than twofold increase in the risk of severe hypoglycaemia (2.33, 21.62 to 3.36, P<0.001). Over a treatment period of five years, 117 to 150 patients would need to be treated to avoid one myocardial infarction and 32 to 142 patients to avoid one episode of microalbuminuria, whereas one severe episode of hypoglycaemia would occur for every 15 to 52 patients. In analysis restricted to high quality studies (Jadad score >3), intensive treatment was not associated with any significant risk of reductions but resulted in a 47% increase in risk of congestive heart failure (P<0.001).

CONCLUSIONS: The overall results of this meta-analysis show limited benefits of intensive glucose lowering treatment on all cause mortality and deaths from cardiovascular causes. We cannot exclude a 9% reduction or a 19% increase in all cause mortality and a 14% reduction or a 43% increase in cardiovascular death. The benefit: risk ratio of intensive glucose lowering treatment in the prevention of macrovascular and microvascular events remains uncertain. The harm associated with severe hypoglycaemia might counterbalance the potential benefit of intensive glucose lowering treatment. More double blind randomised controlled trials are needed to establish the best therapeutic approach in people with type 2 diabetes.


BACKGROUND: Diabetes prevalence is increasing globally, and Sub-Saharan Africa is no exception. With diverse health challenges, health authorities in Sub-Saharan Africa and international donors need robust data on the epidemiology and impact of diabetes in order to plan and prioritise their health programmes. This paper aims to provide a comprehensive and up-to-date review of the epidemiological trends and public health implications of diabetes in Sub-Saharan Africa. METHODS: We conducted a systematic literature review of papers published on diabetes in Sub-Saharan Africa 1999-March 2011, providing data on diabetes prevalence, outcomes (chronic complications, infections, and mortality), access to diagnosis and care and economic impact. RESULTS: Type 2 diabetes accounts for well over 90% of diabetes in Sub-Saharan Africa, and population prevalence proportions ranged from 1% in rural Uganda to 12% in urban Kenya. Reported type 1 diabetes prevalence was low and ranged from 4 per 100,000 in Mozambique to 12 per 100,000 in Zambia. Gestational diabetes prevalence varied from 0% in Tanzania to 9% in Ethiopia. Proportions of patients with diabetic complications ranged from 7-63% for retinopathy, 27-66% for neuropathy, and 10-83% for microalbuminuria. Diabetes is likely to increase the risk of several important infections in the region, including tuberculosis, pneumonia and sepsis. Meanwhile, antiviral treatment for HIV increases the risk of obesity and insulin resistance. Five-year mortality proportions of patients with diabetes varied from 4-57%. Screening studies identified high proportions (> 40%) with previously undiagnosed diabetes, and low levels of adequate glucose control among previously diagnosed diabetics. Barriers to accessing diagnosis and treatment included a lack of diagnostic tools and glucose monitoring equipment and high cost of diabetes treatment. The total annual cost of diabetes in the region was estimated at US$67.03 billion, or US$8836 per diabetic patient. CONCLUSION: Diabetes exerts a significant burden in the region, and this is expected to increase. Many diabetic patients face significant challenges accessing diagnosis and treatment, which contributes to the high mortality and
prevalence of complications observed. The significant interactions between diabetes and important infectious diseases highlight the need and opportunity for health planners to develop integrated responses to communicable and non-communicable diseases.

(49) TRAN AT, STRAAND J, DIEP LM, MEYER HE, et al. Cardiovascular disease by diabetes status in five ethnic minority groups compared to ethnic Norwegians. BMC Public Health. 2011, vol. 11, p.554
http://dx.doi.org/10.1186/1471-2458-11-554

BACKGROUND: The population in Norway has become multi-ethnic due to migration from Asia and Africa over the recent decades. The aim of the present study was to explore differences in the self-reported prevalence of cardiovascular disease (CVD) and associated risk factors by diabetes status in five ethnic minority groups compared to ethnic Norwegians. METHODS: Pooled data from three population-based cross-sectional studies conducted in Oslo between 2000 and 2002 was used. Of 54,473 invited individuals, 24,749 (45.4%) participated. The participants self-reported health status, underwent a clinical examination and blood samples were drawn. A total of 17,854 individuals aged 30 to 61 years born in Norway, Sri-Lanka, Pakistan, Iran, Vietnam or Turkey were included in the study. Chi-square tests, one-way ANOVAs, ANCOVAs, multiple and logistic regression were used. RESULTS: Age- and gender-standardized prevalence of self-reported CVD varied between 5.8% and 8.2% for the ethnic minority groups, compared to 2.9% among ethnic Norwegians (p < 0.001). Prevalence of self-reported diabetes varied from 3.0% to 15.0% for the ethnic minority groups versus 1.8% for ethnic Norwegians (p < 0.001). Among individuals without diabetes, the CVD prevalence was 6.0% versus 2.6% for ethnic minorities and Norwegians, respectively (p < 0.001). Corresponding CVD prevalence rates among individuals with diabetes were 15.3% vs. 12.6% (p = 0.364). For individuals without diabetes, the odds ratio (OR) for CVD in the ethnic minority groups remained significantly higher (range 1.5-2.6) than ethnic Norwegians (p < 0.05), after adjustment for age, gender, education, employment, and body height, except for Turkish individuals. Regardless of diabetes status, obesity and physical inactivity were prevalent in the majority of ethnic minority groups, whereas systolic- and diastolic-blood pressures were higher in Norwegians. In nearly all ethnic groups, individuals with diabetes had higher triglycerides, waist-to-hip ratio (WHR), and body mass index compared to individuals without diabetes. Age, diabetes, hypertension, hypercholesterolemia, and WHR were significant predictors of CVD in both ethnic Norwegians and ethnic minorities, but significant ethnic differences were found for age, diabetes, and hypercholesterolemia. CONCLUSIONS: Ethnic differences in the prevalence of CVD were prominent for individuals without diabetes. Primary CVD prevention including identification of undiagnosed diabetes should be prioritized for ethnic minorities without known diabetes.

http://dx.doi.org/10.1186/1471-2458-11-535

BACKGROUND: This study assessed lay perceptions of issues related to predictive genetic testing for multifactorial diseases. These perceived issues may differ from the "classic" issues, e.g. autonomy, discrimination, and psychological harm that are considered important in predictive testing for monogenic disorders. In this study, type 2 diabetes was used as an example, and perceptions with regard to predictive testing based on DNA test results and family history assessment were compared. METHODS: Eight focus group interviews were held with 45 individuals aged 35-70 years with (n = 3) and without (n = 1) a family history of diabetes, mixed groups of these two (n = 2), and diabetes patients (n = 2). All interviews were transcribed and analysed using Atlas-ti. RESULTS: Most participants believed in the ability of a predictive test to identify people at risk for diabetes and to motivate preventive behaviour. Different reasons underlying motivation were considered when comparing DNA test results and a family history risk assessment. A perceived drawback of DNA testing was that diabetes was considered not severe enough for this type of risk assessment. In addition, diabetes family history assessment was not considered useful by some participants, since there are also other risk factors involved, not everyone has a diabetes family history or knows their family history, and it might have a negative.
influence on family relations. Respect for autonomy of individuals was emphasized more with regard to DNA testing than family history assessment. Other issues such as psychological harm, discrimination, and privacy were only briefly mentioned for both tests. CONCLUSION: The results suggest that most participants believe a predictive genetic test could be used in the prevention of multifactorial disorders, such as diabetes, but indicate points to consider before both these tests are applied. These considerations differ with regard to the method of assessment (DNA test or obtaining family history) and also differ from monogenic disorders.

http://dx.doi.org/10.1186/1471-2458-11-533

BACKGROUND: Self-management is the cornerstone of diabetes control and prevention of complications; however, it is undetermined whether differences in intention to adopt healthy lifestyles and actual healthy behavior exist across race/ethnic groups. This study evaluated the differences across racial-ethnic groups in self-reported medical advice received and health intentions and behaviors among adults with type 2 diabetes mellitus. METHODS: A cross-sectional analysis of the 2007 SHIELD US survey ascertained self-reported health intentions and behaviors for regular exercise, diet, and weight management among Non-Hispanic Caucasian (n = 2526), Non-Hispanic African-American (n = 706), and Hispanic (n = 179) respondents with type 2 diabetes. RESULTS: A similar proportion of respondents from each race-gender group (43%-56%) reported receiving healthcare advice to increase their exercise (P = 0.32). Significantly more minorities reported an intention to follow the exercise recommendation compared with Non-Hispanic Caucasians (P = 0.03). More Non-Hispanic African-American (29%) and Hispanic (27%) men reported exercising regularly compared with other race-gender groups (P = 0.02). Significantly more Non-Hispanic Caucasian women (74%) and Hispanic women (79%) reported trying to lose weight compared with other groups (P < 0.0001). CONCLUSIONS: Differences in health intentions and healthy behaviors were noted across race-gender groups. More Non-Hispanic African-American men reported an intention to follow advice on exercising and self-report of exercising regularly was also higher compared with other race-gender groups. More Hispanic men reported high physical activity levels than other groups. Despite an increased willingness to follow healthcare recommendations for diet, >50% of respondents were obese among all race-gender groups.

(52) MAYOR S. More than one third of diabetic patients have poor blood glucose control, shows audit. BMJ. 2011, vol. 342, p.d4170


(54) DYER C. Hospital trust director is cleared of dishonesty in case of misdiagnosed diabetes. BMJ. 2011, vol. 342, p.d3860

http://dx.doi.org/10.2105/AJPH.2010.300104

Methods for translating the findings of controlled trials, such as the Diabetes Prevention Program, into real-world community application have not been clearly defined. A standardized research methodology for making and evaluating such a transition is needed. We introduce the multisite
translational community trial (mTCT) as the research analog to the multisite randomized controlled trial. The mTCT is adapted to incorporate the principles and practices of community-based participatory research and the increased relevance and generalizability gained from diverse community settings. The mTCT is a tool designed to bridge the gap between what a clinical trial demonstrates can work in principle and what is needed to make it workable and effective in real-world settings. Its utility could be put to the test, in particular with practice-based research networks such as the Prevention Research Centers.

http://dx.doi.org/10.1093/aje/kwr033

The authors aimed to explore optimal cutoffs for high-risk waist circumference (WC) in older adults to assess the health risks of obesity. Prospective data from 4,996 measurements in 2,232 participants aged >/=70 years were collected during 5 triennial measurement cycles (1992/1993-2005/2006) of a population-based cohort study, the Longitudinal Aging Study Amsterdam (Amsterdam, the Netherlands). Cross-sectional associations of WC with pain, mobility limitations, incontinence, knee osteoarthritis, cardiovascular disease, and diabetes were studied. Generalized estimating equations models were fitted with restricted cubic spline functions in order to carefully study the shapes of the associations. Model fits for applying different cutoffs to categorize WC in the association with all outcomes were tested using the quasi-likelihood under the Independence Criterion (QIC). On the basis of the spline regression curves, potential WC cutoffs of approximately 109 cm in men and 98 cm in women were proposed. Based on the model fit, cutoffs between 100 cm and 106 cm were equally applicable in men but should not be higher. In women, the QIC confirmed an optimal cutoff of 99 cm


http://dx.doi.org/10.1186/1471-2458-11-430

BACKGROUND: Safety for diabetic patients means providing the most suitable treatment for each type of diabetic in order to improve monitoring and to prevent the adverse effects of drugs and complications arising from the disease. The aim of this study is to analyze the effect of imparting educational interventions to health professionals regarding the safety of patients with Diabetes Mellitus (DM). METHODS: Design: A cluster randomized trial with a control group. Setting and sample: The study analyzed ten primary healthcare centres (PHC) covering approximately 150,000 inhabitants. Two groups of 5 PHC were selected on the basis of their geographic location (urban, semi-urban and rural), their socio-economic status and the size of their PHC. The interventions and control groups were assigned at random. The study uses computerized patient records to individually assess subjects aged 45 to 75 diagnosed with type 1 and type 2 DM, who met the inclusion conditions and who had the variables of particular interest to the study. Trial: The educational interventions consisted of a standardized teaching course aimed at doctors and nurses. The course lasted 6 hours and was split into three 2-hour blocks with subsequent monthly refresher courses. Measurement: For the health professionals, the study used the Diabetes Attitude Scale (DAS-3) to assess their attitudes and motivation when monitoring diabetes. For the patients, the study assessed factors related to their degree of control over the disease at onset, 6, 12 and 24 months. Main variables: levels of HbA1c. Analysis: The study analyzed the effect of the educational interventions both on the attitudes and motivations of health professionals and on the degree of control over the diabetes in both groups. DISCUSSION: Imparting educational interventions to health professionals would improve the monitoring of diabetic patients. The most effective model involves imparting the course to both doctors and nurses. However, these models...
have not been tested on our Spanish population within the framework of primary healthcare. 
TRIAL REGISTRATION: ClinicalTrials.gov: NCT01087541

http://dx.doi.org/10.1186/1471-2458-11-399

BACKGROUND: Diabetes and related complications are common among ethnic minority groups. Community-based social support interventions are considered promising for improving diabetes self-management. To access such interventions, patients need to disclose their diabetes to others. Research on the disclosure of diabetes in ethnic minority groups is limited. The aim of our study was to explore why diabetes patients from ethnic minority populations either share or do not share their condition with people in their wider social networks. METHODS: We conducted a qualitative study using semi-structured interviews with 32 Surinamese patients who were being treated for type 2 diabetes by general practitioners in Amsterdam, the Netherlands. RESULTS: Most patients disclosed their diabetes only to very close family members. The main factor inhibiting disclosure to people outside this group was the Surinamese cultural custom that talking about disease is taboo, as it may lead to shame, gossip, and social disgrace for the patient and their family. Nevertheless, some patients disclosed their diabetes to people outside their close family circles. Factors motivating this decision were mostly related to a need for facilities or support for diabetes self-management. CONCLUSIONS: Cultural customs inhibited Surinamese patients in disclosing their diabetes to people outside their very close family circles. This may influence their readiness to participate in community-based diabetes self-management programmes that involve other groups. What these findings highlight is that public health researchers and initiatives must identify and work with factors that influence the disclosure of diabetes if they are to develop community-based diabetes self-management interventions for ethnic minority populations.

http://dx.doi.org/10.1186/1471-2458-11-383

BACKGROUND: Metabolic syndrome (MetS) and body mass index (BMI, kg.m(-2)) are established independent risk factors in the development of diabetes; we prospectively examined their relative contributions and joint relationship with incident diabetes in a Middle Eastern cohort. METHOD: participants of the ongoing Tehran lipid and glucose study are followed on a triennial basis. Among non-diabetic participants aged >/= 20 years at baseline (8,121) those with at least one follow-up examination (5,250) were included for the current study. Multivariate logistic regression models were used to estimate sex-specific adjusted odd ratios (ORs) and 95% confidence intervals (CIs) of baseline BMI-MetS categories (normal weight without MetS as reference group) for incident diabetes among 2186 men and 3064 women, aged >/= 20 years, free of diabetes at baseline. RESULT: During follow up (median 6.5 years); there were 369 incident diabetes (147 in men). In women without MetS, the multivariate adjusted ORs (95% CIs) for overweight (BMI 25-30 kg/m(2)) and obese (BMI >/= 30) participants were 2.3 (1.2-4.3) and 2.2 (1.0-4.7), respectively. The corresponding ORs for men without MetS were 1.6 (0.9-2.9) and 3.6 (1.5-8.4) respectively. As compared to the normal-weight/without MetS, normal-weight women and men with MetS, had a multivariate-adjusted ORs for incident diabetes of 8.8 (3.7-21.2) and 3.1 (1.3-7.0), respectively. The corresponding ORs for overweight and obese women with MetS reached to 7.7 (4.0-14.9) and 12.6 (6.9-23.2) and for men reached to 3.4(2.0-5.8) and 5.7(3.9-9.9), respectively. CONCLUSION: This study highlights the importance of screening for MetS in normal weight individuals. Obesity increases diabetes risk in the absence of MetS, underscores the need for more stringent criteria to define healthy metabolic state among obese individuals. Weight reduction measures, thus, should be encouraged in conjunction with achieving metabolic targets not addressed by current definition of MetS, both in every day encounter and public health setting.

BACKGROUND: The potential of web-based interventions in dietary behaviour modification of the diabetics has not been fully explored. We describe the protocol of a 12-month match-design randomised controlled trial of a web-based dietary intervention for type 2 diabetic patients with primary aim to evaluate the effect of the intervention on their dietary knowledge, attitude and behaviour (KAB). The secondary objective of this study is to improve the participants’ dietary practices, physical measurements and biomarkers. METHODS/DESIGN: A minimum total sample of 82 Type 2 diabetics will be randomised, either to the control group, who will receive the standard diabetes care or the e-intervention group, who will participate in a 6-month web-based dietary intervention in addition to the standard care. The dietary recommendations are based on existing guidelines, but personalised according to the patients’ Stages of Change (SOC). The participants will be followed up for 6 months post-intervention with data collection scheduled at baseline, 6-month and 12-month. DISCUSSION: We are aiming for a net improvement in the KAB score in participants of the e-intervention group, besides investigating the impact of the e-intervention on the dietary practices, physical measurements and blood biomarkers of those patients. The successful outcome of this study can be a precursor for policy makers to initiate more rigorous promotion of such web-based programmes in the country. TRIAL REGISTRATION: Clinicaltrials.gov NCT01246687


BACKGROUND: The implementation project of the national diabetes prevention programme in Finland, FIN-D2D, was carried out in primary health care in the area of five hospital districts during 2003-2007. METHODS: The population strategy of FIN-D2D was primarily aimed at increasing the awareness of type 2 diabetes and preventing obesity. To investigate the effects of this strategy, we studied the changes in the prevalence of obesity, overweight, and central obesity among a random independent sample of individuals aged 45-74 years in the FIN-D2D area; and assessed whether they differed from a sample of individuals in the control area, which consisted of four geographical areas not participating in FIN-D2D (FINRISK study). Data was obtained for 5850/6406 (in the beginning/ in the end) individuals. The duration of the observation period varied from three to five years. RESULTS: The mean body weight decreased from 78.7 to 78.1 kg (p = 0.041) in the FIN-D2D area, and from 78.7 to 78.0 kg (p = NS) in the control area. The prevalence of obesity (BMI >/=30 kg/m(2)) decreased in the FIN-D2D area (26.5% vs. 24.4%, p = 0.015), and in the control area (28.4% vs. 25.2%, p = 0.005). The prevalence of morbid obesity (BMI >/=40 kg/m(2)) remained unchanged in the FIN-D2D area, but increased in the control area (1.2% vs. 2.3%, p = 0.007). The mean waist circumference remained unchanged in the FIN-D2D area, but increased in the control area (92.8 vs. 94.0 cm, p = 0.005). CONCLUSIONS: The prevalence of obesity may be decreasing among 45-74 year old Finns. We still need a longer time perspective and future studies to see whether this favourable trend can be sustained in Finland. The actions of this implementation project can at least partly explain the differences in the mean waist circumference and the prevalence of morbid obesity between the intervention and control areas.


BACKGROUND: The context of the study is the increased assessment and treatment of persons with mental illness in general hospital settings by general health staff, as the move away from mental hospitals gathers pace in low and middle income countries. The purpose of the study was to examine whether general attitudes of hospital staff towards persons with mental illness, and extent of mental health training and clinical experience, are associated with different attitudes and
behaviours towards a patient with mental illness than towards a patient with a general health problem - diabetes. METHODS: General hospital health professionals in Malaysia were randomly allocated one of two vignettes, one describing a patient with mental illness and the other a patient with diabetes, and invited to complete a questionnaire examining attitudes and health care practices in relation to the case. The questionnaires completed by respondents included questions on demographics, training in mental health, exposure in clinical practice to people with mental illness, attitudes and expected health care behaviour towards the patient in the vignette, and a general questionnaire exploring negative attitudes towards people with mental illness. Questionnaires with complete responses were received from 654 study participants. RESULTS: Stigmatising attitudes towards persons with mental illness were common. Those responding to the mental illness vignette (N = 356) gave significantly lower ratings on care and support and higher ratings on avoidance and negative stereotype expectations compared with those responding the diabetes vignette (N = 298). CONCLUSIONS: Results support the view that, in the Malaysian setting, patients with mental illness may receive differential care from general hospital staff and that general stigmatising attitudes among professionals may influence their care practices. More direct measurement of clinician behaviours than able to be implemented through survey method is required to support these conclusions.

http://dx.doi.org/10.1186/1471-2458-11-303

BACKGROUND: Immigrants from the Middle-East are at high risk of developing type 2 diabetes (T2D). The aim of the present survey was to measure, in a single deprived neighbourhood, the prevalence rates of impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and T2D in residents originating from Iraq and to compare them to those in residents born in Sweden. An additional aim was to identify metabolic, lifestyle and socioeconomic risk factors associated with IFG/IGT and T2D in these residents. METHODS: The study was conducted February 1'st to March 31'st 2010. Men and women aged 45 to 65 years of Swedish or Iraqi origin, living in the neighbourhood of Rosengard, Malmo, Sweden, were randomly selected from the census register. Each participant signed a written informed consent form, underwent a physical examination and an oral glucose tolerance test (OGTT), provided blood samples and filled in a questionnaire. A total of 175 subjects participated (Swedish origin n = 79, Iraqi origin n = 96), reflecting an overall response rate of almost 60%. RESULTS: In total, 21.9% and 19.0% of the Iraqi and Swedish participants, respectively, suffered from T2D, while 24.0% of the Iraqi participants and 25.3% of the Swedish participants had IFG/IGT. There were no significant differences in prevalence rates relating to country of origin. Obesity (BMI >/= 30 kg/m2) and sedentary leisure time physical activity were highly prevalent in both groups, while a family history of diabetes was more prevalent in participants from Iraq (49.2%) than in those from Sweden (22.8%) (p = 0.001). Being obese or having a sedentary leisure time were, independently associated with T2D (OR 5.43 (95% CI 2.10-14.02) and 2.89 (95% CI 1.03-8.10) respectively), while economic difficulties were independently associated with IFG/IGT (OR 2.55 (95% CI 1.06-6.15)) after adjustment for the confounding effects of other common risk factors for T2D. CONCLUSIONS: This study reveals a high prevalence of T2D, independently of country of origin (Iraq or Sweden), in a socially vulnerable area and additionally presents a risk factor profile that is markedly different from that of Sweden in general.

http://dx.doi.org/10.1186/1471-2458-11-299

BACKGROUND: Public health promotes an ecological approach to chronic disease prevention, however, little research has been conducted to assess the integration of an ecological approach in community-based prevention programs. This study sought to contribute to the evidence base by assessing the extent to which an ecological approach was integrated into an Aboriginal community-based cardiovascular disease (CVD) and type 2 diabetes prevention program, across
The prevalence of diabetes is growing in many countries. Prescription oral medications have been developed to treat the disease since the 1950s. More recently, a group of diabetes drugs, known as the glitazones, have been developed and introduced on to North American and European markets.

Three intervention years. METHODS: Activity implementation forms were completed by interview with implementers and participant observation across three intervention years. A standardised ecological coding procedure was applied to assess participant recruitment settings, intervention targets, intervention strategy types, extent of ecologicalness and organisational partnering. Interrater reliability for two coders was assessed at Kappa = 0.76 (p < .001), 95% CI (0.58, 0.94).

RESULTS: 215 activities were implemented across three intervention years by the health program (HP) with some activities implemented in multiple years. Participants were recruited most frequently through organisational settings in years 1 and 2, and organisational and community settings in year 3. The most commonly utilised intervention targets were the individual (IND) as a direct target, and interpersonal (INT) and organisational (ORG) environments as indirect targets; policy (POL), and community (COM) were targeted least. Direct (HP --> IND) and indirect intervention strategies (i.e., HP --> INT --> IND, HP --> POL --> IND) were used most often; networking strategies, which link at least two targets (i.e., HP -->[ORG-ORG]-->IND), were used the least. The program did not become more ecological over time. CONCLUSIONS: The quantity of activities with IND, INT and ORG targets and the proportion of participants recruited through informal cultural networking demonstrate community commitment to prevention. Integration of an ecological approach would have been facilitated by greater inter-organisational collaboration and centralised planning. The upfront time required for community stakeholders to develop their capacity to mobilise around chronic disease is at odds with short-term funding cycles that emphasise organisational accountability.


BACKGROUND: Individual health education is considered to be essential in the overall care of patients with type 2 diabetes (DM2), although there is some uncertainty regarding its metabolic control benefits. There have been very few randomized studies on the effects of individual education on normal care in DM2 patients with a control group, and none of these have assessed the long-term results. Therefore, this study aims to use this design to assess the effectiveness of the PRECEDE (Predisposing, Reinforcing, Enabling, Causes in Educational Diagnosis, and Evaluation) education model in the metabolic control and the reduction of cardiovascular risk factors, in patients with type 2 diabetes. METHODS: An open community effectiveness study was carried out in 8 urban community health centers in the North-East Madrid Urban Area (Spain). Six hundred patients with DM2 were randomized in two groups: PRECEDE or conventional model for health promotion education. The main outcome measures were glycated hemoglobin A1c, body mass index (BMI), blood pressure, lipids and control criteria during the 2-year follow-up period.

RESULTS: Glycated hemoglobin A1c and systolic blood pressure (SBP) levels decreased significantly in the PRECEDE group (multivariate analysis of covariance, with baseline glycated hemoglobin A1c, SBP, and variables showing statistically significant differences between groups at baseline visits). The decrease levels in diastolic blood pressure (DBP), triglycerides and LDL cholesterol were nonsignificant. PRECEDE increased compliance in all control criteria, except for LDL cholesterol. BMI did not change during the study in either of the two models analyzed.

CONCLUSIONS: PRECEDE health education model is a useful method in the overall treatment in patients with type 2 diabetes, which contributes to decrease glycated hemoglobin A1c and SBP levels and increase the compliance in all the control criteria, except for LDL cholesterol. TRIAL REGISTRATION NUMBER: ClinicalTrials.gov NCT01316367


The prevalence of diabetes is growing in many countries. Prescription oral medications have been developed to treat the disease since the 1950s. More recently, a group of diabetes drugs, known as the glitazones, have been developed and introduced on to North American and European markets.
markets since the late 1990s. When first introduced, the glitazones were widely regarded as 'innovative' pharmaceuticals and have remained on the American and EU markets, among others, throughout the 2000s. Yet, enormous uncertainties about their therapeutic value have remained since they came on the market a decade ago. This paper investigates how socio-political systems of drug development and regulation generate such pharmaceutical uncertainty consequent upon the limited informational value that diabetes drug trials provide about the health risks and benefits of such medications when used in clinical practice. Drawing on documentary research and fieldwork interviews, the first in-depth analysis of regulation of 'innovative' pharmaceuticals in both the US and supranational EU is presented. It is argued that these pharmaceutical uncertainties can be explained by reference to four key factors: regulatory paradigms using surrogate markers for drug efficacy; drug approval standards in policy and legislation; ideological expectations of innovation within regulatory agencies; and pharmaceutical industry shaping of drug evaluation

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The globalization of genetic discourses, especially where ethnicity is treated as a "risk factor" for disease, deserves special attention and concern. In countries such as Mexico, with large indigenous populations, the consequences of the Thrifty Genotype hypothesis and/or the attribution of type 2 diabetes to "family history" may be especially detrimental to poor rural communities, playing as they do into existing racial hierarchies. Based on semi-structured interviews with doctors and patients in a public clinic in a community near Oaxaca, Mexico, the study examines etiologies for type 2 diabetes. While notions of genetic inheritance and family history figure prominently in government and public health discourse, the "explanatory model" of patients places most emphasis on strong emotions, traumatic events, and dietary factors. Clinic doctors emphasize diet and lifestyle factors. The diffusion of "genetic risk" has had little impact on doctor-patient interactions in this community, but can be clearly seen in academic research, government policy, and medical specialties in the region, raising concerns about whether or not interventions will be directed at the social determinants of this growing health concern

http://dx.doi.org/10.1093/ije/dyr029

BACKGROUND: We conducted a systematic review and meta-analysis, the first to our knowledge, summarizing and quantifying the published evidence on associations between type 2 diabetes incidence and socio-economic position (SEP) (measured by educational level, occupation and income) worldwide and when sub-divided into high-, middle- and low-income countries. METHODS: Relevant case-control and cohort studies published between 1966 and January 2010 were searched in PubMed and EMBASE using the keywords: diabetes vs educational level, occupation or income. All identified citations were screened by one author, and two authors independently evaluated and extracted data from relevant publications. Risk estimates from individual studies were pooled using random-effects models quantifying the associations. RESULTS: Out of 5120 citations, 23 studies, including 41 measures of association, were found to be relevant. Compared with high educational level, occupation and income, low levels of these determinants were associated with an overall increased risk of type 2 diabetes; [relative risk (RR) = 1.41, 95% confidence interval (CI): 1.28-1.51], (RR = 1.31, 95% CI: 1.09-1.57) and (RR = 1.40, 95% CI: 1.04-1.88), respectively. The increased risks were independent of the income levels of countries, although based on limited data in middle- and low-income countries. CONCLUSIONS: The risk of getting type 2 diabetes was associated with low SEP in high-, middle- and low-income countries and overall. The strength of the associations was consistent in high-income countries, whereas there is a strong need for further investigation in middle- and low-income countries

BACKGROUND: Accumulating evidence implicates insufficient oxidative capacity in the development of type 2 diabetes. This notion has not been well tested in large, population-based studies. METHODS: To test this hypothesis, we assessed the cross-sectional association of plasma lactate, an indicator of the gap between oxidative capacity and energy expenditure, with type 2 diabetes in 1709 older adults not taking metformin, who were participants in the Atherosclerosis Risk in Communities (ARIC) Carotid MRI Study. RESULTS: The prevalence of type 2 diabetes rose across lactate quartiles (11, 14, 20 and 30%; P for trend <0.0001). Following adjustment for demographic factors, physical activity, body mass index and waist circumference, the relative odds of type 2 diabetes across lactate quartiles were 0.98 [95% confidence interval (CI) 0.59-1.64], 1.64 (95% CI 1.03-2.64) and 2.23 (95% CI 1.38-3.59), respectively. Furthermore, lactate was associated with higher fasting glucose among non-diabetic adults. CONCLUSIONS: Plasma lactate was strongly associated with type 2 diabetes in older adults. Plasma lactate deserves greater attention in studies of oxidative capacity and diabetes risk.

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BACKGROUND: Diabetic patients show an increased prevalence of non-dipping arterial pressure pattern, target organ damage and elevated arterial stiffness. These alterations are associated with increased cardiovascular risk. The objectives of this study are the following: to evaluate the prognostic value of central arterial pressure and pulse wave velocity in relation to the incidence and outcome of target organ damage and the appearance of cardiovascular episodes (cardiovascular mortality, myocardial infarction, chest pain and stroke) in patients with type 2 diabetes mellitus or metabolic syndrome. METHODS/DESIGN: Design: This is an observational prospective study with 5 years duration, of which the first year corresponds to patient inclusion and initial evaluation, and the remaining four years to follow-up. SETTING: The study will be carried out in the urban primary care setting. STUDY POPULATION: Consecutive sampling will be used to include patients diagnosed with type 2 diabetes between 20-80 years of age. A total of 110 patients meeting all the inclusion criteria and none of the exclusion criteria will be included. MEASUREMENTS: Patient age and sex, family and personal history of cardiovascular disease, and cardiovascular risk factors. Height, weight, heart rate and abdominal circumference. Laboratory tests: hemoglobin, lipid profile, creatinine, microalbuminuria, glomerular filtration rate, blood glucose, glycosylated hemoglobin, blood insulin, fibrinogen and high sensitivity C-reactive protein. Clinical and 24-hour ambulatory (home) blood pressure monitoring and self-measured blood pressure. Common carotid artery ultrasound for the determination of mean carotid intima-media thickness. Electrocardiogram for assessing left ventricular hypertrophy. Ankle-brachial index. Retinal vascular study based on funduscopy with non-mydriatic retinography and evaluation of pulse wave morphology and pulse wave velocity using the SphygmoCor system. The medication used for diabetes, arterial hypertension and hyperlipidemia will be registered, together with antiplatelet drugs. DISCUSSION: The results of this study will help to know and quantify the prognostic value of central arterial pressure and pulse wave velocity in relation to the evolution of the subclinical target organ damage markers and the possible incidence of cardiovascular events in patients with type 2 diabetes mellitus.
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BACKGROUND: Differences in life expectancy (LE) between social groups in a specific country are a fundamental measure of health inequalities within that country. Constant monitoring of these differences provides important information on the population's general health. The purpose of the present study is to explore and quantify the socio-economic differences in LE in Germany, focussing on a topic rarely assessed in other studies, the dependency of these LE differences on the presence of myocardial infarction or diabetes mellitus. METHODS: The dataset consists of 13,427 participants (6,725 men, 6,702 women) aged 25-74 years, recruited in the region of Augsburg in Germany through three independent cross-sectional representative surveys conducted in 1984/85, 1989/90, 1994/95, with a mortality follow up in 1998 and 2002. We use a parametric model for the survival function based on the Weibull distribution, in which the hazard function is described in terms of two parameters. We estimate these parameters with a maximum likelihood method that takes into account censoring and data truncation. RESULTS: The difference in LE between the lowest and the highest socio-economic group is estimated to be 3.79 years for men and 4.10 years for women. Diabetes mellitus reduces LE of men from the upper three income quartiles by 4.88 years, and LE of men belonging to the lowest income quartile by 7.97 years. For women, the corresponding figures are 5.79 and 5.72 years. Myocardial infarction reduces LE of men and women from the upper three income quartiles by 3.65 and 3.75 years, respectively, and LE of men and women belonging to the lowest income quartile by 5.11 and 10.95 years, respectively. CONCLUSIONS: This study shows that in Germany the differences in LE by socio-economic status are comparable to those found in other European countries, and that these differences seem to increase when diabetes mellitus or myocardial infarction is present. The statistical method used allows estimates of LE with relatively small datasets.
simultaneously considering PA and television watching suggested that both contributed independently to depression risk

3) MARKS M. *Routine test batteries for cognitive impairment in older people may not be cost effective*. BMJ. 2011, vol. 343, p.d6330  


http://dx.doi.org/10.1001/jama.2011.1282

CONTEXT: Several studies have suggested that depression is associated with an increased risk of stroke; however, the results are inconsistent. OBJECTIVE: To conduct a systematic review and meta-analysis of prospective studies assessing the association between depression and risk of developing stroke in adults. DATA SOURCES: A search of MEDLINE, EMBASE, and PsycINFO databases (to May 2011) was supplemented by manual searches of bibliographies of key retrieved articles and relevant reviews. STUDY SELECTION: We included prospective cohort studies that reported risk estimates of stroke morbidity or mortality by baseline or updated depression status assessed by self-reported scales or clinician diagnosis. DATA EXTRACTION: Two independent reviewers extracted data on depression status at baseline, risk estimates of stroke, study quality, and methods used to assess depression and stroke. Hazard ratios (HRs) were pooled using fixed-effect or random-effects models when appropriate. Associations were tested in subgroups representing different participant and study characteristics. Publication bias was evaluated with funnel plots and Begg test. RESULTS: The search yielded 28 prospective cohort studies (comprising 317,540 participants) that reported 8478 stroke cases (morbidity and mortality) during a follow-up period ranging from 2 to 29 years. The pooled adjusted HRs were 1.45 (95% CI, 1.29-1.63; P for heterogeneity <.001; random-effects model) for total stroke, 1.55 (95% CI, 1.25-1.93; P for heterogeneity = .31; fixed-effects model) for fatal stroke (8 studies), and 1.25 (95% CI, 1.11-1.40; P for heterogeneity = .34; fixed-effects model) for ischemic stroke (6 studies). The estimated absolute risk differences associated with depression were 106 cases for total stroke, 53 cases for ischemic stroke, and 22 cases for fatal stroke per 100,000 individuals per year. The increased risk of total stroke associated with depression was consistent across most subgroups. CONCLUSION: Depression is associated with a significantly increased risk of stroke morbidity and mortality

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The New York City terrorist attacks on Sept 11, 2001 (9/11), killed nearly 2800 people and thousands more had subsequent health problems. In this Review of health effects in the short and medium terms, strong evidence is provided for associations between experiencing or witnessing
events related to 9/11 and post-traumatic stress disorder and respiratory illness, with a correlation between prolonged, intense exposure and increased overall illness and disability. Rescue and recovery workers, especially those who arrived early at the World Trade Center site or worked for longer periods, were more likely to develop respiratory illness than were other exposed groups. Risk factors for post-traumatic stress disorder included proximity to the site on 9/11, living or working in lower Manhattan, rescue or recovery work at the World Trade Center site, event-related loss of spouse, and low social support. Investigators note associations between 9/11 exposures and additional disorders, such as depression and substance use; however, for some health problems association with exposures related to 9/11 is unclear.


BACKGROUND: More than 50,000 people participated in the rescue and recovery work that followed the Sept 11, 2001 (9/11) attacks on the World Trade Center (WTC). Multiple health problems in these workers were reported in the early years after the disaster. We report incidence and prevalence rates of physical and mental health disorders during the 9 years since the attacks, examine their associations with occupational exposures, and quantify physical and mental health comorbidities. METHODS: In this longitudinal study of a large cohort of WTC rescue and recovery workers, we gathered data from 27,449 participants in the WTC Screening, Monitoring, and Treatment Program. The study population included police officers, firefighters, construction workers, and municipal workers. We used the Kaplan-Meier procedure to estimate cumulative and annual incidence of physical disorders (asthma, sinusitis, and gastro-oesophageal reflux disease), mental health disorders (depression, post-traumatic stress disorder [PTSD], and panic disorder), and spirometric abnormalities. Incidence rates were assessed also by level of exposure (days worked at the WTC site and exposure to the dust cloud). FINDINGS: 9-year cumulative incidence of asthma was 27.6% (number at risk: 7027), sinusitis 42.3% (5870), and gastro-oesophageal reflux disease 39.3% (5650). In police officers, cumulative incidence of depression was 7.0% (number at risk: 3648), PTSD 9.3% (3761), and panic disorder 8.4% (3780). In other rescue and recovery workers, cumulative incidence of depression was 27.5% (number at risk: 4200), PTSD 31.9% (4342), and panic disorder 21.2% (4953). 9-year cumulative incidence for spirometric abnormalities was 41.8% (number at risk: 5769); three-quarters of these abnormalities were low forced vital capacity. Incidence of most disorders was highest in workers with greatest WTC exposure. Extensive comorbidity was reported within and between physical and mental health disorders. INTERPRETATION: 9 years after the 9/11 WTC attacks, rescue and recovery workers continue to have a substantial burden of physical and mental health problems. These findings emphasise the need for continued monitoring and treatment of the WTC rescue and recovery population. FUNDING: Centers for Disease Control and Prevention and National Institute for Occupational Safety and Health


Previous studies have found J-shaped relations between volume of alcohol consumed and mortality risk in white Americans but not in African Americans, suggesting the need for studies in which race/ethnicity-defined subgroups are analyzed in separate comparable models. In the present study, the authors utilized mortality follow-up data (through 2006) on respondents from the 1984 and 1995 National Alcohol Surveys, including similar numbers of black, white, and Hispanic respondents by oversampling the minority groups. Cox proportional hazards models controlling for demographic, socioeconomic, mental health, and drug- and tobacco-use measures
were used to estimate mortality risk from all causes. Findings indicated a protective effect of moderate alcohol drinking (2-30 drinks/month for women and 2-60 drinks/month for men) with no monthly >/=5-drink days) relative to lifetime abstention for whites only. Elevated mortality risk relative to moderate drinking was found in former drinkers with lifetime alcohol problems. Moderate drinkers who consumed >/=5 drinks in 1 day at least monthly were also found to have increased risk, suggesting the importance of identifying heavy-occasion drinking for mortality analyses. These differential results regarding lifetime abstainers may suggest bias from differential unmeasured confounding or unmeasured aspects of alcohol consumption pattern or may be due to genetic differences in the health impact of alcohol metabolism


OBJECTIVES: To investigate the proportion of original studies included in systematic reviews and meta-analyses on the diagnostic accuracy of screening tools for depression that appropriately exclude patients who already have a diagnosis of or are receiving treatment for depression and to determine whether these systematic reviews and meta-analyses evaluate possible bias from the inclusion of such patients. DESIGN: Systematic review. DATA SOURCES: Medline, PsycINFO, CINAHL, Embase, ISI, SCOPUS, and Cochrane databases were searched from 1 January 2005 to 29 October 2009. ELIGIBILITY CRITERIA FOR SELECTING STUDIES: Systematic reviews and meta-analyses in any language that reported on the diagnostic accuracy of screening tools for depression. RESULTS: Only eight of 197 (4%) unique publications from 17 systematic reviews and meta-analyses specifically excluded patients who already had a diagnosis of or were receiving treatment for depression. No systematic reviews or meta-analyses commented on possible bias from the inclusion of such patients, even though 10 reviews used quality assessment tools with items to rate risk of bias from composition of the sample of patients. CONCLUSIONS: Studies of the accuracy of screening tools for depression rarely exclude patients who already have a diagnosis of or are receiving treatment for depression, a potential bias that is not evaluated in systematic reviews and meta-analyses. This could result in inflated estimates of accuracy on which clinical practice and preventive care guidelines are often based, a problem that takes on greater importance as the rate of diagnosed and treated depression in the population increases


Glucocorticoids are released in response to stressful experiences and serve many beneficial homeostatic functions. However, dysregulation of glucocorticoids is associated with cognitive impairments and depressive illness. In the hippocampus, a brain region densely populated with receptors for stress hormones, stress and glucocorticoids strongly inhibit adult neurogenesis. Decreased neurogenesis has been implicated in the pathogenesis of anxiety and depression, but direct evidence for this role is lacking. Here we show that adult-born hippocampal neurons are required for normal expression of the endocrine and behavioural components of the stress response. Using either transgenic or radiation methods to inhibit adult neurogenesis specifically, we find that glucocorticoid levels are slower to recover after moderate stress and are less suppressed by dexamethasone in neurogenesis-deficient mice than intact mice, consistent with a role for the hippocampus in regulation of the hypothalamic-pituitary-adrenal (HPA) axis. Relative to controls, neurogenesis-deficient mice also showed increased food avoidance in a novel environment after acute stress, increased behavioural despair in the forced swim test, and decreased sucrose preference, a measure of anhedonia. These findings identify a small subset of neurons within the dentate gyrus that are critical for hippocampal negative control of the HPA axis and support a direct role for adult neurogenesis in depressive illness.
http://dx.doi.org/10.1186/1471-2458-11-601

BACKGROUND: For decades, symptoms of anxiety and depression have been included among psychological factors associated with development of hypertension. Although this has been questioned in recent studies, most findings have been based on a single assessment of mental distress at baseline. We examined these associations using repeated assessments of anxiety, depression and blood pressure.

METHODS: Data on 17,410 men and women aged 20 to 67 participating in the Nord-Trondelag Health Study (HUNT) in Norway in 1984-86 were re-examined 11 and 22 years later. The main outcome was change in mean blood pressure (mm Hg) during follow-up.

RESULTS: We found that a high symptom level score (>=80th percentile) of combined anxiety and depression at baseline, as compared to a lower symptom level, was associated with lower mean systolic (-0.67 mm Hg, p = 0.044) and diastolic (-0.25 mm Hg, p = 0.201) blood pressure at year 22. A high symptom level present at all three examinations was associated with a stronger decrease in mean systolic (-1.59 mm Hg, p = 0.004) and diastolic (-0.78 mm Hg, p = 0.019) blood pressure and with a 20% (p = 0.001) lower risk of developing hypertension (BP >=140/90 mm Hg) at year 22. The associations were only slightly attenuated in multivariate analyses, with no evidence of a mediating effect of alteration in heart rate.

CONCLUSIONS: This study do not support previous hypothesis that emotional stress may be a cause of hypertension. Our findings indicate that symptoms of anxiety and depression are associated with decrease in blood pressure, particularly when a high symptom level can be detected over decades.

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This study explores the effects of socioeconomic status on depression in Japan, Korea, and China, focusing on the differences in their labor market structures. Comparative studies among East Asian societies allow researchers studying depression to analyze the effects of unique institutions within each society while holding constant, to a certain extent, cultural attitudes toward mental disorders. This study uses data from National Family Research of Japan 2003, Korean National Family Survey 2003, and Family Survey of China 2006 to examine the effects of education and labor market positions on depression. The results show that the relationship between socioeconomic status and depression differs among the three societies. In Japan, the type of employment contract has a significant impact on depression, while in Korea, higher educational attainment negatively relates to depression. In China, the type of work organization has a significant impact on depression. Based on these results, two types of labor market structures, aimed at differentiating the relationship between socioeconomic status and depression, are delineated: labor markets with a secured sector, and flexible labor markets.

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Higher rates of major depression (MD) among females, and of alcohol dependence (AD) among males, are among the most routinely reported findings in psychiatric epidemiology. One of the most often pursued explanations for sex differences in both disorders suggests that males and females have a differential vulnerability to stressors, which is manifested in sex-specific ways (MD for females, AD for males). However, existing evidence in support of this explanation is mixed. In the present study, we investigated sex differences in the association between stressful life events and MD and AD in a large national sample of adults in the United States (n = 32,744) using a prospective design. Logistic regression was used to estimate associations between stressful life events and both MD and AD; sex-specific effects of stress on MD and AD were evaluated by testing interaction terms between sex and stressors in the prediction of both outcomes. The
number of stressful life events was predictive of first onset MD and AD. This was true for both males and females, and sex-by-stress interaction terms did not support the hypothesis that sex-specific responses to stressful life events lead to sex differences in first onset of MD and AD among adults. These results indicate the resistance of sex differences in MD and AD to simple explanations, and suggest the need for more nuanced models that incorporate both physiological and social aspects of vulnerability.


OBJECTIVES: We examined whether neighborhood socioeconomic status (NSES) is associated with cognitive functioning in older US women and whether this relationship is explained by associations between NSES and vascular, health behavior, and psychosocial factors. METHODS: We assessed women aged 65 to 81 years (n = 7479) who were free of dementia and took part in the Women's Health Initiative Memory Study. Linear mixed models examined the cross-sectional association between an NSES index and cognitive functioning scores. A base model adjusted for age, race/ethnicity, education, income, marital status, and hysterectomy. Three groups of potential confounders were examined in separate models: vascular, health behavior, and psychosocial factors. RESULTS: Living in a neighborhood with a 1-unit higher NSES value was associated with a level of cognitive functioning that was 0.022 standard deviations higher (P = .02). The association was attenuated but still marginally significant (P < .1) after adjustment for confounders and, according to interaction tests, stronger among younger and non-White women.

CONCLUSIONS: The socioeconomic status of a woman's neighborhood may influence her cognitive functioning. This relationship is only partially explained by vascular, health behavior, or psychosocial factors. Future research is needed on the longitudinal relationships between NSES, cognitive impairment, and cognitive decline.


OBJECTIVES: We examined associations between parental military service and adolescent well-being. METHODS: We used cross-sectional data from the 2008 Washington State Healthy Youth Survey collected in public school grades 8, 10, and 12 (n = 10,606). We conducted multivariable logistic regression analyses to test associations between parental military service and adolescent well-being (quality of life, depressed mood, thoughts of suicide). RESULTS: In 8th grade, parental deployment was associated with higher odds of reporting thoughts of suicide among adolescent girls (odds ratio [OR] = 1.66; 95% confidence interval [CI] = 1.19, 2.32) and higher odds of low quality of life (OR = 2.10; 95% CI = 1.43, 3.10) and thoughts of suicide (OR = 1.75; 95% CI = 1.15, 2.67) among adolescent boys. In 10th and 12th grades, parental deployment was associated with higher odds of reporting low quality of life (OR = 2.74; 95% CI = 1.79, 4.20), depressed mood (OR = 1.50; 95% CI = 1.02, 2.20), and thoughts of suicide (OR = 1.64; 95% CI = 1.13, 2.38) among adolescent boys. CONCLUSIONS: Parental military deployment is associated with increased odds of impaired well-being among adolescents, especially adolescent boys. Military, school-based, and public health professionals have a unique opportunity to develop school- and community-based interventions to improve the well-being of adolescents in military families.


OBJECTIVES: We evaluated the effectiveness of a community-based participatory research-grounded intervention among women receiving Temporary Assistance for Needy Families (TANF)
with chronic health conditions in increasing (1) health care visits, (2) Medicaid knowledge and skills, and (3) health and functional status. METHODS: We used a randomized controlled trial design to assign 432 women to a public health nurse case management plus Medicaid intervention or a wait-control group. We assessed Medicaid outcomes pre- and posttraining; other outcomes were assessed at 3, 6, and 9 months. RESULTS: Medicaid knowledge and skills improved (P < .001 for both). Intervention group participants were more likely to have a new mental health visit (odds ratio [OR] = 1.92; P = .007), and this likelihood increased in higher-risk subgroups (OR = 2.03 and 2.83; P = .04 and .006, respectively). Depression and functional status improved in the intervention group over time (P = .016 for both). No differences were found in routine or preventive care, or general health. CONCLUSIONS: Health outcomes among women receiving TANF can be improved with public health interventions. Additional strategies are needed to further reduce health disparities in this population

(20) ANDERSSON D, MAGNUSSON H, CARSTENSEN J, BORGQUIST L. Co-morbidity and health care utilisation five years prior to diagnosis for depression. A register-based study in a Swedish population. BMC Public Health. 2011, vol. 11, p.552
http://dx.doi.org/10.1186/1471-2458-11-552

BACKGROUND: Depressive disorders have been associated with a number of co-morbidities, and we hypothesized that patients with a depression diagnosis would be heavy users of health care services, not only when first evaluated for depression, but also for preceding years. The aim of this study was to investigate whether increased health care utilisation and co-morbidity could be seen during five years prior to an initial diagnosis of depression. METHODS: We used a longitudinal register-based study design. The setting comprised the general population in the county of Ostergotland, south-east Sweden. All 2470 patients who were 20 years or older in 2006 and who received a new diagnosis of depression (F32 according to ICD-10) in 2006, were selected and followed back to the year 2001, five years before their depression diagnosis. A control group was randomly selected among those who were aged 20 years or over in 2006 and who had received no depression diagnosis during the period 2001-2006. RESULTS: Predictors of a depression diagnosis were a high number of physician visits, female gender, age below 60, age above 80 and a low socioeconomic status. Patients who received a diagnosis of depression used twice the amount of health care (e.g. physician visits and hospital days) during the five year period prior to diagnosis compared to the control group. A particularly strong increase in health care utilisation was seen the last year before diagnosis. These findings were supported with a high level of co-morbidity as for example musculoskeletal disorders during the whole five-year period for patients with a depression diagnosis. CONCLUSIONS: Predictors of a depression diagnosis were a high number of physician visits, female gender, age below 60, age above 80 and a low socioeconomic status. To find early signs of depression in the clinical setting and to use a preventive strategy to handle these patients is important

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BACKGROUND: The reproductive and mental health of women contributes significantly to their overall well-being. Three of the eight Millennium Development Goals are directly related to reproductive and sexual health while mental disorders make up three of the ten leading causes of disease burden in low and middle-income countries. Among mental disorders, depression and anxiety are two of the most prevalent. In the context of slower progress in achieving Millennium Development Goals in developing countries and the ever-increasing man-made and natural disasters in these areas, it is important to understand the association between reproductive health and mental health among women with post-disaster experiences. METHODS: This was a cross-sectional study with a sample of 387 women of reproductive age (15-49 years) randomly selected from the October 2005 earthquake affected areas of Pakistan. Data on reproductive health was collected using the Centers for Disease Control reproductive health assessment toolkit. Depression and anxiety were measured using the Hopkins Symptom Checklist-25, while earthquake experiences were captured using the Harvard Trauma Questionnaire. The association
of either depression or anxiety with socio-demographic variables, earthquake experiences, reproductive health and access to health facilities was estimated using multivariate logistic regression. RESULTS: Post-earthquake reproductive health events together with economic deprivation, lower family support and poorer access to health care facilities explained a significant proportion of differences in the experiencing of clinical levels of depression and anxiety. For instance, women losing resources for subsistence, separation from family and experiencing reproductive health events such as having a stillbirth, having had an abortion, having had abnormal vaginal discharge or having had genital ulcers, were at significant risk of depression and anxiety. CONCLUSION: The relationship between women's post-earthquake mental health and reproductive health, socio-economic status, and health care access is complex and explained largely by the socio-cultural role of women. It is suggested that interventions that consider gender differences and that are culturally appropriate are likely to reduce the incidence


This meta-analysis reviewed existing data on the impact of work-related critical incidents in hospital-based health care professionals. Work-related critical incidents may induce post-traumatic stress symptoms or even post-traumatic stress disorder (PTSD), anxiety, and depression and may negatively affect health care practitioners’ behaviors toward patients. Nurses and doctors often cope by working part time or switching jobs. Hospital administrators and health care practitioners themselves may underestimate the effects of work-related critical incidents. Relevant online databases were searched for original research published from inception to 2009 and manual searches of the Journal of Traumatic Stress, reference lists, and the European Traumatic Stress Research Database were conducted. Two researchers independently decided on inclusion and study quality. Effect sizes were estimated using standardized mean differences with 95% confidence intervals. Consistency was evaluated, using the I(2)-statistic. Meta-analysis was performed using the random effects model. Eleven studies, which included 3866 participants, evaluated the relationship between work-related critical incidents and post-traumatic stress symptoms. Six of these studies, which included 1695 participants, also reported on the relationship between work-related critical incidents and symptoms of anxiety and depression. Heterogeneity among studies was high and could not be accounted for by study quality, character of the incident, or timing of data collection. Pooled effect sizes for the impact of work-related critical incidents on post-traumatic stress symptoms, anxiety, and depression were small to medium. Remarkably, the effect was more pronounced in the longer than in the shorter term. In conclusion, this meta-analysis supports the hypothesis that work-related critical incidents are positively related to post-traumatic stress symptoms, anxiety, and depression in hospital-based health care professionals. Health care workers and their supervisors should be aware of the harmful effects of critical incidents and take preventive measures


BACKGROUND: Exercise may be effective in treating depression, but trials testing its effect in depressed women are rare. AIM: To compare the effect of exercise of preferred intensity with exercise of prescribed intensity in thirty-eight women living with depression. METHODS: A Pragmatic RCT of 12 sessions of exercise at preferred intensity compared with 12 sessions at prescribed intensity. Beck Depression Inventory (BDI), Rosenberg Self Esteem Scale (RSES), General Health Questionnaire 12 (GHQ-12), heart rate (HR), Rating of Perceived Exertion Scale (RPE), Quality of Life in Depression Scale (QLDS), Multi-Dimensional Scale of Perceived Social Support (MDSPSS), SF12 Health Survey and exercise participation rates were compared between groups. RESULTS: Intervention participants had statistically better BDI (t = 2.638, df = 36, p = 0.006, 95% mean (SD) 26.5 (10.7), CI-20.4 to -2.7, d = 0.86), GHQ-12 (t = 3.284, df = 36, p = 0.001, mean (SD) 8.3 (3.7) 95% CI -6.5 to -1.5, d = 1.08), RSES (t = 2.045, df = 36, p = 0.024,
mean (SD) 11.3 (5.8), 95% CI 0.3 -6.4, d = 0.25), QLDS (t = 1.902, df = 36, p = 0.0325, mean (SD) 15.5 (7.9), 95% CI -12.2 -0.4, d = 0.27) RPE scores (t = 1.755, df = 36, p = 0.0475, mean (SD) 9.2 (3.2), 95% CI -5.2 -2.0, d = 0.77) and attended more exercise sessions (t = 1.781, df = 36, p = 0.0415, number of sessions 8 (65%), 95% CI 0.3 -4.8, d = 0.58). SF-12, MSPSS and HR did not differ significantly between groups. CONCLUSIONS: Exercise of preferred intensity improves psychological, physiological and social outcomes, and exercise participation rates in women living with depression. TRIAL REGISTRATION: ClinicalTrials.gov: NCT00546221


BACKGROUND: In developed countries, perinatal death is known to cause major emotional and social effects on mothers. However, little is known about these effects in low income countries which bear the brunt of perinatal mortality burden. This paper reports the impact of perinatal death on psychological status and social consequences among mothers in a rural area of Bangladesh. METHODS: A total of 476 women including 122 women with perinatal deaths were assessed with the Edinburgh Postnatal Depression Scale (EPDS-B) at 6 weeks and 6 months postpartum, and followed up for negative social consequences at 6 months postpartum. Trained female interviewers carried out structured interviews at women's home. RESULTS: Overall 43% (95% CI: 33.7-51.8%) of women with a perinatal loss at 6 weeks postpartum were depressed compared to 17% (95% CI: 13.7-21.9%) with healthy babies (p = < 0.001). Depression status were significantly associated with women reporting negative life changes such as worse relationships with their husband (adjusted OR = 3.89, 95% CI: 1.37-11.04) and feeling guilty (adjusted OR = 2.61, 95% CI: 1.22-5.63) following the results of their last pregnancy outcome after 6 months of childbirth. CONCLUSIONS: This study highlights the greatly increased vulnerability of women with perinatal death to experience negative psychological and social consequences. There is an urgent need to develop appropriate mental health care services for mothers with perinatal deaths in Bangladesh, including interventions to develop positive family support


BACKGROUND: Mental health problems in young people are an important public health issue. Students leaving their hometown and family at a young age to pursue better educational opportunities overseas are confronted with life adjustment stress, which in turn affects their mental health and academic performance. This study aimed to examine the relationships among stress, coping strategies, and depressive symptoms using the stress coping framework in overseas Chinese university preparatory students in Taiwan. METHODS: A cross-sectional study was conducted at an overseas Chinese university preparatory institute in Taiwan. Of enrolled overseas Chinese university preparatory students at 2009, 756 completed a structured questionnaire measuring stress, strategies for coping with it, and the Center for Epidemiologic Studies Depression Scale. RESULTS: High levels of stress significantly predicted the adoption of active, problem-focused coping strategies (R(2) = 0.13, p < .01) and passive, emotion-focused coping strategies (R(2) = 0.24, p < .01). Acceptable CFI, SRMR, and RMSEA values from the structural equation modeling analysis demonstrated that the model satisfactorily fits the stress coping framework, after active coping strategies were eliminated from the model. Results from the Sobel test revealed that passive coping strategies mediated the relation between stress and depressive symptoms (z = 8.06, p < .001). CONCLUSION: Our study results suggested that stress is associated with coping strategies and depressive symptoms and passive strategies mediate the relation between stress and depressive symptoms in overseas Chinese university preparatory students

BACKGROUND: This study aims to look at the prevalence and characteristics of postpartum depression symptomatology (PPDS) among Canadian women. Studies have found that in developed countries, 10-15% of new mothers were affected by major postpartum depression. Mothers who suffer from postpartum depression may endure difficulties regarding their ability to cope with life events, as well as negative clinical implications for maternal-infant attachment.

METHODS: An analysis based on 6,421 Canadian women, who had a live birth between 2005 and 2006 and were part of the Maternity Experience Survey (MES), was performed. PPDS was measured based on the Edinburgh Postnatal Depression Scale. Various factors that assessed socio-economic status, demographic factors, and maternal characteristics were considered for the multinomial regression model. RESULTS: The national prevalence of minor/major and major PPDS was found to be 8.46% and 8.69% respectively. A mother's stress level during pregnancy, the availability of support after pregnancy, and a prior diagnosis of depression were the characteristics that had the strongest significant association with the development of PPDS.

CONCLUSIONS: A significant number of Canadian women experience symptoms of postpartum depression. Findings from this study may be useful to increase both the attainment of treatment and the rate at which it can be obtained among new mothers. Interventions should target those with the greatest risk of experiencing PPDS, specifically immigrant and adolescent mothers.


BACKGROUND: Relatively little empirical attention has focused on the association between social participation and depressive symptoms amongst older adults in Asian nations, where persons over the age of 65 represent a rapidly growing segment of the population. This study explores the dynamic relationship between participation in social activities and trajectories of depressive symptomatology among older Taiwanese adults surveyed over 18 years. METHODS: Data are from a nationally representative sample of 1,388 adults aged 60-64 first surveyed in 1989 and followed over an 18-year time period for a total of six waves. Individual involvement in social activities was categorized into continuous participation, ceased participation before age 70, initiating participation in older adulthood, never participated, and dropped out before age 70. Two domains of depressive symptoms--negative affect and lack of positive affect--were measured using a 10-item version of the Center for Epidemiologic Studies-Depression Scale. RESULTS: Analyses using growth curve modeling showed that continuously participating or initiating participation in social activities later life is significantly associated with fewer depressive symptoms among older Taiwanese adults, even after controlling for the confounding effects of aging, individual demographic differences, and health status. CONCLUSIONS: These findings suggest that maintaining or initiating social participation in later life benefits the mental health of older adults. Facilitating social activities among older adults is a promising direction for programs intended to promote mental health and successful aging among older adults in Taiwan.


Schools are one of the strongest socializing forces in the U.S. and wield considerable influence over individuals' social and economic trajectories. Our study investigates how school-level racial composition, measured by the percentage non-Hispanic white students in a school, affects depressive and somatic symptoms among a representative sample of U.S. adolescents, and whether the association differs by race/ethnicity. We analyzed Wave I data from the US National Longitudinal Study of Adolescent Health, resulting in a sample size of 18,419 students attending 132 junior and senior high schools in 1994/5. After controlling for individual and school characteristics, our multilevel analyses indicated that with increasing percentages of white...
students at their school, black students experienced more depressive symptoms and a higher risk of reporting high levels of somatic symptoms. After including students’ perceptions of discrimination and school attachment, the interaction between black student race and school-level racial composition was no longer significant for either outcome. Our findings suggest that attending predominantly-minority schools may buffer black students from discrimination and increase their school attachment, which may reduce their risk of experiencing depressive and somatic symptoms.

http://dx.doi.org/10.1093/aje/kwr030

Depression contributes substantially to the global burden of disease and disability. Population-level factors that shape depression may be efficient targets for intervention to decrease the depression burden. The authors aimed to identify the relation between neighborhood collective efficacy and major depression. Analyses were conducted on data from the New York Social Environment Study (n = 4,000), a representative study of residents of New York, New York, conducted in 2005. Neighborhood collective efficacy was measured as the average neighborhood response on a well-established scale. Major depression was assessed with the Patient Health Questionnaire. A marginal modeling approach was applied to present results on the additive scale relevant to public health and intervention. Analyses were adjusted for demographic and socioeconomic characteristics, recent life events that could contribute to both depression and change in residence, and individual perception of collective efficacy. Collective efficacy was related to major depression among older adults; marginal models estimated a 6.2% (95% confidence interval: 0.1, 17.5) lower prevalence of depression if all older adults (65 years and older) had lived in high versus low collective efficacy neighborhoods. Similar results were suggested among younger adults; however, the confidence interval crossed the null. These and other study findings suggest that community-randomized trials targeting collective efficacy merit consideration.

http://dx.doi.org/10.1016/j.socscimed.2011.03.024

This paper uses data from the National Longitudinal Study of Adolescent Health to examine the mental health of non-Hispanic black and white young adults in the US. We use latent growth curve modeling to characterize the typical stress trajectories experienced by black and white young adults spanning the bulk of their lives. We identify the following four stress trajectories: 1) relatively stress free; 2) stress peak at age 15 and a subsequent decline; 3) stress peak at age 17 and a subsequent decline; and 4) a moderately high chronic stress. Results indicate that black adolescents have significantly higher risk of being in all three of the stressful classes compared to white adolescents. Stress exposure is strongly associated with depression and the race differences in stress profiles account for a modest amount of the observed race differences in mental health. We do not observe any race differences in behavioral responses to stressors; black youth are no more likely than white youth to engage in poor health behaviors (e.g., smoking, drinking, or obesity) in response to stress. We provide tentative support for the notion that poor health behaviors partially reduce the association between stress and depression for blacks but not whites. These findings contribute to unresolved issues regarding mental and physical health disparities among blacks and whites.

http://dx.doi.org/10.2105/AJPH.2010.197285

OBJECTIVES: We determined racial/ethnic differences in social support and exposure to violence and transphobia, and explored correlates of depression among male-to-female transgender women with a history of sex work (THSW). METHODS: A total of 573 THSW who worked or
resided in San Francisco or Oakland, California, were recruited through street outreach and referrals and completed individual interviews using a structured questionnaire. RESULTS: More than half of Latina and White participants were depressed on the basis of Center For Epidemiologic Studies Depression Scale scores. About three quarters of White participants reported ever having suicidal ideation, of whom 64% reported suicide attempts. Half of the participants reported being physically assaulted, and 38% reported being raped or sexually assaulted before age 18 years. White and African American participants reported transphobia experiences more frequently than did others. Social support, transphobia, suicidal ideation, and levels of income and education were significantly and independently correlated with depression. CONCLUSIONS: For THSW, psychological vulnerability must be addressed in counseling, support groups, and health promotion programs specifically tailored to race/ethnicity.


BACKGROUND: Trafficking in women is a widespread human rights violation commonly associated with poor mental health. Yet, to date, no studies have used psychiatric diagnostic assessment to identify common forms of mental distress among survivors returning to their home country. METHODS: A longitudinal study was conducted of women aged 18 and over who returned to Moldova between December 2007 and December 2008 registered by the International Organisation for Migration as a survivor of human trafficking. Psychiatric diagnoses in women at a mean of 6 months after return (range 2-12 months) were made by a trained Moldavian psychiatrist using the Structured Clinical Interview for DSM-IV, and compared with diagnoses recorded in the same women within 5 days of return. We described the socio-demographic characteristics of the women in the sample including both pre and post-trafficking information. We then described the distribution of mental health diagnoses recorded during the crisis intervention phase (1-5 days after return) and the re-integration phase (2-12 months after return). We compared diagnoses at the patient level between the two time points by tabulating the diagnoses and carrying out a kappa test of agreement and the Stuart-Maxwell test for marginal homogeneity (an extension of the McNemar test to kxk table). RESULTS: 120/176 (68%) eligible women participated. At 2-12 months after their return, 54% met criteria for at least one psychiatric diagnoses comprising post-traumatic stress disorder (PTSD) alone (16%); co-morbid PTSD (20%); other anxiety or mood disorder (18%). 85% of women who had been diagnosed in the crisis phase with co-morbid PTSD or with another anxiety or mood disorder sustained a diagnosis of any psychiatric disorder when followed up during rehabilitation. CONCLUSIONS: Trafficked women returning to their country of origin are likely to suffer serious psychological distress that may endure well beyond the time they return. Women found to have co-morbid PTSD or other forms of anxiety and depression immediately post-return should be offered evidenced-based mental health treatment for at least the standard 12-month period of rehabilitation.


BACKGROUND: Acute stress reaction is a diagnosis given immediately following the experience of an exceptional mental or physical stressor. To the best of our knowledge, no study has examined the association between acute stress reaction diagnosis and suicide. The current study examined this association in a population-based sample. In addition, we examined comorbid psychiatric diagnoses as modifiers of this association. METHODS: Data for the current study were obtained from the nationwide Danish health and administrative registries, which include data for all 5.4 million residents of Denmark. All suicides between 1 January 1994 and 31 December 2006 were included and controls were selected from a sample of all Danish residents. Using this nested case-control design, we examined 9612 suicide cases and 199 306 controls matched to cases with respect to gender, date of birth and time. RESULTS: In total, 95 cases (0.99%) and 165 controls (0.08%) had a diagnosis of acute stress reaction. Those diagnosed with acute stress reaction had 10 times the rate of completed suicide compared with those without this diagnosis,
adjusting for the control to case matching, depression and marital status (95% confidence interval 7.7-14). Additionally, persons with acute stress reaction and depression, or acute stress reaction and substance abuse, had a greater rate of suicide than expected based on their independent effects. CONCLUSIONS: Acute stress reaction is a risk factor for completed suicide


BACKGROUND: Physicians' mental health may be adversely affected by the number of days of work and time spent on-call, and improved by sleep and days-off. The aim of this study was to determine the associations of depressive symptoms with taking days of off duty, hours of sleep, and the number of days of on-call and overnight work among physicians working in Japanese hospitals. METHODS: A cross-sectional study as a national survey was conducted by mail. The study population was 10,000 randomly selected physicians working in hospitals who were also members of the Japan Medical Association (response rate 40.5%). Self-reported anonymous questionnaire was sent to assess the number of days off-duty, overnight work, and on-calls, and the average number of sleep hours on days not working overnight in the previous one month. Depressive state was determined by the Japanese version of the Quick Inventory of Depressive Symptomatology. Logistic regression analysis was used to explore the associations between depressive symptoms and the studied variables. RESULTS: Among the respondents, 8.3% of men and 10.5% of women were determined to be depressed. For both men and women, depressive state was associated with having no off-duty days and averaging less than 5 hours of sleep on days not doing overnight work. Depressive state was positively associated with being on-call more than 5 days per month for men, and more than 8 days per month for women, and was negatively associated with being off-duty more than 8 days per month for men. CONCLUSION: Some physicians need some support to maintain their mental health. Physicians who do not take enough days-off, who reduced sleep hours, and who have certain number of days on-calls may develop depressive symptoms

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ABSTRACT: BACKGROUND: Much remains unknown about the effect of timing and prioritization of vaccination against pandemic (pH1N1) 2009 virus on health outcomes. We adapted a city-level contact network model to study different campaigns on influenza morbidity and mortality. METHODS: We modeled different distribution strategies initiated between July and November 2009 using a compartmental epidemic model that includes age structure and transmission network dynamics. The model represents the Greater Vancouver Regional District, a major North American city and surrounding suburbs with a population of 2 million, and is parameterized using data from the British Columbia Ministry of Health, published studies, and expert opinion. Outcomes are expressed as the number of infections and deaths averted due to vaccination. RESULTS: The model output was consistent with provincial surveillance data. Assuming a basic reproduction number = 1.4, an 8-week vaccination campaign initiated two weeks before the epidemic onset reduced morbidity and mortality by 79-91% and 80-87%, respectively, compared to no vaccination. Prioritizing children and parents for vaccination may have reduced transmission compared to actual practice, but the mortality benefit of this strategy appears highly sensitive to campaign timing. Modeling the actual late October start date resulted in modest reductions in morbidity and mortality (13-25% and 16-20%, respectively) with little variation by prioritization scheme. CONCLUSION: Delays in vaccine production due to technological or logistical barriers
may reduce potential benefits of vaccination for pandemic influenza, and these temporal effects can outweigh any additional theoretical benefits from population targeting. Careful modeling may provide decision makers with estimates of these effects before the epidemic peak to guide production goals and inform policy. Integration of real-time surveillance data with mathematical models holds the promise of enabling public health planners to optimize the community benefits from proposed interventions before the pandemic peak.

(2) SHAFIR SC, O'KEEFE KA, SHOAF KI. Evaluation of the Seroprevalence of Influenza A(H1N1) 2009 on a University Campus: A cross-sectional Study. BMC Public Health. 2011 Dec. 13, vol. 11, n° 1, p.922
http://dx.doi.org/10.1186/1471-2458-11-922

ABSTRACT: BACKGROUND: Human infection with influenza A(H1N1) 2009 was first identified in the United States on 15 April 2009 and on 11 June 2009, WHO declared that the rapidly spreading swine-origin influenza virus constituted a global pandemic. We evaluated the seroprevalence of influenza A(H1N1) 2009 virus on a large public University campus, as well as disparities in demographic, symptomatic and vaccination characteristics of participants.

METHODS: Using a cross-sectional study design, sera was collected from volunteers and then tested for the presence of antibodies to the virus using a [greater than or equal to] 1:40 dilution cut-off by hemagglutination inhibition assay. In conjunction, participants were asked to complete a questionnaire allowing us to estimate risk factors for infection in this population, as well as distinguish artificially derived antibodies from naturally derived antibodies.

RESULTS: 300 total participants were recruited and tested. 158 (52.6%) tested positive for influenza A(H1N1) 2009 via hemagglutination inhibition assay using a [greater than or equal to] 1:40 dilution cut-off. 86 people (54.4%) tested positive for H1N1 but did not report experiencing symptoms during the pandemic meeting the May 2010 CDC definition of influenza-like illness. Furthermore, of those individuals who reported that they had received the H1N1 vaccine, 16% did not test positive.

CONCLUSIONS: Overall, 52.7% of the total study population tested positive for influenza A(H1N1) 2009. 54.4% of those who tested positive for influenza A(H1N1) 2009 using the >1:40 dilution cut-off on the hemagglutination inhibition assay in this study population did not report experiencing symptoms during the pandemic meeting the May 2010 CDC definition of influenza-like illness. 16% of those who reported receiving the H1N1 vaccine did not test positive by HAI. We also found that vaccination coverage for H1N1 vaccine was poor among Blacks and Latinos, despite the fact that vaccine was readily available at no cost.


The liberalisation of the European aviation sector has multiplied paths of entry into the United Kingdom (UK) for the international traveller. These changing mobilities necessitate a reconceptualisation of the border as a series of potentially vulnerable nodes occurring within, and extending beyond, national boundaries. In this paper, we consider the border through the lens of port health, the collective term for various sanitary operations enacted at international transport terminals. In the UK, a critical player in the oversight of port health is the Health Protection Agency (HPA), which became a non-Departmental public body in 2005. A major part of port health is preparedness, a set of techniques aimed at managing, and responding to, emergencies of public health concern. More recently, certain jurisdictions have embarked on public health preparedness work across a number of different geographical scales. Using methods pioneered by the military, this form of ‘distributed preparedness’ is of increased interest to social science and medical scholars. With reference to case studies conducted in localities surrounding two UK regional airports following the 2009-10 H1N1 influenza pandemic, we consider the extent to which distributed preparedness as a concept and a set of practices can inform current debates - in the UK, and beyond - concerning interventions at the border 'within'.

(4) SAVULESCU C, JIMENEZ-JORGE S, DE MS, POZO F, et al. Using surveillance data to estimate pandemic vaccine effectiveness against laboratory confirmed influenza A(H1N1)2009 infection: two case control studies, Spain, season 2009-2010. BMC Public
ABSTRACT: BACKGROUND: Physicians of the Spanish Influenza Sentinel Surveillance System report and systematically swab patients attended to their practices for influenza-like illness (ILI). Within the surveillance system, some Spanish regions also participated in an observational study aiming at estimating influenza vaccine effectiveness (cycEVA study). During the season 2009-2010, we estimated pandemic influenza vaccine effectiveness using both the influenza surveillance data and the cycEVA study. METHODS: We conducted two case-control studies using the test-negative design, between weeks 48/2009 and 8/2010 of the pandemic season. The surveillance-based study included all swabbed patients in the sentinel surveillance system. The cycEVA study included swabbed patients from seven Spanish regions. Cases were laboratory-confirmed pandemic influenza A(H1N1)2009. Controls were ILI patients testing negative for any type of influenza. Variables collected in both studies included demographic data, vaccination status, laboratory results, chronic conditions, and pregnancy. Additionally, cycEVA questionnaire collected data on previous influenza vaccination, smoking, functional status, hospitalisations, visits to the general practitioners, and obesity. We used logistic regression to calculate adjusted odds ratios (OR), computing pandemic influenza vaccine effectiveness as (1-OR)*100. RESULTS: We included 331 cases and 995 controls in the surveillance-based study and 85 cases and 351 controls in the cycEVA study. We detected nine (2.7%) and two (2.4%) vaccine failures in the surveillance-based and cycEVA studies, respectively. Adjusting for variables collected in surveillance database and swabbing month, pandemic influenza vaccine effectiveness was 62% (95% confidence interval (CI): -5; 87). The cycEVA vaccine effectiveness was 64% (95%CI: -225; 96) when adjusting for common variables with the surveillance system and 75% (95%CI: -293; 98) adjusting for all variables collected. CONCLUSION: Point estimates of the pandemic influenza vaccine effectiveness suggested a protective effect of the pandemic vaccine against laboratory-confirmed influenza A(H1N1)2009 in the season 2009-2010. Both studies were limited by the low vaccine coverage and the late start of the vaccination campaign. Routine influenza surveillance provides reliable estimates and could be used for influenza vaccine effectiveness studies in future seasons taken into account the surveillance system limitations


Objectives. We assessed the impact of social determinants of potential exposure to H1N1—which are unequally distributed by race/ethnicity in the United States-on incidence of influenza-like illness (ILI) during the 2009 H1N1 pandemic. Methods. In January 2010 we surveyed a nationally representative sample (n=2079) of US adults from the Knowledge Networks online research panel, with Hispanic and African American oversamples. The completion rate was 56%. Results. Path analysis examining ILI incidence, race, and social determinants of potential exposure to H1N1 demonstrated that higher ILI incidence was related to workplace policies, such as lack of access to sick leave, and structural factors, such as number of children in the household. Hispanic ethnicity was related to a greater risk of ILI attributable to these social determinants, even after we controlled for income and education. Conclusions. The absence of certain workplace policies, such as paid sick leave, confers a population-attributable risk of 5 million additional cases of ILI in the general population and 1.2 million cases among Hispanics. Federal mandates for sick leave could have significant health impacts by reducing morbidity from ILI, especially in Hispanics. (Am J Public Health. Published online ahead of print November 17, 2011: e1-e7. doi:10.2105/AJPH.2011.300307)

Despite considerable research efforts in specific subpopulations, reliable estimates of the infection attack rates and severity of 2009 influenza A (H1N1) in the general population remain scarce. Such estimates are essential to the tailoring of future control strategies. Therefore, 2 serial population-based serologic surveys were conducted, before and after the 2009 influenza A (H1N1) epidemic, in the Netherlands. Random age-stratified samples were obtained using a 2-stage cluster design. Participants donated blood and completed a questionnaire. Data on sentinel general practitioner-attended influenza-like illness and nationwide hospitalization and mortality were used to assess the severity of infection. The estimated infection attack rates were low in the general population (7.6%, 95% confidence interval: 3.6, 11) but high in children aged 5-19 years (35%, 95% confidence interval: 25, 45). The estimated hospitalization and mortality rates per infection increased significantly with age (5-19 years: 0.042% and 0.00094%, respectively; 20-39 years: 0.12% and 0.0025%; 40-59 years: 0.68% and 0.032%; 60-75 years: >0.81% and >0.068%). The high infection attack rate in children and the very low attack rate in older adults, together with the low severity of illness per infection in children but substantial severity in older adults, produced an epidemic with a low overall impact.

(8) LUTEIJN JM, DOLK H, MARNOCH GJ. Differences in pandemic influenza vaccination policies for pregnant women in Europe. BMC Public Health. 2011, vol. 11, p.819
http://dx.doi.org/10.1186/1471-2458-11-819

ABSTRACT: BACKGROUND: An important component of the policy to deal with the H1N1 pandemic in 2009 was to develop and implement vaccination. Since pregnant women were found to be at particular risk of severe morbidity and mortality, the World Health Organization and the European Centers for Disease Control advised vaccinating pregnant women, regardless of trimester of pregnancy. This study reports a survey of vaccination policies for pregnant women in European countries. METHODS: Questionnaires were sent to European competent authorities of 27 countries via the European Medicines Agency and to leaders of registries of European Surveillance of Congenital Anomalies in 21 countries. RESULTS: Replies were received for 24 out of 32 European countries of which 20 had an official pandemic vaccination policy. These 20 countries all had a policy targeting pregnant women. For two of the four countries without official pandemic vaccination policies, some vaccination of pregnant women took place. In 12 out of 20 countries the policy was to vaccinate only second and third trimester pregnant women and in 8 out of 20 countries the policy was to vaccinate pregnant women regardless of trimester of pregnancy. Seven different vaccines were used for pregnant women, of which four contained adjuvants. Few countries had mechanisms to monitor the number of vaccinations given specifically to pregnant women over time. Vaccination uptake varied. CONCLUSIONS: Differences in pandemic vaccination policy and practice might relate to variation in perception of vaccine efficacy and safety, operational issues related to vaccine manufacturing and procurement, and vaccination campaign systems. Increased monitoring of pandemic influenza vaccine coverage of pregnant women is recommended to enable evaluation of the vaccine safety in pregnancy and pandemic vaccination campaign effectiveness.

http://dx.doi.org/10.1001/jama.306.15.1723

OBJECTIVE: To examine the risk of neurological and autoimmune disorders of special interest in people vaccinated against pandemic influenza A (H1N1) with Pandemrix (GlaxoSmithKline, Middlesex, UK) compared with unvaccinated people over 8-10 months. DESIGN: Retrospective cohort study linking individualised data on pandemic vaccinations to an inpatient and specialist database on healthcare utilisation in Stockholm county for follow-up during and after the pandemic period. SETTING: Stockholm county, Sweden. Population All people registered in Stockholm county on 1 October 2009 and who had lived in this region since 1 January 1998; 1,024,019 were vaccinated against H1N1 and 921,005 remained unvaccinated. MAIN OUTCOME MEASURES: Neurological and autoimmune diagnoses according to the European Medicines Agency strategy for monitoring of adverse events of special interest defined using ICD-10 codes for Guillain-Barre syndrome, Bell's palsy, multiple sclerosis, polyneuropathy, anaesthesia or hypoaesthesia, paraesthesia, narcolepsy (added), and autoimmune conditions such as rheumatoid arthritis, inflammatory bowel disease, and type 1 diabetes; and short term mortality according to vaccination status. RESULTS: Excess risks among vaccinated compared with unvaccinated people were of low magnitude for Bell's palsy (hazard ratio 1.25, 95% confidence interval 1.06 to 1.48) and paraesthesia (1.11, 1.00 to 1.23) after adjustment for age, sex, socioeconomic status, and healthcare utilisation. Risks for Guillain-Barre syndrome, multiple sclerosis, type 1 diabetes, and rheumatoid arthritis remained unchanged. The risks of paraesthesia and inflammatory bowel disease among those vaccinated in the early phase (within 45 days from 1 October 2009) of the vaccination campaign were significantly increased; the risk being increased within the first six weeks after vaccination. Those vaccinated in the early phase were at a slightly reduced risk of death than those who were unvaccinated (0.94, 0.91 to 0.98), whereas those vaccinated in the late phase had an overall reduced mortality (0.68, 0.64 to 0.71). These associations could be real or explained, partly or entirely, by residual confounding. CONCLUSIONS: Results for the safety of Pandemrix over 8-10 months of follow-up were reassuring -notably, no change in the risk for Guillain-Barre syndrome, multiple sclerosis, type 1 diabetes, or rheumatoid arthritis. Relative risks were significantly increased for Bell's palsy, paraesthesia, and inflammatory bowel disease after vaccination, predominantly in the early phase of the vaccination campaign. Small numbers of children and adolescents with narcolepsy precluded any meaningful conclusions.


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 TCID(50) (95% CI = 8.8-35 TCID(50) ). The infectivity of wild-type H1N1 virus remains unknown as the data set pooling was unsuccessful.

CONTEXT: Extracorporeal membrane oxygenation (ECMO) can support gas exchange in patients with severe acute respiratory distress syndrome (ARDS), but its role has remained controversial. ECMO was used to treat patients with ARDS during the 2009 influenza A(H1N1) pandemic.

OBJECTIVE: To compare the hospital mortality of patients with H1N1-related ARDS referred, accepted, and transferred for ECMO with matched patients who were not referred for ECMO.

DESIGN, SETTING, AND PATIENTS: A cohort study in which ECMO-referred patients were defined as all patients with H1N1-related ARDS who were referred, accepted, and transferred to 1 of the 4 adult ECMO centers in the United Kingdom during the H1N1 pandemic in winter 2009-2010. The ECMO-referred patients and the non-ECMO-referred patients were matched using data from a concurrent, longitudinal cohort study (Swine Flu Triage study) of critically ill patients with suspected or confirmed H1N1. Detailed demographic, physiological, and comorbidity data were used in 3 different matching techniques (individual matching, propensity score matching, and GenMatch matching).

MAIN OUTCOME MEASURE: Survival to hospital discharge analyzed according to the intention-to-treat principle.

RESULTS: Of 80 ECMO-referred patients, 69 received ECMO (86.3%) and 22 died (27.5%) prior to discharge from the hospital. From a pool of 1756 patients, there were 59 matched pairs of ECMO-referred patients and non-ECMO-referred patients identified using individual matching, 75 matched pairs identified using propensity score matching, and 75 matched pairs identified using GenMatch matching. The hospital mortality rate was 23.7% for ECMO-referred patients vs 52.5% for non-ECMO-referred patients (relative risk [RR], 0.45 [95% CI, 0.26-0.79]; P = .006) when individual matching was used; 24.0% vs 46.7%, respectively (RR, 0.51 [95% CI, 0.31-0.81]; P = .008) when propensity score matching was used; and 24.0% vs 50.7%, respectively (RR, 0.47 [95% CI, 0.31-0.72]; P = .001) when GenMatch matching was used. The results were robust to sensitivity analyses, including amending the inclusion criteria and restricting the location where the non-ECMO-referred patients were treated.

CONCLUSION: For patients with H1N1-related ARDS, referral and transfer to an ECMO center was associated with lower hospital mortality compared with matched non-ECMO-referred patients.

http://dx.doi.org/10.1001/jama.2011.1504

http://dx.doi.org/10.1186/1471-2458-11-758

BACKGROUND: In contrast to seasonal influenza epidemics, where the majority of deaths occur amongst elderly, a considerable part of the 2009 pandemic influenza related deaths concerned relatively young people. In the Netherlands, all deaths associated with laboratory-confirmed influenza A(H1N1) 2009 virus infection had to be notified, both during the 2009-2010 pandemic season and the 2010-2011 influenza season. To assess whether and to what extent pandemic mortality patterns were reverting back to seasonal patterns, a retrospective analyses of all notified fatal cases associated with laboratory-confirmed influenza A(H1N1) 2009 virus infection was performed.

METHODS: The notification database, including detailed information about the clinical characteristics of all notified deaths, was used to perform a comprehensive analysis of all deceased patients with a laboratory-confirmed influenza A(H1N1) 2009 virus infection. Characteristics of the fatalities with respect to age and underlying medical conditions were analysed, comparing the 2009-2010 pandemic and the 2010-2011 influenza season.

RESULTS: A total of 65 fatalities with a laboratory-confirmed influenza A(H1N1) 2009 virus infection were notified in 2009-2010 and 38 in 2010-2011. During the pandemic season, the population mortality rates peaked in persons aged 0-15 and 55-64 years. In the 2010-2011 influenza season, peaks in mortality were seen in persons aged 0-15 and 75-84 years. During the 2010-2011 influenza season, the height of first peak was lower compared to that during the pandemic season.

Underlying immunological disorders were more common in the pandemic season compared to the 2010-2011 season (p = 0.02), and cardiovascular disorders were more common in the 2010-2011
season (p = 0.005). CONCLUSIONS: The mortality pattern in the 2010-2011 influenza season still resembled the 2009-2010 pandemic season with a peak in relatively young age groups, but concurrently a clear shift toward seasonal patterns was seen, with a peak in mortality in the elderly, i.e. ≥ 75 years of age


OBJECTIVE: To assess the impact of the 2009 A/H1N1 influenza pandemic in England during the two waves of activity up to end of February 2010 by estimating the probabilities of cases leading to severe events and the proportion of the population infected. DESIGN: A Bayesian evidence synthesis of all available relevant surveillance data in England to estimate severity of the pandemic. DATA SOURCES: All available surveillance systems relevant to the pandemic 2009 A/H1N1 influenza outbreak in England from June 2009 to February 2010. Pre-existing influenza surveillance systems, including estimated numbers of symptomatic cases based on consultations to the health service for influenza-like illness and cross sectional population serological surveys, as well as systems set up in response to the pandemic, including follow-up of laboratory confirmed cases up to end of June 2009 (FF100 and Fluzone databases), retrospective and prospective follow-up of confirmed hospitalised cases, and reported deaths associated with pandemic 2009 A/H1N1 influenza. Main outcome measures Age specific and wave specific probabilities of infection and symptomatic infection resulting in hospitalisation, intensive care admission, and death, as well as infection attack rates (both symptomatic and total). The probabilities of intensive care admission and death given hospitalisation over time are also estimated to evaluate potential changes in severity across waves. RESULTS: In the summer wave of A/H1N1 influenza, 0.54% (95% credible interval 0.33% to 0.82%) of the estimated 606,100 (419,300 to 886,300) symptomatic cases were hospitalised, 0.05% (0.03% to 0.08%) entered intensive care, and 0.015% (0.010% to 0.022%) died. These correspond to 3200 (2300 to 4700) hospital admissions, 310 (200 to 480) intensive care admissions, and 90 (80 to 110) deaths in the summer wave. In the second wave, 0.55% (0.28% to 0.89%) of the 1,352,000 (829,900 to 2,806,000) estimated symptomatic cases were hospitalised, 0.10% (0.05% to 0.16%) were admitted to intensive care, and 0.025% (0.013% to 0.040%) died. These correspond to 7500 (5900 to 9700) hospitalisations, 1340 (1030 to 1790) admissions to intensive care, and 240 (310 to 380) deaths. Just over a third (35% (26% to 45%)) of infections were estimated to be symptomatic. The estimated probabilities of infections resulting in severe events were therefore 0.19% (0.12% to 0.29%), 0.02% (0.01% to 0.03%), and 0.005% (0.004% to 0.008%) in the summer wave for hospitalisation, intensive care admission, and death respectively. The corresponding second wave probabilities are 0.19% (0.10% to 0.32%), 0.03% (0.02% to 0.06%), and 0.009% (0.004% to 0.014%). An estimated 30% (20% to 43%) of hospitalisations were detected in surveillance systems in the summer, compared with 20% (15% to 25%) in the second wave. Across the two waves, a mid-estimate of 11.2% (7.4% to 18.9%) of the population of England were infected, rising to 29.5% (16.9% to 64.1%) in 5-14 year olds. Sensitivity analyses to the evidence included suggest this infection attack rate could be as low as 5.9% (4.2% to 8.7%) or as high as 28.4% (26.0% to 30.8%). In terms of the probability that an infection leads to death in the second wave, these correspond, respectively, to a high estimate of 0.017% (0.011% to 0.024%) and a low estimate of 0.0027% (0.0024% to 0.0031%). CONCLUSIONS: This study suggests a mild pandemic, characterised by case and infection severity ratios increasing between waves. Results suggest low ascertainment rates, highlighting the importance of systems enabling early robust estimation of severity, to inform optimal public health responses, particularly in light of the apparent resurgence of the 2009 A/H1N1 strain in the 2010-11 influenza season


The calcium-transporting ATPase ATP2A2, also known as SERCA2a, is a critical ATPase responsible for Ca(2+) re-uptake during excitation-contraction coupling. Impaired Ca(2+) uptake
resulting from decreased expression and reduced activity of SERCA2a is a hallmark of heart failure. Accordingly, restoration of SERCA2a expression by gene transfer has proved to be effective in improving cardiac function in heart-failure patients, as well as in animal models. The small ubiquitin-related modifier (SUMO) can be conjugated to lysine residues of target proteins, and is involved in many cellular processes. Here we show that SERCA2a is SUMOylated at lysines 480 and 585 and that this SUMOylation is essential for preserving SERCA2a ATPase activity and stability in mouse and human cells. The levels of SUMO1 and the SUMOylation of SERCA2a itself were greatly reduced in failing hearts. SUMO1 restitution by adeno-associated-virus-mediated gene delivery maintained the protein abundance of SERCA2a and markedly improved cardiac function in mice with heart failure. This effect was comparable to SERCA2A gene delivery. Moreover, SUMO1 overexpression in isolated cardiomyocytes augmented contractility and accelerated Ca(2+) decay. Transgene-mediated SUMO1 overexpression rescued cardiac dysfunction induced by pressure overload concomitantly with increased SERCA2a function. By contrast, downregulation of SUMO1 using small hairpin RNA (shRNA) accelerated pressure-overload-induced deterioration of cardiac function and was accompanied by decreased SERCA2a function. However, knockdown of SERCA2a resulted in severe contractile dysfunction both in vitro and in vivo, which was not rescued by overexpression of SUMO1. Taken together, our data show that SUMOylation is a critical post-translational modification that regulates SERCA2a function, and provide a platform for the design of novel therapeutic strategies for heart failure.

(17) ZHANG Y, MAY L, STOTO MA. Evaluating syndromic surveillance systems at institutions of higher education (IHEs): a retrospective analysis of the 2009 H1N1 influenza pandemic at two universities. BMC Public Health. 2011, vol. 11, p.591

http://dx.doi.org/10.1186/1471-2458-11-591

BACKGROUND: Syndromic surveillance has been widely adopted as a real-time monitoring tool for timely response to disease outbreaks. During the second wave of the pH1N1 pandemic in Fall 2009, two major universities in Washington, DC collected data that were potentially indicative of influenza-like illness (ILI) cases in students and staff. In this study, our objectives were three-fold. The primary goal of this study was to characterize the impact of pH1N1 on the campuses as clearly as possible given the data available and their likely biases. In addition, we sought to evaluate the strengths and weaknesses of the data series themselves, in order to inform these two universities and other institutions of higher education (IHEs) about real-time surveillance systems that are likely to provide the most utility in future outbreaks (at least to the extent that it is possible to generalize from this analysis). METHODS: We collected a wide variety of data that covered both student ILI cases reported to medical and non-medical staff, employee absenteeism, and hygiene supply distribution records (from University A only). Communication data were retrieved from university broadcasts, university preparedness websites, and H1N1-related on campus media reports. Regional data based on the Centers for Disease Control and Prevention Outpatient Influenza-like Illness Surveillance Network (CDC ILINet) surveillance network, American College Health Association (ACHA) pandemic influenza surveillance data, and local Google Flu Trends were used as external data sets. We employed a “triangulation” approach for data analysis in which multiple contemporary data sources are compared to identify time patterns that are likely to reflect biases as well as those that are more likely to be indicative of actual infection rates. RESULTS: Medical personnel observed an early peak at both universities immediately after school began in early September and a second peak in early November; only the second peak corresponded to patterns in the community at large. Self-reported illness to university deans’ offices was also relatively increased during mid-term exam weeks. The overall volume of pH1N1-related communication messages similarly peaked twice, corresponding to the two peaks of student ILI cases. CONCLUSIONS: During the 2009 H1N1 pandemic, both University A and B experienced a peak number of ILI cases at the beginning of the Fall term. This pattern, seen in surveillance systems at these universities and to a lesser extent in data from other IHEs, most likely resulted from students bringing the virus back to campus from their home states coupled with a sudden increase in population density in dormitories and lecture halls. Through comparison of data from different syndromic surveillance data streams, paying attention to the likely biases in each over time, we have determined, at least in the case of the pH1N1
pandemic, that student health center data more accurately depicted disease transmission on
campus at both universities during the Fall 2009 pandemic than other available data sources


OBJECTIVES: We assessed risk factors for 2009 pandemic influenza A (H1N1)-related hospitalization, mechanical ventilation, and death among New Mexico residents. METHODS: We calculated population rate ratios using Poisson regression to analyze risk factors for H1N1-related hospitalization. We performed a cross-sectional analysis of hospitalizations during September 14, 2009 through January 13, 2010, using logistic regression to assess risk factors for mechanical ventilation and death among those hospitalized. RESULTS: During the study period, 926 laboratory-confirmed H1N1-related hospitalizations were identified. H1N1-related hospitalization was significantly higher among American Indians (risk ratio [RR] = 2.6; 95% confidence interval [CI] = 2.2, 3.2), Blacks (RR = 1.7; 95% CI = 1.2, 2.4), and Hispanics (RR = 1.8; 95% CI = 1.5, 2.0) than it was among non-Hispanic Whites, and also was higher among persons of younger age and lower household income. Mechanical ventilation was significantly associated with age 25 years and older, obesity, and lack of or delayed antiviral treatment. Death was significantly associated with male gender, cancer during the previous 12 months, and liver disorder. CONCLUSIONS: This analysis supports recent national efforts to include American Indian/Alaska Native race as a group at high risk for complications of influenza with respect to vaccination and antiviral treatment recommendations


BACKGROUND: During the course of an influenza pandemic, governments know relatively little about the possibly changing influence of government trust, risk perception, and receipt of information on the public's intention to adopt protective measures or on the acceptance of vaccination. This study aims to identify and describe possible changes in and factors associated with public's intentions during the 2009 influenza A (H1N1) pandemic in the Netherlands. METHODS: Sixteen cross-sectional telephone surveys were conducted (N = 8060) between April - November 2009. From these repeated measurements three consecutive periods were categorized based on crucial events during the influenza A (H1N1) pandemic. Time trends in government trust, risk perception, intention to adopt protective measures, and the acceptance of vaccination were analysed. Factors associated with an intention to adopt protective measures or vaccination were identified. RESULTS: Trust in the government was high, but decreased over time. During the course of the pandemic, perceived vulnerability and an intention to adopt protective measures increased. Trust and vulnerability were associated with an intention to adopt protective measures in general only during period one. Higher levels of intention to receive vaccination were associated with increased government trust, fear/worry, and perceived vulnerability. In periods two and three receipt of information was positively associated with an intention to adopt protective measures. Most respondents wanted to receive information about infection prevention from municipal health services, health care providers, and the media. CONCLUSIONS: The Dutch response to the H1N1 virus was relatively muted. Higher levels of trust in the government, fear/worry, and perceived vulnerability were all positively related to an intention to accept vaccination. Only fear/worry was positively linked to an intention to adopt protective measures during the entire pandemic. Risk and crisis communication by the government should focus on building and maintaining trust by providing information about preventing infection in close collaboration with municipal health services, health care providers, and the media
http://dx.doi.org/10.1093/aje/kwr122

Analysis of historical data has strongly shaped our understanding of the epidemiology of pandemic influenza and informs analysis of current and future epidemics. Here, the authors analyzed previously unpublished documents from a large household survey of the “Spanish” H1N1 influenza pandemic, conducted in 1918, for the first time quantifying influenza transmissibility at the person-to-person level during that most lethal of pandemics. The authors estimated a low probability of person-to-person transmission relative to comparable estimates from seasonal influenza and other directly transmitted infections but similar to recent estimates from the 2009 H1N1 pandemic. The authors estimated a very low probability of asymptomatic infection, a previously unknown parameter for this pandemic, consistent with an unusually virulent virus. The authors estimated a high frequency of prior immunity that they attributed to a largely unreported influenza epidemic in the spring of 1918 (or perhaps to cross-reactive immunity). Extrapolating from this finding, the authors hypothesize that prior immunity partially protected some populations from the worst of the fall pandemic and helps explain differences in attack rates between populations. Together, these analyses demonstrate that the 1918 influenza virus, though highly virulent, was only moderately transmissible and thus in a modern context would be considered controllable.

http://dx.doi.org/10.1093/aje/kwr113

Estimation of influenza infection rates is important for determination of the extent of epidemic spread and for calculation of severity indicators. The authors compared estimated infection rates from paired and cross-sectional serologic surveys, rates of influenza like illness (ILI) obtained from sentinel general practitioners (GPs), and ILI samples that tested positive for influenza using data from similar periods collected during the 2009 H1N1 epidemic in Singapore. The authors performed sensitivity analyses to assess the robustness of estimates to input parameter uncertainties, and they determined sample sizes required for differing levels of precision. Estimates from paired seroconversion were 17% (95% Bayesian credible interval (BCI): 14, 20), higher than those from cross-sectional serology (12%, 95% BCI: 9, 17). Adjusted ILI estimates were 15% (95% BCI: 10, 25), and estimates computed from ILI and laboratory data were 12% (95% BCI: 8, 18). Serologic estimates were least sensitive to the risk of input parameter misspecification. ILI-based estimates were more sensitive to parameter misspecification, though this was lessened by incorporation of laboratory data. Obtaining a 5-percentage-point spread for the 95% confidence interval in infection rates would require more than 1,000 participants per serologic study, a sentinel network of 90 GPs, or 50 GPs when combined with laboratory samples. The various types of estimates will provide comparable findings if accurate input parameters can be obtained.

(22) JOSEPH KS, LISTON RM. H1N1 influenza in pregnant women. BMJ. 2011, vol. 342, p.d3237


OBJECTIVES: To follow up a UK national cohort of women admitted to hospital with confirmed 2009/H1N1 influenza in pregnancy in order to obtain a complete picture of pregnancy outcomes and estimate the risks of adverse fetal and infant outcomes. DESIGN: National cohort study. SETTING: 221 hospitals with obstetrician led maternity units in the UK. PARTICIPANTS: 256 women admitted to hospital with confirmed 2009/H1N1 in pregnancy during the second wave of...
pandemic infection between September 2009 and January 2010; 1220 pregnant women for comparison. MAIN OUTCOME MEASURES: Rates of stillbirth, perinatal mortality, and neonatal mortality; odds ratios for infected versus comparison women. RESULTS: Perinatal mortality was higher in infants born to infected women (10 deaths among 256 infants; rate 39 (95% confidence interval 19 to 71) per 1000 total births) than in infants of uninfected women (9 deaths among 1233 infants; rate 7 (3 to 13) per 1000 total births) (P < 0.001). This was principally explained by an increase in the rate of stillbirth (27 per 1000 total births v 6 per 1000 total births; P = 0.001). Infants of infected women were also more likely to be born prematurely than were infants of comparison women (adjusted odds ratio 4.0, 95% confidence interval 2.7 to 5.9). Infected women who delivered preterm were more likely to be infected in their third trimester (P = 0.046), to have been admitted to an intensive care unit (P < 0.001), and to have a secondary pneumonia (P = 0.001) than were those who delivered at term. CONCLUSIONS: This study suggests an increase in the risk of poor outcomes of pregnancy in women infected with 2009/H1N1, which reinforces the message from studies of maternal risk alone. The health of pregnant women is an important public health priority in future waves of this and other influenza pandemics.


BACKGROUND: Privacy concerns by providers have been a barrier to disclosing patient information for public health purposes. This is the case even for mandated notifiable disease reporting. In the context of a pandemic it has been argued that the public good should supersede an individual's right to privacy. The precise nature of these provider privacy concerns, and whether they are diluted in the context of a pandemic are not known. Our objective was to understand the privacy barriers which could potentially influence family physicians' reporting of patient-level surveillance data to public health agencies during the Fall 2009 pandemic H1N1 influenza outbreak. METHODS: Thirty seven family doctors participated in a series of five focus groups between October 29-31 2009. They also completed a survey about the data they were willing to disclose to public health units. Descriptive statistics were used to summarize the amount of patient detail the participants were willing to disclose, factors that would facilitate data disclosure, and the consensus on those factors. The analysis of the qualitative data was based on grounded theory. RESULTS: The family doctors were reluctant to disclose patient data to public health units. This was due to concerns about the extent to which public health agencies are dependable to protect health information (trusting beliefs), and the possibility of loss due to disclosing health information (risk beliefs). We identified six specific actions that public health units can take which would affect these beliefs, and potentially increase the willingness to disclose patient information for public health purposes. CONCLUSIONS: The uncertainty surrounding a pandemic of a new strain of influenza has not changed the privacy concerns of physicians about disclosing patient data. It is important to address these concerns to ensure reliable reporting during future outbreaks.


The role of influenzalike illnesses and influenza vaccination in the development of Guillain-Barre syndrome (GBS), particularly the role of A/H1N1 epidemics and A/H1N1 vaccination, is debated. Data on all incident GBS cases meeting the Brighton Collaboration criteria that were diagnosed at 25 neurology centers in France were prospectively collected between March 2007 and June 2010, covering 3 influenzavirus seasons, including the 2009-2010 A/H1N1 outbreak. A total of 457 general practitioners provided a registry of patients from which 1,080 controls were matched by age, gender, index date (calendar month), and region to 145 cases. Causal relations were assessed by multivariate case-control analysis with adjustment for risk factors (personal and family history of autoimmune disorders, among others), while matching on age, gender, and calendar time. Influenza (seasonal or A/H1N1) or influenzalike symptoms in the 2 months
preceding the index date was associated with GBS, with a matched odds ratio of 2.3 (95% confidence interval (CI): 0.7, 8.2). The difference in the rates of GBS occurring between influenza virus circulation periods and noncirculation periods was highly statistically significant (P = 0.004). Adjusted odds ratios for GBS occurrence within 6 weeks after seasonal and A/H1N1 vaccination were 1.3 (95% CI: 0.4, 4.1) and 0.9 (95% CI: 0.1, 7.6), respectively. Study results confirm that influenza virus is a likely risk factor for GBS. Conversely, no new concerns have arisen regarding influenza vaccination.


BACKGROUND: During the 2009 H1N1 influenza epidemic, policy makers debated over whether, when, and how long to close schools. While closing schools could have reduced influenza transmission thereby preventing cases, deaths, and health care costs, it may also have incurred substantial costs from increased childcare needs and lost productivity by teachers and other school employees. METHODS: A combination of agent-based and Monte Carlo economic simulation modeling was used to determine the cost-benefit of closing schools (vs. not closing schools) for different durations (range: 1 to 8 weeks) and symptomatic case incidence triggers (range: 1 to 30) for the state of Pennsylvania during the 2009 H1N1 epidemic. Different scenarios varied the basic reproductive rate (R(0)) from 1.2, 1.6, to 2.0 and used case-hospitalization and case-fatality rates from the 2009 epidemic. Additional analyses determined the cost per influenza case averted of implementing school closure. RESULTS: For all scenarios explored, closing schools resulted in substantially higher net costs than not closing schools. For R(0) = 1.2, 1.6, and 2.0 epidemics, closing schools for 8 weeks would have resulted in median net costs of $21.0 billion (95% Range: $8.0 - $45.3 billion). The median cost per influenza case averted would have been $14,185 ($5,000 - $45,300).


BACKGROUND: Interest in the use of emergency department (ED) data by syndromic surveillance systems to detect influenza outbreaks has been growing. Evaluations of these systems generally focus on events during influenza seasons. The aims of this study were to identify which emergency department disease codes best correlated with confirmed influenza cases and to determine if these same codes would be useful in the non-influenza season. The 2009 influenza pandemic in Victoria, Australia, provided further opportunity to examine the performance of the syndromic surveillance system during this event. METHODS: We undertook a retrospective analysis of data from the Victorian Department of Health's pilot syndromic surveillance programme, 'SynSurv'. SynSurv automatically captures patient information as it is entered by ED staff. This information includes patient demographics, their presenting symptoms and a preliminary diagnosis using ICD-10 coding. To determine which codes were best correlated with influenza notifications, weekly counts for each of the ICD-10 diagnosis codes ever used in the dataset were calculated and compared with the corresponding weekly count of confirmed influenza cases. Correlations between these codes and confirmed influenza cases in the non-influenza season were then undertaken. The data covered the period from July 2001 until August 2009 and included the 2009 influenza pandemic. RESULTS: There was a marked increase in weekly counts of both laboratory-confirmed influenza cases and relevant ICD-10 codes during the influenza pandemic period. The increase in laboratory confirmed cases was more than four times greater than the previous highest number reported, in 2007, even though the influenza-like-illness
activity in the community was considered comparable to 2003 and 2007. We found five ICD-10 codes to be moderately and significantly correlated with influenza cases. None of these codes was correlated with laboratory confirmed influenza notifications outside the influenza season, at least in part because of the small number of influenza cases notified during that period.

CONCLUSIONS: This study suggests that the choice of codes made by ED staff to record a case of influenza-like illness is influenced by their perceptions of how much influenza is circulating at the time. The ability of syndromic surveillance to detect outbreaks early may be impeded because case diagnosis is influenced by what ED staff believes to be occurring in the community.


BACKGROUND: The province of Ontario, Canada initiated mass immunization clinics with adjuvanted pandemic H1N1 influenza vaccine in October 2009. Due to the scale of the campaign, temporal associations with Guillain-Barre syndrome (GBS) and vaccination were expected. The objectives of this analysis were to estimate the number of background GBS cases expected to occur in the projected vaccinated population and to estimate the number of additional GBS cases which would be expected if an association with vaccination existed. The number of influenza-associated GBS cases was also determined. METHODS: Baseline incidence rates of GBS were determined from published Canadian studies and applied to projected vaccine coverage data to estimate the expected number of GBS cases in the vaccinated population. Assuming an association with vaccine existed, the number of additional cases of GBS expected was determined by applying the rates observed during the 1976 Swine Flu and 1992/1994 seasonal influenza campaigns in the United States. The number of influenza-associated GBS cases expected to occur during the vaccination campaign was determined based on risk estimates of GBS after influenza infection and provincial influenza infection rates using a combination of laboratory-confirmed cases and data from a seroprevalence study. RESULTS: The overall provincial vaccine coverage was estimated to be between 32% and 38%. Assuming 38% coverage, between 6 and 13 background cases of GBS were expected within this projected vaccinated cohort (assuming 32% coverage yielded between 5-11 background cases). An additional 6 or 42 cases would be expected if an association between GBS and influenza vaccine was observed (assuming 32% coverage yielded 5 or 35 additional cases); while up to 31 influenza-associated GBS cases could be expected to occur. In comparison, during the same period, only 7 cases of GBS were reported among vaccinated persons. CONCLUSIONS: Our analyses do not suggest an increased number of GBS cases due to the vaccine. Awareness of expected rates of GBS is crucial when assessing adverse events following influenza immunization. Furthermore, since individuals with influenza infection are also at risk of developing GBS, they must be considered in such analyses, particularly if the vaccine campaign and disease are occurring concurrently.


The objective of this study was to link arsenic exposure and influenza A (H1N1) infection-induced respiratory effects to assess the impact of arsenic-contaminated drinking water on exacerbation risk of A (H1N1)-associated lung function. The homogeneous Poisson process was used to approximate the related processes between arsenic exposure and influenza-associated lung function exacerbation risk. We found that (i) estimated arsenic-induced forced expiratory volume in 1 second (FEV(1)) reducing rates ranged from 0.116 to 0.179 mL/mug for age 15-85 years, (ii) estimated arsenic-induced A (H1N1) viral load increasing rate was 0.5 mL/mug, (iii) estimated A (H1N1) virus-induced FEV(1) reducing rate was 0.10 mL/logTCID50, and (iv) the relationship between arsenic exposure and A (H1N1)-associated respiratory symptoms scores (RSS) can be described by a Hill model. Here we showed that maximum RSS at day 2 postInfection for Taiwan, West Bengal (India), and the United States were estimated to be in the severe range of 0.83,
We concluded that the probability of lung function exacerbations risk induced by arsenic and influenza infection was within the mild and moderate ranges of RSS at day 1 and 2 postinfection. We concluded that avoidance of drinking arsenic-containing water could significantly reduce influenza respiratory illness and that need will become increasingly urgent as the novel H1N1 pandemic influenza virus infects people worldwide.


http://dx.doi.org/10.1186/1471-2458-11-30

**BACKGROUND:** Following the emergence of the influenza A(H1N1)2009 virus, the French ministry of health decided to offer free vaccination against pandemic influenza to the entire French population. Groups of people were defined and prioritised for vaccination. **METHODS:** We took a random sample of the population of mainland France and conducted a retrospective cross-sectional telephone survey to estimate vaccination coverage against seasonal and pandemic influenza and to identify determinants of these vaccinations. **RESULTS:** 10,091 people were included in the survey. Overall seasonal influenza vaccination coverage (IVC) remained stable in the population from the 2008-2009 season to the 2009-2010 season reaching 20.6% and 20.8% respectively. Overall pandemic IVC in the French population is estimated to be 11.1% (CI95%: 9.8 - 12.4). The highest pandemic IVC was observed in the 0-4 years age group. For individuals with health conditions associated with higher risk of influenza, pandemic IVC was estimated to be 12.2% (CI95%: 9.8 - 15.1). The main determinants associated with pandemic influenza vaccine uptake were: living in a household with a child < 5 years ORadj: 2.0 (CI95%: 1.3 - 3.1) or with two children < 5 years or more, ORadj: 2.7 (CI95%: 1.4 - 5.1), living in a household where the head of the family is university graduate (>2 years), ORadj: 2.5 (CI95%: 1.5 - 4.1), or has a higher professional and managerial occupation, ORadj: 3.0 (CI95%: 1.5 - 5.5) and being vaccinated against seasonal influenza, ORadj: 7.1 (CI95%: 5.1 - 10.0). Being an individual with higher risk for influenza was not a determinant for pandemic influenza vaccine uptake. These determinants are not the same as those for seasonal influenza vaccination. **CONCLUSIONS:** Overall A(H1N1)2009 influenza vaccine uptake remained low, particularly among individuals with higher risk for influenza and was lower than that observed for seasonal influenza. The reasons behind people's reluctance to be vaccinated need to be investigated further.


http://dx.doi.org/10.1111/j.1539-6924.2010.01546.x

Sources for human hepatitis E virus (HEV) infections of genotype 3 are largely unknown. Pigs are potential animal reservoirs for HEV. Intervention at pig farms may be desired when pigs are confirmed as a source for human infections, requiring knowledge about transmission routes. These routes are currently understudied. The current study aims to quantify the likelihood of pig feces in causing new HEV infections in pigs due to oral ingestion. We estimated the daily infection risk for pigs by modeling the fate of HEV in the fecal-oral (F-O) pathway. Using parameter values deemed most plausible by the authors based on current knowledge the daily risk of infection was 0.85 (95% interval: 0.03-1). The associated expected number of new infections per day was approximately 4 (2.5% limit 0.1, the 97% limit tending to infinity) compared to 0.7 observed in a transmission experiment with pigs, and the likelihood of feces causing the transmission approached 1. In alternative scenarios, F-O transmission of HEV was also very likely to cause new infections. By reducing the total value of all explanatory variables by 2 orders of magnitude, the expected numbers of newly infected pigs approached the observed number. The likelihood of F-O transmission decreased by decreasing parameter values, allowing for at most 94% of infections being caused by additional transmission routes. Nevertheless, in all scenarios F-O transmission was estimated to contribute to HEV transmission. Thus, despite the difficulty in infecting pigs with HEV via oral inoculation, the F-O route is likely to cause HEV transmission among pigs.

BACKGROUND: Following the emergence of the A/H1N1 2009 influenza pandemic, public health interventions were activated to lessen its potential impact. Computer modelling and simulation can be used to determine the potential effectiveness of the social distancing and antiviral drug therapy interventions that were used at the early stages of the pandemic, providing guidance to public health policy makers as to intervention strategies in future pandemics involving a highly pathogenic influenza strain. METHODS: An individual-based model of a real community with a population of approximately 30,000 was used to determine the impact of alternative interventions strategies, including those used in the initial stages of the 2009 pandemic. Different interventions, namely school closure and antiviral strategies, were simulated in isolation and in combination to form different plausible scenarios. We simulated epidemics with reproduction numbers R0 of 1.5, which aligns with estimates in the range 1.4-1.6 determined from the initial outbreak in Mexico.

RESULTS: School closure of 1 week was determined to have minimal effect on reducing overall illness attack rate. Antiviral drug treatment of 50% of symptomatic cases reduced the attack rate by 6.5%, from an unmitigated rate of 32.5% to 26%. Treatment of diagnosed individuals combined with additional household prophylaxis reduced the final attack rate to 19%. Further extension of prophylaxis to close contacts (in schools and workplaces) further reduced the overall attack rate to 13% and reduced the peak daily illness rate from 120 to 22 per 10,000 individuals. We determined the size of antiviral stockpile required; the ratio of the required number of antiviral courses to population was 13% for the treatment-only strategy, 25% for treatment and household prophylaxis and 40% for treatment, household and extended prophylaxis. Additional simulations suggest that coupling school closure with the antiviral strategies further reduces epidemic impact.

CONCLUSIONS: These results suggest that the aggressive use of antiviral drugs together with extended school closure may substantially slow the rate of influenza epidemic development. These strategies are more rigorous than those actually used during the early stages of the relatively mild 2009 pandemic, and are appropriate for future pandemics that have high morbidity and mortality rates.

Maladies d’Alzheimer


This paper draws on empirical findings from interview studies in the USA and Canada to interrogate the idea that expanding practices of genetic testing are likely to transform kin and family relations in fundamental ways. We argue that in connection with common adult onset disorders in which susceptibility genes with low predictive power are implicated it is unlikely that family relationships will be radically altered as a result of learning about either individual or family genotypes. Rather, pre-existing family dynamics and ideas about family susceptibilities for disease may be reinforced. The case of the ApoE gene and its relationship to Alzheimer's disease is used as an illustrative example. We found that "postgenomic" thinking, in which complexity of disease causation is emphasized, is readily apparent in informant narratives.

Maladies cardio-vasculaires

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CONTEXT: The precise relationship between sodium and potassium intake and cardiovascular (CV) risk remains uncertain, especially in patients with CV disease. OBJECTIVE: To determine the association between estimated urinary sodium and potassium excretion (surrogates for intake) and CV events in patients with established CV disease or diabetes mellitus. DESIGN, SETTING, AND PATIENTS: Observational analyses of 2 cohorts (N = 28,880) included in the ONTARGET and TRANSCEND trials (November 2001-March 2008 from initial recruitment to final follow-up). We estimated 24-hour urinary sodium and potassium excretion from a morning fasting urine sample (Kawasaki formula). We used restricted cubic spline plots to describe the association between sodium and potassium excretion and CV events and mortality, and to identify reference categories for sodium and potassium excretion. We used Cox proportional hazards multivariable models to determine the association of urinary sodium and potassium with CV events and mortality. MAIN OUTCOME MEASURES: CV death, myocardial infarction (MI), stroke, and hospitalization for congestive heart failure (CHF). RESULTS: At baseline, the mean (SD) estimated 24-hour excretion for sodium was 4.77 g (1.61); and for potassium was 2.19 g (0.57). After a median follow-up of 56 months, the composite outcome occurred in 4729 (16.4%) participants, including 2057 CV deaths, 1412 with MI, 1282 with stroke, and 1213 with hospitalization for CHF. Compared with the reference group with estimated baseline sodium excretion of 4 to 5.99 g per day (n = 14,156; 6.3% participants with CV death, 4.6% with MI, 4.2% with stroke, and 3.8% admitted to hospital with CHF), higher baseline sodium excretion was associated with an increased risk of CV death (9.7% for 7-8 g/day; hazard ratio [HR], 1.53; 95% CI, 1.26-1.86; and 11.2% for >8 g/day; HR, 1.66; 95% CI, 1.31-2.10), MI (6.8%; HR, 1.48; 95% CI, 1.11-1.98 for >8 g/day), stroke (6.6%; HR, 1.48; 95% CI, 1.09-2.01 for >8 g/day), and
hospitalization for CHF (6.5%; HR, 1.51; 1.12-2.05 for >8 g/day). Lower sodium excretion was associated with an increased risk of CV death (8.6%; HR, 1.19; 95% CI, 1.02-1.39 for 2-2.99 g/day; 10.6%; HR, 1.37; 95% CI, 1.09-1.73 for <2 g/day), and hospitalization for CHF (5.2%; HR, 1.23; 95% CI, 1.01-1.49 for 2-2.99 g/day) on multivariable analysis. Compared with an estimated potassium excretion of less than 1.5 g per day (n = 2194; 6.2% with stroke), higher potassium excretion was associated with a reduced risk of stroke (4.7% [HR, 0.77; 95% CI, 0.63-0.94] for 1.5-1.99 g/day; 4.3% [HR, 0.73; 95% CI, 0.59-0.90] for 2-2.49 g/day; 3.9% [HR, 0.71; 95% CI, 0.56-0.91] for 2.5-3 g/day; and 3.5% [HR, 0.68; 95% CI, 0.49-0.92] for >3 g/day) on multivariable analysis. CONCLUSIONS: The association between estimated sodium excretion and CV events was J-shaped. Compared with baseline sodium excretion of 4 to 5.99 g per day, sodium excretion of greater than 7 g per day was associated with an increased risk of all CV events, and a sodium excretion of less than 3 g per day was associated with increased risk of CV mortality and hospitalization for CHF. Higher estimated potassium excretion was associated with a reduced risk of stroke.

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CONTEXT: Recurrent stroke prevention guidelines suggest that larger reductions in systolic blood pressure (SBP) are positively associated with a greater reduction in the risk of recurrent stroke and define an SBP level of less than 120 mm Hg as normal. However, the association of SBP maintained at such levels with risk of vascular events after a recent ischemic stroke is unclear.

OBJECTIVE: To assess the association of maintaining low-normal vs high-normal SBP levels with risk of recurrent stroke.

DESIGN, SETTING, AND PATIENTS: Post hoc observational analysis of a multicenter trial involving 20,330 patients (<age >/=50 years) with recent non-cardioembolic ischemic stroke; patients were recruited from 695 centers in 35 countries from September 2003 through July 2006 and followed up for 2.5 years (follow-up ended on February 8, 2008). Patients were categorized based on their mean SBP level: very low-normal (<120 mm Hg), low-normal (120-<130 mm Hg), high-normal (130-<140 mm Hg), high (140-<150 mm Hg), and very high (>/>=150 mm Hg).

MAIN OUTCOME MEASURES: The primary outcome was first recurrence of stroke of any type and the secondary outcome was a composite of stroke, myocardial infarction, or death from vascular causes.

RESULTS: The recurrent stroke rates were 8.0% (95% CI, 6.8%-9.2%) for the very low-normal SBP level group, 7.2% (95% CI, 6.4%-8.0%) for the low-normal SBP group, 6.8% (95% CI, 6.1%-7.4%) for the high-normal SBP group, 8.7% (95% CI, 7.9%-9.5%) for the high SBP group, and 14.1% (95% CI, 13.0%-15.2%) for the very high SBP group.

Compared with patients in the high-normal SBP group, the risk of the primary outcome was higher for patients in the very low-normal SBP group (adjusted hazard ratio [AHR], 1.29; 95% CI, 1.07-1.56), in the high SBP group (AHR, 2.08; 95% CI, 1.83-2.37). Compared with patients in the high-normal SBP group, the risk of secondary outcome was higher for patients in the very low-normal SBP group (AHR, 1.31; 95% CI, 1.13-1.52), in the low-normal SBP group (AHR, 1.16; 95% CI, 1.03-1.31), in the high SBP group (AHR, 1.24; 95% CI, 1.11-1.39), and in the very high SBP group (AHR, 1.94; 95% CI, 1.74-2.16).

CONCLUSION: Among patients with recent non-cardioembolic ischemic stroke, SBP levels during follow-up in the very low-normal (<120 mm Hg), high (140-<150 mm Hg), or very high (>/>=150 mm Hg) range were associated with increased risk of recurrent stroke. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00153062

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CONTEXT: Coronary computed tomography angiography (CCTA) is a new noninvasive diagnostic test for coronary artery disease (CAD), but its association with subsequent clinical management has not been established. OBJECTIVE: To compare utilization and spending associated with functional (stress testing) and anatomical (CCTA) noninvasive cardiac testing in a Medicare population. DESIGN, SETTING, AND PATIENTS: Retrospective, observational cohort study using claims data from a 20% random sample of 2005-2008 Medicare fee-for-service beneficiaries 66 years or older with no claims for CAD in the preceding year, who received nonemergent, noninvasive testing for CAD (n = 282,830). MAIN OUTCOME MEASURES: Cardiac catheterization, coronary revascularization, acute myocardial infarction, all-cause mortality, and total and CAD-related Medicare spending over 180 days of follow-up. RESULTS: Compared with stress myocardial perfusion scintigraphy (MPS), CCTA was associated with an increased likelihood of subsequent cardiac catheterization (22.9% vs 12.1%; adjusted odds ratio [AOR], 2.19 [95% CI, 2.08 to 2.32]; P < .001), percutaneous coronary intervention (7.8% vs 3.4%; AOR, 2.49 [2.28 to 2.72]; P < .001), and coronary artery bypass graft surgery (3.7% vs 1.3%; AOR, 3.00 [2.63 to 3.41]; P < .001). CCTA was also associated with higher total health care spending ($4200 [3193 to 5267]; P < .001), which was almost entirely attributable to payments for any claims for CAD ($4007 [$3256 to 4835]; P < .001). Compared with MPS, there was lower associated spending with stress echocardiography (-$4981 [-$4991 to -$4969]; P < .001) and exercise electrocardiography (-$7449 [-$7452 to -$7444]; P < .001). At 180 days, CCTA was associated with a similar likelihood of all-cause mortality (1.05% vs 1.28%; AOR, 1.11 [0.88 to 1.38]; P = .32) and a slightly lower likelihood of hospitalization for acute myocardial infarction (0.19% vs 0.43%; AOR, 1.05 [0.88 to 1.38]; P < .001). CONCLUSION: Medicare beneficiaries who underwent CCTA in a nonacute setting were more likely to undergo subsequent invasive cardiac procedures and have higher CAD-related spending than patients who underwent stress testing.

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CONTEXT: Few studies have examined the association between the number of coronary heart disease risk factors and outcomes of acute myocardial infarction in community practice. OBJECTIVE: To determine the association between the number of coronary heart disease risk factors in patients with first myocardial infarction and hospital mortality. DESIGN: Observational study from the National Registry of Myocardial Infarction, 1994-2006. PATIENTS: We examined the presence and absence of 5 major traditional coronary heart disease risk factors (hypertension, smoking, dyslipidemia, diabetes, and family history of coronary heart disease) and hospital mortality among 542,008 patients with first myocardial infarction and without prior cardiovascular disease. MAIN OUTCOME MEASURE: All-cause in-hospital mortality. RESULTS: A majority (85.6%) of patients who presented with initial myocardial infarction had at least 1 of the 5 coronary heart disease risk factors, and 14.4% had none of the 5 risk factors. Age varied inversely with the number of coronary heart disease risk factors, from a mean age of 71.5 years with 0 risk factors to 56.7 years with 5 risk factors (P for trend <.001). The total number of in-hospital deaths for all causes was 50,788. Unadjusted in-hospital mortality rates were 14.9%, 10.9%, 7.9%, 5.3%, 4.2%, and 3.6% for patients with 0, 1, 2, 3, 4, and 5 risk factors, respectively. After adjusting for age and other clinical factors, there was an inverse association between the number of coronary heart disease risk factors and hospital mortality adjusted odds ratio (1.54; 95% CI, 1.23-1.94) among individuals with 0 vs 5 risk factors. This association was consistent among several age strata and important patient subgroups. CONCLUSION: Among patients with incident acute myocardial infarction without prior cardiovascular disease, in-hospital mortality was inversely related to the number of coronary heart disease risk factors.

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BACKGROUND: Statins reduce adverse cardiovascular outcomes and slow the progression of coronary atherosclerosis in proportion to their ability to reduce low-density lipoprotein (LDL) cholesterol. However, few studies have either assessed the ability of intensive statin treatments to achieve disease regression or compared alternative approaches to maximal statin administration.

METHODS: We performed serial intravascular ultrasonography in 1039 patients with coronary disease, at baseline and after 104 weeks of treatment with either atorvastatin, 80 mg daily, or rosuvastatin, 40 mg daily, to compare the effect of these two intensive statin regimens on the progression of coronary atherosclerosis, as well as to assess their safety and side-effect profiles.

RESULTS: After 104 weeks of therapy, the rosuvastatin group had lower levels of LDL cholesterol than the atorvastatin group (62.6 vs. 70.2 mg per deciliter [1.62 vs. 1.82 mmol per liter], P<0.001), and higher levels of high-density lipoprotein (HDL) cholesterol (50.4 vs. 48.6 mg per deciliter [1.30 vs. 1.26 mmol per liter], P=0.01). The primary efficacy end point, percent atheroma volume (PAV), decreased by 0.99% (95% confidence interval [CI], -1.19 to -0.63) with atorvastatin and by 1.22% (95% CI, -1.52 to -0.90) with rosuvastatin (P=0.17). The effect on the secondary efficacy end point, normalized total atheroma volume (TAV), was more favorable with rosuvastatin than with atorvastatin: -6.39 mm(3) (95% CI, -7.52 to -5.12), as compared with -4.42 mm(3) (95% CI, -5.98 to -3.26) (P=0.01). Both agents induced regression in the majority of patients: 63.2% with atorvastatin and 68.5% with rosuvastatin for PAV (P=0.07) and 64.7% and 71.3%, respectively, for TAV (P=0.02). Both agents had acceptable side-effect profiles, with a low incidence of laboratory abnormalities and cardiovascular events.

CONCLUSIONS: Maximal doses of rosuvastatin and atorvastatin resulted in significant regression of coronary atherosclerosis. Despite the lower level of LDL cholesterol and the higher level of HDL cholesterol achieved with rosuvastatin, a similar degree of regression of PAV was observed in the two treatment groups.

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CONTEXT: New-onset atrial fibrillation (AF) has been reported in 6% to 20% of patients with severe sepsis. Chronic AF is a known risk factor for stroke and death, but the clinical significance of new-onset AF in the setting of severe sepsis is uncertain. OBJECTIVE: To determine the in-hospital stroke and in-hospital mortality risks associated with new-onset AF in patients with severe sepsis. DESIGN AND SETTING: Retrospective population-based cohort of California State Inpatient Database administrative claims data from nonfederal acute care hospitals for January 1 through December 31, 2007. PATIENTS: Data were available for 3,144,787 hospitalized adults. Severe sepsis (n = 49,082 [1.56%]) was defined by validated International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 995.92. New-onset AF was defined as AF that occurred during the hospital stay, after excluding AF cases present at admission. MAIN OUTCOME MEASURES: A priori outcome measures were in-hospital ischemic stroke (ICD-9-CM codes 433, 434, or 436) and mortality. RESULTS: Patients with severe sepsis were a mean age of 69 (SD, 16) years and 48% were women. New-onset AF occurred in 5.9% of
patients with severe sepsis vs 0.65% of patients without severe sepsis (multivariable-adjusted odds ratio [OR], 6.82; 95% CI, 6.54-7.11; P < .001). Severe sepsis was present in 14% of all new-onset AF in hospitalized adults. Compared with severe sepsis patients without new-onset AF, patients with new-onset AF during severe sepsis had greater risks of in-hospital stroke (75/2896 [2.6%] vs 306/46,186 [0.6%] strokes; adjusted OR, 2.70; 95% CI, 2.05-3.57; P < .001) and in-hospital mortality (1629 [56%] vs 18,027 [39%] deaths; adjusted relative risk, 1.07; 95% CI, 1.04-1.11; P < .001). Findings were robust across 2 definitions of severe sepsis, multiple methods of addressing confounding, and multiple sensitivity analyses. CONCLUSION: Among patients with severe sepsis, patients with new-onset AF were at increased risk of in-hospital stroke and death compared with patients with no AF and patients with preexisting AF.

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BACKGROUND: The effectiveness of durable polymer drug-eluting stents comes at the expense of delayed arterial healing and subsequent late adverse events such as stent thrombosis (ST). We report the 4 year follow-up of an assessment of biodegradable polymer-based drug-eluting stents, which aim to improve safety by avoiding the persistent inflammatory stimulus of durable polymers. METHODS: We did a multicentre, assessor-masked, non-inferiority trial. Between Nov 27, 2006, and May 18, 2007, patients aged 18 years or older with coronary artery disease were randomly allocated with a computer-generated sequence to receive either biodegradable polymer biolimus-eluting stents (BES) or durable polymer sirolimus-eluting stents (SES; 1:1 ratio). The primary endpoint was a composite of cardiac death, myocardial infarction, or clinically-induced target vessel revascularisation (TVR); patients were followed-up for 4 years. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00389220. FINDINGS: 1707 patients with 2472 lesions were randomly allocated to receive either biodegradable polymer BES (857 patients, 1257 lesions) or durable polymer SES (850 patients, 1215 lesions). At 4 years, biodegradable polymer BES were non-inferior to durable polymer SES for the primary endpoint: 160 (18.7%) patients versus 192 (22.6%) patients (rate ratios [RR] 0.81, 95% CI 0.66-1.00, p for non-inferiority <0.0001, p for superiority=0.050). The RR of definite ST was 0.62 (0.35-1.08, p=0.09), which was largely attributable to a lower risk of very late definite ST between years 1 and 4 in the BES group than in the SES group (RR 0.20, 95% CI 0.06-0.67, p=0.004). Conversely, the RR of definite ST during the first year was 0.99 (0.51-1.95; p=0.98) and the test for interaction between RR of definite ST and time was positive (p(interaction)=0.017). We recorded an interaction with time for events associated with ST but not for other events. For primary endpoint events associated with ST, the RR was 0.86 (0.41-1.80) during the first year and 0.17 (0.04-0.78) during subsequent years (p(interaction)=0.049). INTERPRETATION: Biodegradable polymer BES are non-inferior to durable polymer SES and, by reducing the risk of cardiac events associated with very late ST, might improve long-term clinical outcomes for up to 4 years compared with durable polymer SES. FUNDING: Biosensors Europe SA, Switzerland

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CONTEXT: Outcomes following treatment of brain arteriovenous malformations (AVMs) with microsurgery, embolization, stereotactic radiosurgery (SRS), or combinations vary greatly between studies. OBJECTIVES: To assess rates of case fatality, long-term risk of hemorrhage, complications, and successful obliteration of brain AVMs after interventional treatment and to assess determinants of these outcomes. DATA SOURCES: We searched PubMed and EMBASE to March 1, 2011, and hand-searched 6 journals from January 2000 until March 2011. STUDY SELECTION AND DATA EXTRACTION: We identified studies fulfilling predefined inclusion criteria. We used Poisson regression analyses to explore associations of patient and study characteristics with case fatality, complications, long-term risk of hemorrhage, and successful brain AVM obliteration. DATA SYNTHESIS: We identified 137 observational studies including 142 cohorts, totaling 13,698 patients and 46,314 patient-years of follow-up. Case fatality was 0.68 (95% CI, 0.61-0.76) per 100 person-years overall, 1.1 (95% CI, 0.87-1.3; n = 2549) after microsurgery, 0.50 (95% CI, 0.43-0.58; n = 9436) after SRS, and 0.96 (95% CI, 0.67-1.4; n = 1019) after embolization. Intracranial hemorrhage rates were 1.4 (95% CI, 1.3-1.5) per 100 person-years overall, 0.18 (95% CI, 0.10-0.30) after microsurgery, 1.7 (95% CI, 1.5-1.8) after SRS, and 1.7 (95% CI, 1.3-2.3) after embolization. More recent studies were associated with lower case-fatality rates (rate ratio [RR], 0.972; 95% CI, 0.955-0.989) but increased rates of hemorrhage (RR, 1.02; 95% CI, 1.00-1.03). Male sex (RR, 0.964; 95% CI, 0.945-0.984), small brain AVMs (RR, 0.988; 95% CI, 0.981-0.995), and those with strictly deep venous drainage (RR, 0.975; 95% CI, 0.960-0.990) were associated with lower case fatality. Lower hemorrhage rates were associated with male sex (RR, 0.976, 95% CI, 0.964-0.988), small brain AVMs (RR, 0.988, 95% CI, 0.980-0.996), and brain AVMs with deep venous drainage (0.982, 95% CI, 0.969-0.996). Complications leading to permanent neurological deficits or death occurred in a median 7.4% (range, 0%-40%) of patients after microsurgery, 5.1% (range, 0%-21%) after SRS, and 6.6% (range, 0%-28%) after embolization. Successful brain AVM obliteration was achieved in 96% (range, 0%-100%) of patients after microsurgery, 38% (range, 0%-75%) after SRS, and 13% (range, 0%-94%) after embolization. CONCLUSIONS: Although case fatality after treatment has decreased over time, treatment of brain AVM remains associated with considerable risks and incomplete efficacy. Randomized controlled trials comparing different treatment modalities appear justified.


CONTEXT: The degree to which financial factors may influence use of cardiac stress imaging procedures is unknown. OBJECTIVE: To examine the association of physician billing and nuclear stress and stress echocardiography testing following coronary revascularization. DESIGN, SETTING, AND PATIENTS: Using data from a national health insurance carrier. 17,847 patients were identified between November 1, 2004, and June 30, 2007, who had coronary revascularization and an index cardiac outpatient visit more than 90 days following the procedure. Based on overall billings, physicians were classified as billing for both technical (practice/equipment) and professional (supervision/interpretation) fees, professional fees only, or not billing for either. Logistic regression models were used to evaluate the association between physician billing and use of stress testing, after adjusting for patient and other physician factors. MAIN OUTCOME MEASURES: Incidence of nuclear and echocardiographic stress tests within 30 days of an index cardiac-related outpatient visit. RESULTS: The overall cumulative incidence of
nuclear or echocardiography stress testing within 30 days of the index cardiac-related outpatient visit following revascularization was 12.2% (95% CI, 11.8%-12.7%). The cumulative incidence of nuclear stress testing was 12.6% (95% CI, 12.0%-13.2%), 8.8% (95% CI, 7.5%-10.2%), and 5.0% (95% CI, 4.4%-5.7%) among physicians who billed for technical and professional fees, professional fees only, or neither, respectively. For stress echocardiography, the cumulative incidence of testing was 2.8% (95% CI, 2.5%-3.2%), 1.4% (95% CI, 1.0%-1.9%), and 0.4% (95% CI, 0.3%-0.6%) among physicians who billed for the technical and professional fees, professional fees only, or neither, respectively. Adjusted odds ratios (ORs) of nuclear stress testing among patients treated by physicians who billed for technical and professional fees and professional fees only were 2.3 (95% CI, 1.8-2.9) and 1.6 (95% CI, 1.2-2.1), respectively, compared with those patients treated by physicians who did not bill for testing (P < .001). The adjusted OR of stress echocardiography testing among patients treated by physicians billing for both or professional fees only were 12.8 (95% CI, 7.6-21.6) and 7.1 (95% CI, 4.0-12.9), respectively, compared with patients treated by physicians who did not bill for testing (P < .001). CONCLUSION: Nuclear stress testing and stress echocardiography testing following revascularization were more frequent among patients treated by physicians who billed for technical fees, professional fees, or both compared with those treated by physicians who did not bill for these services.


CONTEXT: Patients with symptomatic atherosclerotic internal carotid artery occlusion (AICAO) and hemodynamic cerebral ischemia are at high risk for subsequent stroke when treated medically. OBJECTIVE: To test the hypothesis that extracranial-intracranial (EC-IC) bypass surgery, added to best medical therapy, reduces subsequent ipsilateral ischemic stroke in patients with recently symptomatic AICAO and hemodynamic cerebral ischemia. DESIGN: Parallel-group, randomized, open-label, blinded-adjudication clinical treatment trial conducted from 2002 to 2010. SETTING: Forty-nine clinical centers and 18 positron emission tomography (PET) centers in the United States and Canada. The majority were academic medical centers. PARTICIPANTS: Patients with arteriographically confirmed AICAO causing hemispheric symptoms within 120 days and hemodynamic cerebral ischemia identified by ipsilateral increased oxygen extraction fraction measured by PET. Of 195 patients who were randomized, 97 were randomized to receive surgery and 98 to no surgery. Follow-up for the primary end point until occurrence, 2 years, or termination of trial was 99% complete. No participant withdrew because of adverse events. INTERVENTIONS: Anastomosis of superficial temporal artery branch to a middle cerebral artery cortical branch for the surgical group. Antithrombotic therapy and risk factor intervention were recommended for all participants. MAIN OUTCOME MEASURE: For all participants who were assigned to surgery and received surgery, the combination of (1) all stroke and death from surgery through 30 days after surgery and (2) ipsilateral ischemic stroke within 2 years of randomization. For the nonsurgical group and participants assigned to surgery who did not receive surgery, the combination of (1) all stroke and death from randomization to randomization plus 30 days and (2) ipsilateral ischemic stroke within 2 years of randomization. RESULTS: The trial was terminated early for futility. Two-year rates for the primary end point were 21.0% (95% CI, 12.8% to 29.2%; 20 events) for the surgical group and 22.7% (95% CI, 13.9% to 31.6%; 20 events) for the nonsurgical group (P = .78, Z test), a difference of 1.7% (95% CI, 10.4% to 13.8%). Thirty-day rates for ipsilateral ischemic stroke were 14.4% (14/97) in the surgical group and 2.0% (2/98) in the nonsurgical group, a difference of 12.4% (95% CI, 4.9% to 19.9%). CONCLUSION: Among participants with recently symptomatic AICAO and hemodynamic cerebral ischemia, EC-IC bypass surgery plus medical therapy compared with medical therapy alone did not reduce the risk of recurrent ipsilateral ischemic stroke at 2 years. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00029146


CONTEXT: Despite dual antiplatelet therapy, stent thrombosis remains a devastating and unpredictable complication of percutaneous coronary intervention (PCI). OBJECTIVE: To perform a sequential analysis of clinical and genetic factors associated with definite early stent thrombosis. DESIGN, SETTING, AND PARTICIPANTS: Case-control study conducted in 10 centers in France between January 2007 and May 2010 among 123 patients undergoing PCI who had definite early stent thrombosis and DNA samples available, matched on age and sex with 246 stent thrombosis-free controls. MAIN OUTCOME MEASURE: Accuracy of early stent thrombosis prediction by 23 genetic variants. RESULTS: Among the 23 genetic variants investigated in 15 different genes, the significant determinants of early stent thrombosis were CYP2C19 metabolic status (adjusted odds ratio [OR], 1.99; 95% CI, 1.47-2.69), ABCB1 3435 TT genotype (adjusted OR, 2.16; 95% CI, 1.21-3.88), and ITGB3 PL/A2 carriage (adjusted OR, 0.52; 95% CI, 0.28-0.95). Nongenetic independent correlates were acuteness of PCI (adjusted OR, 3.05; 95% CI, 1.54-6.07), complex lesions (American College of Cardiology/American Heart Association type C) (adjusted OR, 2.33; 95% CI, 1.40-3.89), left ventricular function less than 40% (adjusted OR, 2.25; 95% CI, 1.09-4.70), diabetes mellitus (adjusted OR, 1.82; 95% CI, 1.02-3.24), use of proton pump inhibitors (adjusted OR, 2.19; 95% CI, 1.29-3.75), and higher clopidogrel loading doses (adjusted OR, 0.73; 95% CI, 0.57-0.93). The discriminative accuracy of the clinical-only model was similar to that of a genetic-only model (area under the curve, 0.73 [95% CI, 0.67-0.78] vs 0.68 [95% CI, 0.62-0.74], respectively; P = .34). A combined clinical and genetic model led to a statistically significant increase in the discriminatory power of the model compared with the clinical-only model (area under the curve, 0.78 [95% CI, 0.73-0.83] vs 0.73 [95% CI, 0.67-0.78]; P = .004). CONCLUSIONS: This case-control study identified 3 genes (CYP2C19, ABCB1, and ITGB3) and 2 clopidogrel-related factors (loading dose and proton pump inhibitors) that were independently associated with early stent thrombosis. Future studies are needed to validate the prognostic accuracy of these risk factors in prospective cohorts


BACKGROUND: We assessed patient outcomes 90 days after hospital admission for stroke following a multidisciplinary intervention targeting evidence-based management of fever, hyperglycaemia, and swallowing dysfunction in acute stroke units (ASUs). METHODS: In the Quality in Acute Stroke Care (QASC) study, a single-blind cluster randomised controlled trial, we randomised ASUs (clusters) in New South Wales, Australia, with immediate access to CT and on-site high dependency units, to intervention or control group. Patients were eligible if they spoke English, were aged 18 years or older, had had an ischaemic stroke or intracerebral haemorrhage, and presented within 48 h of onset of symptoms. Intervention ASUs received treatment protocols to manage fever, hyperglycaemia, and swallowing dysfunction with multidisciplinary team building workshops to address implementation barriers. Control ASUs received only an abridged version of existing guidelines. We recruited pre-intervention and post-intervention patient cohorts to compare
90-day death or dependency (modified Rankin scale [mRS] >/=2), functional dependency (Barthel index), and SF-36 physical and mental component summary scores. Research assistants, the statistician, and patients were masked to trial groups. All analyses were done by intention to treat. This trial is registered at the Australia New Zealand Clinical Trial Registry (ANZCTR), number ACTRN12608000563369. FINDINGS: 19 ASUs were randomly assigned to intervention (n=10) or control (n=9). Of 6564 assessed for eligibility, 1696 patients' data were obtained (687 pre-intervention; 1009 post-intervention). Results showed that, irrespective of stroke severity, intervention ASU patients were significantly less likely to be dead or dependent (mRS >/=2) at 90 days than control ASU patients (236 [42%] of 558 patients in the intervention group vs 259 [58%] of 449 in the control group, p=0.002; number needed to treat 6.4; adjusted absolute difference 15.7% [95% CI 5.8-25.4]). They also had a better SF-36 mean physical component summary score (45.6 [SD 10.2] in the intervention group vs 42.5 [10.5] in the control group, p=0.002; adjusted absolute difference 3.4 [95% CI 1.2-5.5]) but no improvement was recorded in mortality (21 [4%] of 558 in intervention group and 24 [5%] of 451 in the control group, p=0.36), SF-36 mean mental component summary score (49.5 [10.9] in the intervention group vs 49.4 [10.6] in the control group, p=0.69) or functional dependency (Barthel Index >/=60: 487 [92%] of 532 patients vs 380 [90%] of 423 patients; p=0.44). INTERPRETATION: Implementation of multidisciplinary supported evidence-based protocols initiated by nurses for the management of fever, hyperglycaemia, and swallowing dysfunction delivers better patient outcomes after discharge from stroke units. Our findings show the possibility to augment stroke unit care.

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Mendelian randomization studies typically have low power. Where there are several valid candidate genetic instruments, precision can be gained by using all the instruments available. However, sporadically missing genetic data can offset this gain. The authors describe 4 Bayesian methods for imputing the missing data based on a missing-at-random assumption: multiple imputations, single nucleotide polymorphism (SNP) imputation, latent variables, and haplotype imputation. These methods are demonstrated in a simulation study and then applied to estimate the causal relation between C-reactive protein and each of fibrinogen and coronary heart disease, based on 3 SNPs in British Women's Heart and Health Study participants assessed at baseline between May 1999 and June 2000. A complete-case analysis based on all 3 SNPs was found to be more precise than analyses using any 1 SNP alone. Precision is further improved by using any of the 4 proposed missing data methods; the improvement is equivalent to about a 25% increase in sample size. All methods gave similar results, which were apparently not overly sensitive to violation of the missing-at-random assumption. Programming code for the analyses presented is available online


CONTEXT: Although the efficacy of carotid stenting has been established in clinical trials, outcomes of the procedure based on operator experience are less certain in clinical practice. OBJECTIVE: To assess association between outcomes and 2 measures of operator experience: annual volume and experience at the time of the procedure among new operators who first performed carotid stenting after a national coverage decision by the Centers for Medicare & Medicaid Services (CMS). DESIGN, SETTING, AND PATIENTS: Observational study using administrative data on fee-for-service Medicare beneficiaries aged 65 years or older undergoing carotid stenting between 2005 and 2007. MAIN OUTCOME MEASURE: Thirty-day mortality stratified by very low, low, medium, and high annual operator volumes (<6, 6-11, 12-23, and >/=24 procedures per year, respectively) and treatment early vs late during a new operator's experience (1st to 11th procedure and 12th procedure or higher). RESULTS: During the study period, 24,701 procedures were performed by 2339 operators. Of these, 11,846 were performed by 1792 new operators who first performed carotid stenting after the CMS national coverage decision. Overall, 30-day mortality was 1.9% (n = 461) and rate of failure to use an embolic protection device was 4.8% (n = 1173). The median annual operator volume among Medicare beneficiaries was 3.0 per year (interquartile range, 1.4-6.5) and 11.6% of operators performed 12 or more procedures per year during the study period. Observed 30-day mortality was higher among patients treated by operators with lower annual volumes (2.5% [95% CI, 2.1%-2.9%], 1.9% [95% CI, 1.6%-2.3%], 1.6% [95% CI, 1.3%-1.9%], and 1.4% [95% CI, 1.1%-1.7%] across the 4 categories; P < .001) and among patients treated early (2.3% [95% CI, 2.0%-2.7%] vs late (1.4%; 95% CI, 1.1%-1.9%; P < .001) during a new operator's experience. Conclusions: Among older patients undergoing carotid stenting, lower annual operator volume and early experience are associated with increased 30-day mortality.
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CONTEXT: Several studies have suggested that depression is associated with an increased risk of stroke; however, the results are inconsistent. OBJECTIVE: To conduct a systematic review and meta-analysis of prospective studies assessing the association between depression and risk of developing stroke in adults. DATA SOURCES: A search of MEDLINE, EMBASE, and PsycINFO databases (to May 2011) was supplemented by manual searches of bibliographies of key retrieved articles and relevant reviews. STUDY SELECTION: We included prospective cohort studies that reported risk estimates of stroke morbidity or mortality by baseline or updated depression status assessed by self-reported scales or clinician diagnosis. DATA EXTRACTION: Two independent reviewers extracted data on depression status at baseline, risk estimates of stroke, study quality, and methods used to assess depression and stroke. Hazard ratios (HRs) were pooled using fixed-effect or random-effects models when appropriate. Associations were tested in subgroups representing different participant and study characteristics. Publication bias was evaluated with funnel plots and Begg test. RESULTS: The search yielded 28 prospective cohort studies (comprising 317,540 participants) that reported 8478 stroke cases (morbidity and mortality) during a follow-up period ranging from 2 to 29 years. The pooled adjusted HRs were 1.45 (95% CI, 1.29-1.63; P for heterogeneity <.001; random-effects model) for total stroke, 1.55 (95% CI, 1.25-1.93; P for heterogeneity = .31; fixed-effects model) for fatal stroke (8 studies), and 1.25 (95% CI, 1.11-1.40; P for heterogeneity = .34; fixed-effects model) for ischemic stroke (6 studies). The estimated absolute risk differences associated with depression were 106 cases for total stroke, 53 cases for ischemic stroke, and 22 cases for fatal stroke per 100,000 individuals per year. The increased risk of total stroke associated with depression was consistent across most subgroups. CONCLUSION: Depression is associated with a significantly increased risk of stroke morbidity and mortality

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CONTEXT: High residual platelet reactivity (HRPR) in patients receiving clopidogrel has been associated with high risk of ischemic events after percutaneous coronary intervention (PCI). OBJECTIVE: To test the hypothesis that HRPR after clopidogrel loading is an independent prognostic marker of risk of long-term thrombotic events in patients with acute coronary syndromes (ACS) undergoing an invasive procedure and antithrombotic treatment adjusted according to the results of platelet function tests. DESIGN, SETTING, AND PATIENTS: Prospective, observational, referral center cohort study of 1789 consecutive patients with ACS undergoing PCI from April 2005 to April 2009 at the Division of Cardiology of Careggi Hospital, Florence, Italy, in whom platelet reactivity was prospectively assessed by light transmittance aggregometry. INTERVENTIONS: All patients received 325 mg of aspirin and a loading dose of 600 mg of clopidogrel followed by a maintenance dosage of 325 mg/d of aspirin and 75 mg/d of clopidogrel for at least 6 months. Patients with HRPR as assessed by adenosine diphosphate test (>70% platelet aggregation) received an increased dose of clopidogrel (150-300 mg/d) or switched to ticlopidine (500-1000 mg/d) under adenosine diphosphate test guidance. MAIN
OUTCOME MEASURES: The primary end point was a composite of cardiac death, myocardial infarction, any urgent coronary revascularization, and stroke at 2-year follow-up. Secondary end points were stent thrombosis and each component of the primary end point. RESULTS: The primary end point event rate was 14.6% (36/247) in patients with HRPR and 8.7% (132/1525) in patients with low residual platelet reactivity (absolute risk increase, 5.9%; 95% CI, 1.6%-11.1%; P = .003). Stent thrombosis was higher in the HRPR group compared with the low residual platelet reactivity group (6.1% [15/247] vs 2.9% [44/1525]; absolute risk increase, 3.2%; 95% CI, 0.4%-6.7%; P = .01). By multivariable analysis, HRPR was independently associated with the primary end point (hazard ratio, 1.49; 95% CI, 1.08-2.05; P = .02) and with cardiac mortality (hazard ratio, 1.81; 95% CI, 1.18-2.76; P = .006). CONCLUSION: Among patients receiving platelet reactivity-guided antithrombotic medication after PCI, HRPR status was significantly associated with increased risk of ischemic events at short- and long-term follow-up. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT01231035


Systemic immunosuppression has been associated with stroke for many years, but the underlying mechanisms are poorly understood. In this study, we demonstrated that stroke induced profound behavioral changes in hepatic invariant NKT (iNKT) cells in mice. Unexpectedly, these effects were mediated by a noradrenergic neurotransmitter rather than a CD1d ligand or other well-characterized danger signals. Blockade of this innervation was protective in wild-type mice after stroke but had no effect in mice deficient in iNKT cells. Selective immunomodulation of iNKT cells with a specific activator (alpha-galactosylceramide) promoted proinflammatory cytokine production and prevented infections after stroke. Our results therefore identify a molecular mechanism that leads to immunosuppression after stroke and suggest an attractive potential therapeutic alternative to antibiotics, namely, immunomodulation of iNKT cells to prevent stroke-associated infections


Coffee consumption has been inconsistently associated with risk of stroke. The authors conducted a meta-analysis of prospective studies to quantitatively assess the association between coffee consumption and stroke risk. Pertinent studies were identified by searching PubMed and Embase from January 1966 through May 2011 and by reviewing the reference lists of retrieved articles. Prospective studies in which investigators reported relative risks of stroke for 3 or more categories of coffee consumption were eligible. Results from individual studies were pooled using a random-effects model. Eleven prospective studies, with 10,003 cases of stroke and 479,689 participants, met the inclusion criteria. There was some evidence of a nonlinear association between coffee consumption and risk of stroke (P for nonlinearity = 0.005). Compared with no coffee consumption, the relative risks of stroke were 0.86 (95% confidence interval (95% CI): 0.78, 0.94) for 2 cups of coffee per day, 0.83 (95% CI: 0.74, 0.92) for 3-4 cups/day, 0.87 (95% CI: 0.77, 0.97) for 6 cups/day, and 0.93 (95% CI: 0.79, 1.08) for 8 cups/day. There was marginal between-study heterogeneity among study-specific trends (I = 12% and I = 20% for the first and second spline transformations, respectively). Findings from this meta-analysis indicate that moderate coffee consumption may be weakly inversely associated with risk of stroke

(43) CHRISTOFFERSEN M, FRIKKE-SCHMIDT R, SCHNOHR P, JENSEN GB, et al. Xanthelasmata, arcus corneae, and ischaemic vascular disease and death in general

OBJECTIVE: To test the hypothesis that xanthelasmata and arcus corneae, individually and combined, predict risk of ischaemic vascular disease and death in the general population.

DESIGN: Prospective population based cohort study. SETTING: The Copenhagen City Heart Study. PARTICIPANTS: 12,745 people aged 20-93 years free of ischaemic vascular disease at baseline and followed from 1976-8 until May 2009 with 100% complete follow-up. MAIN OUTCOME MEASURES: Hazard ratios for myocardial infarction, ischaemic heart disease, ischaemic stroke, ischaemic cerebrovascular disease, and death; odds ratios for severe atherosclerosis. RESULTS: 563 (4.4%) of participants had xanthelasmata and 3159 (24.8%) had arcus corneae at baseline. During 33 years' follow-up (mean 22 years), 1872 developed myocardial infarction, 3699 developed ischaemic heart disease, 1498 developed ischaemic stroke, 1815 developed ischaemic cerebrovascular disease, and 8507 died. Multifactorially adjusted hazard/odds ratios for people with versus those without xanthelasmata were 1.48 (95% confidence interval 1.23 to 1.79) for myocardial infarction, 1.39 (1.20 to 1.60) for ischaemic heart disease, 0.94 (0.73 to 1.21) for ischaemic stroke, 0.91 (0.72 to 1.15) for ischaemic cerebrovascular disease, 1.69 (1.03 to 2.79) for severe atherosclerosis, and 1.14 (1.04 to 1.26) for death. The corresponding hazard/odds ratios for people with versus those without arcus corneae were non-significant. In people with versus those without both xanthelasmata and arcus corneae, hazard/odds ratios were 1.47 (1.09 to 1.99) for myocardial infarction, 1.56 (1.25 to 1.94) for ischaemic heart disease, 0.87 (0.57 to 1.31) for ischaemic stroke, 0.86 (0.58 to 1.26) for ischaemic cerebrovascular disease, 2.75 (0.75 to 10.1) for severe atherosclerosis, and 1.09 (0.93 to 1.28) for death. In all age groups in both women and men, absolute 10 year risk of myocardial infarction, ischaemic heart disease, and death increased in the presence of xanthelasmata. The highest absolute 10 year risks of ischaemic heart disease of 53% and 41% were found in men aged 70-79 years with and without xanthelasmata. Corresponding values in women were 35% and 27%. CONCLUSION: Xanthelasmata predict risk of myocardial infarction, ischaemic heart disease, severe atherosclerosis, and death in the general population, independently of well known cardiovascular risk factors, including plasma cholesterol and triglyceride concentrations. In contrast, arcus corneae is not an important independent predictor of risk.


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Plasma protein S (PS) levels are reportedly low in patients with venous thrombosis but high in coronary heart disease (CHD) patients. The authors examined the association between free PS concentration and CHD or stroke risk and assessed risk in combination with C-reactive protein (CRP) levels. Free PS concentration was determined in 6 annual visits among 3,052 middle-aged (49-64 years) United Kingdom men from the Second Northwick Park Heart Study, with 297 CHD events from 1989 to 2005. The highest (vs. first) quintile was associated with a significantly increased CHD risk after adjustment for all other risk factors and correction for regression dilution bias (hazard ratio = 1.85, 95% confidence interval: 1.08, 3.16; P = 0.024). Models that included all well-known risk factors plus PS quintiles improved prediction of CHD (net reclassification improvement (NRI) = 7.0% (P = 0.007), category-less NRI (>0) = 22.1% (P < 0.001)), and the likelihood ratio statistic increased significantly (P = 0.018). The increase in CHD risk was
particularly strong when subjects also had high CRP levels. There was no association between free PS level and stroke risk. This study confirms the independent association of elevated free PS levels with future risk of CHD, although elevated PS levels added only modestly to prediction metrics. The novel finding of increased CHD risk, particularly when CRP and PS levels are high, requires further study.

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BACKGROUND: Atherosclerotic intracranial arterial stenosis is an important cause of stroke that is increasingly being treated with percutaneous transluminal angioplasty and stenting (PTAS) to prevent recurrent stroke. However, PTAS has not been compared with medical management in a randomized trial. METHODS: We randomly assigned patients who had a recent transient ischemic attack or stroke attributed to stenosis of 70 to 99% of the diameter of a major intracranial artery to aggressive medical management alone or aggressive medical management plus PTAS with the use of the Wingspan stent system. The primary end point was stroke or death within 30 days after enrollment or after a revascularization procedure for the qualifying lesion during the follow-up period or stroke in the territory of the qualifying artery beyond 30 days. RESULTS: Enrollment was stopped after 451 patients underwent randomization, because the 30-day rate of stroke or death was 14.7% in the PTAS group (nonfatal stroke, 12.5%; fatal stroke, 2.2%) and 5.8% in the medical-management group (nonfatal stroke, 5.3%; non-stroke-related death, 0.4%) (P=0.002). Beyond 30 days, stroke in the same territory occurred in 13 patients in each group. Currently, the mean duration of follow-up, which is ongoing, is 11.9 months. The probability of the occurrence of a primary end-point event over time differed significantly between the two treatment groups (P=0.009), with 1-year rates of the primary end point of 20.0% in the PTAS group and 12.2% in the medical-management group. CONCLUSIONS: In patients with intracranial arterial stenosis, aggressive medical management was superior to PTAS with the use of the Wingspan stent system, both because the risk of early stroke after PTAS was high and because the risk of stroke with aggressive medical therapy alone was lower than expected. ( Funded by the National Institute of Neurological Disorders and Stroke and others; SAMMPRIS ClinicalTrials.gov number, NCT00576693.)

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Genome-wide association studies (GWAS) have identified many risk loci for complex diseases, but effect sizes are typically small and information on the underlying biological processes is often lacking. Associations with metabolic traits as functional intermediates can overcome these problems and potentially inform individualized therapy. Here we report a comprehensive analysis of genotype-dependent metabolic phenotypes using a GWAS with non-targeted metabolomics. We identified 37 genetic loci associated with blood metabolite concentrations, of which 25 show effect sizes that are unusually high for GWAS and account for 10-60% differences in metabolite levels per allele copy. Our associations provide new functional insights for many disease-related associations that have been reported in previous studies, including those for cardiovascular and kidney disorders, type 2 diabetes, cancer, gout, venous thromboembolism and Crohn's disease. The study advances our knowledge of the genetic basis of metabolic individuality in humans and generates many new hypotheses for biomedical and pharmaceutical research.


BACKGROUND: Although most cardiovascular disease occurs in low-income and middle-income countries, little is known about the use of effective secondary prevention medications in these communities. We aimed to assess use of proven effective secondary preventive drugs (antiplatelet drugs, beta blockers, angiotensin-converting enzyme [ACE] inhibitors or angiotensin-receptor blockers [ARBs], and statins) in individuals with a history of coronary heart disease or stroke. METHODS: In the Prospective Urban Rural Epidemiological (PURE) study, we recruited individuals aged 35-70 years from rural and urban communities in countries at various stages of economic development. We assessed rates of previous cardiovascular disease (coronary heart disease or stroke) and use of proven effective secondary preventive drugs and blood-pressure-lowering drugs with standardised questionnaires, which were completed by telephone interviews, household visits, or on patient's presentation to clinics. We report estimates of drug use at national, community, and individual levels. FINDINGS: We enrolled 153,996 adults from 628 urban and rural communities in countries with incomes classified as high (three countries), upper middle (seven), lower-middle (three), or low (four) between January, 2003, and December, 2009. 5650 participants had a self-reported coronary heart disease event (median 5.0 years previously [IQR 2.0-10.0]) and 2292 had stroke (4.0 years previously [2.0-8.0]). Overall, few individuals with cardiovascular disease took antiplatelet drugs (25.3%), beta blockers (17.4%), ACE inhibitors or ARBs (19.5%), or statins (14.6%). Use was highest in high-income countries (antiplatelet drugs 62.0%, beta blockers 40.0%, ACE inhibitors or ARBs 49.8%, and statins 66.5%), lowest in low-income countries (8.8%, 9.7%, 5.2%, and 3.3%, respectively), and decreased in line with reduction of country economic status (p[trend]<0.0001 for every drug type). Fewest patients received no drugs in high-income countries (11.2%), compared with 45.1% in upper middle-income countries, 69.3% in lower middle-income countries, and 80.2% in low-income countries. Drug use was higher in urban than rural areas (antiplatelet drugs 28.7% urban vs 21.3% rural, beta blockers 23.5%vs 15.6%, ACE inhibitors or ARBs 22.8%vs 15.5%, and statins 19.9%vs 11.6%; all p<0.0001), with greatest variation in poorest countries (p[interaction]<0.0001 for urban vs rural differences by country economic status). Country-level factors (eg, economic status) affected rates of drug use more than did individual-level factors (eg, age, sex, education, smoking status, body-mass index, and hypertension and diabetes statuses). INTERPRETATION: Because
use of secondary prevention medications is low worldwide—especially in low-income countries and rural areas—systematic approaches are needed to improve the long-term use of basic, inexpensive, and effective drugs. FUNDING: Full funding sources listed at end of paper (see Acknowledgments)

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BACKGROUND: Vitamin K antagonists are highly effective in preventing stroke in patients with atrial fibrillation but have several limitations. Apixaban is a novel oral direct factor Xa inhibitor that has been shown to reduce the risk of stroke in a similar population in comparison with aspirin.

METHODS: In this randomized, double-blind trial, we compared apixaban (at a dose of 5 mg twice daily) with warfarin (target international normalized ratio, 2.0 to 3.0) in 18,201 patients with atrial fibrillation and at least one additional risk factor for stroke. The primary outcome was ischemic or hemorrhagic stroke or systemic embolism. The trial was designed to test for noninferiority, with key secondary objectives of testing for superiority with respect to the primary outcome and to the rates of major bleeding and death from any cause.

RESULTS: The median duration of follow-up was 1.8 years. The rate of the primary outcome was 1.27% per year in the apixaban group, as compared with 1.60% per year in the warfarin group (hazard ratio with apixaban, 0.79; 95% confidence interval [CI], 0.66 to 0.95; P<0.001 for noninferiority; P=0.01 for superiority). The rate of major bleeding was 2.13% per year in the apixaban group, as compared with 3.09% per year in the warfarin group (hazard ratio, 0.69; 95% CI, 0.60 to 0.80; P<0.001), and the rates of death from any cause were 3.52% and 3.94%, respectively (hazard ratio, 0.89; 95% CI, 0.80 to 0.99; P=0.047). The rate of hemorrhagic stroke was 0.24% per year in the apixaban group, as compared with 0.47% per year in the warfarin group (hazard ratio, 0.51; 95% CI, 0.35 to 0.75; P<0.001), and the rate of ischemic or uncertain type of stroke was 0.97% per year in the apixaban group and 1.05% per year in the warfarin group (hazard ratio, 0.92; 95% CI, 0.74 to 1.13; P=0.42).

CONCLUSIONS: In patients with atrial fibrillation, apixaban was superior to warfarin in preventing stroke or systemic embolism, caused less bleeding, and resulted in lower mortality. (Funded by Bristol-Myers Squibb and Pfizer; ARISTOTLE ClinicalTrials.gov number, NCT00412984.)

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BACKGROUND: The JUPITER trial showed that some patients with LDL-cholesterol concentrations less than 3.37 mmol/L (<130 mg/dL) and high-sensitivity C-reactive protein (hsCRP) concentrations of 2 mg/L or more benefit from treatment with rosvuastatin, although absolute rates of cardiovascular events were low. In a population eligible for JUPITER, we established whether coronary artery calcium (CAC) might further stratify risk; additionally we
compared hsCRP with CAC for risk prediction across the range of low and high hsCRP values.

METHODS: 950 participants from the Multi-Ethnic Study of Atherosclerosis (MESA) met all criteria for JUPITER entry. We compared coronary heart disease and cardiovascular disease event rates and multivariable-adjusted hazard ratios after stratifying by burden of CAC (scores of 0, 1-100, or >100). We calculated 5-year number needed to treat (NNT) by applying the benefit recorded in JUPITER to the event rates within each CAC strata. FINDINGS: Median follow-up was 5.8 years (IQR 5.7-5.9). 444 (47%) patients in the MESA-JUPITER population had CAC scores of 0 and, in this group, rates of coronary heart disease events were 0.8 per 1000 person-years. 74% of all coronary events were in the 239 (25%) of participants with CAC scores of more than 100 (20.2 per 1000 person-years). For coronary heart disease, the predicted 5-year NNT was 549 for CAC score 0, 94 for scores 1-100, and 24 for scores greater than 100. For cardiovascular disease, the NNT was 124, 54, and 19. In the total study population, presence of CAC was associated with a hazard ratio of 4.29 (95% CI 1.99-9.25) for coronary heart disease, and of 2.57 (1.48-4.48) for cardiovascular disease. hsCRP was not associated with either disease after multivariable adjustment. INTERPRETATION: CAC seems to further stratify risk in patients eligible for JUPITER, and could be used to target subgroups of patients who are expected to derive the most, and the least, absolute benefit from statin treatment. Focusing of treatment on the subset of individuals with measurable atherosclerosis could allow for more appropriate allocation of resources. FUNDING: National Institutes of Health-National Heart, Lung, and Blood Institute


BACKGROUND: Prevalence of smoking is increasing in women in some populations and is a risk factor for coronary heart disease. Whether smoking confers the same excess risk of coronary heart disease for women as it does for men is unknown. Therefore, we aimed to estimate the effect of smoking on coronary heart disease in women compared with men after accounting for sex differences in other major risk factors. METHODS: We undertook a systematic review and meta-analysis of prospective cohort studies published between Jan 1, 1966, and Dec 31, 2010, from four online databases. We selected cohort studies that were stratified by sex with measures of relative risk (RR), and associated variability, for coronary heart disease and current smoking compared with not smoking. We pooled data with a random effects model with inverse variance weighting, and estimated RR ratios (RRRs) between men and women. FINDINGS: We reviewed 8005 abstracts and included 26 articles with data for 3,912,809 individuals and 67,075 coronary heart disease events from 86 prospective trials. In 75 cohorts (2.4 million participants) that adjusted for cardiovascular risk factors other than coronary heart disease, the pooled adjusted female-to-male RRR of smoking compared with not smoking for coronary heart disease was 1.25 (95% CI 1.12-1.39, p<0.0001). This outcome was unchanged after adjustment for potential publication bias and there was no evidence of important between-study heterogeneity (p=0.21). The RRR increased by 2% for every additional year of study follow-up (p=0.03). In pooled data from 53 studies, there was no evidence of a sex difference in the RR between participants who had previously smoked compared with those who never had (RRR 0.96, 95% CI 0.86-1.08, p=0.53). INTERPRETATION: Whether mechanisms underlying the sex difference in risk of coronary heart disease are biological or related to differences in smoking behaviour between men and women is unclear. Tobacco-control programmes should consider women, particularly in those countries where smoking among young women is increasing in prevalence. FUNDING: None
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BACKGROUND: Stroke and myocardial infarction (MI) are serious public health burdens in the US. These burdens vary by geographic location with the highest mortality risks reported in the southeastern US. While these disparities have been investigated at state and county levels, little is known regarding disparities in risk at lower levels of geography, such as neighborhoods. Therefore, the objective of this study was to investigate spatial patterns of stroke and MI mortality risks in the East Tennessee Appalachian Region so as to identify neighborhoods with the highest risks. METHODS: Stroke and MI mortality data for the period 1999-2007, obtained free of charge upon request from the Tennessee Department of Health, were aggregated to the census tract (neighborhood) level. Mortality risks were age-standardized by the direct method. To adjust for spatial autocorrelation, population heterogeneity, and variance instability, standardized risks were smoothed using Spatial Empirical Bayesian technique. Spatial clusters of high risks were identified using spatial scan statistics, with a discrete Poisson model adjusted for age and using a 5% scanning window. Significance testing was performed using 999 Monte Carlo permutations. Logistic models were used to investigate neighborhood level socioeconomic and demographic predictors of the identified spatial clusters. RESULTS: There were 3,824 stroke deaths and 5,018 MI deaths. Neighborhoods with significantly high mortality risks were identified. Annual stroke mortality risks ranged from 0 to 182 per 100,000 population (median: 55.6), while annual MI mortality risks ranged from 0 to 243 per 100,000 population (median: 65.5). Stroke and MI mortality risks exceeded the state risks of 67.5 and 85.5 in 28% and 32% of the neighborhoods, respectively. Six and ten significant (p < 0.001) spatial clusters of high risk of stroke and MI mortality were identified, respectively. Neighborhoods belonging to high risk clusters of stroke and MI mortality tended to have high proportions of the population with low education attainment. CONCLUSIONS: These methods for identifying disparities in mortality risks across neighborhoods are useful for identifying high risk communities and for guiding population health programs aimed at addressing health disparities and improving population health.

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BACKGROUND: The use of warfarin reduces the rate of ischemic stroke in patients with atrial fibrillation but requires frequent monitoring and dose adjustment. Rivaroxaban, an oral factor Xa inhibitor, may provide more consistent and predictable anticoagulation than warfarin. METHODS: In a double-blind trial, we randomly assigned 14,264 patients with nonvalvular atrial fibrillation who were at increased risk for stroke to receive either rivaroxaban (at a daily dose of 20 mg) or dose-adjusted warfarin. The per-protocol, as-treated primary analysis was designed to determine whether rivaroxaban was noninferior to warfarin for the primary end point of stroke or systemic embolism. RESULTS: In the primary analysis, the primary end point occurred in 188 patients in the rivaroxaban group (1.7% per year) and in 241 in the warfarin group (2.2% per year) (hazard ratio in the rivaroxaban group, 0.79; 95% confidence interval [CI], 0.66 to 0.96; P<0.001 for noninferiority). In the intention-to-treat analysis, the primary end point occurred in 269 patients in the rivaroxaban group (2.1% per year) and in 306 patients in the warfarin group (2.4% per year) (hazard ratio, 0.88; 95% CI, 0.74 to 1.03; P<0.001 for noninferiority; P=0.12 for superiority). Major and nonmajor clinically relevant bleeding occurred in 1475 patients in the rivaroxaban group (14.9% per year) and in 1449 in the warfarin group (14.5% per year) (hazard ratio, 1.03; 95% CI, 0.96 to 1.11; P=0.44), with significant reductions in intracranial hemorrhage (0.5% vs. 0.7%, P=0.02) and fatal bleeding (0.2% vs. 0.5%, P=0.003) in the rivaroxaban group. CONCLUSIONS: In patients with atrial fibrillation, rivaroxaban was noninferior to warfarin for the prevention of
stroke or systemic embolism. There was no significant between-group difference in the risk of major bleeding, although intracranial and fatal bleeding occurred less frequently in the rivaroxaban group. (Fundied by Johnson & Johnson and Bayer; ROCKET AF ClinicalTrials.gov number, NCT00403767.)

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Longitudinal cohort studies normally identify and adjudicate incident events detected during follow-up by retrieving medical records. There are several reasons why the adjudication process may not be successfully completed for a suspected event including the inability to retrieve medical records from hospitals and an insufficient time between the suspected event and data analysis. These "incomplete adjudications" are normally assumed not to be events, an approach which may be associated with loss of precision and introduction of bias. In this article, the authors evaluate the use of multiple imputation methods designed to include incomplete adjudications in analysis. Using data from the REasons for Geographic And Racial Differences in Stroke (REGARDS) Study, 2008-2009, they demonstrate that this approach may increase precision and reduce bias in estimates of the relations between risk factors and incident events.

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OBJECTIVE: To compare the predictive power of the main existing and recently proposed schemes for stratification of risk of stroke in older patients with atrial fibrillation. DESIGN: Comparative cohort study of eight risk stratification scores. SETTING: Trial of thromboprophylaxis in stroke, the Birmingham Atrial Fibrillation in the Aged (BAFTA) trial. PARTICIPANTS: 665 patients aged 75 or over with atrial fibrillation based in the community who were randomised to the BAFTA trial and were not taking warfarin throughout or for part of the study period. MAIN OUTCOME MEASURES: Events rates of stroke and thromboembolism. RESULTS: 54 (8%) patients had an ischaemic stroke, four (0.6%) had a systemic embolism, and 13 (2%) had a transient ischaemic attack. The distribution of patients classified into the three risk categories (low, moderate, high) was similar across three of the risk stratification scores (revised CHADS(2), NICE, ACC/AHA/ESC), with most patients categorised as high risk (65-69%, n = 460-457) and the remaining classified as moderate risk. The original CHADS(2) (Congestive heart failure, Hypertension, Age >/= 75 years, Diabetes, previous Stroke) score identified the lowest number as high risk (27%, n = 180). The incremental risk scores of CHADS(2), Rietbrock modified CHADS(2), and CHA(2)DS(2)-VASC (CHA(2)DS(2)-Vascular disease, Age 65-74 years, Sex) failed to show an increase in risk at the upper range of scores. The predictive accuracy was similar across the tested schemes with C statistic ranging from 0.55 (original CHADS(2)) to 0.62 (Rietbrock modified CHADS(2)), with all except the original CHADS(2) predicting better than...
chance. Bootstrapped paired comparisons provided no evidence of significant differences between the discriminatory ability of the schemes. CONCLUSIONS: Based on this single trial population, current risk stratification schemes in older people with atrial fibrillation have only limited ability to predict the risk of stroke. Given the systematic undertreatment of older people with anticoagulation, and the relative safety of warfarin versus aspirin in those aged over 70, there could be a pragmatic rationale for classifying all patients over 75 as "high risk" until better tools are available.


(74) NESTEL AR. Test for inflammatory markers. BMJ. 2011, vol. 342, p.d3685

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Sex differences in cardiovascular disease mortality are more pronounced among non-Hispanic whites than other racial/ethnic groups, but it is unknown whether this variation is present in the earlier subclinical stages of disease. The authors examined racial/ethnic variation in sex differences in coronary artery calcification (CAC) and carotid intimal media thickness at baseline in 2000-2002 among participants (n = 6,726) in the Multi-Ethnic Study of Atherosclerosis using binomial and linear regression. Models adjusted for risk factors in several stages: age, traditional cardiovascular disease risk factors, behavioral risk factors, psychosocial factors, and adult socioeconomic position. Women had a lower prevalence of any CAC and smaller amounts of CAC when present than men in all racial/ethnic groups. Sex differences in the prevalence of CAC were more pronounced in non-Hispanic whites than in African Americans and Chinese Americans after adjustment for traditional cardiovascular disease risk factors, and further adjustment for behavioral factors, psychosocial factors, and socioeconomic position did not modify these results (for race/sex, P(interaction) = 0.047). Similar patterns were observed for amount of CAC among adults with CAC. Racial/ethnic variation in sex differences for carotid intimal media thickness was less pronounced. In conclusion, coronary artery calcification is differentially patterned by sex across racial/ethnic groups.


(77) MAYOR S. Four in one polypill halves predicted cardiovascular risk, international study shows. BMJ. 2011, vol. 342, p.d3355

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The aims of the present study were to analyze the association between incident stroke, occupational class and stress and to examine whether the association is found in both men and women in a prospective study of Japanese male and female workers. A total of 3190 male and 3363 female Japanese community-dwelling workers aged 65 or under with no history of cardiovascular disease were followed. Occupational stress was evaluated using a demand-control questionnaire. The impact on stroke was examined in stratified analyses of occupational classes. We identified 147 incident strokes (91 in men and 56 in women) during the 11-year follow-up period. Men with high strain jobs (combination of high job demand and low job control) were nearly three times more likely to suffer from a stroke than men with low strain jobs (combination of low job demand and high job control). Among male workers in low occupational classes (blue-collar and non-managerial work), job strain was associated with a higher risk of stroke. In contrast, there was no association between job strain and incident stroke among male workers in high occupational classes (white-collar and managerial work). No statistically significant differences were found for stroke incidence among the job characteristic categories in all the female participants. However, significant, over five-fold excess risks were found among white-collar and managerial female workers exposed to high job strain, compared with their counterparts with low strain jobs. Our study of Japanese workers provided supportive evidence for vulnerability to occupational stress among lower occupational class workers in males but not in females.

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Social isolation confers increased risk for coronary heart disease (CHD) events and mortality. In two recent studies, low levels of social integration among older adults were related to higher levels of C-reactive protein (CRP), a marker of inflammation, suggesting a possible biological link between social isolation and CHD. The current study examined relationships among social isolation, CRP, and 15-year CHD death in a community sample of US adults aged 40 years and older without a prior history of myocardial infarction. A nested case-cohort study was conducted from a parent cohort of community-dwelling adults from the southeastern New England region of the United States (N = 2321) who were interviewed in 1989 and 1990. CRP levels were measured from stored sera provided by the nested case-cohort (n = 370), which included all cases of CHD death observed through 2005 (n = 48), and a random sample of non-cases. We found that the most socially isolated individuals had two-and-a-half times the odds of elevated CRP levels compared to the most socially integrated. In separate logistic regression models, both social isolation and CRP predicted later CHD death. The most socially isolated continued to have more than twice the odds of CHD death compared to the most socially integrated in a model adjusting for CRP and more traditional CHD risk factors. The current findings support social isolation as an independent risk factor of both high levels of CRP and CHD death in middle-aged adults without a prior history of myocardial infarction. Prospective study of inflammatory pathways related to social isolation and mortality are needed to fully delineate whether and how CRP or other inflammatory markers contribute to mechanisms linking social isolation to CVD health.
BACKGROUND: A 6-month abstinence from alcohol is usually required before patients with severe alcoholic hepatitis are considered for liver transplantation. Patients whose hepatitis is not responding to medical therapy have a 6-month survival rate of approximately 30%. Since most alcoholic hepatitis deaths occur within 2 months, early liver transplantation is attractive but controversial. METHODS: We selected patients from seven centers for early liver transplantation. The patients had no prior episodes of alcoholic hepatitis and had scores of 0.45 or higher according to the Lille model (which calculates scores ranging from 0 to 1, with a score >/= 0.45 indicating nonresponse to medical therapy and an increased risk of death in the absence of transplantation) or rapid worsening of liver function despite medical therapy. Selected patients also had supportive family members, no severe coexisting conditions, and a commitment to alcohol abstinence. Survival was compared between patients who underwent early liver transplantation and matched patients who did not. RESULTS: In all, 26 patients with severe alcoholic hepatitis at high risk of death (median Lille score, 0.88) were selected and placed on the list for a liver transplant within a median of 13 days after nonresponse to medical therapy. Fewer than 2% of patients admitted for an episode of severe alcoholic hepatitis were selected. The centers used 2.9% of available grafts for this indication. The cumulative 6-month survival rate (+/-SE) was higher among patients who received early transplantation than among those who did not (77 +/- 8% vs. 23 +/- 8%, P<0.001). This benefit of early transplantation was maintained through 2 years of follow-up (hazard ratio, 6.08; P = 0.004). Three patients resumed drinking alcohol: one at 720 days, one at 740 days, and one at 1140 days after transplantation. CONCLUSIONS: Early liver transplantation can improve survival in patients with a first episode of severe alcoholic hepatitis not responding to medical therapy. (Fundied by Societe Nationale Francaise de Gastroenterologie.)

BACKGROUND: Mortality among patients with severe acute alcoholic hepatitis is high, even among those treated with glucocorticoids. We investigated whether combination therapy with glucocorticoids plus N-acetylcysteine would improve survival. METHODS: We randomly assigned 174 patients to receive prednisolone plus N-acetylcysteine (85 patients) or only prednisolone (89 patients). All patients received 4 weeks of prednisolone. The prednisolone-N-acetylcysteine group received intravenous N-acetylcysteine on day 1 (at a dose of 150, 50, and 100 mg per kilogram of body weight in 250, 500, and 1000 ml of 5% glucose solution over a period of 30 minutes, 4 hours, and 16 hours, respectively) and on days 2 through 5 (100 mg per kilogram per day in 1000 ml of 5% glucose solution). The prednisolone-only group received an infusion in 1000 ml of 5% glucose solution per day on days 1 through 5. The primary outcome was 6-month survival. Secondary outcomes included survival at 1 and 3 months, hepatitis complications, adverse events related to N-acetylcysteine use, and changes in bilirubin levels on days 7 and 14. RESULTS: Mortality was not significantly lower in the prednisolone-N-acetylcysteine group than in the prednisolone-only group at 6 months (27% vs. 38%, P = 0.07). Mortality was significantly lower at 1 month (8% vs. 24%, P = 0.006) but not at 3 months (22% vs. 34%, P = 0.06). Death due to the hepatorenal syndrome was less frequent in the prednisolone-N-acetylcysteine group than in the prednisolone-only group at 6 months (9% vs. 22%, P = 0.02). In a multivariate analysis, factors associated with 6-month survival were a younger age (P<0.001), a shorter prothrombin time (P<0.001), a lower level of bilirubin at baseline (P<0.001), and a decrease in bilirubin on day 14 (P<0.001). Infections were less frequent in the prednisolone-N-acetylcysteine group than in the prednisolone-only group (P = 0.001); other side effects were similar in the two groups. CONCLUSIONS: Although combination therapy with prednisolone plus N-acetylcysteine
increased 1-month survival among patients with severe acute alcoholic hepatitis, 6-month survival, the primary outcome, was not improved. (Fundied by Programme Hospitalier de Recherche Clinique; AAH-NAC ClinicalTrials.gov number, NCT00863785.)

(4) O’DOWD A. Minister admits government has not convinced public of the harms of excessive drinking. BMJ. 2011, vol. 343, p.d6999

(5) HOLMWOOD C. Alcohol and drug problems in older people. BMJ. 2011, vol. 343, p.d6761

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Previous studies have found J-shaped relations between volume of alcohol consumed and mortality risk in white Americans but not in African Americans, suggesting the need for studies in which race/ethnicity-defined subgroups are analyzed in separate comparable models. In the present study, the authors utilized mortality follow-up data (through 2006) on respondents from the 1984 and 1995 National Alcohol Surveys, including similar numbers of black, white, and Hispanic respondents by oversampling the minority groups. Cox proportional hazards models controlling for demographic, socioeconomic, mental health, and drug- and tobacco-use measures were used to estimate mortality risk from all causes. Findings indicated a protective effect of moderate alcohol drinking (2-30 drinks/month for women and 2-60 drinks/month for men) with no monthly >/=5-drink days) relative to lifetime abstention for whites only. Elevated mortality risk relative to moderate drinking was found in former drinkers with lifetime alcohol problems. Moderate drinkers who consumed >/=5 drinks in 1 day at least monthly were also found to have increased risk, suggesting the importance of identifying heavy-occasion drinking for mortality analyses. These differential results regarding lifetime abstainers may suggest bias from differential unmeasured confounding or unmeasured aspects of alcohol consumption pattern or may be due to genetic differences in the health impact of alcohol metabolism.

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BACKGROUND: Kisumu has shown a rising HIV prevalence over the past sentinel surveillance surveys, and most new infections are occurring among youth. We conducted a qualitative study to explore risk situations that can explain the high HIV prevalence among youth in Kisumu town, Kenya METHODS: We conducted in-depth interviews with 150 adolescents aged 15 to 20, held 4 focus group discussions, and made 48 observations at places where youth spend their free time.
RESULTS: Porn video shows and local brew dens were identified as popular events where unprotected multipartner, concurrent, coerced and transactional sex occurs between adolescents. Video halls - rooms with a TV and

(11) SLOPEN N, WILLIAMS DR, FITZMAURICE GM, GILMAN SE. *Sex, stressful life events, and adult onset depression and alcohol dependence: are men and women equally vulnerable?* Soc Sci Med. 2011 Aug., vol. 73, n° 4, pp.615-622 http://dx.doi.org/10.1016/j.socscimed.2011.06.022

Higher rates of major depression (MD) among females, and of alcohol dependence (AD) among males, are among the most routinely reported findings in psychiatric epidemiology. One of the most often pursued explanations for sex differences in both disorders suggests that males and females have a differential vulnerability to stressors, which is manifested in sex-specific ways (MD for females, AD for males). However, existing evidence in support of this explanation is mixed. In the present study, we investigated sex differences in the association between stressful life events and MD and AD in a large national sample of adults in the United States (n = 32,744) using a prospective design. Logistic regression was used to estimate associations between stressful life events and both MD and AD; sex-specific effects of stress on MD and AD were evaluated by testing interaction terms between sex and stressors in the prediction of both outcomes. The number of stressful life events was predictive of first onset MD and AD. This was true for both males and females, and sex-by-stress interaction terms did not support the hypothesis that sex-specific responses to stressful life events lead to sex differences in first onset of MD and AD among adults. These results indicate the resistance of sex differences in MD and AD to simple explanations, and suggest the need for more nuanced models that incorporate both physiological and social aspects of vulnerability.


BACKGROUND: Inpatient care for alcohol intoxication is increasing in Sweden, especially among young women. Since it is well known that alcohol disorder is a chronic relapsing illness, this study examines the extent to which people return for more care. METHOD: All inpatients with alcohol-related diagnoses in Stockholm County during 1997 were followed prospectively to 2007 through registers. The proportion reappearing for the same diagnosis, other alcohol-related inpatient, or outpatient care each year after baseline, as well as the number of years the inpatients reappeared were calculated (n = 2735). Three diagnoses were examined separately; alcohol dependence, harmful use of alcohol, and alcohol intoxication. RESULTS: Three out of five inpatients with an alcohol diagnoses reappeared for more alcohol-related inpatient care during the following decade. The proportion returning was largest the year after baseline and then decreased curvilinearly over time. The inclusion of outpatient care increased proportions, but did not change patterns. Of those with an alcohol dependence diagnosis at baseline 42 percent returned for more alcohol-related inpatient care the first, 28 percent the fifth, and 25 percent the tenth year. Corresponding proportions for harmful use and intoxication were smaller. One in five among those with an alcohol dependence returned for more than five of the ten years. Ordered logistic regressions confirmed that besides diagnosis, age and gender were independently related to the number of years returning to care. CONCLUSIONS: While middle-aged males with alcohol dependence were in a revolving door, young female inpatients with intoxication diagnosis returned to a comparably lower degree.


BACKGROUND: Alcohol dependence affects approximately 3% of the English population, and accounts for significant medical and psychiatric morbidity. Only 5.6% of alcohol-dependent
individuals ever access specialist treatment and only a small percentage ever seek treatment. As people who are alcohol dependent are more likely to have experienced health problems leading to frequent attendance at acute hospitals it would seem both sensible and practical to ensure that this setting is utilised as a major access point for treatment, and to test the effectiveness of these treatments. METHODS/DESIGN: This is a randomised controlled trial with a primary hypothesis that extended brief interventions (EBI) delivered to alcohol-dependent patients in a hospital setting by an Alcohol Specialist Nurse (ASN) will be effective when compared to usual care in reducing overall alcohol consumption and improving on the standard measures of alcohol dependence. Consecutive patients will be screened for alcohol misuse in the Emergency Department (ED) of a district general hospital. On identification of an alcohol-related problem, following informed written consent, we aim to randomize 130 patients per group. The ASN will discharge to usual clinical care all control group patients, and plan a programme of EBI for treatment group patients. Follow-up interview will be undertaken by a researcher blinded to the intervention at 12 and 24 weeks. The primary outcome measure is level of alcohol dependence as determined by the Severity of Alcohol Dependence Questionnaire (SADQ) score. Secondary outcome measures include; Alcohol Use Disorders Identification Test (AUDIT) score, quantity and frequency of alcohol consumption, health-related quality of life measures, service utilisation, and patient experience. The trial will also allow an assessment of the cost-effectiveness of EBI in an acute hospital setting. In addition, patient experience will be assessed using qualitative methods. DISCUSSION: This paper presents a protocol for a RCT of EBI delivered to alcohol dependent patients by an ASN within an ED. Importantly; the trial will also seek to understand patients' perceptions and experiences of being part of a RCT and of receiving this form of intervention. TRIAL REGISTRATION NUMBER: ISRCTN: ISRCTN78062794


BACKGROUND: It is thought that small volumes of alcohol may have positive effects on health. However, excessive drinking results in serious health problems. An accurate method to determine individual alcohol use behaviors are needed to assess objectively the extent to which drinking affects health. This study investigated the association between risk of metabolic syndrome (MetS) and alcohol use behaviors in middle-aged South Korean men using the Alcohol Use Disorders Identification Test. METHODS: This study used data from the South Korea National Health and Nutrition Examination (KNHANES) IV (2008), which extracted the standard survey household by using the proportional systematic sampling method. Data of 714 participants from KNHANES IV, 2008 were analyzed using Surveyfreq and Surveylogistic regression to investigate the association between MetS and alcohol use behaviors in middle-aged South Korean men. RESULTS: After adjustment for education, smoking, and physical activity, alcohol use behaviors were significantly associated with an increased risk of hypertension [odds ratio (OR) = 2.54, 95% confidence interval (CI) = 1.5-4.06 in the hazardous group; OR = 2.99, 95% CI = 1.84-4.92 in the problem group]; impaired fasting glucose [OR = 2.15, 95% CI = 1.16-3.99 in the hazardous group; OR = 2.48, 95% CI = 1.42-4.33 in the problem group]; dyslipidemia (OR = 2.19, 95% CI = 1.38-3.47 in the problem group); abdominal obesity (OR = 1.93, 95% CI = 1.7-3.19 in the hazardous group; OR = 1.85, 95% CI = 1.7-2.92 in the problem group); and MetS (OR = 2.16, 95% CI = 1.24-3.77 in the hazardous group; OR = 2.99, 95% CI = 1.61-5.1 in the problem group). CONCLUSIONS: This study found that excessive alcohol use behaviors increased the risk of hypertension, diabetes, dyslipidemia, abdominal obesity, and MetS. Considering the rising rate of alcohol consumption and heavy drinking at single sittings, a culture of less risky alcohol consumption must be established to promote health among middle-aged men.


BACKGROUND: The Australian Government launched a mass media campaign in 2009 to raise awareness of the harms and costs associated risky drinking among young Australians. The aim of
this study was to assess if young people attending a music festival who report frequent risky single occasions of drinking (RSOD) recognise the key message of the campaign, "Binge drinking can lead to injuries and regrets", compared to young people who report less frequent RSOD.

METHODS: A cross-sectional behavioural survey of young people (aged 16-29 years) attending a music festival in Melbourne, Australia, was conducted in January 2009. We collected basic demographics, information on alcohol and other drug use and sexual health and behaviour during the previous 12 months, and measured recognition of the Australian National Binge Drinking Campaign key message. We calculated the odds of recognition of the key slogan of the Australian National Binge Drinking Campaign among participants who reported frequent RSOD (defined as reported weekly or more frequent RSOD during the previous 12 months) compared to participants who reported less frequent RSOD. RESULTS: Overall, three-quarters (74.7%) of 1072 participants included in this analysis recognised the campaign message. In the adjusted analysis, those reporting frequent RSOD had significantly lower odds of recognising the campaign message compared to those not reporting frequent RSOD (OR 0.7, 95% CI 0.5-0.9), whilst females had significantly greater odds of recognising the campaign message compared to males (OR 1.8, 95% CI 1.4-2.1). CONCLUSIONS: Whilst a high proportion of the target group recognised the campaign, our analysis suggests that participants that reported frequent R

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BACKGROUND: In the post-Soviet period, Russian working-age men have suffered unusually high mortality rates. Earlier quantitative work found that part of this is attributable to hazardous and harmful patterns of alcohol consumption, which increased in the period of transition at a time of massive social and economic disruption and uncertainty. However, there has been very little work done to document and understand in detail the downward life trajectories of individual men who died prematurely from alcohol-related conditions. Building on an earlier case-control study, this unique qualitative study investigates the perceived interplay between men's drinking careers, their employment and family history, health and eventual death. METHODS: In-depth interviews were conducted with close relatives (most often the widow) of 19 men who died between 2003 and 2005 aged 25-54 years whose close relatives reported that alcohol contributed to their death. The study was conducted in a typical medium-sized Russian city. The relative's accounts were analysed using thematic content analysis. RESULTS: The accounts describe how hazardous drinking both contributed to serious employment, family and health problems, and was simultaneously used as a coping mechanism to deal with life crises and a decline in social status. The interviews highlighted the importance of the workplace and employment status for shaping men's drinking patterns. Common themes emerged around a culture of drinking in the workplace, peer pressure from colleagues to drink, use of alcohol as remuneration, consuming non-beverage alcohols, Russian-specific drinking patterns, attitudes to treatment, and passive attitudes towards health and drinking. CONCLUSIONS: The study provides a unique insight into the personal decline that lies behind the extremely high working-age mortality due to heavy drinking in Russia, and highlights how health status and hazardous drinking are often closely intertwined with economic and social functioning. Descriptions of the development of drinking careers, hazardous drinking patterns and treatment experiences can be used to plan effective interventions relevant in the Russian context.

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This paper examines the real life contexts in which decisions surrounding heavy drinking are made by young adults (that is, on occasions when five or more alcoholic drinks are consumed within a few hours). It presents a conceptual model that views such decision making as a multi-faceted and multi-staged process. The mixed method study draws on purposive data gathered through direct observation of eight social networks consisting of 81 young adults aged between 18 and 25 years in Perth, Western Australia, including in-depth interviews with 31 participants.
Qualitative and some basic quantitative data were gathered using participant observation and in-depth interviews undertaken over an eighteen month period. Participants explained their decision to engage in heavy drinking as based on a variety of factors. These elements relate to sociocultural norms and expectancies that are best explained by the theory of planned behaviour. A framework is proposed that characterises heavy drinking as taking place in a multi-staged manner, with young adults having: 1. A generalised orientation to the value of heavy drinking shaped by wider influences and norms; 2. A short-term orientation shaped by situational factors that determines drinking intentions for specific events; and 3. An evaluative orientation shaped by moderating factors. The value of qualitative studies of decision making in real life contexts is advanced to complement the mostly quantitative research that dominates research on alcohol decision making.


BACKGROUND: In 2008 the World Health Organization (WHO) reported that South Africa had the highest tuberculosis (TB) incidence in the world. This high incidence rate is linked to a number of factors, including HIV co-infection and alcohol use disorders. The diagnosis and treatment package for TB and HIV co-infection is relatively well established in South Africa. However, because alcohol use disorders may present more insidiously, making it difficult to diagnose, those patients with active TB and misusing alcohol are not easily cured from TB. With this in mind, the primary purpose of this cluster randomized controlled trial is to provide screening for alcohol misuse and to test the efficacy of brief interventions in reducing alcohol intake in those patients with active TB found to be misusing alcohol in primary health care clinics in three provinces in South Africa. METHODS/DESIGN: Within each of the three selected health districts with the highest TB burden in South Africa, 14 primary health care clinics with the highest TB caseloads will be selected. Those agreeing to participate will be stratified according to TB treatment caseload and the type of facility (clinic or community health centre). Within strata from 14 primary care facilities, 7 will be randomly selected into intervention and 7 to control study clinics (42 clinics, 21 intervention clinics and 21 control clinics). At the clinic level systematic sampling will be used to recruit newly diagnosed TB patients. Those consenting will be screened for alcohol misuse using the AUDIT. Patients who screen positive for alcohol misuse over a 6-month period will be given either a brief intervention based on the Information-Motivation-Behavioural Skills (IMB) Model or an alcohol use health education leaflet. A total sample size of 520 is expected. DISCUSSION: The trial will evaluate the impact of alcohol screening and brief interventions for patients with active TB in primary care settings in South Africa. The findings will impact public health and will enable the health ministry to formulate policy related to comprehensive treatment for TB and alcohol misuse, which will result in reduction in alcohol use and ultimately improve the TB cure rates. TRIAL REGISTRATION NUMBER: PACTR: PACTR201105000297151


BACKGROUND: Although social environments may influence alcohol-related behaviours in youth, the relationship between neighbourhood socioeconomic context and effectiveness of school-based prevention against underage drinking has been insufficiently investigated. We study whether the social environment affects the impact of a new school-based prevention programme on alcohol use among European students. METHODS: During the school year 2004-2005, 7079 students 12-14 years of age from 143 schools in nine European centres participated in this cluster randomised controlled trial. Schools were randomly assigned to either control or a 12-session standardised curriculum based on the comprehensive social influence model. Randomisation was blocked within socioeconomic levels of the school environment. Alcohol use and alcohol-related problem behaviours were investigated through a self-completed anonymous questionnaire at
baseline and 18 months thereafter. Data were analysed using multilevel models, separately by socioeconomic level. RESULTS: At baseline, adolescents in schools of low socioeconomic level were more likely to report problem drinking than other students. Participation in the programme was associated in this group with a decreased odds of reporting episodes of drunkenness (OR = 0.60, 95% CI = 0.44-0.83), intention to get drunk (OR = 0.60, 95% CI = 0.45-0.79), and marginally alcohol-related problem behaviours (OR = 0.70, 95% CI = 0.46-1.06). No significant programme's effects emerged for students in schools of medium or high socioeconomic level. Effects on frequency of alcohol consumption were also stronger among students in disadvantaged schools, although the estimates did not attain statistical significance in any subgroup. CONCLUSIONS: It is plausible that comprehensive social influence programmes have a more favourable effect on problematic drinking among students in underprivileged social environments. TRIAL REGISTRATION: ISRCTN: ISRCTN18092805

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BACKGROUND: The alcohol-attributable fraction for injury mortality is defined as the proportion of fatal injury that would disappear if consumption went to zero. Estimating this fraction has previously been based on a simplistic view of drinking and associated risk. This paper develops a new way to calculate the alcohol-attributable fraction for injury based on different dimensions of drinking, mortality data, experimental data, survey research, new risk scenarios, and by incorporating different distributions of consumption within populations. For this analysis, the Canadian population in 2005 was used as the reference population. METHODS: Binge drinking and average daily consumption were modeled separately with respect to the calculation of the AAF. The acute consumption risk was calculated with a probability-based method that accounted for both the number of binge drinking occasions and the amount of alcohol consumed per occasion. The average daily consumption was computed based on the prevalence of daily drinking at various levels. These were both combined to get an overall estimate. 3 sensitivity analyses were performed using different alcohol consumption parameters to test the robustness of the model. Calculation of the variance to generate confidence limits around the point estimates was accomplished via Monte Carlo resampling methods on randomly generated AAFs that were based on the distribution and prevalence of drinking in the Canadian population. RESULTS: Overall, the AAFs decrease with age and are significantly lower for women than men across all ages. As binge drinking increases, the injury mortality AAF also increases. Motor vehicle collisions show the largest relative increases in AAF as alcohol consumption is increased, with over a 100% increase in AAF from the lowest to highest consumption category. Among non-motor vehicle collisions, the largest change in total AAF occurred both for homicide and other intentional injuries at about a 15% increase in the AAF from the lowest to the highest binge consumption scenarios. CONCLUSIONS: This method combines the best available evidence to generate new alcohol-attributable fractions for alcohol-attributable injury mortality. Future research is needed to refine the risk function for non-motor vehicle injury types and to investigate potential interactions between binge drinking and average volume of alcohol consumption

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BACKGROUND: As the promotion of alcohol and tobacco to young people through direct advertising has become increasingly restricted, there has been greater interest in whether images of certain behaviours in films are associated with uptake of those behaviours in young people. Associations have been reported between exposure to smoking images in films and smoking initiation, and between exposure to film alcohol images and initiation of alcohol consumption, in younger adolescents in the USA and Germany. To date no studies have reported on film images of recreational drug use and young people’s own drug use. METHODS: Cross sectional multivariable logistic regression analysis of data collected at age 19 (2002-4) from a cohort of
young people (502 boys, 500 girls) previously surveyed at ages 11 (in 1994-5), 13 and 15 in schools in the West of Scotland. Outcome measures at age 19 were: exceeding the 'sensible drinking' guidelines ('heavy drinkers') and binge drinking (based on alcohol consumption reported in last week), and ever use of cannabis and of 'hard' drugs. The principle predictor variables were an estimate of exposure to images of alcohol, and of drug use, in films, controlling for factors related to the uptake of substance use in young people. RESULTS: A third of these young adults (33%) were classed as 'heavy drinkers' and half (47%) as 'binge drinkers' on the basis of their previous week's consumption. Over half (56%) reported ever use of cannabis and 13% ever use of one or more of the 'hard' drugs listed. There were linear trends in the percentage of heavy drinkers (p = .018) and binge drinkers (p = 0.012) by film alcohol exposure quartiles, and for ever use of cannabis by film drug exposure (p = .000), and for ever use of 'hard' drugs (p = .033). The odds ratios for heavy drinking (1.56, 95% CI 1.06-2.29 comparing highest with lowest quartile of film alcohol exposure) and binge drinking (1.59, 95% CI 1.10-2.30) were attenuated by adjustment for gender, social class, family background (parental structure, parental care and parental control), attitudes to risk-taking and rule-breaking, and qualifications (OR heavy drinking 1.42, 95% CI 0.95-2.13 and binge drinking 1.49, 95% CI 1.01-2.19), and further so when adjusting for friends' drinking status (when the odds ratios were no longer significant). A similar pattern was seen for ever use of cannabis and 'hard' drugs (unadjusted OR 1.80, 95% CI 1.24-2.62 and 1.57, 95% CI 0.91-2.69 respectively, 'fully' adjusted OR 1.41 (0.90-2.22 and 1.28 (0.66-2.47) respectively).

CONCLUSIONS: Despite some limitations, which are discussed, these cross-sectional results add to a body of work which suggests that it is important to design good longitudinal studies which can determine whether exposure to images of potentially health-damaging behaviours lead to uptake of these behaviours during adolescence and early adulthood, and to examine factors that might mediate this relationship

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OBJECTIVES: We assessed the relation of alcohol consumption in young adulthood to problem alcohol consumption 10 years later and to educational attainment and labor market outcomes at midlife. We considered whether these relations differ between Blacks and Whites. METHODS: We classified individuals on the basis of their drinking frequency patterns with data from the 1982 to 1984 National Longitudinal Survey of Youth 1979 (respondents aged 19-27 years). We assessed alcohol consumption from the 1991 reinterview (respondents aged 26-34 years) and midlife outcomes from the 2006 reinterview (respondents aged 41-49 years). RESULTS: Black men who consumed 12 or more drinks per week at baseline had lower earnings at midlife, but no corresponding relation for Black women or Whites was found. Black men and Black women who consumed 12 or more drinks per week at baseline had lower occupational attainment than did White male non-drinkers and White female non-drinkers, respectively, but this result was not statistically significant. CONCLUSIONS: The relation between alcohol consumption in young adulthood and important outcomes at midlife differed between Blacks and Whites and between Black men and Black women, although Blacks' alcohol consumption at baseline was lower on average than was that of Whites

Paludisme sommaire

http://dx.doi.org/10.1016/S0140-6736(11)61826-6

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(3) WATTS G. Lost in translation. BMJ. 2011, vol. 343, p.d7047

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BACKGROUND: An ongoing phase 3 study of the efficacy, safety, and immunogenicity of candidate malaria vaccine RTS,S/AS01 is being conducted in seven African countries. METHODS: From March 2009 through January 2011, we enrolled 15,460 children in two age categories—6 to 12 weeks of age and 5 to 17 months of age—for vaccination with either RTS,S/AS01 or a non-malaria comparator vaccine. The primary end point of the analysis was vaccine efficacy against clinical malaria during the 12 months after vaccination in the first 6000 children 5 to 17 months of age at enrollment who received all three doses of vaccine according to protocol. After 250 children had an episode of severe malaria, we evaluated vaccine efficacy against severe malaria in both age categories. RESULTS: In the 14 months after the first dose of vaccine, the incidence of first episodes of clinical malaria in the first 6000 children in the older age category was 0.32 episodes per person-year in the RTS,S/AS01 group and 0.55 episodes per person-year in the control group, for an efficacy of 50.4% (95% confidence interval [CI], 45.8 to 54.6) in the intention-to-treat population and 55.8% (97.5% CI, 50.6 to 60.4) in the per-protocol population. Vaccine efficacy against severe malaria was 45.1% (95% CI, 23.8 to 60.5) in the intention-to-treat population and 47.3% (95% CI, 22.4 to 64.2) in the per-protocol population. Vaccine efficacy against severe malaria in the combined age categories was 34.8% (95% CI, 16.2 to 49.2) in the per-protocol population during an average follow-up of 11 months. Serious adverse events occurred with a similar frequency in the two study groups. Among children in the older age category, the rate of generalized convulsive seizures after RTS,S/AS01 vaccination was 1.04 per 1000 doses (95% CI, 0.62 to 1.64). CONCLUSIONS: The RTS,S/AS01 vaccine provided protection against both clinical and severe malaria in African children. (Funded by GlaxoSmithKline Biologicals and the PATH Malaria Vaccine Initiative; RTS,S ClinicalTrials.gov number, NCT00866619.)

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http://dx.doi.org/10.1038/477395a

(14) HAWKES N. Gains in malaria control will be lost if funding stalls. BMJ. 2011, vol. 343, p.d5970

http://dx.doi.org/10.1056/NEJMc1100670

http://dx.doi.org/10.1056/NEJMoa1008115

BACKGROUND: Blood-stage malaria vaccines are intended to prevent clinical disease. The malaria vaccine FMP2.1/AS02(A), a recombinant protein based on apical membrane antigen 1 (AMA1) from the 3D7 strain of Plasmodium falciparum, has previously been shown to have immunogenicity and acceptable safety in Malian adults and children. METHODS: In a double-blind, randomized trial, we immunized 400 Malian children with either the malaria vaccine or a control (rabies) vaccine and followed them for 6 months. The primary end point was clinical malaria, defined as fever and at least 2500 parasites per cubic millimeter of blood. A secondary end point was clinical malaria caused by parasites with the AMA1 DNA sequence found in the vaccine strain. RESULTS: The cumulative incidence of the primary end point was 48.4% in the malaria-vaccine group and 54.4% in the control group; efficacy against the primary end point was 17.4% (hazard ratio for the primary end point, 0.83; 95% confidence interval [CI], 0.63 to 1.09; P=0.18). Efficacy against the first and subsequent episodes of clinical malaria, as defined on the basis of various parasite-density thresholds, was approximately 20%. Efficacy against clinical malaria caused by parasites with AMA1 corresponding to that of the vaccine strain was 64.3% (hazard ratio, 0.36; 95% CI, 0.08 to 0.86; P=0.03). Local reactions and fever after vaccination were more frequent with the malaria vaccine. CONCLUSIONS: On the basis of the primary end point, the malaria vaccine did not provide significant protection against clinical malaria, but on the basis of secondary results, it may have strain-specific efficacy. If this finding is confirmed, AMA1 might be useful in a multicomponent malaria vaccine. (Funded by the National Institute of Allergy and Infectious Diseases and others; ClinicalTrials.gov number, NCT00460525.)

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Our goal is to develop a vaccine that sustainably prevents Plasmodium falciparum (Pf) malaria in >/=80% of recipients. Pf sporozoites (PfSPZ) administered by mosquito bites are the only
immunogens shown to induce such protection in humans. Such protection is thought to be mediated by CD8(+) T cells in the liver that secrete interferon-gamma (IFN-gamma). We report that purified irradiated PfSPZ administered to 80 volunteers by needle inoculation in the skin was safe, but suboptimally immunogenic and protective. Animal studies demonstrated that intravenous immunization was critical for inducing a high frequency of PfSPZ-specific CD8(+), IFN-gamma-producing T cells in the liver (nonhuman primates, mice) and conferring protection (mice). Our results suggest that intravenous administration of this vaccine will lead to the prevention of infection with Pf malaria.


BACKGROUND: Many investigators have suggested that malaria infection predisposes individuals to bacteraemia. We tested this hypothesis with mendelian randomisation studies of children with the malaria-protective phenotype of sickle-cell trait (HbAS). METHODS: This study was done in a defined area around Kilifi District Hospital, Kilifi, Kenya. We did a matched case-control study to identify risk factors for invasive bacterial disease, in which cases were children aged 3 months to 13 years who were admitted to hospital with bacteraemia between Sept 16, 1999, and July 31, 2002. We aimed to match two controls, by age, sex, location, and time of recruitment, for every case. We then did a longitudinal case-control study to assess the relation between HbAS and invasive bacterial disease as malaria incidence decreased. Cases were children aged 0-13 years who were admitted to hospital with bacteraemia between Jan 1, 1999, and Dec 31, 2007. Controls were born in the study area between Jan 1, 2006, and June 23, 2009. Finally, we modelled the annual incidence of bacteraemia against the community prevalence of malaria during 9 years with Poisson regression. RESULTS: In the matched case-control study, we recruited 292 cases—we recruited two controls for 236, and one for the remaining 56. Sickle-cell disease, HIV, leucocyte haemozoin pigment, and undernutrition were positively associated with bacteraemia and HbAS was strongly negatively associated with bacteraemia (odds ratio 0.36; 95% CI 0.20-0.65). In the longitudinal case-control study, we assessed data from 1454 cases and 10,749 controls. During the study period, the incidence of admission to hospital with malaria per 1000 child-years decreased from 28.5 to 3.45, with a reduction in protection afforded by HbAS against bacteraemia occurring in parallel (p=0.0008). The incidence of hospital admissions for bacteraemia per 1000 child-years also decreased from 2.59 to 1.45. The bacteraemia incidence rate ratio associated with malaria parasitaemia was 6.69 (95% CI 1.31-34.3) and, at a community parasite prevalence of 29% in 1999, 62% (8.2-91) of bacteraemia cases were attributable to malaria. INTERPRETATION: Malaria infection strongly predisposes individuals to bacteraemia and can account for more than half of all cases of bacteraemia in malaria-endemic areas. Interventions to control malaria will have a major additional benefit by reducing the burden of invasive bacterial disease. FUNDING: Wellcome Trust


Synthetic biology is an emerging field focused on engineering biomolecular systems and cellular capabilities for a variety of applications. Substantial progress began a little over a decade ago with the creation of synthetic gene networks inspired by electrical engineering. Since then, the field has
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designed and built increasingly complex circuits and constructs and begun to use these systems in a variety of settings, including the clinic. These efforts include the development of synthetic biology therapies for the treatment of infectious diseases and cancer, as well as approaches in vaccine development, microbiome engineering, cell therapy, and regenerative medicine. Here, we highlight advances in the biomedical application of synthetic biology and discuss the field's clinical potential.

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BACKGROUND: Health workers' malaria case-management practices often differ from national guidelines. We assessed whether text messages sent to health workers' mobile phones could improve and maintain their adherence to treatment guidelines for outpatient paediatric malaria in Kenya. METHODS: From March 6, 2009, to May 31, 2010, we did a cluster-randomised controlled trial at 107 rural health facilities in 11 districts in coastal and western Kenya. With a computer-generated sequence, health facilities were randomly allocated to either the intervention group, in which all health workers received text messages on their personal mobile phones on malaria case-management for 6 months, or the control group, in which health workers did not receive any text messages. Health workers were not masked to the intervention, although patients were unaware of whether they were in an intervention or control facility. The primary outcome was correct management with artemether-lumefantrine, defined as a dichotomous composite indicator of treatment, dispensing, and counselling tasks concordant with Kenyan national guidelines. The primary analysis was by intention to treat. The trial is registered with Current Controlled Trials, ISRCTN72328636. FINDINGS: 119 health workers received the intervention. Case-management practices were assessed for 2269 children who needed treatment (1157 in the intervention group and 1112 in the control group). Intention-to-treat analysis showed that correct artemether-lumefantrine management improved by 23.7 percentage points (95% CI 7.6-40.0; p=0.004) immediately after intervention and by 24.5 percentage points (8.1-41.0; p=0.003) 6 months later. INTERPRETATION: In resource-limited settings, malaria control programmes should consider use of text messaging to improve health workers' case-management practices. FUNDING: The Wellcome Trust

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BACKGROUND: There is limited uptake of measures to prevent malaria by pregnant women in Nigeria which is often related to the lack of knowledge on Malaria in Pregnancy (MIP) and its effects on mother and foetus. This study, explored peer to peer education as a tool in raising knowledge of MIP among women of child bearing age. METHODS: 1105 women of child bearing age were interviewed in their households using a structured questionnaire about their knowledge of malaria in general, MIP and use of preventive measures. Thereafter, a peer education campaign was launched to raise the level of knowledge in the community. The interviews were repeated after the campaign and the responses between the pre- and post-intervention were compared. RESULTS: In the pre-assessment women on average answered 64.8% of the question on malaria and its possibility to prevent malaria correctly. The peer education campaign had a significant impact in raising the level of knowledge among the women; after the campaign the respondents answered on average 73.8% of the questions correctly. Stratified analysis on pre and post assessment scores for malaria in general (68.8 & 72.9%) and MIP (61.7 & 76.3%) showed also significant increase. Uptake of bed nets was reported to be low: 11.6% CONCLUSION: Peer
education led to a significant increase in knowledge of malaria and its prevention but we could not
assess its influence on the use of preventive measures.

(25) DICKO A, TOURE SO, TRAORE M, SAGARA I, et al. Increase in EPI vaccines coverage after
implementation of intermittent preventive treatment of malaria in infant with Sulfadoxine-
pyrimethamine in the district of Kolokani, Mali: results from a cluster randomized control
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BACKGROUND: Even though the efficacy of Intermittent Preventive Treatment in infants (IPTi)
with Sulfadoxine-Pyrimethamine (SP) against clinical disease and the absence of its interaction
with routine vaccines of the Expanded Immunization Programme (EPI) have been established,
there are still some concerns regarding the addition of IPTi, which may increase the work burden
and disrupt the routine EPI services especially in Africa where the target immunization coverage
remains to be met. However IPTi may also increase the adherence of the community to EPI
services and improve EPI coverage, once the benefit of strategy is perceived. METHODS: To
assess the impact of IPTi implementation on the coverage of EPI vaccines, 22 health areas of the
district of Kolokani were randomized at a 1:1 ratio to either receive IPTi-SP or to serve as a
control. The EPI vaccines coverage was assessed using cross-sectional surveys at baseline in
November 2006 and after one year of IPTi pilot-implementation in December 2007. RESULTS: At
baseline, the proportion of children of 9-23 months who were completely vaccinated (defined as
children who received BGG, 3 doses of DTP/Polio, measles and yellow fever vaccines) was
36.7% (95% CI 25.3%-48.0%). After one year of implementation of IPTi-SP using routine health
services, the proportion of children completely vaccinated rose to 53.8% in the non intervention
zone and 69.5% in the IPTi intervention zone (P <0.001). The proportion of children in the target
age groups who received IPTi with each of the 3 vaccinations DTP2, DTP3 and Measles, were
89.2% (95% CI 85.9%-92.0%), 91.0% (95% CI 87.6%-93.7%) and 77.4% (95% CI 70.7%-83.2%)
respectively. The corresponding figures in non intervention zone were 2.3% (95% CI 0.9%-4.7%),
2.6% (95% CI 1.0%-5.6%) and 1.7% (95% CI 0.4%-4.9%). CONCLUSION: This study shows
that high coverage of the IPTi can be obtained when the strategy is implemented using routine
health services and implementation results in a significant increase in coverage of EPI vaccines in
the district of Kolokani, Mali.

(26) LORDAN G, TANG KK, CARMIGNANI F. Has HIV/AIDS displaced other health funding
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In recent times there has been a sense that HIV/AIDS control has been attracting a significantly
larger portion of donor health funding to the extent that it crowds out funding for other health
concerns. Although there is no doubt that HIV/AIDS has absorbed a large share of development
assistance for health (DAH), whether HIV/AIDS is actually diverting funding away from other
health concerns has yet to be analyzed fully. To fill this vacuum, this study aims to test if a higher
level of HIV/AIDS funding is related to a displacement in funding for other health concerns, and if
yes, to quantify the magnitude of the displacement effect. Specifically, we consider whether
HIV/AIDS DAH has displaced i) TB, ii) malaria iii) health sector and ‘other’ DAH in terms of the
dollar amount received for aid. We consider this question within a regression framework
controlling for time and recipient heterogeneity. We find displacement effects for malaria and
health sector funding but not TB. In particular, the displacement effect for malaria is large and
worrying.

(27) GINGRICH CD, HANSON K, MARCHANT T, MULLIGAN JA, et al. Price subsidies and the
market for mosquito nets in developing countries: A study of Tanzania’s discount voucher
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This study uses a partial equilibrium simulation model to explore how price subsidies for
insecticide-treated mosquito nets (ITNs) affect households' purchases of ITNs. The model
describes the ITN market in a typical developing country and is applied to the situation in Tanzania, where the Tanzania National Voucher Scheme (TNVS) provides a targeted subsidy to vulnerable population groups by means of a discount voucher. The data for this study come from a nationally-representative household survey completed July-August 2006 covering over 4300 households in 21 districts. The simulation results show the impact of the voucher program on ITN coverage among target households, namely those that experienced the birth of a child. More specifically, the share of target households purchasing an ITN increased from 18 to 62 percent because of the discount voucher. The model also suggests that the voucher program could cause the retail ITN price to rise due to an overall increase in demand. As a result, ITN purchases by households without a voucher may actually decline. The simulation model suggests that additional increases toward the stated goal of 80 percent ITN coverage for pregnant women and children could best be achieved through a combination of "catch up" mass distribution programs and expanding the target group for the voucher program to cover additional households. The model can be employed in other countries considering use of a targeted price subsidy for ITNs, and could be adapted to assess the impact of subsidies for other public health commodities

(28) PARRY J. Global Fund pressures China to engage with civil society groups. BMJ. 2011, vol. 342, p.d3327

Pathologies liées à l'obésité

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BACKGROUND: Obesity in childhood is associated with increased cardiovascular risk. It is uncertain whether this risk is attenuated in persons who are overweight or obese as children but not obese as adults. METHODS: We analyzed data from four prospective cohort studies that measured childhood and adult body-mass index (BMI, the weight in kilograms divided by the square of the height in meters). The mean length of follow-up was 23 years. To define high adiposity status, international age-specific and sex-specific BMI cutoff points for overweight and obesity were used for children, and a BMI cutoff point of 30 was used for adults. RESULTS: Data were available for 6328 subjects. Subjects with consistently high adiposity status from childhood to adulthood, as compared with persons who had a normal BMI as children and were nonobese as adults, had an increased risk of type 2 diabetes (relative risk, 5.4; 95% confidence interval [CI], 3.4 to 8.5), hypertension (relative risk, 2.7; 95% CI, 2.2 to 3.3), elevated low-density lipoprotein cholesterol levels (relative risk, 1.8; 95% CI, 1.4 to 2.3), reduced high-density lipoprotein cholesterol levels (relative risk, 2.1; 95% CI, 1.8 to 2.5), elevated triglyceride levels (relative risk, 3.0; 95% CI, 2.4 to 3.8), and carotid-artery atherosclerosis (increased intima-media thickness of the carotid artery) (relative risk, 1.7; 95% CI, 1.4 to 2.2) (P ≤ 0.002 for all comparisons). Persons
who were overweight or obese during childhood but were nonobese as adults had risks of the outcomes that were similar to those of persons who had a normal BMI consistently from childhood to adulthood (P>0.20 for all comparisons). CONCLUSIONS: Overweight or obese children who were obese as adults had increased risks of type 2 diabetes, hypertension, dyslipidemia, and carotid-artery atherosclerosis. The risks of these outcomes among overweight or obese children who became nonobese by adulthood were similar to those among persons who were never obese. (Funded by the Academy of Finland and others.)

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BACKGROUND: Obesity and its cardiovascular complications are extremely common medical problems, but evidence on how to accomplish weight loss in clinical practice is sparse.

METHODS: We conducted a randomized, controlled trial to examine the effects of two behavioral weight-loss interventions in 415 obese patients with at least one cardiovascular risk factor. Participants were recruited from six primary care practices; 63.6% were women, 41.0% were black, and the mean age was 54.0 years. One intervention provided patients with weight-loss support remotely--through the telephone, a study-specific Web site, and e-mail. The other intervention provided in-person support during group and individual sessions, along with the three remote means of support. There was also a control group in which weight loss was self-directed. Outcomes were compared between each intervention group and the control group and between the two intervention groups. For both interventions, primary care providers reinforced participation at routinely scheduled visits. The trial duration was 24 months. RESULTS: At baseline, the mean body-mass index (the weight in kilograms divided by the square of the height in meters) for all participants was 36.6, and the mean weight was 103.8 kg. At 24 months, the mean change in weight from baseline was -0.8 kg in the control group, -4.6 kg in the group receiving remote support only (P<0.001 for the comparison with the control group), and -5.1 kg in the group receiving in-person support (P<0.001 for the comparison with the control group). The percentage of participants who lost 5% or more of their initial weight was 18.8% in the control group, 38.2% in the group receiving remote support only, and 41.4% in the group receiving in-person support. The change in weight from baseline did not differ significantly between the two intervention groups. CONCLUSIONS: In two behavioral interventions, one delivered with in-person support and the other delivered remotely, without face-to-face contact between participants and weight-loss coaches, obese patients achieved and sustained clinically significant weight loss over a period of 24 months. (Funded by the National Heart, Lung, and Blood Institute and others; ClinicalTrials.gov number, NCT00783315.)

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BACKGROUND: Calls for primary care providers (PCPs) to offer obese patients behavioral weight-loss counseling have not been accompanied by adequate guidance on how such care could be delivered. This randomized trial compared weight loss during a 2-year period in response to three lifestyle interventions, all delivered by PCPs in collaboration with auxiliary health professionals (lifestyle coaches) in their practices. METHODS: We randomly assigned 390 obese adults in six primary care practices to one of three types of intervention: usual care, consisting of quarterly PCP visits that included education about weight management; brief lifestyle counseling, consisting of quarterly PCP visits combined with brief monthly sessions with lifestyle coaches who instructed participants about behavioral weight control; or enhanced brief lifestyle counseling, which provided the same care as described for the previous intervention but included meal
replacements or weight-loss medication (orlistat or sibutramine), chosen by the participants in consultation with the PCPs, to potentially increase weight loss. RESULTS: Of the 390 participants, 86% completed the 2-year trial, at which time, the mean (+/-SE) weight loss with usual care, brief lifestyle counseling, and enhanced brief lifestyle counseling was 1.7+/-0.7, 2.9+/-0.7, and 4.6+/-0.7 kg, respectively. Initial weight decreased at least 5% in 21.5%, 26.0%, and 34.9% of the participants in the three groups, respectively. Enhanced lifestyle counseling was superior to usual care on both these measures of success (P=0.003 and P=0.02, respectively), with no other significant differences among the groups. The benefits of enhanced lifestyle counseling remained even after participants given sibutramine were excluded from the analyses. There were no significant differences between the intervention groups in the occurrence of serious adverse events. CONCLUSIONS: Enhanced weight-loss counseling helps about one third of obese patients achieve long-term, clinically meaningful weight loss. (Funded by the National Heart, Lung, and Blood Institute; POWER-UP ClinicalTrials.gov number, NCT00826774.)


OBJECTIVE: To assess the effectiveness of a range of weight management programmes in terms of weight loss. DESIGN: Eight arm randomised controlled trial. SETTING: Primary care trust in Birmingham, England. PARTICIPANTS: 740 obese or overweight men and women with a comorbid disorder identified from general practice records. INTERVENTIONS: Weight loss programmes of 12 weeks’ duration: Weight Watchers; Slimming World; Rosemary Conley; group based, dietetics led programme; general practice one to one counselling; pharmacy led one to one counselling; choice of any of the six programmes. The comparator group was provided with 12 vouchers enabling free entrance to a local leisure (fitness) centre. MAIN OUTCOME MEASURES: The primary outcome was weight loss at programme end (12 weeks). Secondary outcomes were weight loss at one year, self reported physical activity, and percentage weight loss at programme end and one year. RESULTS: Follow-up data were available for 658 (88.9%) participants at programme end and 522 (70.5%) at one year. All programmes achieved significant weight loss from baseline to programme end (range 1.37 kg (general practice) to 4.43 kg (Weight Watchers)), and all except general practice and pharmacy provision resulted in significant weight loss at one year. At one year, only the Weight Watchers group had significantly greater weight loss than did the comparator group (2.5 (95% confidence interval 0.8 to 4.2) kg greater loss.). The commercial programmes achieved significantly greater weight loss than did the primary care programmes at programme end (mean difference 2.3 (1.3 to 3.4) kg). The primary care programmes were the most costly to provide. Participants allocated to the choice arm did not have better outcomes than those randomly allocated to a programme. CONCLUSIONS: Commercially provided weight management services are more effective and cheaper than primary care based services led by specially trained staff, which are ineffective. Trial registration Current Controlled Trials ISRCTN25072883


BACKGROUND: After weight loss, changes in the circulating levels of several peripheral hormones involved in the homeostatic regulation of body weight occur. Whether these changes are transient or persist over time may be important for an understanding of the reasons behind the high rate of weight regain after diet-induced weight loss. METHODS: We enrolled 50 overweight or obese patients without diabetes in a 10-week weight-loss program for which a very-low-energy diet was prescribed. At baseline (before weight loss), at 10 weeks (after program completion), and at 62 weeks, we examined circulating levels of leptin, ghrelin, peptide YY, gastric inhibitory polypeptide, glucagon-like peptide 1, amylin, pancreatic polypeptide, cholecystokinin, and insulin and subjective ratings of appetite. RESULTS: Weight loss (mean [+/-SE], 13.5+/-0.5 kg) led to significant reductions in levels of leptin, peptide YY, cholecystokinin, insulin (P<0.001 for all comparisons), and amylin (P=0.002) and to increases in levels of ghrelin (P<0.001), gastric inhibitory polypeptide (P=0.004), and pancreatic polypeptide (P=0.008). There was also a significant increase in subjective appetite (P<0.001). One year after the initial weight loss, there were still significant differences from baseline in the mean levels of leptin (P<0.001), peptide YY (P<0.001), cholecystokinin (P=0.04), insulin (P=0.01), ghrelin (P<0.001), gastric inhibitory polypeptide (P<0.001), and pancreatic polypeptide (P=0.002), as well as hunger (P<0.001). CONCLUSIONS: One year after initial weight reduction, levels of the circulating mediators of appetite that encourage weight regain after diet-induced weight loss do not revert to the levels recorded before weight loss. Long-term strategies to counteract this change may be needed to prevent obesity relapse. (Funded by the National Health and Medical Research Council and others; ClinicalTrials.gov number, NCT00870259.)


OBJECTIVE: To test the effect of a multidimensional lifestyle intervention on aerobic fitness and adiposity in predominantly migrant preschool children. DESIGN: Cluster randomised controlled single blinded trial (Ballabeina study) over one school year; randomisation was performed after stratification for linguistic region. SETTING: 40 preschool classes in areas with a high migrant population in the German and French speaking regions of Switzerland. PARTICIPANTS: 652 of the 727 preschool children had informed consent and were present for baseline measures (mean age 5.1 years (SD 0.7), 72% migrants of multicultural origins). No children withdrew, but 26 moved away. INTERVENTION: The multidimensional culturally tailored lifestyle intervention included a physical activity programme, lessons on nutrition, media use (use of television and computers), and sleep and adaptation of the built environment of the preschool class. It lasted from August 2008 to June 2009. MAIN OUTCOME MEASURES: Primary outcomes were aerobic fitness (20 m shuttle run test) and body mass index (BMI). Secondary outcomes included motor agility, balance, percentage body fat, waist circumference, physical activity, eating habits, media use, sleep, psychological health, and cognitive abilities. RESULTS: Compared with controls, children in the intervention group had an increase in aerobic fitness at the end of the intervention (adjusted mean difference: 0.32 stages (95% confidence interval 0.07 to 0.57; P=0.01) but no difference in BMI (-0.07 kg/m²), -0.19 to 0.06; P=0.31). Relative to controls, children in the intervention group had beneficial effects in motor agility (-0.54 s, -0.90 to -0.17; P=0.004), percentage body fat (-1.1%, -2.0 to -0.2; P=0.02), and waist circumference (-1.0 cm, -1.6 to -0.4; P=0.001). There were also significant benefits in the intervention group in reported physical activity, sleep, psychological health, and cognitive abilities.

(19) MAYOR S. Specialists condemn government's obesity plan as too simplistic. BMJ. 2011, vol. 343, p.d6688

activity, media use, and eating habits, but not in the remaining secondary outcomes.
CONCLUSIONS: A multidimensional intervention increased aerobic fitness and reduced body fat but not BMI in predominantly migrant preschool children. Trial registration Clinical Trials NCT00674544


OBJECTIVE: To study the risk of adverse pregnancy outcomes in women with polycystic ovary syndrome, taking into account maternal characteristics and assisted reproductive technology.

DESIGN: Population based cohort study.
PARTICIPANTS: By linkage with the Swedish patient register, 3787 births among women with a diagnosis of polycystic ovary syndrome and 1,191,336 births among women without such a diagnosis.

MAIN OUTCOME MEASURES: Risk of adverse pregnancy outcomes (gestational diabetes, pre-eclampsia, preterm birth, stillbirth, neonatal death, low Apgar score (<7 at five minutes), meconium aspiration, large for gestational age, macrosomia, small for gestational age), adjusted for maternal characteristics (body mass index, age), socioeconomic factors (educational level, and cohabitating with infant's father), and assisted reproductive technology.

RESULTS: Women with polycystic ovary syndrome were more often obese and more commonly used assisted reproductive technology than women without such a diagnosis (60.6% vs 34.8% and 13.7% vs 1.5%). Polycystic ovary syndrome was strongly associated with pre-eclampsia (adjusted odds ratio 1.45, 95% confidence interval 1.24 to 1.69) and very preterm birth (2.21, 1.69 to 2.90) and the risk of gestational diabetes was more than doubled (2.32, 1.88 to 2.88). Infants born to mothers with polycystic ovary syndrome were more prone to be large for gestational age (1.39, 1.19 to 1.62) and were at increased risk of meconium aspiration (2.02, 1.13 to 3.61) and having a low Apgar score (<7) at five minutes (1.41, 1.09 to 1.83).

CONCLUSIONS: Women with polycystic ovary syndrome are at increased risk of adverse pregnancy and birth outcomes that cannot be explained by assisted reproductive technology. These women may need increased surveillance during pregnancy and parturition

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OBJECTIVES: The United States has the highest prevalence of obesity and one of the lowest life expectancies among high-income countries. We investigated the relationship between these 2 phenomena.

METHODS: We estimated the fraction of deaths attributable to obesity by country, age, and sex and reestimated life tables after removing these deaths. To allow for a possible secular decline in obesity risks, we employed alternative risks from a more recent period.

RESULTS: In our baseline analysis, obesity reduced US life expectancy at age 50 years in 2006 by 1.54 years (95% confidence interval [CI] = 1.37, 1.93) for women and by 1.85 years (95% CI =
1.62, 2.10) for men. Removing the effects of obesity reduced the US shortfall by 42% (95% CI = 36, 48) for women and 67% (95% CI = 57, 76) for men, relative to countries with higher life expectancies. Using more recently recorded risk data, we estimated that differences in obesity still accounted for a fifth to a third of the shortfall. CONCLUSIONS: The high prevalence of obesity in the United States contributes substantially to its poor international ranking in longevity (26)


The authors hypothesized that the absence of cross-sectional associations of body mass index (BMI; weight (kg)/height (m)(2)) with peripheral arterial disease (PAD) in prior studies may reflect lower weight among persons who smoke or have poor health status. They conducted an observational study among 5,419 noninstitutionalized residents of 4 US communities aged >/= 65 years at baseline (1989-1990 or 1992-1993). Ankle brachial index was measured, and participants reported their history of PAD procedures. Participants were followed longitudinally for adjudicated incident PAD events. At baseline, mean BMI was 26.6 (standard deviation, 4.6), and 776 participants (14%) had prevalent PAD. During 13.2 (median) years of follow-up through June 30, 2007, 276 incident PAD events occurred. In cross-sectional analysis, each 5-unit increase in BMI was inversely associated with PAD (prevalence ratio (PR) = 0.92, 95% confidence interval (CI): 0.85, 1.00). However, among persons in good health who had never smoked, the direction of association was opposite (PR = 1.20, 95% CI: 0.94, 1.52). Similar results were observed between BMI calculated using weight at age 50 years and PAD prevalence (PR = 1.30, 95% CI: 1.11, 1.51) and between BMI at baseline and incident PAD events occurring during follow-up (hazard ratio = 1.32, 95% CI: 1.00, 1.76) among never smokers in good health. Greater BMI is associated with PAD in older persons who remain healthy and have never smoked. Normal weight maintenance may decrease PAD incidence and associated comorbidity in older age (27)


BACKGROUND: The increasing prevalence of overweight and obesity needs effective approaches for weight loss in primary care and community settings. We compared weight loss with standard treatment in primary care with that achieved after referral by the primary care team to a commercial provider in the community. METHODS: In this parallel group, non-blinded, randomised controlled trial, 772 overweight and obese adults were recruited by primary care practices in Australia, Germany, and the UK. Participants were randomly assigned with a computer-generated simple randomisation sequence to receive either 12 months of standard care as defined by national treatment guidelines, or 12 months of free membership to a commercial programme (Weight Watchers), and followed up for 12 months. The primary outcome was weight change over 12 months. Analysis was by intention to treat (last observation carried forward [LOCF] and baseline observation carried forward [BOCF]) and in the population who completed the 12-month assessment. This trial is registered, number ISRCTN85485463. FINDINGS: 377 participants were assigned to the commercial programme, of whom 230 (61%) completed the 12-month assessment; and 395 were assigned to standard care, of whom 214 (54%) completed the
12-month assessment. In all analyses, participants in the commercial programme group lost twice as much weight as did those in the standard care group. Mean weight change at 12 months was -5.06 kg (SE 0.31) for those in the commercial programme versus -2.25 kg (0.21) for those receiving standard care (adjusted difference -2.77 kg, 95% CI -3.50 to -2.03) with LOCF; -4.06 kg (0.31) versus -1.77 kg (0.19; adjusted difference -2.29 kg, -2.99 to -1.58) with BOCF; and -6.65 kg (0.43) versus -3.26 kg (0.33; adjusted difference -3.16 kg, -4.23 to -2.11) for those who completed the 12-month assessment. Participants reported no adverse events related to trial participation.

INTERPRETATION: Referral by a primary health-care professional to a commercial weight loss programme that provides regular weighing, advice about diet and physical activity, motivation, and group support can offer a clinically useful early intervention for weight management in overweight and obese people that can be delivered at large scale. FUNDING: Weight Watchers International, through a grant to the UK Medical Research Council.

http://dx.doi.org/10.1038/477166a

http://dx.doi.org/10.1056/NEJMoa1104119

BACKGROUND: Recent pooled analyses show an increased risk of death with increasing levels of the body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) of 25.0 or higher in populations of European ancestry, a weaker association among East Asians, and no association of an increased BMI with an increased risk of death among South Asians. The limited data available on blacks indicate that the risk of death is increased only at very high levels of BMI (>/=35.0). METHODS: We prospectively assessed the relation of both BMI and waist circumference to the risk of death among 51,695 black women with no history of cancer or cardiovascular disease who were 21 to 69 years of age at study enrollment. Our analysis was based on follow-up data from 1995 through 2008 in the Black Women's Health Study. Multivariable proportional-hazards models were used to estimate hazard ratios and 95% confidence intervals. RESULTS: Of 1773 deaths identified during follow-up, 770 occurred among 33,916 women who had never smoked. Among nonsmokers, the risk of death was lowest for a BMI of 20.0 to 24.9. For a BMI above this range, the risk of death increased as the BMI increased. With a BMI of 22.5 to 24.9 as the reference category, multivariable-adjusted hazard ratios were 1.12 (95% confidence interval [CI], 0.87 to 1.44) for a BMI of 25.0 to 27.4, 1.31 (95% CI, 1.01 to 1.72) for a BMI of 27.5 to 29.9, 1.27 (95% CI, 0.99 to 1.64) for a BMI of 30.0 to 34.9, 1.51 (95% CI, 1.13 to 2.02) for a BMI of 35.0 to 39.9, and 2.19 (95% CI, 1.62 to 2.95) for a BMI of 40.0 to 49.9 (P<0.001 for trend). A large waist circumference was associated with an increased risk of death from any cause among women with a BMI of less than 30.0. CONCLUSIONS: The risk of death from any cause among black women increased with an increasing BMI of 25.0 or higher, which is similar to the pattern observed among whites. Waist circumference appeared to be associated with an increased risk of death only among nonobese women. (Funded by the National Cancer Institute.)

http://dx.doi.org/10.1038/nature10383

PPARgamma is the functioning receptor for the thiazolidinedione (TZD) class of antidiabetes drugs including rosiglitazone and pioglitazone. These drugs are full classical agonists for this nuclear receptor, but recent data have shown that many PPARgamma-based drugs have a separate biochemical activity, blocking the obesity-linked phosphorylation of PPARgamma by Cdk5. Here we describe novel synthetic compounds that have a unique mode of binding to PPARgamma, completely lack classical transcriptional agonism and block the Cdk5-mediated
phosphorylation in cultured adipocytes and in insulin-resistant mice. Moreover, one such
compound, SR1664, has potent antidiabetic activity while not causing the fluid retention and
weight gain that are serious side effects of many of the PPARgamma drugs. Unlike TZDs,
SR1664 also does not interfere with bone formation in culture. These data illustrate that new
classes of antidiabetes drugs can be developed by specifically targeting the Cdk5-mediated
phosphorylation of PPARgamma

(33) LUO J, HORN K, OCKENE JK, SIMON MS, et al. Interaction between smoking and obesity
and the risk of developing breast cancer among postmenopausal women: the Women’s
http://dx.doi.org/10.1093/aje/kwr192

Obesity is a well-established risk factor for postmenopausal breast cancer. Recent studies
suggest that smoking increases the risk of breast cancer. However, the effect of co-occurrence of
smoking and obesity on breast cancer risk remains unclear. A total of 76,628 women aged 50-79
years enrolled in the Women’s Health Initiative Observational Study were followed through August
14, 2009. Cox proportional hazards regression models were used to estimate hazard ratios and
95% confidence intervals. Over an average 10.3 years of follow-up, 3,378 incident cases of
invasive breast cancer were identified. The effect of smoking on the risk of developing invasive
breast cancer was modified significantly by obesity status among postmenopausal women,
regardless of whether the obesity status was defined by body mass index (P(interaction) = 0.01)
or waist circumference (P(interaction) = 0.02). A significant association between smoking and
breast cancer was noted in nonobese women (hazard ratio = 1.25, 95% confidence interval:
1.05, 1.47) but not in obese women (hazard ratio = 0.96, 95% confidence interval: 0.69, 1.34). In
conclusion, this study suggests that the effect of smoking exposure on breast cancer risk was
modified by obesity among postmenopausal women. The modification effect did not differ by
general versus abdominal obesity

(34) BAUR LA. Changing perceptions of obesity--recollections of a paediatrician. Lancet. 2011
Aug. 27, vol. 378, n° 9793, pp.762-763

(35) HOLT E. Hungary to introduce broad range of fat taxes. Lancet. 2011 Aug. 27, vol. 378, n°
9793, p.755

(36) MA J, FLANDERS WD, WARD EM, JEMAL A. Body mass index in young adulthood and
premature death: analyses of the US National Health Interview Survey linked mortality files.
http://dx.doi.org/10.1093/aje/kwr169

Knowledge of the association between body mass index (weight (kg)/height (m)(2)) and
premature death in young adulthood is very limited, especially for specific causes of death. Using
the US National Health Interview Survey linked mortality files, the authors examined the relation
between body mass index and premature death from all causes, cardiovascular disease (CVD),
and cancer among 112,328 persons aged 18-39 years who participated in the National Health
Interview Survey in the years 1987, 1988, and 1990-1995. During an average of 16 years of
follow-up (ending on December 31, 2006), there were 3,178 deaths: 573 from CVD and 733 from
cancer. Hazard ratios and 95% confidence intervals were estimated using multivariate
proportional hazards models adjusting for age, gender, race/ethnicity, education, and smoking
status. In analyses restricted to participants who had never smoked, the hazard ratios for death
from all causes were 1.07 (95% confidence interval (CI): 0.91, 1.26) for overweight participants,
1.41 (95% CI: 1.16, 1.73) for obese participants, and 2.46 (95% CI: 1.91, 3.16) for extremely
obese participants, compared with those of normal weight. Monotonically increasing risks for
excess body weight were also observed for deaths from cancer and CVD. The associations found
in this young cohort were much stronger than those in middle-aged or older populations
Rising prevalence of obesity is a worldwide health concern because excess weight gain within populations forecasts an increased burden from several diseases, most notably cardiovascular diseases, diabetes, and cancers. In this report, we used a simulation model to project the probable health and economic consequences in the next two decades from a continued rise in obesity in two ageing populations—the USA and the UK. These trends project 65 million more obese adults in the USA and 11 million more obese adults in the UK by 2030, consequently accruing an additional 6-8.5 million cases of diabetes, 5.7-7.3 million cases of heart disease and stroke, 492,000-669,000 additional cases of cancer, and 26-55 million quality-adjusted life years forgone for USA and UK combined. The combined medical costs associated with treatment of...
these preventable diseases are estimated to increase by $48-66 billion/year in the USA and by £1.9-2 billion/year in the UK by 2030. Hence, effective policies to promote healthier weight also have economic benefits.

http://dx.doi.org/10.1016/S0140-6736(11)60813-1

The simultaneous increases in obesity in almost all countries seem to be driven mainly by changes in the global food system, which is producing more processed, affordable, and effectively marketed food than ever before. This passive overconsumption of energy leading to obesity is a predictable outcome of market economies predicated on consumption-based growth. The global food system drivers interact with local environmental factors to create a wide variation in obesity prevalence between populations. Within populations, the interactions between environmental and individual factors, including genetic makeup, explain variability in body size between individuals. However, even with this individual variation, the epidemic has predictable patterns in subpopulations. In low-income countries, obesity mostly affects middle-aged adults (especially women) from wealthy, urban environments; whereas in high-income countries it affects both sexes and all ages, but is disproportionately greater in disadvantaged groups. Unlike other major causes of preventable death and disability, such as tobacco use, injuries, and infectious diseases, there are no exemplar populations in which the obesity epidemic has been reversed by public health measures. This absence increases the urgency for evidence-creating policy action, with a priority on reduction of the supply-side drivers.

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http://dx.doi.org/10.1016/S0140-6736(11)61218-X

http://dx.doi.org/10.1016/S0140-6736(11)61261-0

http://dx.doi.org/10.1016/S0140-6736(11)61356-1


http://dx.doi.org/10.1093/aje/kwr200

The role of cannabis and endocannabinoids in appetite regulation has been extensively studied, but the association of cannabis use with weight in the general population is not known. The
authors used data from 2 representative epidemiologic studies of US adults aged 18 years or older, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; 2001-2002) and the National Comorbidity Survey-Replication (NCS-R; 2001-2003), to estimate the prevalence of obesity as a function of cannabis use. The adjusted prevalences of obesity in the NESARC and the NCS-R were 22.0% and 25.3%, respectively, among participants reporting no use of cannabis in the past 12 months and 14.3% and 17.2%, respectively, among participants reporting the use of cannabis at least 3 days per week. These differences were not accounted for by tobacco smoking status. Additionally, after adjustment for sex and age, the use of cannabis was associated with body mass index differences in both samples. The authors conclude that the prevalence of obesity is lower in cannabis users than in nonusers.

http://dx.doi.org/10.2105/AJPH.2011.300175

OBJECTIVES: We examined the relations of meeting or not meeting the 2008 Physical Activity Guidelines for Americans recommendations for muscular strengthening activities with percentage of body fat, body mass index (BMI; defined as weight in kilograms divided by height in meters, squared), muscular strength, and obesity classification in women. METHODS: We analyzed data on 918 women aged 20 to 83 years in the Women's Injury Study from 2007 to 2009. A baseline orthopedic examination included measurement of height, body weight, skinfolds, and muscle strength. RESULTS: Women who met muscle strengthening activity recommendations had significantly lower BMI and percentage of body fat and higher muscle strength. Women not meeting those recommendations were more likely to be obese (BMI >/= 30) compared with women who met the recommendations after we adjusted for age, race, and aerobic physical activity (odds ratio = 2.28; 95% confidence interval = 1.61, 3.23). CONCLUSIONS: There was a small but significant positive association between meeting muscle strengthening activity recommendations and muscular strength, a moderate inverse association with body fat percentage, and a strong inverse association with obesity classification, providing preliminary support for the muscle strengthening activity recommendation for women.

http://dx.doi.org/10.1001/jama.2011.1203

Health literacy is the degree to which individuals have the capacity to obtain, process, and understand health information, skills, and services needed to make informed health decisions and take informed actions. Narratives from Mr J, a 76-year-old man with multiple medical problems and limited health literacy, and his physician exhibit some of the difficulties experienced by patients with limited health literacy. Clinicians can help patients with limited health literacy by removing unneeded complexity in their treatment regimens and in the health care system and by using teach-back methods to assess and improve understanding. Rather than a selective screening approach for limited health literacy, a patient-based universal precaution approach for confirming patient comprehension of critical self-care activities helps ensure that all patients have their health literacy needs identified.

http://dx.doi.org/10.1186/1471-2458-11-607

BACKGROUND: This paper describes Project FIT, a collaboration between the public school system, local health systems, physicians, neighborhood associations, businesses, faith-based leaders, community agencies and university researchers to develop a multi-faceted approach to promote physical activity and healthy eating toward the general goal of preventing and reducing
childhood obesity among children in Grand Rapids, MI, USA. METHODS/DESIGN: There are four overall components to Project FIT: school, community, social marketing, and school staff wellness - all that focus on: 1) increasing access to safe and affordable physical activity and nutrition education opportunities in the schools and surrounding neighborhoods; 2) improving the affordability and availability of nutritious food in the neighborhoods surrounding the schools; 3) improving the knowledge, self-efficacy, attitudes and behaviors regarding nutrition and physical activity among school staff, parents and students; 4) impacting the ‘culture’ of the schools and neighborhoods to incorporate healthful values; and 5) encouraging dialogue among all community partners to leverage existing programs and introduce new ones. DISCUSSION: At baseline, there was generally low physical activity (70% do not meet recommendation of 60 minutes per day), excessive screen time (75% do not meet recommendation of < 2 hours per day), and low intake of vegetables and whole grains and high intake of sugar-sweetened beverages, French fries and chips and desserts as well as a high prevalence of overweight and obesity (48.5% including 6% with severe obesity) among low income, primarily Hispanic and African American 3rd-5th grade children (n = 403). TRIAL REGISTRATION: ClinicalTrials.gov NCT01385046

(51) AUTIER P, BONIOL M, GAVIN A, VATTEN LJ. Breast cancer mortality in neighbouring European countries with different levels of screening but similar access to treatment: trend analysis of WHO mortality database. BMJ. 2011, vol. 343, p.d4411

OBJECTIVE: To compare trends in breast cancer mortality within three pairs of neighbouring European countries in relation to implementation of screening. DESIGN: Retrospective trend analysis. SETTING: Three country pairs (Northern Ireland (United Kingdom) v Republic of Ireland, the Netherlands v Belgium and Flanders (Belgian region south of the Netherlands), and Sweden v Norway). DATA SOURCES: WHO mortality database on cause of death and data sources on mammography screening, cancer treatment, and risk factors for breast cancer mortality. MAIN OUTCOME MEASURES: Changes in breast cancer mortality calculated from linear regressions of log transformed, age adjusted death rates. Joinpoint analysis was used to identify the year when trends in mortality for all ages began to change. RESULTS: From 1989 to 2006, deaths from breast cancer decreased by 29% in Northern Ireland and by 26% in the Republic of Ireland; by 25% in the Netherlands and by 20% in Belgium and 25% in Flanders; and by 16% in Sweden and by 24% in Norway. The time trend and year of downward inflexion were similar between Northern Ireland and the Republic of Ireland and between the Netherlands and Flanders. In Sweden, mortality rates have steadily decreased since 1972, with no downward inflexion until 2006. Countries of each pair had similar healthcare services and prevalence of risk factors for breast cancer mortality but differing implementation of mammography screening, with a gap of about 10-15 years. CONCLUSIONS: The contrast between the time differences in implementation of mammography screening and the similarity in reductions in mortality between the country pairs suggest that screening did not play a direct part in the reductions in breast cancer mortality

http://dx.doi.org/10.1016/j.socscimed.2011.05.048

Obesity is understood as a major medical and public health challenge, but the stigma attached to it also creates extraordinary suffering. The perversiveness of morally negative views toward the overweight and obese, such as laziness and lack of self-control, are undeniable in mainstream U.S. society, situated both institutionally (such as health care barriers or media stereotypes) and interpersonally (such as the negative comments of others). To test basic pathways related to the etiology of women's vulnerability to feeling "fat-stigma" in interpersonal relationships, we present a study conducted between August and November 2009 that combines social network, anthropometric, body image, and interview data for 112 women aged 18-45 years, living in Phoenix, Arizona, U.S., and linked follow-up interviews with 823 of their social ties. Based on the proposition that some social network characteristics should amplify the personal experience of stigma, and others should ameliorate it, we ask: what relationship qualities make women more sensitive to the judgments of others about their weight? We find that what others say about women has only a very limited influence on how women judge others' negative views of their
weight once actual body size is taken into account, but that women are more influenced by the opinions of those they are closer to and interact with more often. Ultimately, the degree to which women perceive themselves to be judged by others regarding their weight is not well explained by the actual opinions of people in their networks, either known or unknown to them. The assumption that social network norms exert considerable influence on people's stigma experiences needs to be carefully evaluated, at least in the domain of overweight and obesity


http://dx.doi.org/10.1186/1471-2458-11-585

**BACKGROUND:** Brazil is currently experiencing a nutrition transition: the displacement of traditional diets with foods high in saturated fat, sodium, and cholesterol and an increase in sedentary lifestyles. Despite these trends, our understanding of child obesity in Brazil is limited. Thus, the aims of this study were (1) to investigate the current prevalence of overweight and obesity in a large sample of children and adolescents living in Sao Paulo, Brazil, and (2) to identify the lifestyle behaviors associated with an increased risk of obesity in young Brazilians.

**METHODS:** A total of 3,397 children and adolescents (1,596 male) aged 7-18 years were randomly selected from 22 schools in Sao Paulo, Brazil. Participants were classified as normal weight, overweight, or obese based on international age- and sex-specific body mass index thresholds. Selected sociodemographic, physical activity, and nutrition behaviors were assessed via questionnaire. **RESULTS:** Overall, 19.4% of boys and 16.1% of girls were overweight while 8.9% and 4.3% were obese. Two-way analysis of variance revealed that the prevalence of overweight and obesity was significantly higher in boys and in younger children when compared to girls and older children, respectively (P < 0.05 for both). Logistic regression analysis revealed that overweight was associated with more computer usage, parental encouragement to be active, and light soft drink consumption after controlling for differences in sex, age, and parental education (P < 0.05 for all). Conversely, overweight was associated with less active transport to school, eating before sleep, and consumption of breakfast, full-sugar soft drinks, fried food and confectionery (P < 0.05 for all).

**CONCLUSIONS:** Our results show that obesity in Sao Paulo children and adolescents has reached a level equivalent to that seen in many developed countries. We have also identified three key modifiable factors related to obesity that may be appropriate targets for future intervention in Brazilian youth: transport mode to school, computer usage, and breakfast consumption


http://dx.doi.org/10.2105/AJPH.2011.300221

**OBJECTIVES:** We estimated the association between state policy changes and adolescent soda consumption and body mass index (BMI) percentile, overall and by race/ethnicity. **METHODS:** We obtained data on whether states required or recommended that schools prohibit junk food in vending machines, snack bars, concession stands, and parties from the 2000 and 2006 School Health Policies and Programs Study. We used linear mixed models to estimate the association between 2000-2006 policy changes and 2007 soda consumption and BMI percentile, as reported by 90 730 students in 33 states and the District of Columbia in the Youth Risk Behavior Survey, and to test for racial/ethnic differences in the associations. **RESULTS:** Policy changes targeting concession stands were associated with 0.09 fewer servings of soda per day among students (95% confidence interval [CI] = -0.17, -0.01); the association was more pronounced among non-Hispanic Blacks (0.19 fewer servings per day). Policy changes targeting parties were associated with 0.07 fewer servings per day (95% CI = -0.13, 0.00). Policy changes were not associated with BMI percentile in any group. **CONCLUSIONS:** State policies targeting junk food in schools may reduce racial/ethnic disparities in adolescent soda consumption, but their impact appears to be too weak to reduce adolescent BMI percentile
BACKGROUND: The number of overweight children in America has doubled to an estimated 10 million in the past 20 years. Establishing healthy dietary behaviors must begin early in childhood and include parents. The Healthy Toddlers intervention focuses on promoting healthy eating habits in 1- to 3-year-old children utilizing the Social Cognitive Theory and a learner-centered approach using Adult Learning principles. This Healthy Toddlers Trial aims to determine the efficacy of a community-based randomized controlled trial of an in-home intervention with economically and educationally disadvantaged mothers of toddlers. The intervention focuses on: (a) promoting healthy eating behaviors in toddlers while dietary habits are forming; and (b) providing initial evidence for the potential of Healthy Toddlers as a feasible intervention within existing community-based programs. METHODS/DESIGN: This describes the study protocol for a randomized control trial, a multi-state project in Colorado, Michigan, and Wisconsin with economically and educationally disadvantaged mother-toddler dyads; toddlers are between 12 and 36 months. The Healthy Toddlers intervention consists of eight in-home lessons and four reinforcement telephone contacts, focusing on fruit, vegetable, and sweetened beverage consumption and parental behaviors, taught by paraprofessional instructors. Healthy Toddlers uses a randomized, experimental, short-term longitudinal design with intervention and control groups. In-home data collection (anthropometric measurements, feeding observations, questionnaires, 3-day dietary records) occurs at baseline, immediately following the intervention, and 6 months after the intervention. Main toddler outcomes include: a) increased fruit and vegetable consumption and decreased sweetened beverage consumption; and b) improved toddler-eating skills (self-feeding and self-serving). Main parent outcomes include: a) improved psychosocial attributes (knowledge, attitudes, self-efficacy, feeding style) related to child feeding; b) provision of a more positive mealtime physical environment (turning off the TV); and c) creation of a more positive mealtime social environment (sitting down together for meals). DISCUSSION: If this project is successful, the expected outcomes are that the intervention will be effective in helping toddlers develop healthy eating skills that contribute to improve overall health and development and to the prevention of obesity. TRIAL REGISTRATION: Current Controlled Trials ACTRN12610000981022

BACKGROUND: Metabolic syndrome (MS) is associated with subsequent appearance of diabetes and cardiovascular disease. As compared to other Spanish regions, Murcia (southern Spain) registers increased obesity as well as cardiovascular morbidity and mortality. The aim of this study was to assess the prevalence of MS and its components, awareness of obesity as a health risk and associated lifestyles. METHODS: A population-based, cross-sectional study was conducted in 2003, covering a sample of 1555 individuals 20 years and over. MS was defined according to the Revised National Cholesterol Education Program Adult Treatment Panel III (R-ATPIII), International Diabetes Federation (IDF) and Joint Interim Statement (JIS) criteria. Both low (94/80) and high (102/88) waist circumference (WC) thresholds were considered. RESULTS: Prevalence of MS was 27.2% (95%CI: 25.2-29.2), 32.2% (95%CI: 30.1-34.3) and 33.2% (95%CI: 31.2-35.3) according to the R-ATPIII, IDF and JIS94/80 respectively. It increased with age until reaching 52.6% (R-ATPIII) or 60.3% (JIS94/80) among persons aged 70 years and over, and was higher in persons with little or no formal education (51.7% R-ATPIII, 57.3% JIS94/80). The most common risk factors were hypertension (46.6%) and central obesity (40.7% and 66.1% according to high and low WC cut-off points respectively). Although most persons were aware that obesity increased health risks, regular exercise was very unusual (13.0% centrally obese, 27.2% non-centrally obese). Adherence to dietary recommendations was similar among centrally obese and non-centrally obese subjects. CONCLUSIONS: Prevalence of MS is high in our population, is comparable to that found in northern Europe and varies with the definition used. Adherence to
preventive recommendations and to adequate weight promotion is very low. In the absence of a specific treatment for MS, integrated intervention based on a sustained increase in physical activity and changes in diet should be reinforced.


Obesity, gastroesophageal reflux, and smoking have repeatedly been shown to be important and independent risk factors for adenocarcinoma of the esophagus (EAC) and of the gastroesophageal junction (GEJAC). There have been few attempts, however, to quantify the proportion of disease associated with these potentially modifiable factors. The authors have estimated the population attributable fraction of EAC and GEJAC attributable to obesity, symptoms of gastroesophageal reflux, and smoking using data from a population-based case-control study conducted in Australia between 2002 and 2005. Cases were patients with EAC (n = 364) or GEJAC (n = 425). Controls (n = 1,580) were randomly sampled from a population register. Combinations of smoking, body mass index (weight in kilograms divided by height in meters squared), and gastroesophageal reflux together accounted for 76% (95% confidence interval: 66, 84) of EAC cases and 69% (95% confidence interval: 58, 78) of GEJAC cases. Individually, high body mass index (/>=30) and frequent acid reflux (/>=1 time/week) accounted for the greatest proportions of EAC (23% and 36%, respectively), and smoking and frequent symptoms of acid reflux accounted for the greatest proportions of GEJAC (43% and 28%, respectively). The present study suggests that these cancers may be largely prevented by maintaining healthy body mass index, avoiding smoking, and controlling symptomatic gastroesophageal reflux.


BACKGROUND: Weight loss is challenging and maintenance of weight loss is problematic among midlife and older rural women. Finding effective interventions using innovative delivery methods that can reach underserved and vulnerable populations of overweight and obese rural women is a public health challenge. METHODS/DESIGN: This Women Weigh-In for Wellness (The WWW study) randomized-controlled trial is designed to compare the effectiveness of theory-based behavior-change interventions using (1) website only, (2) website with peer-led support, or (3) website with professional email-counseling to facilitate initial weight loss (baseline to 6 months), guided continuing weight loss and maintenance (7-18 months) and self-directed weight maintenance (19-30 months) among rural women ages 45-69 with a BMI of 28-45. Recruitment efforts using local media will target 306 rural women who live within driving distance of a community college site where assessments will be conducted at baseline, 3, 6, 12, 18, 24 and 30 months by research nurses blinded to group assignments. Primary outcomes include changes in body weight, % weight loss, and eating and activity behavioral and biomarkers from baseline to each subsequent assessment. Secondary outcomes will be percentage of women achieving at least 5% and 10% weight loss without regain from baseline to 6, 18, and 30 months and achieving healthy eating and activity targets. Data analysis will use generalized estimating equations to analyze average change across groups and group differences in proportion of participants achieving target weight loss levels. DISCUSSION: The Women Weigh-In for Wellness study compares innovative web-based alternatives for providing lifestyle behavior-change interventions for promoting weight loss and weight maintenance among rural women. If effective, such interventions would offer potential for reducing overweight and obesity among a vulnerable, hard-to-reach, population of rural women. TRIAL REGISTRATION: ClinicalTrials.gov: NCT01307644

BACKGROUND: Intensive combined lifestyle interventions are the recommended treatment for severely obese children and adolescents, but there is a lack of studies and their cost-effectiveness. The objective of this study is to compare the cost-effectiveness of two intensive one-year inpatient treatments and usual care for severely obese children and adolescents.

METHODS/DESIGN: Participants are 40 children aged 8-13 and 40 adolescents aged 13-18 with severe obesity (SDS-BMI ≥ 3.0 or SDS-BMI ≥ 2.3 with obesity related co-morbidity). They will be randomized into two groups that will receive a comprehensive treatment program of 12 months that focuses on nutrition, physical activity and behavior change of the participant and their parents. The two programs are the same in total duration (12 months), but differ in inpatient treatment duration. Group A will participate in a 6 month intensive inpatient treatment program during weekdays, followed by six monthly return visits of 2 days. Group B will participate in a 2 month intensive inpatient treatment program during weekdays, followed by biweekly return visits of 2 days during the next four months, followed by six monthly return visits of 2 days. Several different health care professionals are involved, such as pediatricians, dieticians, psychologists, social workers, nurses and physiotherapists. Results will also be compared to a control group that receives usual care. The primary outcome is SDS-BMI. Secondary outcomes include quality of life using the EQ-5D and cardiovascular risk factors. Data will be collected at baseline and after 6, 12 and 24 months. An economic evaluation will be conducted alongside this study. Healthcare consumption will be based on actual resource use, using prospective data collection during 2 years through cost diaries. Quality Adjusted Life Years (QALYs) will be calculated using the EQ-5D. DISCUSSION: This study will provide useful information on the effectiveness and cost-effectiveness of inpatient treatment in severely obese children and adolescents. Valuable information on long term effects, after 2 years, is also included. TRIAL REGISTRATION: Netherlands Trial Register (NTR): NTR1678


OBJECTIVE: To investigate the relations between causes of death, social position, and obesity in women who had never smoked. DESIGN: Prospective cohort study. SETTING: Renfrew and Paisley, Scotland. PARTICIPANTS: 8353 women and 7049 men aged 45-64 were recruited to the Renfrew and Paisley Study in 1972-6. Of these, 3613 women had never smoked and were the focus of this study. They were categorised by occupational class (I and II, III non-manual, III manual, and IV and V) and body mass index groups (normal weight, overweight, moderately obese, and severely obese). MAIN OUTCOME MEASURES: All cause and cause specific mortality during 28 years of follow-up by occupational class and body mass index, using Cox proportional hazards models adjusted for age and other confounders. RESULTS: The women in lower occupational classes who had never smoked were on average shorter and had poorer lung function and higher systolic blood pressure than women in the higher occupational classes. Overall, 43% (n = 1555) were overweight, 14% (n = 515) moderately obese, and 5% (n = 194) severely obese. Obesity rates were higher in lower occupational classes and much higher in all occupational classes than in current smokers in the full cohort. Half the women died, 51% (n = 916) from cardiovascular disease and 27% (n = 487) from cancer. Relative to occupational class I and II, all cause mortality rates were more than a third higher in occupational classes III manual (relative rate 1.35, 95% confidence interval 1.16 to 1.57) and IV and V (1.34, 1.17 to 1.55) and largely explained by differences in obesity, systolic blood pressure, and lung function. Similar upward gradients were seen for cardiovascular disease and respiratory disease but not for cancer. Mortality rates were highest in severely obese women in the lowest occupational classes. CONCLUSIONS: Women who had never smoked and were not obese had the lowest mortality rates, regardless of their social position. Where obesity is socially patterned as in this cohort, it may contribute to health inequalities and increase pressure on health and social services serving more disadvantaged populations

MACKENBACH JP. What would happen to health inequalities if smoking were eliminated? BMJ. 2011, vol. 342, p.d3460
BACKGROUND: Dental caries (decay) is the most prevalent disease of childhood. It is often left untreated and can impact negatively on general health, and physical, developmental, social and learning outcomes. Similar to other health issues, the greatest burden of dental caries is seen in those of low socio-economic position. In addition, a number of diet-related risk factors for dental caries are shared risk factors for the development of childhood obesity. These include high and frequent consumption of refined carbohydrates (predominately sugars), and soft drinks and other sweetened beverages, and low intake of (fluoridated) water. The prevalence of childhood obesity is also at a concerning level in most countries and there is an opportunity to determine interventions for addressing both of these largely preventable conditions through sustainable and equitable solutions. This study aims to prospectively examine the impact of drink choices on child obesity risk and oral health status. METHODS/DESIGN: This is a two-stage study using a mixed methods research approach. The first stage involves qualitative interviews of a sub-sample of recruited parents to develop an understanding of the processes involved in drink choice, and inform the development of the Discrete Choice Experiment analysis and the measurement instruments to be used in the second stage. The second stage involves the establishment of a prospective birth cohort of 500 children from disadvantaged communities in rural and regional Victoria, Australia (with and without water fluoridation). This longitudinal design allows measurement of changes in the child's diet over time, exposure to fluoride sources including water, dental caries progression, and the risk of childhood obesity. DISCUSSION: This research will provide a unique contribution to integrated health, education and social policy and program directions, by providing clearer policy relevant evidence on strategies to counter social and environmental factors which predispose infants and children to poor health, wellbeing and social outcomes; and evidence-based strategies to promote health and prevent disease through the adoption of healthier lifestyles and diet. Further, given the absence of evidence on the processes and effectiveness of contemporary policy implementation, such as community water fluoridation in rural and regional communities it's approach and findings will be extremely informative.


BACKGROUND: Inexpensive, reliable objective methods are needed to measure physical activity (PA) in large scale trials. This study compared the number of pedometer step counts with accelerometer data in pregnant women in free-living conditions to assess agreement between these measures. METHODS: Pregnant women (n = 58) with body mass index >/=25 kg/m(2) at median 13 weeks' gestation wore a GT1M Actigraph accelerometer and a Yamax Digi-Walker CW-701 pedometer for four consecutive days. The Spearman rank correlation coefficients were determined between pedometer step counts and various accelerometer measures of PA. Total
agreement between accelerometer and pedometer step counts was evaluated by determining the 95% limits of agreement estimated using a regression-based method. Agreement between the monitors in categorising participants as active or inactive was assessed by determining Kappa.

RESULTS: Pedometer step counts correlated moderately ($r = 0.36$ to $0.54$) with most accelerometer measures of PA. Overall step counts recorded by the pedometer and the accelerometer were not significantly different (medians 5961 vs. 5687 steps/day, $p = 0.37$). However, the 95% limits of agreement ranged from -2690 to 2656 steps/day for the mean step count value (6026 steps/day) and changed substantially over the range of values. Agreement between the monitors in categorising participants to active and inactive varied from moderate to good depending on the criteria adopted. CONCLUSIONS: Despite statistically significant correlations and similar median step counts, the overall agreement between pedometer and accelerometer step counts was poor and varied with activity level. Pedometer and accelerometer steps cannot be used interchangeably in overweight and obese pregnant women.

(66) MCPHAIL D, CHAPMAN GE, BEAGAN BL. "Too much of that stuff can't be good": Canadian teens, morality, and fast food consumption. Soc Sci Med. 2011 July, vol. 73, n° 2, pp.301-307
http://dx.doi.org/10.1016/j.socscimed.2011.05.022

Recently, public health agents and the popular media have argued that rising levels of obesity are due, in part, to "obesogenic" environments, and in particular to the clustering of fast food establishments in Western urban centers that are poor and working class. Our findings from a multi-site, cross-national qualitative study of teenaged Canadians’ eating practices in urban and rural areas offer another perspective on this topic, showing that fast food consumption is not simply a function of the location of fast food outlets, and that Canadian teens engage in complex ways with the varied dimensions of choosing (or rejecting) fast foods. Drawing on evidence gleaned from semi-structured interviews with 132 teenagers (77 girls and 55 boys, ages 13-19 years) carried out between 2007 and 2009, we maintain that no easy relationship exists between the geographical availability of fast food and teen eating behaviors. We use critical obesity literature that challenges widely accepted understandings about obesity prevalence and etiology, as well as Lamont's (1992, 2000) concept of "moral boundary work," to argue that teen fast food consumption and avoidance is multifaceted and does not stem exclusively nor directly from spatial proximity or social class. Through moral boundary work, in which teens negotiated with moralistic notions of healthy eating, participants made and re-made themselves as "good" and successful subjects by Othering those who were "bad" in references to socially derived discourses of healthy eating.

http://dx.doi.org/10.1016/j.socscimed.2011.04.014

This paper uses recent longitudinal data about a cohort of young children born in the United States to mostly unmarried parents to examine the association between increasingly-complex patterns of family instability and physical health in early childhood. The analyses assess whether, and how, the association between family instability and child health varies across a number of family types. We consider several measures of children's health at age five (overweight/obesity, asthma diagnosis and overall health) and examine to what extent the association between family instability and child health varies across outcomes and depends on the number and timing of any familial transitions. We also explore a number of potential mechanisms through which family instability may affect child health. The results suggest that familial instability is related to worse child health, particularly among children born to coresident (married or cohabiting) biological parents and for children who experience high levels of residential instability.

http://dx.doi.org/10.2105/AJPH.2010.300115

OBJECTIVES: We investigated whether exposure to negative aspects of close relationships was
associated with subsequent increase in body mass index (BMI) and waist circumference. METHODS: Data came from a prospective cohort study (Whitehall II) of 9425 civil servants aged 35 to 55 years at baseline (phase 1: 1985-1988). We assessed negative aspects of close relationships with the Close Persons Questionnaire (range 0-12) at phases 1 and 2 (1989-1990). We measured BMI and waist circumference at phases 3 (1991-1994) and 5 (1997-1999). Covariates at phase 1 included gender, age, marital status, ethnicity, BMI, employment grade, smoking, physical activity, fruit and vegetable consumption, and common mental disorder. RESULTS: After adjustment for sociodemographic characteristics and health behaviors, participants with higher exposure to negative aspects of close relationships had a higher likelihood of a 10% or greater increase in BMI and waist circumference (odds ratios per 1-unit increase 1.08 [95% confidence interval (CI) =1.02, 1.14; P = .007] and 1.09 [CI = 1.04, 1.14; P \leq .001], respectively) as well as a transition from the overweight (25 \leq BMI < 30) to the obese (BMI \geq 30) category. CONCLUSIONS: Adverse social relationships may contribute to weight gain


In Canada, tax incentives have been recently introduced to promote physical activity and reduce rates of obesity. The most prominent of these is the federal government's Children's Fitness Tax Credit, which came into effect in 2007. We critically assess the potential benefits and limitations of using tax measures to promote physical activity. Careful design could make these measures more effective, but any tax-based measures have inherent limitations, and the costs of such programs are substantial. Therefore, it is important to consider whether public funds are better spent on other strategies that could instead provide direct public funding to address environmental and systemic factors


BACKGROUND: The Swiss Health Survey (SHS) provides the only source of data for monitoring overweight and obesity in the general population in Switzerland. However, this survey reports body mass index (BMI) based on self-reported height and weight, and is therefore subject to measurement errors. Moreover, it is not possible to differentiate between overall and abdominal overweight. In this study, we aimed to gain a better understanding of the need for weight management in the general population of Switzerland by exploring and comparing prevalence rates of BMI and waist circumference (WC) based on physical measurements by trained observers, based on data from the 2009 National Blood Pressure Week (NBPW). METHODS: Sample selection was based on a one-stage cluster design. A total of 385 pharmacies representing 3,600 subjects were randomly selected from pharmacies participating in NBPW. BMI measures based on physical weight and height (NBPW) were compared with self-reported BMI measures from the SHS. BMI and WC measurements from NBPW were then used to produce population estimates of overweight and obesity. RESULTS: BMI-based overall prevalence of overweight and obesity was 43.6%, which was 4.7% higher than the value based on the respective SHS data. Overweight and obesity were more common in men (54.3%) than in women (33.5%). However, the overall prevalence of increased WC in the general population was estimated to be 64.4%, with more women (68.4%) than men (60.1%) exhibiting a WC above the threshold. The prevalence of subjects requiring weight management in the Swiss population remained high, even after adjusting WC for false positive and negative cases. CONCLUSIONS: Firstly, it may be more appropriate for health promotion programs to address the wider group identified by WC, which includes subjects who need to reduce their weight, or gain no further weight. Secondly, the gender differences are reversed depending on the use of WC or BMI to identify subjects suitable for health promotion programs; more women than men are identified by WC, and more men than women using BMI. These differences should be accounted for in gender-specific health promotion programs
http://dx.doi.org/10.1093/aje/kwr093

The authors aimed to explore optimal cutoffs for high-risk waist circumference (WC) in older adults to assess the health risks of obesity. Prospective data from 4,996 measurements in 2,232 participants aged >/=70 years were collected during 5 triennial measurement cycles (1992/1993-2005/2006) of a population-based cohort study, the Longitudinal Aging Study Amsterdam (Amsterdam, the Netherlands). Cross-sectional associations of WC with pain, mobility limitations, incontinence, knee osteoarthritis, cardiovascular disease, and diabetes were studied. Generalized estimating equations models were fitted with restricted cubic spline functions in order to carefully study the shapes of the associations. Model fits for applying different cutoffs to categorize WC in the association with all outcomes were tested using the quasi-likelihood under the Independence Criterion (QIC). On the basis of the spline regression curves, potential WC cutoffs of approximately 109 cm in men and 98 cm in women were proposed. Based on the model fit, cutoffs between 100 cm and 106 cm were equally applicable in men but should not be higher. In women, the QIC confirmed an optimal cutoff of 99 cm.

http://dx.doi.org/10.1093/ije/dyr085

http://dx.doi.org/10.1186/1471-2458-11-438

BACKGROUND: Large soft drinks sizes increase consumption, and thereby contribute to obesity. Portion size labelling may help consumers to select more appropriate food portions. This study aimed to assess the effectiveness of portion size and caloric Guidelines for Daily Amounts (GDA) labelling on consumers' portion size choices and consumption of regular soft drinks. METHODS: A field experiment that took place on two subsequent evenings in a Dutch cinema. Participants (n=101) were asked to select one of five different portion sizes of a soft drink. Consumers were provided with either portion size and caloric GDA labelling (experimental condition) or with millilitre information (control condition). RESULTS: Labelling neither stimulated participants to choose small portion sizes (OR = .75, p = .61, CI: .25 - 2.25), nor did labelling dissuade participants to choose large portion sizes (OR = .51, p = .36, CI: .12 - 2.15). CONCLUSIONS: Portion size and caloric GDA labelling were found to have no effect on soft drink intake. Further research among a larger group of participants combined with pricing strategies is required. The results of this study are relevant for the current public health debate on food labelling.

http://dx.doi.org/10.1186/1471-2458-11-431

BACKGROUND: More than 20% of US children ages 2-5 yrs are classified as overweight or obese. Parents greatly influence the behaviors their children adopt, including those which impact weight (e.g., diet and physical activity). Unfortunately, parents often fail to recognize the risk for excess weight gain in young children, and may not be motivated to modify behavior. Research is needed to explore intervention strategies that engage families with young children and motivate parents to adopt behaviors that will foster healthy weight development. METHODS: This study tests the efficacy of the 35-week My Parenting SOS intervention. The intervention consists of 12 sessions; initial sessions focus on general parenting skills (stress management, effective parenting styles, child behavior management, coparenting, and time management) and later sessions apply these skills to promote healthier eating and physical activity habits. The primary
outcome is change in child percent body fat. Secondary measures assess parent and child dietary intake (three 24-hr recalls) and physical activity (accelerometry), general parenting style and practices, nutrition- and activity-related parenting practices, and parent motivation to adopt healthier practices. DISCUSSION: Testing of these new approaches contributes to our understanding of how general and weight-specific parenting practices influence child weight, and whether or not they can be changed to promote healthy weight trajectories. TRIAL REGISTRATION: ClinicalTrials.gov: NCT00998348


OBJECTIVE: To determine whether initial improvements in obstructive sleep apnoea after a very low energy diet were maintained after one year in patients with moderate to severe obstructive sleep apnoea. DESIGN: Single centre, prospective observational follow-up study. SETTING: Outpatient obesity clinic in a university hospital in Stockholm, Sweden. PARTICIPANTS: 63 men aged 30-65 with body mass index (BMI) 30-40 and moderate to severe obstructive sleep apnoea defined as an apnoea-hypopnoea index $\geq$ 15 (events/hour), all treated with continuous positive airway pressure. INTERVENTION: A one year weight loss programme, consisting of an initial very low energy diet for nine weeks (seven weeks of 2.3 MJ/day and two weeks of gradual introduction of normal food) followed by a weight loss maintenance programme. MAIN OUTCOME MEASURE: Apnoea-hypopnoea index, the main index for severity of obstructive sleep apnoea. Data from all patients were analysed (baseline carried forward for missing data). RESULTS: Of 63 eligible patients, 58 completed the very low energy diet period and started the weight maintenance programme and 44 completed the full programme; 49 had complete measurements at one year. At baseline the mean apnoea-hypopnoea index was 36 events/hour. After the very low energy diet period, apnoea-hypopnoea index was improved by -21 events/hour (95% confidence interval -17 to -25) and weight by -18 kg (-16 to -19; both P<0.001). After one year the apnoea-hypopnoea index had improved by -17 events/hour (-13 to -21) and body weight by -12 kg (-10 to -14) compared with baseline (both P<0.001). Patients with severe obstructive sleep apnoea at baseline had greater improvements in apnoea-hypopnoea index (-25 events/hour) compared with patients with moderate disease (-7 events/hour, P<0.001). At one year, 30/63 (48%, 95% confidence interval 35% to 60%) no longer required continuous positive airway pressure and 6/63 (10%, 2% to 17%) had total remission of obstructive sleep apnoea (apnoea-hypopnoea index <5 events/hour). There was a dose-response association between weight loss and apnoea-hypopnoea index at follow-up (beta = 0.50 events/kg, 0.11 to 0.88; P = 0.013). CONCLUSION: Initial improvements in obstructive sleep apnoea after treatment with a very low energy diet can be maintained after one year in obese men with moderate to severe disease. Those who lose the most weight or have severe sleep apnoea at baseline benefit most. Trial registration Current Controlled Trials 70090382


BACKGROUND: We examined ethnic differences between levels of body mass index (BMI) based on self-reported and measured body height and weight and the validity of self-reports used to estimate the prevalence of obesity (BMI$\geq$30 kg/m2) in Turkish, Moroccan, and Dutch people in the Netherlands. Furthermore, we investigated whether BMI levels and the prevalence of obesity in Turkish and Moroccan people with incomplete self-reports (missing height or weight) differ from those with complete self-reports. METHODS: Data on self-reported and measured height and weight were collected in a population-based survey among 441 Dutch, 414 Turks and 344 Moroccans aged 18 to 69 years in Amsterdam, the Netherlands in 2004. BMI and obesity were calculated from self-reported and measured height and weight. RESULTS: The difference between measured and estimated BMI was larger in Turkish and Moroccan women than in Dutch women, which was explained by the higher BMI of the Turkish and Moroccan women. In men we
found no ethnic differences between measured and estimated BMI. Sensitivity to detect obesity was low and specificity was high. In participants with available self-reported and measured height and weight, self-reports produced a similar underestimation of the obesity prevalence in all ethnic groups. However, many obese Turkish and Moroccan women had incomplete self-reports, missing height or weight, resulting in an additional underestimation of the prevalence of obesity. Among men (all ethnicities) and Dutch women, the availability of height or weight by self-report did not differ between obese and non-obese participants. CONCLUSIONS: BMI based on self-reports is underestimated more by Turkish and Moroccan women than Dutch women, which is explained by the higher BMI of Turkish and Moroccan women. Further, in women, ethnic differences in the estimation of obesity prevalence based on self-reports do exist and are due to incomplete self-reports in obese Turkish and Moroccan women. In men, ethnicity is not associated with discrepancies between levels of BMI and obesity prevalence based on measurements and self-reports. Hence, our results indicate that using measurements to accurately determine levels of BMI and obesity prevalence in public health research seems even more important in Turkish and Moroccan migrant women than in other populations.

http://dx.doi.org/10.1186/1471-2458-11-378

BACKGROUND: To avoid strong declines in the quality of life due to population ageing, and to ensure sustainability of the health care system, reductions in the burden of disability among elderly populations are urgently needed. Life style interventions may help to reduce the years lived with one or more disabilities, but it is not fully understood which life style factor has the largest potential for such reductions. Therefore, the primary aim of this paper is to compare the effect of BMI, smoking and alcohol consumption on life expectancy with disability, using the Sullivan life table method. A secondary aim is to assess potential improvement of the Sullivan method by using information on the association of disability with time to death. METHODS: Data from the Dutch Permanent Survey of the Living Situation (POLS) 1997-1999 with mortality follow-up until 2006 (n = 6,446) were used. Using estimated relative mortality risks by risk factor exposure, separate life tables were constructed for groups defined in terms of BMI, smoking status and alcohol consumption. Logistic regression models were fitted to predict the prevalence of ADL and mobility disabilities in relationship to age and risk factor exposure. Using the Sullivan method, predicted age-specific prevalence rates were included in the life table to calculate years lived with disability at age 55. In further analysis we assessed whether adding information on time to death in both the regression models and the life table estimates would lead to substantive changes in the results. RESULTS: Life expectancy at age 55 differed by 1.4 years among groups defined in terms of BMI, 4.0 years by smoking status, and 3.0 years by alcohol consumption. Years lived with disability differed by 2.8 years according to BMI, 0.2 years by smoking and 1.6 by alcohol consumption. Obese persons could expect to live more years with disability (5.9 years) than smokers (3.8 years) and drinkers (3.1 years). Employing information on time to death led to lower estimates of years lived with disability, and to smaller differences in these years according to BMI (2.1 years), alcohol (1.2 years), and smoking (0.1 years). CONCLUSIONS: Compared with smoking and drinking alcohol, obesity is most strongly associated with an increased risk of spending many years of life with disability. Although employing information on the relation of disability with time to death improves the precision of Sullivan life table estimates, the relative importance of risk factors remained unchanged.

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BACKGROUND: Snus is a moist smokeless tobacco product which has recently reached beyond its original market of Scandinavia. Snus is now being increasingly used in both the United States and South Africa. The effect of snus use on weight is unknown. This study has therefore investigated the relationship between the use of snus, weight gain (>/>=5%) and the incidence of obesity (body mass index >/=30 kg/m(2)). METHODS: The study participants (n = 9,954 males living in Stockholm County, Sweden) were recruited in 2002 and reassessed in 2007. Tobacco
use was categorized according to information obtained in both the baseline and follow-up surveys. Outcomes were assessed by comparing self-reported weight and body mass index between the baseline and follow-up surveys. RESULTS: Stable current snus use (according to both surveys), compared to never having used any kind of tobacco, seemed to be associated with both weight gain (odds ratio = 1.31, 95% confidence interval: 1.04-1.65) and incident obesity (odds ratio = 1.93, 95% confidence interval: 1.13-3.30) after adjustment for age, baseline weight, alcohol consumption, physical activity, education, consumption of fruit and berries, and the frequency of having breakfast. No associations with incident obesity or weight gain were seen for stable former users of snus (according to both surveys) or among men who quit or began using snus during follow-up. CONCLUSIONS: These data suggest that the use of snus is moderately associated with weight gain and incident obesity among men.

http://dx.doi.org/10.1186/1471-2458-11-365

BACKGROUND: Obesity is on the rise worldwide, not sparing developing countries. Both demographic and socio-economic factors play parts in obesity causation. Few surveys have been conducted in Tanzania to determine the magnitude of obesity and its association with these risk factors. This study aimed at determining the prevalence of obesity and its associated risk factors among adults aged 18 - 65 years in Kinondoni municipality, Dar es Salaam, Tanzania from April 2007 to April 2008. METHODS: Random sampling of households was performed. Interviews and anthropometric measurement were carried out to eligible and consenting members of the selected households. Obesity was defined using Body Mass Index (BMI). RESULTS: Out of 1249 subjects recruited, 814 (65.2%) were females. The overall prevalence of obesity was 19.2% (240/1249). However, obesity was significantly more prevalent in women (24.7%) than men (9%), p < 0.001, among respondents with high socio-economic status (29.2%) as compared to those with medium (14.3%) and low socio-economic status (11.3%), p value for trend < 0.001, and among respondents with light intensity activities (26.0%), p value for trend < 0.001. CONCLUSION: This study revealed a higher prevalence of obesity among Kinondoni residents than previously reported in other parts of the country. Independent predictors of obesity in the population studied were increasing age, marriage and cohabitation, high SES, female sex and less vigorous physical activities.

http://dx.doi.org/10.1186/1471-2458-11-363

BACKGROUND: Weight loss is known to decrease the health risks associated with being overweight and obese. Awareness of overweight status is an important determinant of weight loss attempts and may have more of an impact on one's decision to lose weight than objective weight status. We therefore investigated the perception of weight among adults attending primary care clinics in Karachi, Pakistan, and compared it to their weight categories based on BMI (Body Mass Index), focusing on the underestimation of weight in overweight and obese individuals. We also explored the factors associated with underestimation of weight in these individuals. METHODS: This was a cross sectional study conducted on 493 adults presenting to the three primary care clinics affiliated with a tertiary care hospital in Karachi, Pakistan. We conducted face to face interviews to gather data on a pre-coded questionnaire. The questionnaire included detail on demographics, presence of comorbid conditions, and questions regarding weight assessment. We measured height and weight of the participants and calculated the BMI. The BMI was categorized into normal weight, overweight and obese based on the revised definitions for Asian populations. Perception about weight was determined by asking the study participants the following question: Do you consider yourself to be a) thin b) just right c) overweight d) obese. We compared the responses with the categorized BMI. To identify factors associated with underestimation of weight, we used simple and multiple logistic regression to calculate crude odds Ratios (OR) and adjusted Odds Ratios (AOR) with 95% Confidence Intervals. RESULTS: Overall 45.8% (n = 226) of the
study participants were obese and 18% (n = 89) were overweight. There was poor agreement between self perception and actual BMI (Kappa = 0.24, SE = 0.027, p < 0.001). Among obese participants a large proportion (73%) did not perceive themselves as obese, although half (n = 102) of them thought they may be overweight. Among the overweight participants, half (n = 41) of them didn't recognize themselves as overweight. Factors associated with misperception of weight in overweight and obese participants were age >/= 40 years (AOR = 3.4; 95% CI: 1.8-6.4), male gender (AOR = 2.97; 95% CI: 1.6-5.5), being happy with ones' weight (AOR = 6.4; 95% CI: 3.4-12.1), and not knowing one's ideal weight (AOR = 2.45, 95% CI: 1.10-5.47). CONCLUSION: In this cross sectional survey, we observed marked discordance between the actual and perceived weight. Underestimation of individual weight was more common in older participants (>/= 40 years), men, participants happy with their weight and participants not aware of their ideal weight. Accurate perception of one's actual weight is critical for individuals to be receptive to public health messages about weight maintenance or weight loss goals. Therefore educating people about their correct weight, healthy weights and prevention of weight gain are important steps towards addressing the issue of obesity in Pakistan

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BACKGROUND: Studies have confirmed that the rate of mental illness is no higher in rural Australians than that of urban Australians. However, the rate of poor mental health outcomes, and in particular suicide, is significantly raised in rural populations. This is thought to be due to lack of early diagnosis, health service access, the distance-decay effect, poor physical health determinants and access to firearms. Research conducted by the National Centre for Farmer Health between 2004 and 2009 reveals that there is a correlation between obesity and psychological distress among the farming community where suicide rates are recognised as high. Chronic stress overstimulates the regulation of the hypothalamic-pituitary-adrenal (HPA) axis that is associated with abdominal obesity. Increasing physical activity may block negative thoughts, increase social contact, positively influence brain chemistry and improve both physical and mental health. This paper describes the design of the Farming Fit study that aims to identify the effect of physical activity on psychological distress, obesity and health behaviours such as diet patterns and smoking in farm men and women. METHODS/DESIGN: For this quasi-experimental (convenience sample) control-intervention study, overweight (Body Mass Index >/=25 kg/m(2)) farm men and women will be recruited from Sustainable Farm Families (SFF) programs held across Victoria, Australia. Baseline demographic data, health data, depression anxiety stress scale (DASS) scores, dietary information, physical activity data, anthropometric data, blood pressure and biochemical analysis of plasma and salivary cortisol levels will be collected. The intervention group will receive an exercise program and regular phone coaching in order to increase their physical activity. Analysis will evaluate the impact of the intervention by longitudinal data (baseline and post intervention) comparison of intervention and control groups.

DISCUSSION: This study is designed to examine the effect of physical activity on psychological health and other co-morbidities such as obesity, impaired glucose tolerance, hypertension and dyslipidaemia within a high-risk cohort. The outcomes of this research will be relevant to further research and service delivery programs, in particular those tailored to rural communities. TRIAL REGISTRATION: ACTRN12610000827033

http://dx.doi.org/10.1186/1471-2458-11-350

BACKGROUND: The implementation project of the national diabetes prevention programme in Finland, FIN-D2D, was carried out in primary health care in the area of five hospital districts during 2003-2007. METHODS: The population strategy of FIN-D2D was primarily aimed at increasing the awareness of type 2 diabetes and preventing obesity. To investigate the effects of this strategy, we studied the changes in the prevalence of obesity, overweight, and central obesity among a
random independent sample of individuals aged 45-74 years in the FIN-D2D area; and assessed whether they differed from a sample of individuals in the control area, which consisted of four geographical areas not participating in FIN-D2D (FINRISK study). Data was obtained for 5850/6406 (in the beginning/ in the end) individuals. The duration of the observation period varied from three to five years. RESULTS: The mean body weight decreased from 78.7 to 78.1 kg (p = 0.041) in the FIN-D2D area, and from 78.7 to 78.0 kg (p = NS) in the control area. The prevalence of obesity (BMI >/=30 kg/m(2)) decreased in the FIN-D2D area (26.5% vs. 24.4%, p = 0.015), and in the control area (28.4% vs. 25.2%, p = 0.005). The prevalence of morbidity obesity (BMI >/=40 kg/m(2)) remained unchanged in the FIN-D2D area, but increased in the control area (1.2% vs. 2.3%, p = 0.007). The mean waist circumference remained unchanged in the FIN-D2D area, but increased in the control area (92.8 vs. 94.0 cm, p = 0.005). CONCLUSIONS: The prevalence of obesity may be decreasing among 45-74 year old Finns. We still need a longer time perspective and future studies to see whether this favourable trend can be sustained in Finland. The actions of this implementation project can at least partly explain the differences in the mean waist circumference and the prevalence of morbid obesity between the intervention and control areas.

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BACKGROUND: Overweight and obesity have a dramatic negative impact on children's health not only during the childhood but also throughout the adult life. Preventing the development of obesity in children is therefore a world-wide health priority. There is an obvious urge for sustainable and evidenced-based interventions that are suitable for families with young children, especially for families with overweight or obese parents. We have developed a prevention program, Early STOPP, combating multiple obesity-promoting behaviors such as unbalanced diet, physical inactivity and disturbed sleeping patterns. We also aim to evaluate the effectiveness of the early childhood obesity prevention in a well-characterized population of overweight or obese parents. This protocol outlines methods for the recruitment phase of the study. DESIGN AND METHODS: This randomized controlled trial (RCT) targets overweight and/or obese parents with infants, recruited from the Child Health Care Centers (CHCC) within the Stockholm area. The intervention starts when infants are one year of age and continues until they are six and is regularly delivered by a trained coach (dietitian, physiotherapist or a nurse). The key aspects of Early STOPP family intervention are based on Swedish recommendations for CHCC, which include advices on healthy food choices and eating patterns, increasing physical activity/reducing sedentary behavior and regulating sleeping patterns. DISCUSSION: The Early STOPP trial design addresses weaknesses of previous research by recruiting from a well-characterized population, defining a feasible, theory-based intervention and assessing multiple measurements to validate and interpret the program effectiveness. The early years hold promise as a time in which obesity prevention may be most effective. To our knowledge, this longitudinal RCT is the first attempt to demonstrate whether an early, long-term, targeted health promotion program focusing on healthy eating, physical activity/reduced sedentary behaviors and normalizing sleeping patterns could be effective. If proven so, Early STOPP may protect children from the development of overweight and obesity. TRIAL REGISTRATION: The protocol for this study is registered with the clinical trials registry clinicaltrials.gov, ID: ES-2010)

http://dx.doi.org/10.1186/1471-2458-11-333

BACKGROUND: With the increasing prevalence of childhood obesity, the metabolic syndrome has been studied among children in many countries but not in Malaysia. Hence, this study aimed to compare metabolic risk factors between overweight/obese and normal weight children and to determine the influence of gender and ethnicity on the metabolic syndrome among school children aged 9-12 years in Kuala Lumpur and its metropolitan suburbs. METHODS: A case control study was conducted among 402 children, comprising 193 normal-weight and 209 overweight/obese.
Weight, height, waist circumference (WC) and body composition were measured, and WHO (2007) growth reference was used to categorise children into the two weight groups. Blood pressure (BP) was taken, and blood was drawn after an overnight fast to determine fasting blood glucose (FBG) and full lipid profile, including triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC). International Diabetes Federation (2007) criteria for children were used to identify metabolic syndrome.

RESULTS: Participants comprised 60.9% (n = 245) Malay, 30.9% (n = 124) Chinese and 8.2% (n = 33) Indian. Overweight/obese children showed significantly poorer biochemical profile, higher body fat percentage and anthropometric characteristics compared to the normal-weight group. Among the metabolic risk factors, WC >/=90th percentile was found to have the highest odds (OR = 189.0; 95%CI 70.8, 504.8), followed by HDL-C</=1.03 mmol/L (OR = 5.0; 95%CI 2.4, 11.1) and high BP (OR = 4.2; 95%CI 1.3, 18.7). Metabolic syndrome was found in 5.3% of the overweight/obese children but none of the normal-weight children (p < 0.01). Overweight/obese children had higher odds (OR = 16.3; 95%CI 2.2, 461.1) of developing the metabolic syndrome compared to normal-weight children. Binary logistic regression showed no significant association between age, gender and family history of communicable diseases with the metabolic syndrome. However, for ethnicity, Indians were found to have higher odds (OR = 5.5; 95%CI 1.5, 20.5) compared to Malays, with Chinese children (OR = 0.3; 95%CI 0.0, 2.7) having the lowest odds.

CONCLUSIONS: We conclude that being overweight or obese poses a greater risk of developing the metabolic syndrome among children. Indian ethnicity is at higher risk compared to their counterparts of the same age. Hence, primary intervention strategies are required to prevent this problem from escalating.

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BACKGROUND: Obesity has increased since the early 1980s, and despite numerous attempts, effective strategies to counter this worldwide epidemic are lacking. Food preferences are established early in life and are difficult to change later. There is therefore a need to identify factors that influence the development of food preferences. Our aim was therefore, to investigate cross-sectional and prospective associations between TV viewing habits and food preferences and habits, respectively. We hypothesized that more TV viewing was associated with less healthy concomitant and future food preferences and food habits. METHODS: Data are from the Danish part of European Youth Heart Study (EYHS) I and II, a prospective cohort study conducted among 8-10-year-old and 14-16-year-old Danes in 1997-98. Six years later 2003-04 the 8-10-year-olds were followed up at age 14-16 years, and a new group of 8-10-year olds were included. Data were analysed using mixed linear regression analysis. Cross-sectional analyses included 697 8-10-year-olds and 495 14-16-year-olds. Prospective analyses included 232 pupils with complete data at baseline and follow-up. Associations between TV viewing habits and the sum of healthy food preferences (SigmaHFP), and the sum of healthy food habits (SigmaHFH), respectively, were examined. RESULTS: Inverse cross-sectional associations between TV viewing (h/day) and both SigmaHFP and SigmaHFH were present for both the 8-10-year-old and the 14-16-year-old boys and girls. The frequency of meals in front of the TV (times/week) was also inversely associated with SigmaHFP among 8-10-year-old boys, and with SigmaHFH in all sex- and age groups. Among girls, baseline TV viewing (h/day) was directly associated with adverse development in the SigmaHFP during follow-up. The concomitant 6-year changes in SigmaHFP and TV viewing (h/day) were inversely associated in boys. CONCLUSIONS: Long time spent on TV viewing, and possibly to a lesser degree, frequent consumption of meals during TV viewing, seem to be associated with generally having unhealthy food preferences and food habits among school-aged children. These associations, however, were not generally persistent after 6 years of follow-up.

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Obesity prevalence among inmates in the United States is unknown. Since incarceration disproportionately affects minorities, excluding inmates from surveys may bias national obesity estimates. Including inmates may also help explain racial obesity disparities among men. This descriptive study summarizes obesity prevalence among US male inmates and analyzes the effect of incarceration on national prevalence estimates. Data for male inmates came from the 2002 Survey of Inmates in Local Jails and the 2004 Survey of Inmates in State and Federal Correctional Facilities. Data for the non-incarcerated US adult male population came from the 2004 National Health Interview Survey. Self-reported weight and height data were analyzed from men aged 25-59 years for all surveys (obesity equaled BMI >= 30.0 kg/m(2)). Pooled inmate obesity prevalence was less than non-incarcerated estimates across all race/ethnic-education subgroups. However, unlike non-incarcerated estimates, inmates had obesity disparities between Hispanics and non-Hispanic Whites. Merging inmate and non-incarcerated estimates lowered obesity prevalence among men aged 25-39 with lower education levels. Merged estimates showed a positive obesity gradient within Whites by education. This study indicates that the exclusion of inmates from national obesity estimates leads to overestimates in obesity prevalence, particularly for low SES White and Black men.


The rapid speed of the recent rise in obesity rates suggest environmental causes. There is therefore a need to determine which components of the environment may be contributing to this increase. In this cross-sectional study, we examined the associations between adiposity and the characteristics of areas around homes, schools and routes to school among 1995 9-10 year old boys and girls in Norfolk, UK. The relationships between Fat Mass Index (FMI, calculated as fat mass (kg)/height (m)(2)) and objectively computed environmental indicators describing access to food outlets and physical activity facilities, the safety and connectivity of the road network, and the mix of land uses present were investigated. Multivariable hierarchical regression models were fitted with log-transformed FMI as the outcome, and stratification by gender and mode of travel to school. Among girls, better access to healthy food outlets (supermarkets and greengrocers) in the home environment was associated with lower FMI while better access to unhealthy outlets (takeaways and convenience stores) around homes and schools was associated with higher FMI. Also in girls, a higher proportion of accessible open land and a lower mix of land uses around the school were associated with higher FMI. Among boys the presence of major roads in the home neighbourhood was associated with higher FMI among non-active travellers, while major roads in the school neighbourhood were associated with lower FMI among active travellers. No significant associations were seen between FMI and any of the route characteristics. While the relative paucity of associations provides few indicators for the design of effective interventions, there was some evidence that environmental characteristics may be more important among active travellers than non-active travellers, and among girls than boys, suggesting that future interventions should be sensitive to such differences.


Childhood obesity is a public health concern with significant health and economic impacts. We conducted a prospective experimental study in 4 classrooms in central Texas to determine the effect of desks that encourage standing rather than sitting on caloric expenditure in children. Students were monitored with calorie expenditure-measuring arm-bands worn for 10 days in the fall and spring. The treatment group experienced significant increases in calorie expenditure over the control group, a finding that has implications for policy and practice.
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BACKGROUND: A novel approach is explored for improving causal inference in observational studies by comparing cohorts from high-income with low- or middle-income countries (LMIC), where confounding structures differ. This is applied to assessing causal effects of breastfeeding on child blood pressure (BP), body mass index (BMI) and intelligence quotient (IQ). METHODS: Standardized approaches for assessing the confounding structure of breastfeeding by socio-economic position were applied to the British Avon Longitudinal Study of Parents and Children (ALSPAC) (N approximately 5000) and Brazilian Pelotas 1993 cohorts (N approximately 1000). This was used to improve causal inference regarding associations of breastfeeding with child BP, BMI and IQ. Analyses were extended to include results from a meta-analysis of five LMICs (N approximately 10 000) and compared with a randomized trial of breastfeeding promotion. Findings Although higher socio-economic position was strongly associated with breastfeeding in ALSPAC, there was little such patterning in Pelotas. In ALSPAC, breastfeeding was associated with lower BP, lower BMI and higher IQ, adjusted for confounders, but in the directions expected if due to socioeconomic patterning. In contrast, in Pelotas, breastfeeding was not strongly associated with BP or BMI but was associated with higher IQ. Differences in associations observed between ALSPAC and the LMIC meta-analysis were in line with those observed between ALSPAC and Pelotas, but with robust evidence of heterogeneity detected between ALSPAC and the LMIC meta-analysis associations. Trial data supported the conclusions inferred by the cross-cohort comparisons, which provided evidence for causal effects on IQ but not for BP or BMI. CONCLUSION: While reported associations of breastfeeding with child BP and BMI are likely to reflect residual confounding, breastfeeding may have causal effects on IQ. Comparing associations between populations with differing confounding structures can be used to improve causal inference in observational studies

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OBJECTIVES: We used qualitative and quantitative data collection methods to identify the health concerns of African American residents in an urban community and analyzed the extent to which there were consistencies across methods in the concerns identified. METHODS: We completed 9 focus groups with 51 residents, 27 key informant interviews, and 201 community health surveys with a random sample of community residents to identify the health issues participants considered of greatest importance. We then compared the issues identified through these methods. RESULTS: Focus group participants and key informants gave priority to cancer and cardiovascular diseases, but most respondents in the community health survey indicated that sexually transmitted diseases, substance abuse, and obesity were conditions in need of intervention. How respondents ranked their concerns varied in the qualitative versus the quantitative methods. CONCLUSIONS: Using qualitative and quantitative approaches simultaneously is useful in determining community health concerns. Although quantitative approaches yield concrete evidence of community needs, qualitative approaches provide a context for how these issues can be addressed. Researchers should develop creative ways to address multiple issues that arise when using a mixed-methods approach

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BACKGROUND: Dietary studies differ in design and quality making it difficult to compare results. This study quantifies the prospective association between dietary energy density (DED) and adiposity in children using a meta-analysis method that adjusts for differences in design and
quality through eliciting and incorporating expert opinion on the biases and their uncertainty. 

METHOD: Six prospective studies identified by a previous systematic literature search were included. Differences in study quality and design were considered respectively as internal and external biases and captured in bias checklists. Study results were converted to correlation coefficients; biases were considered either additive or proportional on this scale. The extent and uncertainty of the internal and external biases in each study were elicited in a formal process by five quantitatively-trained assessors and five subject-matter specialists. Biases for each study were combined across assessors using median pooling and results combined across studies by random-effects meta-analysis. 

RESULTS: The unadjusted combined correlation between DED and adiposity change was 0.06 (95%CI 0.01, 0.11; p = 0.013), but with considerable heterogeneity (I(2) = 52%). After bias-adjustment the pooled correlation was 0.17 (95%CI - 0.11, 0.45; p = 0.24), and the studies were apparently compatible (I(2) = 0%). 

CONCLUSIONS: This method allowed quantitative synthesis of the prospective association between DED and adiposity change in children, which is important for the development of evidence-informed policy. Bias adjustment increased the magnitude of the positive association but the widening confidence interval reflects the uncertainty of the assessed biases and implies that higher quality studies are required.


BACKGROUND: Childhood overweight and obesity is the most prevalent and, arguably, politically complex child health problem internationally. Governments, communities and industry have important roles to play, and are increasingly expected to deliver an evidence-informed system-wide prevention program. However, efforts are impeded by a lack of organisational access to and use of research evidence. This study aims to identify feasible, acceptable and ideally, effective knowledge translation (KT) strategies to increase evidence-informed decision-making in local governments, within the context of childhood obesity prevention as a national policy priority.

METHODS/DESIGN: This paper describes the methods for KT4LG, a cluster randomised controlled trial which is exploratory in nature, given the limited evidence base and methodological advances. KT4LG aims to examine a program of KT strategies to increase the use of research evidence in informing public health decisions in local governments. KT4LG will also assess the feasibility and acceptability of the intervention. The intervention program comprises a facilitated program of evidence awareness, access to tailored research evidence, critical appraisal skills development, networking and evidence summaries and will be compared to provision of evidence summaries alone in the control program. 28 local governments were randomised to intervention or control, using computer generated numbers, stratified by budget tertile (high, medium or low). Questionnaires will be used to measure impact, costs, and outcomes, and key informant interviews will be used to examine processes, feasibility, and experiences. Policy tracer studies will be included to examine impact of intervention on policies within relevant government policy documents. 

DISCUSSION: Knowledge translation intervention studies with a focus on public health and prevention are very few in number. Thus, this study will provide essential data on the experience of program implementation and evaluation of a system-integrated intervention program employed within the local government public health context. Standardised programs of system, organisational and individual KT strategies have not been described or rigorously evaluated. As such, the findings will make a significant contribution to understanding whether a facilitated program of KT strategies hold promise for facilitating evidence-informed public health decision making within complex multisectoral government organisations. 

TRIAL REGISTRATION: Australia and New Zealand Clinical Trials Register (ANZCTR): ACTRN12609000953235
BACKGROUND: Although smokers tend to have a lower body-mass index than non-smokers, smoking may favour abdominal body fat accumulation. To our knowledge, no population-based studies have assessed the relationship between smoking and body fat composition. We assessed the association between cigarette smoking and waist circumference, body fat, and body-mass index. METHODS: Height, weight, and waist circumference were measured among 6,123 Caucasians (ages 35-75) from a cross-sectional population-based study in Switzerland. Abdominal obesity was defined as waist circumference >/= 102 cm for men and >/= 88 cm for women. Body fat (percent total body weight) was measured by electrical bioimpedance. Age- and sex-specific body fat cut-offs were used to define excess body fat. Cigarettes smoked per day were assessed by self-administered questionnaire. Age-adjusted means and odds ratios were calculated using linear and logistic regression. RESULTS: Current smokers (29% of men and 24% of women) had lower mean waist circumference, body fat percentage, and body-mass index compared with non-smokers. Age-adjusted mean waist circumference and body fat increased with cigarettes smoked per day among smokers. The association between cigarettes smoked per day and body-mass index was non-significant. Compared with light smokers, the adjusted odds ratio (OR) for abdominal obesity in men was 1.28 (0.78-2.10) for moderate smokers and 1.94 (1.15-3.27) for heavy smokers (P = 0.03 for trend), and 1.07 (0.72-1.58) and 2.15 (1.26-3.64) in female moderate and heavy smokers, respectively (P < 0.01 for trend). Compared with light smokers, the OR for excess body fat in men was 1.05 (95% CI: 0.58-1.92) for moderate smokers and 1.15 (0.60-2.20) for heavy smokers (P = 0.75 for trend) and 1.34 (0.89-2.00) and 2.11 (1.25-3.57), respectively in women (P = 0.07 for trend). CONCLUSION: Among smokers, cigarettes smoked per day were positively associated with central fat accumulation, particularly in women.

BACKGROUND: Childhood obesity is a continuing problem in the UK and South Asian children represent a group that are particularly vulnerable to its health consequences. The relationship between body dissatisfaction and obesity is well documented in older children and adults, but is less clear in young children, particularly South Asians. A better understanding of this relationship in young South Asian children will inform the design and delivery of obesity intervention programmes. The aim of this study is to describe body image size perception and dissatisfaction, and their relationship to weight status in primary school aged UK South Asian children.

METHODS: Objective measures of height and weight were undertaken on 574 predominantly South Asian children aged 5-7 (296 boys and 278 girls). BMI z-scores, and weight status (underweight, healthy weight, overweight or obese) were calculated based on the UK 1990 BMI reference charts. Figure rating scales were used to assess perceived body image size (asking children to identify their perceived body size) and dissatisfaction (difference between perceived current and ideal body size). The relationship between these and weight status were examined using multivariate analyses. RESULTS: Perceived body image size was positively associated with weight status (partial regression coefficient for overweight/obese vs. non-overweight/obese was 0.63 (95% CI 0.26-0.99) and for BMI z-score was 0.21 (95% CI 0.10-0.31), adjusted for sex, age and ethnicity). Body dissatisfaction was also associated with weight status, with overweight and obese children more likely to select thinner ideal body size than healthy weight children (adjusted partial regression coefficient for overweight/obese vs. non-overweight/obese was 1.47 (95% CI 0.99-1.96) and for BMI z-score was 0.54 (95% CI 0.40-0.67). CONCLUSIONS: Awareness of body image size and increasing body dissatisfaction with higher weight status is established at a young age in this population. This needs to be considered when designing interventions to reduce obesity in young children, in terms of both benefits and harms.
OBJECTIVE: Interpretation of meta-analyses of published observational studies is problematic because of numerous sources of bias. We develop bias assessment, elicitation and adjustment methods, and apply them to a systematic review of longitudinal observational studies of the relationship between objectively measured physical activity and subsequent change in adiposity in children. METHODS: We separated internal biases that reflect study quality from external biases that reflect generalizability to a target setting. Since published results were presented in different formats, these were all converted to correlation coefficients. Biases were considered as additive or proportional on the correlation scale. Opinions about the extent of each bias in each study, together with its uncertainty, were elicited in a formal process from quantitatively trained assessors for the internal biases and subject-matter specialists for the external biases. Bias-adjusted results for each study were combined across assessors using median pooling, and results combined across studies by random-effects meta-analysis. RESULTS: Before adjusting for bias, the pooled correlation is difficult to interpret because the studies varied substantially in quality and design, and there was considerable heterogeneity. After adjusting for both the internal and external biases, the pooled correlation provides a meaningful quantitative summary of all available evidence, and the confidence interval incorporates the elicited uncertainties about the extent of the biases. In the adjusted meta-analysis, there was no apparent heterogeneity. CONCLUSION: This approach provides a viable method of bias adjustment for meta-analyses of observational studies, allowing the quantitative synthesis of evidence from otherwise incompatible studies. From the meta-analysis of longitudinal observational studies, we conclude that there is no evidence that physical activity is associated with gain in body fat.

BACKGROUND: Accumulating evidence implicates insufficient oxidative capacity in the development of type 2 diabetes. This notion has not been well tested in large, population-based studies. METHODS: To test this hypothesis, we assessed the cross-sectional association of plasma lactate, an indicator of the gap between oxidative capacity and energy expenditure, with type 2 diabetes in 1709 older adults not taking metformin, who were participants in the Atherosclerosis Risk in Communities (ARIC) Carotid MRI Study. RESULTS: The prevalence of type 2 diabetes rose across lactate quartiles (11, 14, 20 and 30%; P for trend <0.0001). Following adjustment for demographic factors, physical activity, body mass index and waist circumference, the relative odds of type 2 diabetes across lactate quartiles were 0.98 [95% confidence interval (CI) 0.59-1.64], 1.64 (95% CI 1.03-2.64) and 2.23 (95% CI 1.38-3.59), respectively. Furthermore, lactate was associated with higher fasting glucose among non-diabetic adults. CONCLUSIONS: Plasma lactate was strongly associated with type 2 diabetes in older adults. Plasma lactate deserves greater attention in studies of oxidative capacity and diabetes risk.

BACKGROUND: Few studies have examined socioeconomic disparities in health and behavioral risk factors by gender in Asian countries and in South Korea, specifically. We investigated the relationship between socioeconomic position (education, income, and occupation) and subjective and acute and chronic health outcomes and behavioral risk factors by gender, and compared results from 1998 and 2005, in the Republic of Korea. METHODS: We examined data from a nationally representative stratified random sample of 4213 men and 4618 women from the 1998 Korea National Health and Nutrition Examination Survey, and 8289 men and 8827 women from the 2005 Korea National Health and Nutrition Examination Survey using General Linear Modeling.
and multiple logistic regression methods. RESULTS: Controlling for behavioral risk factors (smoking, drinking, obesity, exercise, and sleep), those in lower socioeconomic positions had poorer health outcomes in both self-reported acute and chronic disease and subjective measures; differences were especially pronounced among women. A socioeconomic gradient for education and income was found for both men and women for morbidity and self-reported health status, but the gradient was more pronounced in women. In 1998, the odds ratios (ORs) of higher morbidity for illiterate vs. college educated females was 5.4:1 and 1.9:1 for females in the lowest income quintile vs. the highest. The OR for education decreased in 2005 to 2.9:1 and that for income quintiles remained the same at 1.9:1. The OR of lower self-reported health status for illiterate vs. college educated females was 2.9:1 and 1.6:1 for females in the lowest income quintile vs. the highest in 1998, and 3.3:1 and 2.3:1 in 2005. CONCLUSIONS: Among Korean adults, men and women in lower socioeconomic position, as denoted by education, income, and somewhat less by occupation, experience significantly higher levels of morbidity and lower self-reported health status, even after controlling for standard behavioral risk factors. Disparities were more pronounced for women than for men. Efforts to reduce health disparities in South Korea require attention to the root causes of socioeconomic inequality and gender differences in the impact of socioeconomic position on health.


BACKGROUND: Validity of self-reported height and weight has not been adequately evaluated in diverse adolescent populations. In fact there are no reported validity studies conducted in Asian children and adolescents. This study aims to examine the accuracy of self-reported weight, height, and resultant BMI values in Chinese adolescents, and of the adolescents’ subsequent classification into overweight categories. METHODS: Weight and height were self-reported and measured in 1761 adolescents aged 12-16 years in a cross-sectional survey in Xi’an city, China. BMI was calculated from both reported values and measured values. Bland-Altman plots with 95% limits of agreement, Pearson's correlation and Kappa statistics were calculated to assess the agreement. RESULTS: The 95% limits of agreement were -11.16 and 6.46 kg for weight, -4.73 and 7.45 cm for height, and -4.93 and 2.47 kg/m2 for BMI. Pearson correlation between measured and self-reported values was 0.912 for weight, 0.935 for height and 0.809 for BMI. Weighted Kappa was 0.859 for weight, 0.906 for height and 0.754 for BMI. Sensitivity for detecting overweight (includes obese) in adolescents was 56.1%, and specificity was 98.6%. Subjects’ area of residence, age and BMI were significant factors associated with the errors in self-reporting weight, height and relative BMI. CONCLUSIONS: Reported weight and height does not have an acceptable agreement with measured data. Therefore, we do not recommend the application of self-reported weight and height to screen for overweight adolescents in China. Alternatively, self-reported data could be considered for use, with caution, in surveillance systems and epidemiology studies.


BACKGROUND: There is ample evidence that childhood overweight is associated with increased risk of chronic disease in adulthood. The aim of this study was to investigate associations between childhood overweight and common childhood health problems. METHODS: Data were used from a general population sample of 3960 8-year-old children, participating in the Dutch PIAMA birth cohort study. Weight and height, measured by the investigators, were used to define BMI status (thinness, normal weight, moderate overweight, obesity). BMI status was studied cross-sectionally in relation to the following parental reported outcomes: a general health index, GP visits, school absenteeism due to illness, health-related functional limitations, doctor diagnosed respiratory infections and use of antibiotics. RESULTS: Obesity was significantly associated with a lower general health score, more GP visits, more school absenteeism and more...
health-related limitations, (adjusted odds ratios around 2.0 for most outcomes). Obesity was also significantly associated with bronchitis (adjusted odds ratio (aOR) and 95% confidence intervals (95%CI): 5.29 (2.58;10.85) and with the use of antibiotics (aOR (95%CI): 1.79 (1.09;2.93)). Associations with flu/severe cold, ear infection and throat infection were positive, but not statistically significant. Moderate overweight was not significantly associated with the health outcomes studied. CONCLUSION: Childhood obesity is not merely a risk factor for disease in adulthood, but obese children may experience more illness and health related problems already in childhood. The high prevalence of the outcomes studied implies a high burden of disease in terms of absolute numbers of sick children


BACKGROUND: Low- to middle-income countries are undergoing a health transition with non-communicable diseases contributing substantially to disease burden, despite persistence of undernutrition and infectious diseases. This study aimed to investigate the prevalence and patterns of stunting and overweight/obesity, and hence risk for metabolic disease, in a group of children and adolescents in rural South Africa. METHODS: A cross-sectional growth survey was conducted involving 3511 children and adolescents 1-20 years, selected through stratified random sampling from a previously enumerated population living in Agincourt sub-district, Mpumalanga Province, South Africa. Anthropometric measurements including height, weight and waist circumference were taken using standard procedures. Tanner pubertal assessment was conducted among adolescents 9-20 years. Growth z-scores were generated using 2006 WHO standards for children up to five years and 1977 NCHS/WHO reference for older children. Overweight and obesity for those <18 years were determined using International Obesity Task Force BMI cut-offs, while adult cut-offs of BMI > or = 25 and > or = 30 kg/m2 for overweight and obesity respectively were used for those > or = 18 years. Waist circumference cut-offs of > or = 94 cm for males and > or = 80 cm for females and waist-to-height ratio of 0.5 for both sexes were used to determine metabolic disease risk in adolescents. RESULTS: About one in five children aged 1-4 years was stunted; one in three of those aged one year. Concurrently, the prevalence of combined overweight and obesity, almost non-existent in boys, was substantial among adolescent girls, increasing with age and reaching approximately 20-25% in late adolescence. Central obesity was prevalent among adolescent girls, increasing with sexual maturation and reaching a peak of 35% at Tanner Stage 5, indicating increased risk for metabolic disease. CONCLUSIONS: The study highlights that in transitional societies, early stunting and adolescent obesity may co-exist in the same socio-geographic population. It is likely that this profile relates to changes in nutrition and diet, but variation in factors such as infectious disease burden and physical activity patterns, as well as social influences, need to be investigated. As obesity and adult short stature are risk factors for metabolic syndrome and Type 2 diabetes, this combination of early stunting and adolescent obesity may be an explosive combination


BACKGROUND: Metabolic syndrome (MS) is combination of medical disorders that increase people's risk for cardiovascular disease and diabetes mellitus. Little data exists on the prevalence of MS of rural original adults in NingXia of China. METHODS: A cross-sectional survey method was used and the participants were interviewed by trained health workers under a structured questionnaire in rural of NingXia in 2008. The number of research subjects was 1612. MS was defined by International Diabetes Federation IDF (2005). RESULTS: The age-adjusted prevalence of the metabolic syndrome was 11.8%, whereas ethnic-specific prevalence was 10.3% in Han ethnic group and 13.7% in Hui ethnic group. Components of MS and MS were more common in Hui ethnic group than Han ethnic group. The mean levels and prevalence of abnormal value increased with increasing age in both ethnic groups (Cochran-Artimage test for trend, Hui ethnic group P < 0.05, Han ethnic group P < 0.01). CONCLUSIONS: The prevalence of MS was high in
rural residents' adults in Ningxia. Clustering of MS components and MS was increased with age. The components of MS have big differences among different ethnic groups

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BACKGROUND: Different populations have diverse patterns of relationships between Impaired Fasting Glucose (IFG) and obesity and lipid markers, it is important to investigate the characteristics of associations between IFG and other related risk factors including body mass index (BMI), waist circumstance (WC), serum lipids and blood pressure (BP) in a Chinese population. METHODS: This was a case-control study of 648 IFG subjects and 1,296 controls derived from a large-scale, community-based, cross-sectional survey of 10,867 participants. Each subject received a face-to-face interview, physical examination, and blood tests, including fasting blood glucose and lipids. Student's t-test, Chi-square test, Spearman correlation and multiple logistic regressions were used for the statistical analyses. RESULTS: Fasting plasma glucose (FPG) was positively correlated with BMI, WC, systolic blood pressure (SBP), diastolic blood pressure (DBP), triglyceride (TG), and total cholesterol (TC), and was negatively correlated with high density lipoprotein-cholesterol (HDL-C) (all p < 0.05). BMI was more strongly correlated with IFG than with WC. The correlation coefficient of FPG was remarkably higher with TG (0.244) than with TC (0.134) and HDL-C (-0.192). TG was an important predictor of IFG, with odds ratios of 1.76 (95%CI: 1.31-2.36) for subjects with borderline high TG level (1.70 mmol/l < or = TG < 2.26 mmol/l) and 3.13 (95% CI: 2.50-3.91) for those with higher TG level (TG > or = 2.26 mmol/l), when comparing to subjects with TG < 1.70 mmol/l. There was a significant dose-response relationship between the number of abnormal variables and increased risk of IFG. CONCLUSIONS: In this Chinese population, both BMI and WC were important predictors of IFG. Abnormal TG as a lipid marker was more strongly associated with IFG than were TC and HDL-C. These factors should be taken into consideration simultaneously for prevention of IFG
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BACKGROUND: Antiretroviral therapy (ART) is indicated during tuberculosis treatment in patients infected with human immunodeficiency virus type 1 (HIV-1), but the timing for the initiation of ART when tuberculosis is diagnosed in patients with various levels of immune compromise is not known. METHODS: We conducted an open-label, randomized study comparing earlier ART (within 2 weeks after the initiation of treatment for tuberculosis) with later ART (between 8 and 12 weeks after the initiation of treatment for tuberculosis) in HIV-1 infected patients with CD4+ T-cell counts of less than 250 per cubic millimeter and suspected tuberculosis. The primary end point was the proportion of patients who survived and did not have a new (previously undiagnosed) acquired immunodeficiency syndrome (AIDS)-defining illness at 48 weeks. RESULTS: A total of 809 patients with a median baseline CD4+ T-cell count of 77 per cubic millimeter and an HIV-1 RNA level of 5.43 log(10) copies per milliliter were enrolled. In the earlier-ART group, 12.9% of patients had a new AIDS-defining illness or died by 48 weeks, as compared with 16.1% in the later-ART group (95% confidence interval [CI], 1.8 to 8.1; P=0.45). Among patients with screening CD4+ T-cell counts of less than 50 per cubic millimeter, 15.5% of patients in the earlier-ART group versus 26.6% in the later-ART group had a new AIDS-defining illness or died (95% CI, 1.5 to 20.5; P=0.02). Tuberculosis-associated immune reconstitution inflammatory syndrome was more common with earlier ART than with later ART (11% vs. 5%, P=0.002). The rate of viral suppression at 48 weeks was 74% and did not differ between the groups (P=0.39).

CONCLUSIONS: Overall, earlier ART did not reduce the rate of new AIDS-defining illnesses and death, as compared with later ART. In persons with CD4+ T-cell counts of less than 50 per cubic millimeter, earlier ART was associated with a lower rate of new AIDS-defining illnesses and death. (Funded by the National Institutes of Health and others; ACTG A5221 ClinicalTrials.gov number, NCT00108862.)

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The 5’-leader of the HIV-1 genome regulates multiple functions during viral replication via mechanisms that have yet to be established. We developed a nuclear magnetic resonance approach that enabled direct detection of structural elements within the intact leader (712-nucleotide dimer) that are critical for genome packaging. Residues spanning the gag start codon (AUG) form a hairpin in the monomeric leader and base pair with residues of the unique-5’ region.
(U5) in the dimer. U5:AUG formation promotes dimerization by displacing and exposing a dimer-promoting hairpin and enhances binding by the nucleocapsid (NC) protein, which is the cognate domain of the viral Gag polyprotein that directs packaging. Our findings support a packaging mechanism in which translation, dimerization, NC binding, and packaging are regulated by a common RNA structural switch.

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OBJECTIVES: To estimate life expectancy for people with HIV undergoing treatment compared with life expectancy in the general population and to assess the impact on life expectancy of late treatment, defined as CD4 count <200 cells/mm(3) at start of antiretroviral therapy. DESIGN: Cohort study. SETTING: Outpatient HIV clinics throughout the United Kingdom. Population Adult patients from the UK Collaborative HIV Cohort (UK CHIC) Study with CD4 count ≤350 cells/mm(3) at start of antiretroviral therapy in 1996-2008. MAIN OUTCOME MEASURES: Life expectancy at the exact age of 20 (the average additional years that will be lived by a person after age 20), according to the cross sectional age specific mortality rates during the study period. RESULTS: 1248 of 17,661 eligible patients died during 91,203 person years' follow-up. Life expectancy (standard error) at exact age 20 increased from 30.0 (1.2) to 45.8 (1.7) years from 1996-9 to 2006-8. Life expectancy was 39.5 (0.45) for male patients and 50.2 (0.45) years for female patients compared with 57.8 and 61.6 years for men and women in the general population (1996-2006). Starting antiretroviral therapy later than guidelines suggest resulted in up to 15 years' loss of life: at age 20, life expectancy was 37.9 (1.3), 41.0 (2.2), and 53.4 (1.2) years in those starting antiretroviral therapy with CD4 count <100, 100-199, and 200-350 cells/mm(3), respectively. CONCLUSIONS: Life expectancy in people treated for HIV infection has increased by over 15 years during 1996-2008, but is still about 13 years less than that of the UK population. The higher life expectancy in women is magnified in those with HIV. Earlier diagnosis and subsequent timely treatment with antiretroviral therapy might increase life expectancy.

(14) LOSINA E, FREEDBERG KA. Life expectancy in HIV. BMJ. 2011, vol. 343, p.d6015

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http://dx.doi.org/10.1056/NEJMp1107621


http://dx.doi.org/10.1038/477036a


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Broadly neutralizing antibodies against highly variable viral pathogens are much sought after to treat or protect against global circulating viruses. Here we probed the neutralizing antibody repertoires of four human immunodeficiency virus (HIV)-infected donors with remarkably broad and potent neutralizing responses and rescued 17 new monoclonal antibodies that neutralize broadly across clades. Many of the new monoclonal antibodies are almost tenfold more potent than the recently described PG9, PG16 and VRC01 broadly neutralizing monoclonal antibodies and 100-fold more potent than the original prototype HIV broadly neutralizing monoclonal antibodies. The monoclonal antibodies largely recapitulate the neutralization breadth found in the corresponding donor serum and many recognize novel epitopes on envelope (Env) glycoprotein gp120, illuminating new targets for vaccine design. Analysis of neutralization by the full complement of anti-HIV broadly neutralizing monoclonal antibodies now available reveals that certain combinations of antibodies should offer markedly more favourable coverage of the enormous diversity of global circulating viruses than others and these combinations might be sought in active or passive immunization regimes. Overall, the isolation of multiple HIV broadly neutralizing monoclonal antibodies from several donors that, in aggregate, provide broad coverage at low concentrations is a highly positive indicator for the eventual design of an effective antibody-based HIV vaccine.

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Latency and ongoing replication have both been proposed to explain the drug-insensitive human immunodeficiency virus (HIV) reservoir maintained during antiretroviral therapy. Here we explore a novel mechanism for ongoing HIV replication in the face of antiretroviral drugs. We propose a model whereby multiple infections per cell lead to reduced sensitivity to drugs without requiring drug-resistant mutations, and experimentally validate the model using multiple infections per cell by cell-free HIV in the presence of the drug tenofovir. We then examine the drug sensitivity of cell-to-cell spread of HIV, a mode of HIV transmission that can lead to multiple infection events per target cell. Infections originating from cell-free virus decrease strongly in the presence of
antiretrovirals tenofovir and efavirenz whereas infections involving cell-to-cell spread are markedly less sensitive to the drugs. The reduction in sensitivity is sufficient to keep multiple rounds of infection from terminating in the presence of drugs. We examine replication from cell-to-cell spread in the presence of clinical drug concentrations using a stochastic infection model and find that replication is intermittent, without substantial accumulation of mutations. If cell-to-cell spread has the same properties in vivo, it may have adverse consequences for the immune system, lead to therapy failure in individuals with risk factors, and potentially contribute to viral persistence and hence be a barrier to curing HIV infection.

[http://dx.doi.org/10.1126/science.1207532](http://dx.doi.org/10.1126/science.1207532)

Antibody VRC01 is a human immunoglobulin that neutralizes about 90% of HIV-1 isolates. To understand how such broadly neutralizing antibodies develop, we used x-ray crystallography and 454 pyrosequencing to characterize additional VRC01-like antibodies from HIV-1-infected individuals. Crystal structures revealed a convergent mode of binding for diverse antibodies to the same CD4-binding-site epitope. A functional genomics analysis of expressed heavy and light chains revealed common pathways of antibody-heavy chain maturation, confined to the IGHV1-2*02 lineage, involving dozens of somatic changes, and capable of pairing with different light chains. Broadly neutralizing HIV-1 immunity associated with VRC01-like antibodies thus involves the evolution of antibodies to a highly affinity-matured state required to recognize an invariant viral structure, with lineages defined from thousands of sequences providing a genetic roadmap of their development.

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Determination of the prevalence of accumulated antiretroviral drug resistance among persons infected with human immunodeficiency virus (HIV) is complicated by the lack of routine measurement in clinical care. By using data from 8 clinic-based cohorts from the North American AIDS Cohort Collaboration on Research and Design, drug-resistance mutations from those with genotype tests were determined and scored using the Genotypic Resistance Interpretation Algorithm developed at Stanford University. For each year from 2000 through 2005, the prevalence was calculated using data from the tested subset, assumptions that incorporated clinical knowledge, and multiple imputation methods to yield a complete data set. A total of 9,289 patients contributed data to the analysis; 3,959 had at least 1 viral load above 1,000 copies/mL, of whom 2,962 (75%) had undergone at least 1 genotype test. Using these methods, the authors estimated that the prevalence of accumulated resistance to 2 or more antiretroviral drug classes had increased from 14% in 2000 to 17% in 2005 (P < 0.001). In contrast, the prevalence of resistance in the tested subset declined from 57% to 36% for 2 or more classes. The authors’ use of clinical knowledge and multiple imputation methods revealed trends in HIV drug resistance among patients in care that were markedly different from those observed using only data from patients who had undergone genotype tests.

[http://dx.doi.org/10.2105/AJPH.2011.300259](http://dx.doi.org/10.2105/AJPH.2011.300259)

Thirty years ago, the Centers for Disease Control and Prevention reported the first cases of AIDS in the United States. Since then, more than half a million Americans have died of AIDS, and 1.1 million people are currently living with HIV in the United States. In an attempt to reinvigorate the domestic response to the HIV epidemic, the Obama administration developed and released the National HIV/AIDS Strategy for the United States (NHAS). The NHAS has 3 focus areas: reducing
new infections, improving access to care and health outcomes, and reducing HIV-related disparities. With ambitious five-year targets set for each goal, the NHAS requires significant fiscal investment to achieve its desired impact on the domestic HIV epidemic.


BACKGROUND: Vitamin A deficiency (VAD) is known to be a major public health problem among women of reproductive age in South East Asia and Africa. In Ethiopia, there are no studies conducted on serum vitamin A status of HIV-infected pregnant women. Therefore, the present study was aimed at determining the level of serum vitamin A and VAD among pregnant women with and without HIV infection in tropical settings of Northwest Ethiopia. METHODS: In this cross-sectional study, blood samples were collected from 423 pregnant women and from 55 healthy volunteers who visited the University of Gondar Hospital. Serum concentration of vitamin A was measured by high performance liquid chromatography. RESULTS: After controlling for total serum protein, albumin and demographic variables, the mean +/- SD serum vitamin A in HIV seropositive pregnant women (0.96 +/- 0.42 mumol/L) was significantly lower than that in pregnant women without HIV infection (1.10 +/- 0.45 mumol/L, P < 0.05). Likewise, the level of serum vitamin A in HIV seropositive non-pregnant women (0.74 +/- 0.39) was significantly lower than that in HIV negative non-pregnant women (1.18 +/- 0.59 mumol/L, P < 0.004). VAD (serum retinol < 0.7 mumol/L) was observed in 18.4% and 17.7% of HIV infected and uninfected pregnant women, respectively. Forty six percent of non-pregnant women with HIV infection had VAD while only 28% controls were deficient for vitamin A (P = 0.002). CONCLUSION: The present study shows that VAD is a major public health problem among pregnant women in the tropical settings of Northwest Ethiopia. Considering the possible implications of VAD during pregnancy, we recommend multivitamin (which has a lower level of vitamin A) supplementation in the care and management of pregnant women with or without HIV infection.


BACKGROUND: Women with severe maternal morbidity are at high risk of dying. Quality and prompt management and sometimes luck have been suggested to reduce on the risk of dying. The objective of the study was to identify the direct and indirect causes of severe maternal morbidity, predictors of progression from severe maternal morbidity to maternal mortality in Mulago hospital, Kampala, Uganda. METHODS: This was a longitudinal follow up study at the Mulago hospital's Department of Obstetrics and Gynaecology. Participants were 499 with severe maternal morbidity admitted in Mulago hospital between 15th November 2001 and 30th November 2002 were identified, recruited and followed up until discharge or death. Potential prognostic factors were HIV status and CD4 cell counts, socio demographic characteristics, medical and gynaecological history, past and present obstetric history and intra- partum and postnatal care. RESULTS: Severe pre eclampsia/eclampsia, obstructed labour and ruptured uterus, severe post partum haemorrhage, severe abruptio and placenta praevia, puerperal sepsis, post abortal sepsis and severe anaemia were the causes for the hospitalization of 499 mothers. The mortality incidence rate was 8% (n = 39), maternal mortality ratio of 7815/100,000 live births and the ratio of severe maternal morbidity to mortality was 12.8:1. The independent predictors of maternal mortality were HIV/AIDS (OR 5.1 95% CI 2-12.8), non attendance of antenatal care (OR 4.0, 95% CI 1.3-9.2), non use of oxytocics (OR 4.0, 95% CI 1.7-9.7), lack of essential drugs (OR 3.6, 95% CI 1.1-11.3) and non availability of blood for transfusion (OR 53.7, 95% CI (15.7-183.9) and delivery of amale baby (OR 4.0, 95% CI 1.6-10.1). CONCLUSION: The predictors of progression from severe maternal morbidity to mortality were: residing far from hospital, low socio economic status, non attendance of antenatal care, poor intrapartum care, and HIV/AIDS. There is need to improve on the referral system, economic empowerment of women and to offer comprehensive emergency obstetric care so as to reduce the maternal morbidity and mortality in our community.
http://dx.doi.org/10.2105/AJPH.2011.300242

(31) PARRY J. Global Fund pressures China to engage with civil society groups. BMJ. 2011, vol. 342, p.d3327

http://dx.doi.org/10.1186/1471-2458-10-180

BACKGROUND: Since 1989 when the first 146 HIV positives in China were identified, Dehong Prefecture had been one of the areas hardest-hit by HIV in China. The local and national governments have put substantial financial resources into tackling the HIV epidemic in Dehong from 2004. The objective of this study was to track dynamic changes in HIV-1 prevalence and incidence among five focal populations in Dehong and to assess the impact of HIV prevention and control efforts. METHODS: Consecutive cross-sectional surveys conducted in five focal populations between 2004 and 2008. Specimens seropositive for HIV were tested with the BED IgG capture enzyme immunoassay to identify recent seroconversions (median, 155 days) using normalized optical density of 0.8 and adjustments. RESULTS: From 2004 to 2008, estimated annual HIV incidence among injecting drug users (IDUs) decreased significantly [from 15.0% (95% CI = 11.4%-18.5%) in 2004 to 4.3% (95% CI = 2.4%-6.2%) in 2008; trend test P < 0.0001]. The incidence among other focal populations, such as HIV discordant couples (varying from 5.5% to 4.7%), female sex workers (varying from 1.4% to 1.3%), pregnant women (0.1%), and pre-marital couples (0.2 to 0.1%) remained stable. Overall, the proportion of recent HIV-1 infections was higher among females than males (P < 0.0001). CONCLUSIONS: The HIV epidemic in Dehong continued to expand during a five-year period but at a slowing rate among IDUs, and HIV incidence remains high among IDUs and discordant couples. Intensive prevention measures should target sub-groups at highest risk to further slow the epidemic and control the migration of HIV to other areas of China, and multivariate analysis is needed to explore which measures are more effective for different populations.

Tuberculose

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OBJECTIVE: To assess the cost effectiveness of the Find and Treat service for diagnosing and managing hard to reach individuals with active tuberculosis. DESIGN: Economic evaluation using a discrete, multiple age cohort, compartmental model of treated and untreated cases of active
tuberculosis. SETTING: London, United Kingdom. Population Hard to reach individuals with active pulmonary tuberculosis screened or managed by the Find and Treat service (48 mobile screening unit cases, 188 cases referred for case management support, and 180 cases referred for loss to follow-up), and 252 passively presenting controls from London’s enhanced tuberculosis surveillance system. MAIN OUTCOME MEASURES: Incremental costs, quality adjusted life years (QALYs), and cost effectiveness ratios for the Find and Treat service. RESULTS: The model estimated that, on average, the Find and Treat service identifies 16 and manages 123 active cases of tuberculosis each year in hard to reach groups in London. The service has a net cost of £1.4 million/year and, under conservative assumptions, gains 220 QALYs. The incremental cost effectiveness ratio was £4.

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BACKGROUND: We previously reported that integrating antiretroviral therapy (ART) with tuberculosis treatment reduces mortality. However, the timing for the initiation of ART during tuberculosis treatment remains unresolved. METHODS: We conducted a three-group, open-label, randomized, controlled trial in South Africa involving 642 ambulatory patients, all with tuberculosis (confirmed by a positive sputum smear for acid-fast bacilli), human immunodeficiency virus infection, and a CD4+ T-cell count of less than 500 per cubic millimeter. Findings in the earlier-ART group (ART initiated within 4 weeks after the start of tuberculosis treatment, 214 patients) and later-ART group (ART initiated during the first 4 weeks of the continuation phase of tuberculosis treatment, 215 patients) are presented here. RESULTS: At baseline, the median CD4+ T-cell count was 150 per cubic millimeter, and the median viral load was 161,000 copies per milliliter, with no significant differences between the two groups. The incidence rate of the acquired immunodeficiency syndrome (AIDS) or death was 6.9 cases per 100 person-years in the earlier-ART group (18 cases) as compared with 7.8 per 100 person-years in the later-ART group (19 cases) (incidence-rate ratio, 0.89; 95% confidence interval [CI], 0.44 to 1.79; P=0.73). However, among patients with CD4+ T-cell counts of less than 50 per cubic millimeter, the incidence rates of AIDS or death were 8.5 and 26.3 cases per 100 person-years, respectively (incidence-rate ratio, 0.32; 95% CI, 0.07 to 1.13; P=0.06). The incidence rates of the immune
reconstitution inflammatory syndrome (IRIS) were 20.1 and 7.7 cases per 100 person-years, respectively (incidence-rate ratio, 2.62; 95% CI, 1.48 to 4.82; P<0.001). Adverse events requiring a switching of antiretroviral drugs occurred in 10 patients in the earlier-ART group and 1 patient in the later-ART group (P=0.006). CONCLUSIONS: Early initiation of ART in patients with CD4+ T-cell counts of less than 50 per cubic millimeter increased AIDS-free survival. Deferral of the initiation of ART to the first 4 weeks of the continuation phase of tuberculosis therapy in those with higher CD4+ T-cell counts reduced the risks of IRIS and other adverse events related to ART without increasing the risk of AIDS or death. ( Funded by the U.S. President’s Emergency Plan for AIDS Relief and others; SAPIT ClinicalTrials.gov number, NCT00398996.)


BACKGROUND: Antiretroviral therapy (ART) is indicated during tuberculosis treatment in patients infected with human immunodeficiency virus type 1 (HIV-1), but the timing for the initiation of ART when tuberculosis is diagnosed in patients with various levels of immune compromise is not known. METHODS: We conducted an open-label, randomized study comparing earlier ART (within 2 weeks after the initiation of treatment for tuberculosis) with later ART (between 8 and 12 weeks after the initiation of treatment for tuberculosis) in HIV-1 infected patients with CD4+ T-cell counts of less than 250 per cubic millimeter and suspected tuberculosis. The primary end point was the proportion of patients who survived and did not have a new (previously undiagnosed) acquired immunodeficiency syndrome (AIDS)-defining illness at 48 weeks. RESULTS: A total of 809 patients with a median baseline CD4+ T-cell count of 77 per cubic millimeter and an HIV-1 RNA level of 5.43 log(10) copies per milliliter were enrolled. In the earlier-ART group, 12.9% of patients had a new AIDS-defining illness or died by 48 weeks, as compared with 16.1% in the later-ART group (95% confidence interval [CI], -1.8 to 8.1; P=0.45). Among patients with screening CD4+ T-cell counts of less than 50 per cubic millimeter, 15.5% of patients in the earlier-ART group versus 26.6% in the later-ART group had a new AIDS-defining illness or died (95% CI, 1.5 to 20.5; P=0.02). Tuberculosis-associated immune reconstitution inflammatory syndrome was more common with earlier ART than with later ART (11% vs. 5%, P=0.002). The rate of viral suppression at 48 weeks was 74% and did not differ between the groups (P=0.38).

CONCLUSIONS: Overall, earlier ART did not reduce the rate of new AIDS-defining illness and death, as compared with later ART. In persons with CD4+ T-cell counts of less than 50 per cubic millimeter, earlier ART was associated with a lower rate of new AIDS-defining illnesses and death. ( Funded by the National Institutes of Health and others; ACTG A5221 ClinicalTrials.gov number, NCT00108862.)


BACKGROUND: Tuberculosis remains an important cause of death among patients infected with the human immunodeficiency virus (HIV). Robust data are lacking with regard to the timing for the initiation of antiretroviral therapy (ART) in relation to the start of antituberculosis therapy. METHODS: We tested the hypothesis that the timing of ART initiation would significantly affect mortality among adults not previously exposed to antiretroviral drugs who had newly diagnosed tuberculosis and CD4+ T-cell counts of 200 per cubic millimeter or lower. After beginning the standard, 6-month treatment for tuberculosis, patients were randomly assigned to either earlier treatment (2 weeks after beginning tuberculosis treatment) or later treatment (8 weeks after) with stavudine, lamivudine, and efavirenz. The primary end point was survival. RESULTS: A total of 661 patients were enrolled and were followed for a median of 25 months. The median CD4+ T-cell count was 25 per cubic millimeter, and the median viral load was 5.64 log(10) copies per milliliter. The risk of death was significantly reduced in the group that received ART earlier, with 59 deaths among 332 patients (18%), as compared with 90 deaths among 329 patients (27%) in the later-ART group (hazard ratio, 0.62; 95% confidence interval [CI]; 0.44 to 0.86; P=0.006). The risk of tuberculosis-associated immune reconstitution inflammatory syndrome was significantly increased
in the earlier-ART group (hazard ratio, 2.51; 95% CI, 1.78 to 3.59; P<0.001). Irrespective of the study group, the median gain in the CD4+ T-cell count was 114 per cubic millimeter, and the viral load was undetectable at week 50 in 96.5% of the patients. CONCLUSIONS: Initiating ART 2 weeks after the start of tuberculosis treatment significantly improved survival among HIV-infected adults with CD4+ T-cell counts of 200 per cubic millimeter or lower. (Funded by the French National Agency for Research on AIDS and Viral Hepatitis and the National Institutes of Health; CAMELIA ClinicalTrials.gov number, NCT01300481.)

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OBJECTIVES: Almost 20% of people smoke tobacco worldwide—a percentage projected to rise in many poor countries. Smoking has been linked to increased individual risk of tuberculosis infection and mortality, but it remains unclear how these risks affect population-wide tuberculosis rates. DESIGN: We constructed a state transition, compartmental, mathematical model of tuberculosis epidemics to estimate the impact of alternative future smoking trends on tuberculosis control. We projected tuberculosis incidence, prevalence, and mortality in each World Health Organization region from 2010 to 2050, and incorporated changing trends in smoking, case detection, treatment success, and HIV prevalence. RESULTS: The model predicted that smoking would produce an excess of 18 million tuberculosis cases (standard error 16-20) and 40 million deaths from tuberculosis (39-41) between 2010 and 2050, if smoking trends continued along current trajectories. The effect of smoking was anticipated to increase the number of tuberculosis cases by 7% (274 million v 256 million) and deaths by 66% (101 million v 61 million), compared with model predictions that did not account for smoking. Smoking was also expected to delay the millennium development goal target to reduce tuberculosis mortality by half from 1990 to 2015. The model estimated that aggressive tobacco control (achieving a 1% decrease in smoking prevalence per year down to eradication) would avert 27 million smoking attributable deaths from tuberculosis by 2050. However, if the prevalence of smoking increased to 50% of adults (as observed in countries with high tobacco use), the model estimated that 34 million additional deaths from tuberculosis would occur by 2050. CONCLUSIONS: Tobacco smoking could substantially increase tuberculosis cases and deaths worldwide in coming years, undermining progress towards tuberculosis mortality targets. Aggressive tobacco control could avert millions of deaths from tuberculosis

(18) RODRIGUES LC, MANGTANI P, ABUBAKAR I. How does the level of BCG vaccine protection against tuberculosis fall over time? BMJ. 2011, vol. 343, p.d5974

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http://dx.doi.org/10.1016/S0140-6736(11)61531-6

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We examined how different drivers of infectious disease could interact to threaten control efforts in Europe. We considered projected trends through 2020 for 3 broad groups of drivers: globalization and environmental change, social and demographic change, and health system capacity. Eight plausible infectious disease threats with the potential to be significantly more problematic than they are today were identified through an expert consultation: extensively drug-resistant bacteria, vector-borne diseases, sexually transmitted infections, food-borne infections, resurgence of vaccine-preventable diseases, health care-associated infections, multidrug-resistant tuberculosis, and pandemic influenza. Preemptive measures to be taken by the public health community to counteract these threats were identified

(23) MOSZYNSKI P. Treatment for multidrug resistant TB fails in a quarter of cases in Europe, says WHO. BMJ. 2011, vol. 343, p.d5852


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http://dx.doi.org/10.1093/aje/kwr159

The presence of tuberculosis (TB) in patients with silicosis increases mortality risk. To characterize silicosis-respiratory TB comorbidity in the United States, the authors used 1968-2006
National Center for Health Statistics multiple cause-of-death data for decedents aged \( \geq 25 \) years. The authors calculated proportionate mortality ratios (PMRs) using available information on decedents’ industries and occupations reported from 26 states from 1985 through 1999. Among 16,648 silicosis deaths, 2,278 (13.7%) had respiratory TB listed on the death certificate. Of silicosis-respiratory TB deaths, 1,666 decedents (73.1%) were aged \( \geq 65 \) years, 2,255 (99.0%) were male, and 1,893 (83.1%) were white. Silicosis-respiratory TB deaths declined 99.5% during the study period \( (P < 0.001 \) for time-related trend), from 239.8 per year during 1968-1972 to 1.2 per year during 2002-2006, with no reported deaths in 2006. Silicosis-respiratory TB deaths reported from Pennsylvania \( (n = 525; 1.29 \) per million population), Ohio \( (n = 258; 0.81 \) per million), and West Virginia \( (n = 146; 2.35 \) per million) accounted for 40.8% of all such deaths in the United States. The highest PMR for silicosis-respiratory TB death was associated with the "miscellaneous nonmetallic mineral and stone products" industry \( (PMR = 73.7, 95\% \) confidence interval: 33.8, 139.8). In the United States, 2006 marked the first year since 1968 with no silicosis-respiratory TB deaths. The substantial decline in silicosis-respiratory TB comortality probably reflects prevention and control measures for both diseases.


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BACKGROUND: In Malawi, high case fatality rates in patients with tuberculosis, who were also co-infected with HIV, and high early death rates in people living with HIV during the initiation of antiretroviral treatment (ART) adversely impacted on treatment outcomes for the national tuberculosis and ART programmes respectively. This article i) discusses the operational research that was conducted in the country on cotrimoxazole preventive therapy, ii) outlines the steps that were taken to translate these findings into national policy and practice, iii) shows how the implementation of cotrimoxazole preventive therapy for both TB patients and HIV-infected patients starting ART was associated with reduced death rates, and iv) highlights lessons that can be learnt for other settings and interventions. DISCUSSION: District and facility-based operational research was undertaken between 1999 and 2005 to assess the effectiveness of cotrimoxazole preventive therapy in reducing death rates in TB patients and subsequently in patients starting ART under routine programme conditions. Studies demonstrated significant reductions in case fatality in HIV-infected TB patients receiving cotrimoxazole and in HIV-infected patients about to start ART. Following the completion of research, the findings were rapidly disseminated nationally at stakeholder meetings convened by the Ministry of Health and internationally through conferences and peer-reviewed scientific publications. The Ministry of Health made policy changes based on the available evidence, following which there was countrywide distribution of the updated policy and guidelines. Policy was rapidly moved to practice with the development of monitoring tools, drug procurement and training packages. National programme performance improved which showed a significant decrease in case fatality rates in TB patients as well as a reduction in early death in people with HIV starting ART. SUMMARY: Key lessons for moving this research endeavour through to policy and practice were the importance of placing operational research within the programme, defining relevant questions, obtaining “buy-in” from national programme staff at the beginning of projects and having key actors or “policy entrepreneurs” to push forward the policy-making process. Ultimately, any change in policy and practice has to benefit patients, and the ultimate judge of success is whether treatment outcomes improve or not.

http://dx.doi.org/10.1016/j.socscimed.2011.05.045
In recent times there has been a sense that HIV/AIDS control has been attracting a significantly larger portion of donor health funding to the extent that it crowds out funding for other health concerns. Although there is no doubt that HIV/AIDS has absorbed a large share of development assistance for health (DAH), whether HIV/AIDS is actually diverting funding away from other health concerns has yet to be analyzed fully. To fill this vacuum, this study aims to test if a higher level of HIV/AIDS funding is related to a displacement in funding for other health concerns, and if yes, to quantify the magnitude of the displacement effect. Specifically, we consider whether HIV/AIDS DAH has displaced i) TB, ii) malaria iii) health sector and ‘other’ DAH in terms of the dollar amount received for aid. We consider this question within a regression framework controlling for time and recipient heterogeneity. We find displacement effects for malaria and health sector funding but not TB. In particular, the displacement effect for malaria is large and worrying


BACKGROUND: In 2005, Rwanda drafted a national TB/HIV policy and began scaling-up collaborative TB/HIV activities. Prior to the scale-up, we evaluated existing TB/HIV practices, possible barriers to policy and programmatic implementation, and patient treatment outcomes. We then used our evaluation data as a baseline for evaluating the national scale-up of collaborative TB/HIV activities from 2005 through 2009. METHODS: Our baseline evaluation included a cross-sectional evaluation of 23/161 TB clinics. We conducted structured interviews with patients and clinic staff and reviewed TB registers and patient records to assess HIV testing practices, provision of HIV care and treatment for people with TB that tested positive for HIV, and patients' TB treatment outcomes. Following our baseline evaluation, we used nationally representative TB/HIV surveillance data to monitor the scale-up of collaborative TB/HIV activities RESULTS: Of 207 patients interviewed, 76% were offered HIV testing, 99% accepted, and 49% reported positive test results. Of 40 staff interviewed, 68% reported offering HIV testing to >50% of patients. From 2005-2009, scaled-up TB/HIV activities resulted in increased HIV testing of patients with TB (69% to 97%) and provision of cotrimoxazole (15% to 92%) and antiretroviral therapy (13% to 49%) for patients with TB disease and HIV infection (TB/HIV). The risk of death among patients with TB/HIV relative to patients with TB not infected with HIV declined from 2005 (RR = 6.1, 95%CI 2.6, 14.0) to 2007 (RR = 1.8, 95%CI 1.68, 1.94). CONCLUSIONS: Our baseline evaluation highlighted that staff and patients were receptive to HIV testing. However, expanded access to testing, care, and treatment was needed based on the proportion of patients with TB having unknown HIV status and the high rate of HIV infection and poorer TB treatment outcomes for patients with TB/HIV. Following our evaluation, scale-up of TB/HIV services resulted in almost all patients with TB knowing their HIV status. Scale-up also resulted in dramatic increases in the uptake of lifesaving HIV care and treatment coinciding with a decline in the risk of death among patients with TB/HIV


BACKGROUND: The study was conducted at a high TB-HIV burden primary health community clinic in Cape Town, South Africa. We describe the management of children under five years of age in household contact with a smear and/or culture-positive adult TB case. METHODS: This study was a record review of routinely-collected programme data. RESULTS: A total of 1094 adult TB case folders were reviewed. From all identified contacts, 149 children should have received IPT based on local guidelines; in only 2/149 IPT was initiated. Management of child contacts of sputum smear and/or culture-positive compared to sputum-negative TB patients were similar. CONCLUSIONS: IPT delivery to children remains an operational challenge, especially in high TB-HIV burden communities. A tool to improve IPT management and targeting sputum smear and/or
culture-positive TB child contacts may overcome some of these challenges and should be
developed and piloted in such settings

(32) AYISI JG, VANT HOOG AH, AGAYA JA, MCHEMBERE W, et al. Care seeking and attitudes
towards treatment compliance by newly enrolled tuberculosis patients in the district
treatment programme in rural western Kenya: a qualitative study. BMC Public Health. 2011,
vol. 11, p.515
http://dx.doi.org/10.1186/1471-2458-11-515

BACKGROUND: The two issues mostly affecting the success of tuberculosis (TB) control
programmes are delay in presentation and non-adherence to treatment. It is important to
understand the factors that contribute to these issues, particularly in resource limited settings,
where rates of tuberculosis are high. The objective of this study is to assess health-seeking
behaviour and health care experiences among persons with pulmonary tuberculosis, and identify
the reasons patients might not complete their treatment. METHODS: We performed qualitative
one-on-one in-depth interviews with pulmonary tuberculosis patients in nine health facilities in
rural western Kenya. Thirty-one patients, 18 women and 13 men, participated in the study. All
reside in an area of western Kenya with a Health and Demographic Surveillance System (HDSS).
They had attended treatment for up to 4 weeks on scheduled TB clinic days in September and
October 2005. The nine sites all provide diagnostic and treatment services. Eight of the facilities
were public (3 hospitals and 5 health centres) and one was a mission health centre. RESULTS:
Most patients initially self-treated with herbal remedies or drugs purchased from kiosks or
pharmacies before seeking professional care. The reported time from initial symptoms to TB
diagnosis ranged from 3 weeks to 9 years. Misinterpretation of early symptoms and financial
constraints were the most common reasons reported for the delay. We also explored potential
reasons that patients might discontinue their treatment before completing it. Reasons included
being unaware of the duration of TB treatment, stopping treatment once symptoms subsided, and
lack of family support. CONCLUSIONS: This qualitative study highlighted important challenges to
TB control in rural western Kenya, and provided useful information that was further validated in a
quantitative study in the same area

(33) KAN X, CHIANG CY, ENARSON DA, CHEN W, et al. Indoor solid fuel use and tuberculosis in
http://dx.doi.org/10.1186/1471-2458-11-498

BACKGROUND: China ranks second among the 22 high burden countries for tuberculosis. A
modeling exercise showed that reduction of indoor air pollution could help advance tuberculosis
control in China. However, the association between indoor air pollution and tuberculosis is not yet
well established. A case control study was conducted in Anhui, China to investigate whether use
of solid fuel is associated with tuberculosis. METHODS: Cases were new sputum smear positive
tuberculosis patients. Two controls were selected from the neighborhood of each case matched
by age and sex using a pre-determined procedure. A questionnaire containing demographic
information, smoking habits and use of solid fuel for cooking or heating was used for interview.
Solid fuel (coal and biomass) included coal/lignite, charcoal, wood, straw/shrubs/grass, animal
dung, and agricultural crop residue. A household that used solid fuel either for cooking and (/or)
heating was classified as exposure to combustion of solid fuel (indoor air pollution). Odds ratios
and their corresponding 95% confidence limits for categorical variables were determined by
Mantel-Haenszel estimate and multivariate conditional logistic regression. RESULTS: There were
202 new smear positive tuberculosis cases and 404 neighborhood controls enrolled in this study.
The proportion of participants who used solid fuels for cooking was high (73.8% among cases and
72.5% among controls). The majority reported using a griddle stove (85.2% among cases and
86.7% among controls), had smoke removed by a hood or chimney (92.0% among cases and
92.8% among controls), and cooked in a separate room (24.8% among cases and 28.0% among
controls) or a separate building (67.8% among cases and 67.6% among controls). Neither using
solid fuel for cooking (odds ratio (OR) 1.08, 95% CI 0.62-1.87) nor using solid fuel for heating (OR
1.04, 95% CI 0.54-2.02) was significantly associated with tuberculosis. Determinants significantly
associated with tuberculosis were household tuberculosis contact (adjusted OR, 27.23, 95% CI
8.19-90.58) and ever smoking tobacco (adjusted OR 1.64, 96% CI 1.01-2.66). CONCLUSION: In
a population where the majority had proper ventilation in cooking places, the association between use of solid fuel for cooking or for heating and tuberculosis was not statistically significant.


BACKGROUND: Tuberculosis remains a major public health problem in India with the country accounting for 1 in 5 of all TB cases reported globally. An advocacy, communication and social mobilisation project for Tuberculosis control was implemented and evaluated in Odisha state of India. The purpose of the study was to identify the impact of project interventions including the use of Interface NGOs and involvement of community groups such as women's self-help groups, local government bodies, village health sanitation committees, and general health staff in promoting TB control efforts. METHODS: The study utilized a rapid assessment and response (RAR) methodology. The approach combined both qualitative field work approaches, including semi-structured interviews and focus group discussions with empirical data collection and desk research. RESULTS: Results revealed that a combination of factors including the involvement of Interface NGOs, coupled with increased training and engagement of front line health workers and community groups, and dissemination of community based resources, contributed to improved awareness and knowledge about TB in the targeted districts. Project activities also contributed towards improving health worker and community effectiveness to raise the TB agenda, and improved TB literacy and treatment adherence. Engagement of successfully treated patients also assisted in reducing community stigma and discrimination. CONCLUSION: The expanded use of advocacy, communication and social mobilisation activities in TB control has resulted in a number of benefits. These include bridging pre-existing gaps between the health system and the community through support and coordination of general health services stakeholders, NGOs and the community. The strategic use of ‘tailored messages’ to address specific TB problems in low performing areas also led to more positive behavioural outcomes and improved efficiencies in service delivery. Implications for future studies are that a comprehensive and well planned range of ACSM activities can enhance TB knowledge, attitudes and behaviours while also mobilising specific community groups to build community efficacy to combat TB. The use of rapid assessments combined with other complementary evaluation approaches can be effective when reviewing the impact of TB advocacy, communication and social mobilisation activities.


BACKGROUND: In 2008 the World Health Organization (WHO) reported that South Africa had the highest tuberculosis (TB) incidence in the world. This high incidence rate is linked to a number of factors, including HIV co-infection and alcohol use disorders. The diagnosis and treatment package for TB and HIV co-infection is relatively well established in South Africa. However, because alcohol use disorders may present more insidiously, making it difficult to diagnose, those patients with active TB and misusing alcohol are not easily cured from TB. With this in mind, the primary purpose of this cluster randomized controlled trial is to provide screening for alcohol misuse and to test the efficacy of brief interventions in reducing alcohol intake in those patients with active TB found to be misusing alcohol in primary health care clinics in three provinces in South Africa. METHODS/DESIGN: Within each of the three selected health districts with the highest TB burden in South Africa, 14 primary health care clinics with the highest TB caseloads
will be selected. Those agreeing to participate will be stratified according to TB treatment caseload and the type of facility (clinic or community health centre). Within strata from 14 primary care facilities, 7 will be randomly selected into intervention and 7 to control study clinics (42 clinics, 21 intervention clinics and 21 control clinics). At the clinic level systematic sampling will be used to recruit newly diagnosed TB patients. Those consenting will be screened for alcohol misuse using the AUDIT. Patients who screen positive for alcohol misuse over a 6-month period will be given either a brief intervention based on the Information-Motivation-Behavioural Skills (IMB) Model or an alcohol use health education leaflet. A total sample size of 520 is expected.

**DISCUSSION:** The trial will evaluate the impact of alcohol screening and brief interventions for patients with active TB in primary care settings in South Africa. The findings will impact public health and will enable the health ministry to formulate policy related to comprehensive treatment for TB and alcohol misuse, which will result in reduction in alcohol use and ultimately improve the TB cure rates. **TRIAL REGISTRATION NUMBER:** PACTR: PACTR201105000297151

(37) **LONG Q, SMITH H, ZHANG T, TANG S, et al.** 
**Patient medical costs for tuberculosis treatment and impact on adherence in China: a systematic review.** 
BMC Public Health. 2011, vol. 11, p.393

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**BACKGROUND:** Charging for tuberculosis (TB) treatment could reduce completion rates, particularly in the poor. We identified and synthesised studies that measure costs of TB treatment, estimates of adherence and the potential impact of charging on treatment completion in China.

**METHODS:** Inclusion criteria were primary research studies, including surveys and studies using qualitative methods, conducted in mainland China. We searched MEDLINE, PUBMED, EMBASE, Science Direct, HEED, CNKI to June 2010; and web pages of relevant Chinese and international organisations. Cost estimates were extracted, transformed, and expressed in absolute values and as a percentage of household income.

**RESULTS:** Low income patients, defined at household or district level, pay a total of US$ 149 to 724 (RMB 1241 to 5228) for medical costs for a treatment course; as a percentage of annual household income, estimates range from 42% to 119%. One national survey showed 73% of TB patients at the time of the survey had interrupted or suspended treatment, and estimates from 9 smaller more recent studies showed that the proportion of patients at the time of the survey who had run out of drugs or were not taking them ranged from 3 to 25%. Synthesis of surveys and qualitative research indicate that cost is the most cited reason for default.

**CONCLUSIONS:** Despite a policy of free drug treatment for TB in China, health services charge all income groups, and costs are high. Adherence measured in cross sectional surveys is often low, and the cumulative failure to adhere is likely to be much higher. These findings may be relevant to those concerned with the development and spread of multi-drug resistant TB. New strategies need to take this into account and ensure patient adherence

(38) **BORGDORFF MW, VAN DEN HS, KALISVAART N, KREMER K, et al.** 
**Influence of sampling on clustering and associations with risk factors in the molecular epidemiology of tuberculosis.** 

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Molecular epidemiologic studies may use genotypic clustering of isolates as an indicator of recent transmission. It has been shown that missing cases lead to underestimating clustering, and modelling studies suggested that they may also lead to underestimating odds ratios for clustering. Using a national, comprehensive database from the Netherlands covering 15 years between 1993 and 2007 and including over 12,000 patients and their isolates, the authors determined the effects of sampling at random, in time, and by geographic area. As expected, sampling reduced the observed clustering percentages. However, sampling did not reduce the observed odds ratios for clustering. The main explanations for this discrepancy with model outcomes were that a substantial proportion of clustered cases were found in large clusters and that risk factors for clustering tended to be among clustered cases—also risk factors for large clusters. The authors conclude that, in settings where risk factors for clustering may be interpreted as risk factors for recent transmission, these risk factors are also associated with larger cluster sizes. As a result, odds ratios would show limited sampling bias

BACKGROUND: Emilia Romagna, a northern Italian region, has a population of 4.27 million, of which 9.7% are immigrants. The objective of this study was to investigate the epidemiology of tuberculosis (TB) during the period 1996-2006 in not Italy-born compared to Italy-born cases.

METHODS: Data was obtained from the Regional TB surveillance system, from where personal data, clinical features and risk factors of all notified TB cases were extracted. RESULTS: 5377 TB cases were reported. The proportion of immigrants with TB, over the total number of TB cases had progressively increased over the years, from 19.1% to 53.3%. In the not Italy-born population, TB incidence was higher than in Italians (in 2006: 100.7 cases per 100,000 registered not Italy-born subjects and 83.9/100,000 adding 20% of estimated irregular presences to the denominators. TB incidence among Italians was 6.5/100,000 Italians). A progressive rise in the not Italy-born incident cases was observed but associated with a decline in TB incidence. Not Italy-born cases were younger compared to the Italy-born cases, and more frequently classified as "new cases" (OR 2.0 95%CI 1.61-2.49 for age group 20-39); 60.7% had pulmonary TB, 31.6% extra pulmonary and 7.6% disseminated TB. Risk factors for TB in this population group were connected to lower income status (homeless: OR 149.9 95%CI 20.7-1083.3 for age group 40-59).

CONCLUSIONS: In low-incidence regions, prevention and control of TB among sub-groups at risk such as the foreign-born population is a matter of public health concern. In addition, increasing immigration rates may affect TB epidemiology. TB among immigrants is characterized by particular clinical features and risk factors, which should be analyzed in order to plan effective action


BACKGROUND: The tuberculosis register is a critical data source for the information system of national tuberculosis control programs. From the information in the tuberculosis case register, it is possible to extend the standard analysis of age and sex characteristics among sputum smear-positive cases to all tuberculosis case categories. National tuberculosis programs might utilize such information to identify problems related to referral and access to diagnosis and treatment.

OBJECTIVES: Based on the electronic database we created, our objectives were to provide a detailed description of age and sex characteristics of tuberculosis patients at registration and to provide a comparison of age-specific sex characteristics among incident and prevalent sputum smear-positive cases. METHODS: A representative sample of tuberculosis case registers from 1 January 2003 to 31 December 2005 was selected in Cambodia, two provinces in China and Viet Nam. Age and sex characteristics of cases in the three separate prevalence surveys in the three jurisdictions (Cambodia: year 2002; China: year 2000; and Viet Nam: year 2006-2007) were obtained for comparison. RESULTS: A total 37,635 patients had been registered during the period in the selected units in the three countries. Cases were more frequently male in all three countries with 53%, 71%, and 69% in Cambodia, China, and Viet Nam, respectively. The ratios of the female-to-male odds in the notification system to that in the prevalence survey in smear-positive cases in Cambodia, China and Viet Nam were 2.1, 0.9, and 1.8, respectively. Because of the small proportion of extrapulmonary tuberculosis registered in China, we limited the analysis on age and sex distribution for extrapulmonary cases to Cambodia and Viet Nam. The proportion with extrapulmonary tuberculosis among all cases was 18.5% in Cambodia and 15.7% in Viet Nam, decreasing in frequency with increasing age. CONCLUSIONS: Characteristics of patients greatly differed between countries and between patient categories. In Cambodia and Viet Nam, efforts should be made for improved case-finding of sputum smear-positive tuberculosis among males

BACKGROUND: Several FIDELIS projects (Fund for Innovative DOTS Expansion through Local Initiatives to Stop TB) in Tanzania were conducted by the National Tuberculosis and Leprosy Programme (NTLP) during the years 2004-2008 to strengthen diagnostic and treatment services. These projects collected information on treatment delay and some of it was available for research purposes. With this database our objective was to assess the duration and determinants of treatment delay among new smear positive pulmonary tuberculosis (TB) patients in FIDELIS projects, and to compare delay according to provider visited prior to diagnosis. METHODS: Treatment delay among new smear positive TB patients was recorded for each patient at treatment initiation and this information was available and fairly complete in 6 out of 57 districts with FIDELIS projects enrolling patients between 2004 and 2007; other districts had discarded their forms at the time of analysis. It was analysed as a cross sectional study. RESULTS: We included 1161 cases, 10% of all patients recruited in the FIDELIS projects in Tanzania. Median delay was 12 weeks. The median duration of cough, weight loss and haemoptysis was 12, 8 and 3 weeks, respectively. Compared to Hai district Handeni had patients with longer delays and Mbozi had patients with shorter delays. Urban and rural patients reported similar delays. Patients aged 15-24 years and patients of 65 years or older had longer delays. Patients reporting contact with traditional healers before diagnosis had a median delay of 15 weeks compared to 12 weeks among those who did not. Patients with dyspnoea and with diarrhoea had longer delays. CONCLUSION: In this patient sample in Tanzania half of the new smear positive pulmonary tuberculosis patients had a treatment delay longer than 12 weeks. Delay was similar in men and women and among urban and rural patients, but longer in the young and older age groups. Patients using traditional healers had a 25% longer median delay.


The objective of this article is to characterize the risk of infection from airborne Mycobacterium tuberculosis bacilli exposure in commercial passenger trains based on a risk-based probabilistic transmission modeling. We investigated the tuberculosis (TB) infection risks among commercial passengers by inhaled aerosol M. tuberculosis bacilli and quantify the patterns of TB transmission in Taiwan High Speed Rail (THSR). A deterministic Wells-Riley mathematical model was used to account for the probability of infection risk from M. tuberculosis bacilli by linking the cough-generated aerosol M. tuberculosis bacilli concentration and particle size distribution. We found that (i) the quantum generation rate of TB was estimated with a lognormal distribution of geometric mean (GM) of 54.29 and geometric standard deviation (GSD) of 3.05 quantum/h at particle size </= 5 mum and (ii) the basic reproduction numbers (R(0)) were estimated to be 0.69 (0.06-6.79), 2.82 (0.32-20.97), and 2.31 (0.25-17.69) for business, standard, and nonreserved cabins, respectively. The results indicate that commercial passengers taking standard and nonreserved cabins had higher transmission risk than those in business cabins based on conservatism. Our results also reveal that even a brief exposure, as in the bronchoscopy cases, can also result in a transmission when the quantum generation rate is high. This study could contribute to a better understanding of the dynamics of TB transmission in commercial passenger trains by assessing the relationship between TB infectiousness, passenger mobility, and key model parameters such as seat occupancy, ventilation rate, and exposure duration.


BACKGROUND: Afar pastoralists live in the northeast of Ethiopia, confined to the most arid part of the country, where there is least access to educational, health and other social services. Tuberculosis (TB) is one of the major public health problems in Afar region. Lack of knowledge...
about TB could affect the health-seeking behaviour of patients and sustain the transmission of the disease within the community. In this study, we assessed the knowledge and perception of apparently healthy individuals about pulmonary tuberculosis (PTB) in pastoral communities of Afar. METHODS: Between March and May 2009, a community-based cross-sectional questionnaire survey involving 818 randomly selected healthy individuals was conducted in pastoral communities of Afar region. Moreover, two focus group discussions (FGDs), one with men and one with women, were conducted in each of the study area to supplement the quantitative study. RESULTS: The majority (95.6%) of the interviewees reported that they have heard about PTB (known locally as "Labadore"). However, the participants associated the cause of PTB with exposure to cold air (45.9%), starvation (38%), dust (21.8%) or smoking/chewing Khat (Catha edulis) (16.4%). The discussants also suggested these same factors as the cause of PTB. All the discussants and the majority (74.3%) of the interviewees reported that persistent cough as the main symptom of PTB. About 87.7% of the interviewees and all the discussants suggested that PTB is treatable with modern drugs. All the discussants and the majority (95%) of the interviewees mentioned that the disease can be transmitted from a patient to another person. Socio-cultural practices, e.g. sharing cups (87.6%), and house type (59.8%) were suggested as risk factors for exposure to PTB in the study areas, while shortage of food (69.7%) and chewing khat (53.8%) were mentioned as factors favouring disease development. Almost all discussants and a considerable number (20.4%) of the interviewees thought that men were the highest risk group to get PTB as well as playing a major role in the epidemiology of the disease. CONCLUSION: The findings indicate that pastoral communities had basic awareness about the disease. Nevertheless, health education to transform their traditional beliefs and perceptions about the disease to biomedical knowledge is crucial.


BACKGROUND: Delays seeking care worsen the burden of tuberculosis and cost of care for patients, families and the public health system. This study investigates costs of tuberculosis diagnosis incurred by patients, escorts and the public health system in 10 districts of Ethiopia. METHODS: New pulmonary tuberculosis patients > or = 15 years old were interviewed regarding their health care seeking behaviour at the time of diagnosis. Using a structured questionnaire patients were interviewed about the duration of delay at alternative care providers and the public health system prior to diagnosis. Costs incurred by patients, escorts and the public health system were quantified through patient interview and review of medical records. RESULTS: Interviews were held with 537 (58%) smear positive patients and 387 (42%) smear negative pulmonary patients. Of these, 413 (45%) were female; 451 (49%) were rural residents; and the median age was 34 years. The mean (median) days elapsed for consultation at alternative care providers and public health facilities prior to tuberculosis diagnosis was 5 days (0 days) and 3 (3 days) respectively. The total median cost incurred from first consultation to diagnosis was $27 per patient (mean = $59). The median costs per patient incurred by patient, escort and the public health system were $16 (mean = $29), $3 (mean = $23) and $3 (mean = $7) respectively. The total cost per patient diagnosed was higher for women, rural residents; those who received government food for work support, patients with smear negative pulmonary tuberculosis and patients who were not screened for TB in at least one district diagnostic centers. CONCLUSIONS: The costs of tuberculosis diagnosis incurred by patients and escorts represent a significant portion of their monthly income. The costs arising from time lost in seeking care comprised a major portion of the total cost of diagnosis, and may worsen the economic position of patients and their families. Getting treatment from alternative sources and low index of suspicion public health providers were key problems contributing to increased cost of tuberculosis diagnosis. Thus, the institution of effective systems of referral, ensuring screening of suspects across the district public health system and the involvement of alternative care providers in district tuberculosis control can reduce delays and the financial burden to patients and escorts.

(45) SIDDIQI K, KHAN A, AHMAD M, SHAFIQ UR. An intervention to stop smoking among patients suspected of TB--evaluation of an integrated approach. BMC Public Health. 2010,
BACKGROUND: In many low- and middle-income countries, where tobacco use is common, tuberculosis is also a major problem. Tobacco use increases the risk of developing tuberculosis, secondary mortality, poor treatment compliance and relapses. In countries with TB epidemic, even a modest relative risk leads to a significant attributable risk. Treating tobacco dependence, therefore, is likely to have benefits for controlling tuberculosis in addition to reducing the non-communicable disease burden associated with smoking. In poorly resourced health systems which face a dual burden of disease secondary to tuberculosis and tobacco, an integrated approach to tackle tobacco dependence in TB control could be economically desirable. During TB screening, health professionals come across large numbers of patients with respiratory symptoms, a significant proportion of which are likely to be tobacco users. These clinical encounters, considered to be “teachable moments”, provide a window of opportunity to offer treatment for tobacco dependence. METHODS/DESIGN: We aim to develop and trial a complex intervention to reduce tobacco dependence among TB suspects based on the WHO ‘five steps to quit’ model. This model relies on assessing personal motivation to quit tobacco use and uses it as the basis for assessing suitability for the different therapeutic options for tobacco dependence. We will use the Medical Research Council framework approach for evaluating complex interventions to: (a) design an evidence-based treatment package (likely to consist of training materials for health professionals and education tools for patients); (b) pilot the package to determine the delivery modalities in TB programme (c) assess the incremental cost-effectiveness of the package compared to usual care using a cluster RCT design; (d) to determine barriers and drivers to the provision of treatment of tobacco dependence within TB programmes; and (e) support long term implementation. The main outcomes to assess the effectiveness would be point abstinence at 4 weeks and continuous abstinence up to 6 months. DISCUSSION: This work will be carried out in Pakistan and is expected to have relevance for other low and middle income countries with high tobacco use and TB incidence. This will enhance our knowledge of the cost-effectiveness of treating tobacco dependence in patients suspected of TB. TRIAL REGISTRATION: Trial Registration Number: ISRCTN08829879