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

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Pathologies suivies

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

Revues surveillées

American journal of epidemiology  
American journal of public health  
BMC public health  
BMJ (Clinical research ed.) - British medical journal  
International journal of epidemiology  
JAMA : the journal of the American Medical Association  
Lancet  
Nature  
Risk analysis : an official publication of the Society for Risk Analysis  
Science  
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Bronchite chronique

(1) [Chronic occupational bronchitis: problems and prospects (review of literature)]. Med Tr Prom Ekol. 2011, n° 12, pp.32-38

The authors analysed history of "occupational bronchitis" term establishment, presented various points of view on defining occupational bronchial obstruction diseases, their classification and connections with other diseases. Evaluating pathogenetic features of occupational bronchitis, the authors emphasized studies of disordered "proteolysis-antiproteolysis" system role, xenobiotics biotransformation and free-radical processes. The authors pointed promising role of molecular genetic studies for better and more individual system of medical care for workers

(2) [On parity in development of obstructive and restrictive changes in miners]. Med Tr Prom Ekol. 2011, n° 12, pp.17-20

Spirometric studies in 397 miners having pneumoconiosis and chronic dust bronchitis demonstrated 80% occurrence of respiratory failure with equally marked obstructive and restrictive disorders. Therefore, bronchopulmonary diseases in miners do not match the criteria of chronic obstructive lung disease


Chronic obstructive pulmonary disease (COPD), including emphysema and chronic bronchitis, is a progressive condition in which airflow becomes limited, making it difficult to breathe. Chronic lower respiratory diseases, primarily COPD, are the third leading cause of death in the United States, and 5.1% of U.S. adults report a diagnosis of emphysema or chronic bronchitis. Smoking is the primary cause of COPD, and at least 75% of COPD deaths are attributable to smoking in the
United States. Information on state-specific prevalence of COPD is sparse, as are data on the use of COPD-related health-care resources. To understand how COPD affects adults in North Carolina and what resources are used by persons with COPD, 2007 and 2009 data from the North Carolina COPD module of the Behavioral Risk Factor Surveillance System (BRFSS) were analyzed. Among 26,227 respondents, 5.7% reported ever having been told by a health professional that they had COPD. Most adults with COPD reported ever having had a diagnostic breathing test (76.4% in 2007 and 82.4% in 2009). Among adults with COPD, 43.0% reported having gone to a physician and 14.9% visited an emergency department (ED) or were admitted to a hospital (2007) for COPD-related symptoms in the previous 12 months. Only 48.1% of persons reported daily use of medications for their COPD (2007). These results indicate that many adults with COPD might not have had adequate diagnostic spirometry, and many who might benefit from daily medications, such as long-acting bronchodilators and inhaled corticosteroids, are not taking them. Continued and expanded surveillance is needed to evaluate the effectiveness of prevention and intervention programs and support efforts to educate the public and physicians about COPD symptoms, diagnosis, and treatment.


Cigarette smoke (CS) exposure induces mucus obstruction and the development of chronic bronchitis (CB). While many of these responses are determined genetically, little is known about the effects CS can exert on pulmonary epithelia at the protein level. We, therefore, tested the hypothesis that CS exerts direct effects on the CFTR protein, which could impair airway hydration, leading to the mucus stasis characteristic of both cystic fibrosis and CB. In vivo and in vitro studies demonstrated that CS rapidly decreased CFTR activity, leading to airway surface liquid (ASL) volume depletion (i.e., dehydration). Further studies revealed that CS induced internalization of CFTR. Surprisingly, CS-internalized CFTR did not colocalize with lysosomal proteins. Instead, the bulk of CFTR shifted to a detergent-resistant fraction within the cell and colocalized with the intermediate filament vimentin, suggesting that CS induced CFTR movement into an aggresome-like, perinuclear compartment. To test whether airway dehydration could be reversed, we used hypertonic saline (HS) as an osmolyte to rehydrate ASL. HS restored ASL height in CS-exposed, dehydrated airway cultures. Similarly, inhaled HS restored mucous transport and increased clearance in patients with CB. Thus, we propose that CS exposure rapidly impairs CFTR function by internalizing CFTR, leading to ASL dehydration, which promotes mucus stasis and a failure of mucus clearance, leaving smokers at risk for developing CB. Furthermore, our data suggest that strategies to rehydrate airway surfaces may provide a novel form of therapy for patients with CB.


Chronic bronchitis (CB) is an indicator of an increased risk of developing COPD, but its symptoms are often underestimated. Demographic and socio-economic conditions might influence its prevalence, reporting and impact. Data from a large epidemiological survey of the French general population were analyzed to determine the burden of CB, the magnitude of under-diagnosis and the influence of age, gender and socio-economic conditions. Altogether, 9050 participants aged 45 years or more provided complete data. The prevalence of symptoms and diagnosis of CB was 3.5% and 3.4%, respectively. CB was associated with impaired health status and activity and, in women, work loss. Among subjects with symptoms of CB, only 28.6% declared a known diagnosis of respiratory disease. Factors associated with symptoms of CB in multivariate analysis were male gender, active smoking, lower income and occupational category: the highest prevalence was...
observed in manual workers (5.6%) and self-employed subjects (5.2%). The under-diagnosis of CB was more marked in men and subjects of higher socio-economic categories. These results confirm that CB is markedly under-diagnosed in the general population. Socio-economic conditions influence both its prevalence (higher in low categories) and rate of diagnosis (lower in high categories), which should be considered when elaborating prevention and detection campaigns.


While previous reports have described the bronchopulmonary profile of the fluoroquinolones in healthy volunteers, limited data are available in infected patients. The purpose of this study was to determine the intrapulmonary profile of high-dose (750 mg) levofloxacin in patients during an acute exacerbation of chronic bronchitis (AECB). Twenty-four patients experiencing clinical signs and symptoms of AECB were enrolled. Once enrolled, patients received levofloxacin 750 mg once daily x 5 days. Bronchoalveolar lavage aspirates and simultaneous plasma samples were obtained at 4 h, 12 h or 24 h after the third dose. Concentrations in biologic matrixes were determined with a validated HPLC method. Epithelial lining fluid (ELF) concentrations were calculated using the urea dilution method. Five patients did not complete the trial, 19 patients underwent bronchoscopy, 18 (52 +/- 13 yrs) had sufficient samples for analysis and confirmed medication compliance. Mean plasma concentrations at 4, 12, and 24 h were 8.0 +/- 2.5, 5.8 +/- 1.2, and 2.2 +/- 1.2 mug/mL. Mean ELF values at 4, 12, and 24 h were 7.5 +/- 3.0, 8.3 +/- 6.0, and 1.2 +/- 0.9 mug/mL. Mean alveolar macrophage (AM) concentrations at 4, 12, and 24 h were 38.5 +/- 43.7, 13.4 +/- 14.4, and 9.0 +/- 7.5 mug/mL. The penetration (ELF/plasma ratio) into the infection site was 113%. In these subjects with AECB, levofloxacin 750 mg once daily reached adequate exposures in the plasma, ELF, and AMs for the most commonly associated pathogens.


Cement dust exposure has previously been associated with airway symptoms and ventilatory impairment. The aim of the present study was to examine lung function and airway symptoms among employees in different jobs and at different levels of exposure to thoracic dust in the cement production industry. At the start of a 4-yr prospective cohort study in 2007, exposure to cement dust, symptoms and lung function were recorded cross-sectionally in 4,265 employees in 24 European cement plants. Bronchial exposure was assessed by 2,670 full-shift dust samples with cyclones collecting the thoracic aerosol fraction. A job exposure matrix was constructed by grouping dust concentrations according to job type and plant. Elevated odds ratios for symptoms and airflow limitation (range 1.2-2.6 in the highest quartile), but not for chronic bronchitis, were found in the higher quartiles of exposure compared with the lowest quartile. Forced expiratory volume in 1 s (FEV(1)) showed an exposure-response relationship with a 270-mL deficit of FEV(1) (95% CI 190-300 mL) in the highest compared with the lowest exposure level. The results support the hypothesis that exposure to dust in cement production may lead to respiratory symptoms and airway obstruction.
Cancer du poumon


(5) HAWKES N. Diesel exhausts may expose city dwellers to raised cancer risk. BMJ. 2012, vol. 344, p.e1669

(6) MASON GA. Cancer of the lung; review of 1,000 cases. Lancet. 1949 Oct. 1, vol. 2, n° 6579, pp.587-591


Dengue

Although low- and middle-income countries still bear the burden of major infectious diseases, chronic noncommunicable diseases are becoming increasingly common due to rapid demographic, epidemiologic, and nutritional transitions. However, information is generally scant in these countries regarding chronic disease incidence, social determinants, and risk factors. The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) aims to contribute relevant information with respect to the development and progression of clinical and subclinical chronic diseases, particularly cardiovascular diseases and diabetes. In this report, the authors delineate the study's objectives, principal methodological features, and timeline. At baseline, ELSA-Brasil enrolled 15,105 civil servants from 5 universities and 1 research institute. The baseline examination (2008-2010) included detailed interviews, clinical and anthropometric examinations, an oral glucose tolerance test, overnight urine collection, a 12-lead resting electrocardiogram, measurement of carotid intima-media thickness, echocardiography, measurement of pulse wave velocity, hepatic ultrasonography, retinal fundus photography, and an analysis of heart rate variability. Long-term biologic sample storage will allow investigation of biomarkers that may predict cardiovascular diseases and diabetes. Annual telephone surveillance, initiated in 2009, will continue for the duration of the study. A follow-up examination is scheduled for 2012-2013.

BACKGROUND: As countries in sub-Saharan Africa develop their economies, it is important to understand the health of employees and its impact on productivity and absenteeism. While previous studies have assessed the impact of single conditions on absenteeism, the current study evaluates multiple health factors associated with absenteeism in a large worker population across several sectors in Namibia. METHODS: From March 2009 to June 2010, PharmAccess Namibia conducted a series of cross-sectional surveys of 7,666 employees in 7 sectors of industry in Namibia. These included a self-reported health questionnaire and biomedical screenings for certain infectious diseases and non-communicable disease (NCD) risk factors. Data were collected on demographics, absenteeism over a 90-day period, smoking behavior, alcohol use, hemoglobin, blood pressure, blood glucose, cholesterol, waist circumference, body mass index (BMI), HIV status, and presence of hepatitis B antigens and syphilis antibodies. The associations of these factors to absenteeism were ascertained using negative binomial regression. RESULTS:
Controlling for demographic and job-related factors, high blood glucose and diabetes had the largest effect on absenteeism (IRR: 3.67, 95%CI: 2.06-6.55). This was followed by anemia (IRR: 1.59, 95%CI: 1.17-2.18) and being HIV positive (IRR: 1.47; 95%CI: 1.12-1.95). In addition, working in the fishing or services sectors was associated with an increased incidence of sick days (IRR: 1.53, 95%CI: 1.23-1.90; and IRR: 1.70, 95%CI: 1.32-2.20 respectively). The highest prevalence of diabetes was in the services sector (3.6%, 95%CI: 2.5-4.7). The highest prevalence of HIV was found in the fishing sector (14.3%, 95%CI: 10.1-18.5). CONCLUSION: Both NCD risk factors and infectious diseases are associated with increased rates of short-term absenteeism of formal sector employees in Namibia. Programs to manage these conditions could help employers avoid costs associated with absenteeism. These programs could include basic health care insurance including regular wellness screenings.


We have reported results from the formative stage of a community health worker intervention designed to improve diabetes management among Bangladeshi patients in New York City. Trained community health workers conducted focus groups (n = 47) and surveys (n = 169) with Bangladeshi individuals recruited from community locations. Results indicated that participants faced numerous barriers to care, had high rates of limited English proficiency, and had low levels of knowledge about diabetes. Most participants expressed interest in participating in a community health worker intervention.


OBJECTIVE: Recently, diabetes prevalence has increased in South Asians making it a global public health priority. There are suggestions that pre-diabetes, including impaired glucose tolerance (IGT), may not be increasing. We conducted a systematic review to explore the paradox. Research Design and Methods We searched electronic databases from inception to June 2009 for cross-sectional studies providing prevalence of pre-diabetes (using WHO criteria) in South Asian adult populations. Two reviewers independently screened articles, performed data extraction, quality appraisal and study classification with any discrepancies resolved by consensus. Repeated cross-sectional studies, categorized by pre-specified criteria, were used for the primary analysis, supplemented by analysis of comparable and all studies. RESULTS: In total, 79 cross-sectional data sets (from 69 published studies) were identified resulting in the inclusion of 179 408 people. Four sets of repeated cross-sectional studies, conducted in Chennai, rural
Tamil Nadu, Mauritius and Singapore (n = 30,399), provided time trend information. Three of them showed an increase in diabetes prevalence (P < 0.001) whereas IGT fell in two (P < 0.05), and was stable in the remainder. A similar pattern was seen among three other sets of comparable studies (n = 58,820) and in scatterplots of all 79 data sets. CONCLUSION: This novel systematic review is the first to assess secular trends of pre-diabetes in any population. The data show diabetes prevalence is rising, whereas IGT prevalence is stable or falling. Explanations include: recent environmental or lifestyle changes favouring an increased rate of conversion from IGT to diabetes, or a cohort effect with improving maternal and infant nutrition resulting in reduced IGT with a fall in diabetes to follow.


BACKGROUND: Guidelines for coronary heart disease (CHD) prevention recommend using multifactorial risk prediction algorithms, particularly the Framingham risk score. We sought to examine whether adding information on job strain to the Framingham model improves its predictive power in a low-risk working population. METHODS: Our analyses are based on data from the prospective Whitehall II cohort study, UK. Job strain among 5533 adults (mean age 48.9 years, 1666 women) was ascertained in Phases 1 (1985-88), 2 (1989-90) and 3 (1991-93). Variables comprising the Framingham score (blood lipids, blood pressure, diabetes and smoking) were measured at Phase 3. In men and women who were CHD free at baseline, CHD mortality and non-fatal myocardial infarction (MI) were ascertained from 5-yearly screenings and linkage to mortality and hospital records until Phase 7 (2002-04). RESULTS: A total of 160 coronary deaths and non-fatal MIs occurred during the mean follow-up period of 11.3 years. The addition of indicators of job strain to the Framingham score increased the C-statistics from 0.725 [95% confidence intervals (95% CIs): 0.575-0.854] to only 0.726 (0.577-0.855), corresponding to a net reclassification improvement of 0.7% (95% CIs: -4.2 to 5.6%). The findings were similar after inclusion of definite angina in the CHD outcome (352 total cases) and when using alternative operational definitions for job strain. CONCLUSION: In this middle-aged low-risk working population, job strain was associated with an increased risk of CHD. However, when compared with the Framingham algorithm, adding job strain did not improve the model's predictive performance.


BACKGROUND: Adults with type 2 diabetes mellitus often have limitations in mobility that increase with age. An intensive lifestyle intervention that produces weight loss and improves fitness could slow the loss of mobility in such patients. METHODS: We randomly assigned 5145 overweight or obese adults between the ages of 45 and 74 years with type 2 diabetes to either an intensive lifestyle intervention or a diabetes support-and-education program; 5016 participants
contributed data. We used hidden Markov models to characterize disability states and mixed-effects ordinal logistic regression to estimate the probability of functional decline. The primary outcome was self-reported limitation in mobility, with annual assessments for 4 years. RESULTS: At year 4, among 2514 adults in the lifestyle-intervention group, 517 (20.6%) had severe disability and 969 (38.5%) had good mobility; the numbers among 2502 participants in the support group were 656 (26.2%) and 798 (31.9%), respectively. The lifestyle-intervention group had a relative reduction of 48% in the risk of loss of mobility, as compared with the support group (odds ratio, 0.52; 95% confidence interval, 0.44 to 0.63; P<0.001). Both weight loss and improved fitness (as assessed on treadmill testing) were significant mediators of this effect (P<0.001 for both variables). Adverse events that were related to the lifestyle intervention included a slightly higher frequency of musculoskeletal symptoms at year 1. CONCLUSIONS: Weight loss and improved fitness slowed the decline in mobility in overweight adults with type 2 diabetes. (Fund by the Department of Health and Human Services and others; ClinicalTrials.gov number, NCT00017953.)


OBJECTIVES: To determine the incidence of any and referable diabetic retinopathy in people with type 2 diabetes mellitus attending an annual screening service for retinopathy and whose first screening episode indicated no evidence of retinopathy. DESIGN: Retrospective four year analysis. SETTING: Screenings at the community based Diabetic Retinopathy Screening Service for Wales, United Kingdom. PARTICIPANTS: 57,199 people with type 2 diabetes mellitus, who were diagnosed at age 30 years or older and who had no evidence of diabetic retinopathy at their first screening event between 2005 and 2009. 49,763 (87%) had at least one further screening event within the study period and were included in the analysis. MAIN OUTCOME MEASURES: Annual incidence and cumulative incidence after four years of any and referable diabetic retinopathy. Relations between available putative risk factors and the onset and progression of retinopathy. RESULTS: Cumulative incidence of any and referable retinopathy at four years was 360.27 and 11.64 per 1000 people, respectively. From the first to fourth year, the annual incidence of any retinopathy fell from 124.94 to 66.59 per 1000 people, compared with referable retinopathy, which increased slightly from 2.02 to 3.54 per 1000 people. Incidence of referable retinopathy was independently associated with known duration of diabetes, age at diagnosis, and use of insulin treatment. For participants needing insulin treatment with a duration of diabetes of 10 years or more, cumulative incidence of referable retinopathy at one and four years was 9.61 and 30.99 per 1000 people, respectively. CONCLUSIONS: Our analysis supports the extension of the screening interval for people with type 2 diabetes mellitus beyond the currently recommended 12 months, with the possible exception of those with diabetes duration of 10 years or more and on insulin treatment.
Dépression


It has been shown that the psychosocial environment perceived by school staff is associated with children's academic performance and wellbeing. In this study we examined the associations between organizational justice (procedural and relational justice) as reported by school staff and pupils’ perceptions of their school environment, health problems, academic performance, and absenteeism. We combined data from two surveys: for the staff (the Finnish Public Sector Study, n = 1946) and pupils (the Finnish school health promotion survey, n = 11,781 boys and 12,842 girls) of 136 secondary schools, collected during 2004-2005. Multilevel cumulative logistic regression analyses showed that after adjustment for potential individual and school-level confounding factors, low procedural justice was associated with pupils’ dissatisfaction with school-going. Low relational justice was associated with a 1.30 times higher risk of poor academic performance, 1.15 times higher risk of psychosomatic symptoms and 1.13 times higher risk of depressive symptoms among pupils. Both organizational justice components were associated with truancy. We concluded that staff perceptions of organizational justice at school are associated with pupils’ reports of their psychosocial school environment, health, performance, and absenteeism due to truancy. Improving managerial and decision making procedures among school personnel may be an important factor for protecting pupils’ academic performance and wellbeing.


BACKGROUND: Depression is a major cause of disability, particularly among women; poverty heightens the risk for depression. Beyond its direct effects, maternal depression can harm children’s health and development. This study aimed to assess the effects of a large-scale anti-poverty programme in Mexico (Oportunidades) on maternal depressive symptoms. METHODS: In 2003, 5050 women living in rural communities who had participated in Oportunidades since its inception were assessed and compared with a group of 1293 women from matched communities, whose families had received no exposure to Oportunidades at the time of assessment but were later enrolled. Self-reported depressive symptoms were measured using the Center for Epidemiologic Studies Depression Scale (CES-D). Ordinary least squares regressions were used to evaluate the treatment effect of programme participation on depression while adjusting for covariates and clustering at the community level. RESULTS: Women in the treatment group had lower depressive symptoms than those in the comparison group (unadjusted mean CES-D scores: 16.9 +/- 9.8 vs 18.6 +/- 10.2). In multivariable analyses, programme participation was associated with lower depression whilst controlling for maternal age, education and household demographic, ethnicity and socio-economic variables [beta= -1.7 points, 95% confidence interval (95% CI) -2.46 to -0.96, P < 0.001]. Reductions in perceived stress and increases in perceived control were mediators of programme effects on women. CONCLUSIONS: Although Oportunidades did not target maternal mental health directly, we found modest but clinically meaningful effects on depressive symptoms. Our design permits stronger causal inference than observational studies that have linked poverty and depressive symptoms. Our results emphasize that the well-being of individuals is responsive to macro-level economic policies and programmes...
BACKGROUND: The incidence of depressive symptoms increases during adolescence, from 10.0% to 24.5% at age 11 to 15, respectively. Experiencing elevated levels of depressive symptoms increases the risk of a depressive disorder in adulthood. A universal school-based depression prevention program Op Volle Kracht (OVK) was developed, based on the Penn Resiliency Program, aimed at preventing the increase of depressive symptoms during adolescence and enhancing positive development. In this study the effectiveness of OVK will be tested and possible mediators of program effects will be focus of study as well. METHOD: The effectiveness of OVK will be tested in a randomized controlled trial with two conditions, intervention (OVK) and control condition (care as usual). Schools are randomly assigned to research conditions. OVK will be incorporated in the school curriculum, maximizing program attendance. OVK consists of 16 lessons of 50 min, given by trained psychologists to groups of 11-15 students. OVK contains Cognitive Behavioral Therapy, social skills training, problem solving and decision making. Outcomes are measured at 6, 12, 18 and 24 months follow up, to monitor long term program effects. Primary outcome is level of depressive symptoms, secondary outcomes are: anxiety, hopelessness, cognitive bias, substance use, truancy, life satisfaction, coping, self-efficacy, optimism, happiness, friendship, school performance and school attitude. The questionnaires for students will be administered in the school setting. Parents will complete a questionnaire at baseline only. DISCUSSION: In this paper the study into the effectiveness of the depression prevention program OVK was described. It is expected that OVK will prevent the increase in depressive symptoms during adolescence and enhance positive development in the intervention condition, compared to the control condition. If OVK will be effective, it can be implemented in the school context by which numerous adolescents can be reached. TRIAL REGISTRATION: Netherlands Trial Register (NTR): NTR2879
(2005). The actual role of general practice in the dutch health-care system. Results of the second dutch national survey of general practice. Medizinische Klinik (Munich), 100(10), 656-661


OBJECTIVES: We examined whether attaining a higher educational degree after 25 years of age was associated with fewer depressive symptoms and better self-rated health at midlife than was not attaining a higher educational degree. METHODS: We analyzed data from National Longitudinal Survey of Youth, restricting our sample to respondents who had not attained a bachelor's degree by 25 years of age (n = 7179). We stratified all regression models by highest degree attained by 25 years of age. RESULTS: Among respondents with no degree, a high school diploma, or a post-high school certificate at 25 years of age, attaining at least a bachelor's degree by midlife was associated with fewer depressive symptoms and better self-rated health at midlife compared with respondents who did not attain a higher degree by midlife. Those with an associate's degree at 25 years of age who later attained a bachelor's degree or higher reported better health at midlife. CONCLUSIONS: Attaining at least a bachelor's degree after 25 years of age is associated with better midlife health. Other specifications of educational timing and its health effects across the life course should be studied.


OBJECTIVES: We investigated associations between stress and mental health (positive affect, depressive symptoms) among HIV-negative and HIV-positive midlife and older gay-identified men, along with the mediating and moderating effects of mastery and emotional support. We also studied the mental health effects of same-sex marriage. METHODS: We obtained data from self-administered questionnaires completed in 2009 or 2010 by a subsample (n = 202; average age = 56.91 years; age range = 44-75 years) of participants in the University of California, Los Angeles component of the Multicenter AIDS Cohort Study, one of the largest and longest-running natural-history studies of HIV/AIDS in the United States. RESULTS: Both sexual minority stress (perceived gay-related stigma, excessive HIV bereavements) and aging-related stress (independence and fiscal concerns) appeared to have been detrimental to mental health. Sense of mastery partially mediated these associations. Being legally married was significantly protective net of all covariates, including having a domestic partner but not being married. Education, HIV status, and race/ethnicity had no significant effects. CONCLUSIONS: Sexual minority and aging-related stress significantly affected the emotional lives of these men. Personal sense of mastery may help to sustain them as they age. We observed specific mental health benefits of same-sex legal marriage.

(2) BENKIMOUN P. Higher prices and plain packaging are part of plan to halve smoking in France by 2025. BMJ. 2012, vol. 344, p.e1647


BACKGROUND: No studies have so far evaluated the impact of the metabolic syndrome (MetS) as an entity on ovarian cancer risk. The authors aimed to examine the association between factors in the MetS, individually and combined, and risk of ovarian cancer incidence and mortality.

METHODS: Altogether, 290,000 women from Austria, Norway and Sweden were enrolled during 1974-2005, with measurements taken of height, weight, blood pressure and levels of glucose, cholesterol and triglycerides. Relative risks (RRs) of ovarian cancer were estimated using Cox regression for each MetS factor in quintiles and for standardized levels (z-scores), and for a composite z-score for the MetS. RRs were corrected for random error in measurements.

RESULTS: During follow-up, 644 epithelial ovarian cancers and 388 deaths from ovarian cancer were identified. There was no overall association between MetS and ovarian cancer risk. Increasing levels of cholesterol [RR 1.52, 95% confidence interval (95% CI) 1.01-2.29, per 1-U increment of z-score] and blood pressure (RR 1.79, 95% CI 1.12-2.86) conferred, however, increased risks of mucinous and endometrioid tumours, respectively. In women below the age of 50 years, there was increased risk of ovarian cancer mortality for MetS (RR 1.52, 95% CI 1.00-2.30). Increasing levels of BMI (RR 1.17, 95% CI 1.01-1.37) conferred increased risk of ovarian cancer mortality in women above the age of 50 years. CONCLUSION: There was no overall association between MetS and ovarian cancer risk. However, increasing levels of cholesterol and blood pressure increased the risks of mucinous and endometrioid tumours, respectively. Increasing levels of BMI conferred an increased risk of ovarian cancer mortality in women above the age of 50 years

(4) CHAPMAN S. The tobacco industry is terrified of plain packs. BMJ. 2012, vol. 344, p.e1617


BACKGROUND: Large blood-based prospective studies can provide reliable assessment of the complex interplay of lifestyle, environmental and genetic factors as determinants of chronic disease. METHODS: The baseline survey of the China Kadoorie Biobank took place during 2004-08 in 10 geographically defined regions, with collection of questionnaire data, physical measurements and blood samples. Subsequently, a re-survey of 25,000 randomly selected participants was done (80% responded) using the same methods as in the baseline. All participants are being followed for cause-specific mortality and morbidity, and for any hospital admission through linkages with registries and health insurance (HI) databases.

RESULTS: Overall, 512,891 adults aged 30-79 years were recruited, including 41% men, 56% from rural
areas and mean age was 52 years. The prevalence of ever-regular smoking was 74% in men and 3% in women. The mean blood pressure was 132/79 mmHg in men and 130/77 mmHg in women. The mean body mass index (BMI) was 23.4 kg/m\(^2\) in men and 23.8 kg/m\(^2\) in women, with only 4% being obese (>30 kg/m\(^2\)), and 3.2% being diabetic. Blood collection was successful in 99.98% and the mean delay from sample collection to processing was 10.6 h. For each of the main baseline variables, there is good reproducibility but large heterogeneity by age, sex and study area. By 1 January 2011, over 10,000 deaths had been recorded, with 91% of surviving participants already linked to HI databases. CONCLUSION: This established large biobank will be a rich and powerful resource for investigating genetic and non-genetic causes of many common chronic diseases in the Chinese population.


BACKGROUND: High serum alanine aminotransferase (ALT) levels have been associated with increased risk of diabetes and with increased mortality, but associations of variations of ALT in the normal range with outcomes have been less well studied. METHODS: We studied the relationship between ALT, mortality and cardiovascular events in the West of Scotland Coronary Prevention Study (WOSCOPS) and the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) trials that explicitly excluded subjects with clinically significant liver damage, plus the Leiden 85-plus, a study of survivors to age 85 years. The associations between ALT and morbidity and mortality outcomes were investigated using Cox proportional hazard models adjusting for a comprehensive panel of cardiovascular risk factors. RESULTS: In all three study cohorts, ALT displayed an independent inverse relationship with all-cause mortality so that hazard ratios for fourth versus first quarter of ALT were all below 1.0; HRs 0.64 [95% confidence interval (CI) 0.50-0.81], 0.86 (0.73-1.01), 0.66 (0.50-0.87); WOSCOPS, PROSPER, Leiden 85-plus, respectively. In WOSCOPS and PROSPER, ALT was also inversely associated with risk of fatal plus non-fatal cardiovascular events, including coronary heart disease (CHD) events and stroke. CONCLUSIONS: In three independent populations, ALT in the normal range displayed an inverse relationship with total mortality, cardiovascular events and non-cardiovascular events in middle-to-older aged subjects without evidence of clinically significant liver damage, independent of traditional cardiovascular and other risk factors. These findings indicate that the relationship between ALT and clinical outcomes is more complex than generally appreciated.


BACKGROUND: Cigarette smoking is associated with lower body mass index (BMI), and a commonly cited reason for unwillingness to quit smoking is a concern about weight gain. Common variation in the CHRNA5-CHRNA3-CHRNB4 gene region (chromosome 15q25) is robustly associated with smoking quantity in smokers, but its association with BMI is unknown. We hypothesized that genotype would accurately reflect smoking exposure and that, if smoking were causally related to weight, it would be associated with BMI in smokers, but not in never smokers. METHODS: We stratified nine European study samples by smoking status and, in each stratum, analysed the association between genotype of the 15q25 SNP, rs1051730, and BMI. We meta-analysed the results (n = 24,198) and then tested for a genotype x smoking status interaction. RESULTS: There was no evidence of association between BMI and genotype in the never smokers (difference per T-allele: 0.05 kg/m\(^2\) [95% confidence interval (95% CI): -0.05 to 0.18]; P = 0.25). However, in ever smokers, each additional smoking-related T-allele was associated with a 0.23 kg/m\(^2\) (95% CI: 0.13-0.31) lower BMI (P = 8 x 10(-6)). The effect size was larger in current [0.33 kg/m\(^2\)] lower BMI per T-allele (95% CI: 0.18-0.48); P = 6 x 10(-5)], than in former
smokers [0.16 kg/m(2) (95% CI: 0.03-0.29); P = 0.01]. There was strong evidence of genotype x smoking interaction (P = 0.0001). CONCLUSIONS: Smoking status modifies the association between the 15q25 variant and BMI, which strengthens evidence that smoking exposure is causally associated with reduced BMI. Smoking cessation initiatives might be more successful if they include support to maintain a healthy BMI.


BACKGROUND: Few studies have examined the possible effects of reproductive factors on cardiovascular disease (CVD) risks in Asian women. METHODS: A cohort of 267,400 female textile workers in Shanghai, China, was administered a questionnaire at enrolment (1989-91) and followed for mortality through 2000. Relative risks (hazard ratios) for ischaemic heart disease (IHD), ischaemic stroke and haemorrhagic stroke were calculated using Cox proportional hazards modelling, adjusting for relevant co-variates. RESULTS: Risks were not consistently associated with age at menopause, parity, stillbirths, miscarriages or duration of lactation. An increasing trend in IHD mortality risk, but not stroke, was observed with decreasing age at menarche. There was no evidence of increased CVD mortality risk by oral or injectable contraceptive use or induced abortions. As expected, greater mortality rates from CVD and increased CVD risks were also observed with smoking. CONCLUSIONS: Use of steroid contraceptives, induced abortions and reduced parity from China’s one-child-per-family policy has not had an adverse effect on risk of CVD mortality in this cohort.


BACKGROUND: Cross-sectional studies have suggested that elevated cortisol is associated with worse physical performance, a surrogate of ageing. We examined the relationship between repeat cortisol measures over 20 years and physical performance in later life. METHODS: Middle-aged men (45-59 years) were recruited between 1979 and 1983 (Phase 1) from the Caerphilly Prospective Study (CaPS) and re-examined 20 years later at 65-83 years of age (Phase 5). Participants included 750 and 898 subjects with either Phase 1 and/or Phase 5 data on exposure and outcomes. Outcome measures were walking speed and balance time and exposures included morning fasting serum cortisol (Phase 1) and four salivary samples on 2 consecutive days (Phase 5). RESULTS: Faster walking speed was associated with higher morning cortisol at Phase 1 [coefficient per standard deviation (SD) increase 0.68, 95% confidence interval (95% CI) 0.09-1.27; P=0.02] though this was attenuated after adjustment for covariates (coefficient per SD increase 0.45; 95% CI -0.16 to 1.07; P=0.15). Higher night-time cortisol at Phase 5 was associated with slower speed (coefficient per SD increase -1.06; 95% CI -1.60 to -0.52; P<0.001) and poorer balance (odds ratio of top tertile vs bottom 2.49; 95% CI 1.63-3.81; P<0.001). Worst performance was seen for men with a poor morning response (Phase 1) and less nocturnal decline (Phase 5). CONCLUSIONS: Dysregulation of the hypothalamic pituitary adrenal (HPA) axis is associated with worse physical performance in later life. This may reflect a causal effect of the HPA axis on ageing or that ageing itself is associated with reduced HPA reactivity.

(10) GLANTZ S, GONZALEZ M. Effective tobacco control is key to rapid progress in reduction of non-communicable diseases. Lancet. 2012 Mar. 31, vol. 379, n° 9822, pp.1269-1271

BACKGROUND: Particularly in groups of adolescents with lower educational level the smoking prevalence is still high and constitutes a serious public health problem. There is limited evidence of effective smoking cessation interventions in this group. Individualised text messaging (SMS) based interventions are promising to support smoking cessation and could be provided to adolescents irrespective of their motivation to quit. The aim of the current paper is to outline the study protocol of a trial testing the efficacy of an SMS based intervention for smoking cessation in apprentices. METHODS/DESIGN: A two-arm cluster-randomised controlled trial will be conducted to test the efficacy of an SMS intervention for smoking cessation in adolescents and young adults compared to an assessment only control group. A total of 910 daily or occasional (≥ 4 cigarettes in the preceding month and ≥ 1 cigarette in the preceding week) smoking apprentices will be proactively recruited in vocational school classes and, using school class as a randomisation unit, randomly assigned to an intervention group (n = 455) receiving the SMS based intervention or an assessment only control group (n = 455). Individualised text messages taking into account demographic data and the individuals’ smoking behaviours will be sent to the participants of the intervention group over a period of 3 months. Participants will receive two text messages promoting smoking cessation per week. Program participants who intend to quit smoking have the opportunity to use a more intensive SMS program to prepare for their quit day and to prevent a subsequent relapse. The primary outcome measure will be the proportion of participants with 7-day point prevalence smoking abstinence assessed at 6-months follow-up. The research assistants conducting the baseline and the follow-up assessments will be blinded regarding group assignment. DISCUSSION: It is expected that the program offers an effective and inexpensive way to promote smoking cessation among adolescents and young adults including those with lower educational level and independent of their motivation to quit. TRIAL REGISTRATION NUMBER: ISRCTN: ISRCTN19739792


BACKGROUND: Guidelines for coronary heart disease (CHD) prevention recommend using multifactorial risk prediction algorithms, particularly the Framingham risk score. We sought to examine whether adding information on job strain to the Framingham model improves its predictive power in a low-risk working population. METHODS: Our analyses are based on data from the prospective Whitehall II cohort study, UK. Job strain among 5533 adults (mean age 48.9 years, 1666 women) was ascertained in Phases 1 (1985-88), 2 (1989-90) and 3 (1991-93). Variables comprising the Framingham score (blood lipids, blood pressure, diabetes and smoking) were measured at Phase 3. In men and women who were CHD free at baseline, CHD mortality and non-fatal myocardial infarction (MI) were ascertained from 5-yearly screenings and linkage to mortality and hospital records until Phase 7 (2002-04). RESULTS: A total of 160 coronary deaths and non-fatal MIs occurred during the mean follow-up period of 11.3 years. The addition of indicators of job strain to the Framingham score increased the C-statistics from 0.725 [95% confidence intervals (95% CIs): 0.575-0.854] to only 0.726 (0.577-0.855), corresponding to a net reclassification improvement of 0.7% (95% CIs: -4.2 to 5.6%). The findings were similar after inclusion of definite angina in the CHD outcome (352 total cases) and when using alternative operational definitions for job strain. CONCLUSION: In this middle-aged low-risk working population, job strain was associated with an increased risk of CHD. However, when compared with the Framingham algorithm, adding job strain did not improve the model's predictive performance

We systematically evaluated smoking-related costs in multiunit housing. From 2008 to 2009, we surveyed California multiunit housing owners or managers on their past-year smoking-related costs and smoke-free policies. A total of 27.1% of respondents had incurred smoking-related costs (mean $4935), and 33.5% reported complete smoke-free policies, which lowered the likelihood of incurring smoking-related costs. Implementing statewide complete smoke-free policies may save multiunit housing property owners $18,094,254 annually.


Most diseases, injuries, and other health conditions experienced by working people are multifactorial, especially as the workforce ages. Evidence supporting the role of work and personal risk factors in the health of working people is frequently underused in developing interventions. Achieving a longer, healthy working life requires a comprehensive preventive approach. To help develop such an approach, we evaluated the influence of both occupational and personal risk factors on workforce health. We present 32 examples illustrating 4 combinatorial models of occupational hazards and personal risk factors (genetics, age, gender, chronic disease, obesity, smoking, alcohol use, prescription drug use). Models that address occupational and personal risk factors and their interactions can improve our understanding of health hazards and guide research and interventions.


(18) WHO global report : mortality attributable to tobacco

L’Organisation Mondiale de la Santé (OMS) vient de publier un rapport sur les conséquences du tabagisme dans le monde. Il présente sous forme de fiches, par continent, par zone géographique et par pays, les taux de mortalité attribuables au tabac par catégorie d’âge et par sexe, prenant en compte les maladies transmissibles (tuberculose et autres maladies infectieuses) et non transmissibles (cancers, maladies cardio-vasculaires, maladies du système respiratoire…). Chaque fiche présente des tableaux comprenant les taux de mortalité imputables à la consommation de tabac ainsi que la part des décès due au tabac selon chacune des maladies. Afin de contextualiser ces chiffres, un rappel des données démographiques générales (répartition de la population par âge et par sexe) est proposé pour chaque fiche. Les auteurs rappellent que 12% des décès chez les personnes de 30 ans et plus dans le monde sont attribuables à la consommation de tabac et que 5 millions de personnes dans cette catégorie d’âge sont décédées suite à la consommation directe de tabac en 2004.

Rapport en anglais

ABSTRACT: BACKGROUND: Public health emergencies have the potential to disproportionately impact disadvantaged populations due to pre-established social and economic inequalities. Internationally, prior to the 2009 H1N1 influenza pandemic, existing pandemic plans were created with limited public consultation; therefore, the unique needs and characteristics of some First Nations communities may not be ethically and adequately addressed. Engaging the public in pandemic planning can provide vital information regarding local values and beliefs that may ultimately lead to increased acceptability, feasibility, and implementation of pandemic plans. Thus, the objective of the present study was to elicit and address First Nations community members’ suggested modifications to their community-level pandemic plans after the 2009 H1N1 influenza pandemic. METHODS: The study area included three remote and isolated First Nations communities located in sub-arctic Ontario, Canada. A community-based participatory approach and community engagement process (i.e., semi-directed interviews (n=13), unstructured interviews (n=4), and meetings (n=27)) were employed. Participants were purposively sampled and represented various community stakeholders (e.g., local government, health care, clergy, education, etc.) involved in the community’s pandemic response. Collected data were manually transcribed and coded using deductive and inductive thematic analysis. The data subsequently informed the modification of the community-level pandemic plans. RESULTS: The primary modifications incorporated in the community-level pandemic plans involved adding community-specific detail. For example, ‘supplies’ emerged as an additional category of pandemic preparedness and response, since including details about supplies and resources was important due to the geographical remoteness of the study communities. Furthermore, it was important to add details of how, when, where, and who was responsible for implementing recommendations outlined in the pandemic plans. Additionally, the roles and responsibilities of the involved organizations were further clarified. CONCLUSIONS: Our results illustrate the importance of engaging the public, especially First Nations, in pandemic planning to address local perspectives. The community engagement process used was successful in incorporating community-based input to create up-to-date and culturally-appropriate community-level pandemic plans. Since these pandemic plans are dynamic in nature, we recommend that the plans are continuously updated to address the communities’ evolving needs. It is hoped that these modified plans will lead to an improved pandemic response capacity and health outcomes, during the next public health emergency, for these remote and isolated First Nations communities. Furthermore, the suggested modifications presented in this paper may help inform updates to the community-level pandemic plans of other similar communities.


Data from all reported cases of 2009 pandemic influenza A (H1N1) were obtained from the China Information System for Disease Control and Prevention. The spatiotemporal distribution patterns of cases were characterized through spatial analysis. The impact of travel-related risk factors on invasion of the disease was analyzed using survival analysis, and climatic factors related to local transmission were identified using multilevel Poisson regression, both at the county level. The results showed that the epidemic spanned a large geographic area, with the most affected areas being in western China. Significant differences in incidence were found among age groups, with
incidences peaking in school-age children. Overall, the epidemic spread from southeast to northwest. Proximity to airports and being intersected by national highways or freeways but not railways were variables associated with the presence of the disease in a county. Lower temperature and lower relative humidity were the climatic factors facilitating local transmission after correction for the effects of school summer vacation and public holidays, as well as population density and the density of medical facilities. These findings indicate that interventions focused on domestic travel, population density, and climatic factors could play a role in mitigating the public health impact of future influenza pandemics.


Objectives. We evaluated the relationship between maternal H1N1 vaccination and fetal and neonatal outcomes among singleton births during the 2009-2010 H1N1 pandemic. Methods. We used a population-based perinatal database in Ontario, Canada, to examine preterm birth (PTB), small-for-gestational-age (SGA) births, 5-minute Apgar score below 7, and fetal death via multivariable regression. We compared outcomes between women who did and did not receive an H1N1 vaccination during pregnancy. Results. Of the 55,570 mothers with a singleton birth, 23,340 (42.0%) received an H1N1 vaccination during pregnancy. Vaccinated mothers were less likely to have an SGA infant based on the 10th (adjusted risk ratio [RR] = 0.90; 95% confidence interval [CI] = 0.85, 0.96) and 3rd (adjusted RR = 0.81; 95% CI = 0.72, 0.92) growth percentiles; PTB at less than 32 weeks' gestation (adjusted RR = 0.73; 95% CI = 0.58, 0.91) and fetal death (adjusted RR = 0.66; 95% CI = 0.47, 0.91) were also less likely among these women. Conclusions. Our results suggest that second- or third-trimester H1N1 vaccination was associated with improved fetal and neonatal outcomes during the recent pandemic. Our findings need to be confirmed in future studies with designs that can better overcome concerns regarding biased estimates of vaccine efficacy. (Am J Public Health. Published online ahead of print April 19, 2012: e1-e8. doi:10.2105/AJPH.2011.300606)
Maladie d’Alzheimer


Alzheimer’s disease (AD) is associated with impaired clearance of beta-amyloid (Abeta) from the brain, a process normally facilitated by apolipoprotein E (apoE). ApoE expression is transcriptionally induced through the action of the nuclear receptors peroxisome proliferator-activated receptor gamma and liver X receptors in coordination with retinoid X receptors (RXRs). Oral administration of the RXR agonist bexarotene to a mouse model of AD resulted in enhanced clearance of soluble Abeta within hours in an apoE-dependent manner. Abeta plaque area was reduced more than 50% within just 72 hours. Furthermore, bexarotene stimulated the rapid reversal of cognitive, social, and olfactory deficits and improved neural circuit function. Thus, RXR activation stimulates physiological Abeta clearance mechanisms, resulting in the rapid reversal of a broad range of Abeta-induced deficits


Cognitive decline is a debilitating feature of most neurodegenerative diseases of the central nervous system, including Alzheimer’s disease. The causes leading to such impairment are only poorly understood and effective treatments are slow to emerge. Here we show that cognitive capacities in the neurodegenerating brain are constrained by an epigenetic blockade of gene transcription that is potentially reversible. This blockade is mediated by histone deacetylase 2, which is increased by Alzheimer’s-disease-related neurotoxic insults in vitro, in two mouse models of neurodegeneration and in patients with Alzheimer’s disease. Histone deacetylase 2 associates with and reduces the histone acetylation of genes important for learning and memory, which show a concomitant decrease in expression. Importantly, reversing the build-up of histone deacetylase 2 by short-hairpin-RNA-mediated knockdown unlocks the repression of these genes, reinstates structural and synaptic plasticity, and abolishes neurodegeneration-associated memory impairments. These findings advocate for the development of selective inhibitors of histone deacetylase 2 and suggest that cognitive capacities following neurodegeneration are not entirely lost, but merely impaired by this epigenetic blockade

Maladies cardio-vasculaires


CONTEXT: In populations of older adults, prediction of coronary heart disease (CHD) events through traditional risk factors is less accurate than in middle-aged adults. Electrocardiographic (ECG) abnormalities are common in older adults and might be of value for CHD prediction.
OBJECTIVE: To determine whether baseline ECG abnormalities or development of new and persistent ECG abnormalities are associated with increased CHD events. DESIGN, SETTING, AND PARTICIPANTS: A population-based study of 2192 white and black older adults aged 70 to 79 years from the Health, Aging, and Body Composition Study (Health ABC Study) without known cardiovascular disease. Adjudicated CHD events were collected over 8 years between 1997-1998 and 2006-2007. Baseline and 4-year ECG abnormalities were classified according to the Minnesota Code as major and minor. Using Cox proportional hazards regression models, the addition of ECG abnormalities to traditional risk factors were examined to predict CHD events.
MAIN OUTCOME MEASURE: Adjudicated CHD events (acute myocardial infarction [MI], CHD death, and hospitalization for angina or coronary revascularization). RESULTS: At baseline, 276 participants (13%) had minor and 506 (23%) had major ECG abnormalities. During follow-up, 351 participants had CHD events (96 CHD deaths, 101 acute MIs, and 154 hospitalizations for angina or coronary revascularizations). Both baseline minor and major ECG abnormalities were associated with an increased risk of CHD after adjustment for traditional risk factors (17.2 per 1000 person-years among those with no abnormalities; 29.3 per 1000 person-years; hazard ratio [HR], 1.35; 95% CI, 1.02-1.81; for minor abnormalities; and 31.6 per 1000 person-years; HR, 1.51; 95% CI, 1.20-1.90; for major abnormalities). When ECG abnormalities were added to a model containing traditional risk factors alone, 13.6% of intermediate-risk participants with both major and minor ECG abnormalities were correctly reclassified (overall net reclassification improvement [NRI], 7.4%; 95% CI, 3.1%-19.0%; integrated discrimination improvement, 0.99%; 95% CI, 0.32%-2.15%). After 4 years, 208 participants had new and 416 had persistent abnormalities. Both new and persistent ECG abnormalities were associated with an increased risk of subsequent CHD events (HR, 2.01; 95% CI, 1.33-3.02; and HR, 1.66; 95% CI, 1.18-2.34; respectively). When added to the Framingham Risk Score, the NRI was not significant (5.7%; 95% CI, -0.4% to 11.8%). CONCLUSIONS: Major and minor ECG abnormalities among older adults were associated with an increased risk of CHD events. Depending on the model, adding ECG abnormalities was associated with improved risk prediction beyond traditional risk factors.

(3) BATHULA R, HUGHES AD, PANERAI RB, POTTER JF, et al. South Asians have adverse cerebrovascular haemodynamics, despite equivalent blood pressure, compared with Europeans. This is due to their greater hyperglycaemia. Int J Epidemiol. 2011 Dec., vol. 40, n° 6, pp.1490-1498

BACKGROUND: South Asians have a 1.5-fold increased stroke mortality compared with Europeans, despite similar blood pressures (BP). We hypothesized that it is the greater hyperglycaemia in South Asians that increases stroke risk, by adversely affecting cerebrovascular haemodynamics. METHODS: A population-based sample of 149 Europeans and 151 South...
Asians underwent metabolic profiling and concurrent measurement of finger BP using a Finapres and middle cerebral artery (MCA) blood flow velocity using transcranial Doppler ultrasound. Cerebrovascular autoregulation, cerebrovascular resistance [resistive index (RI) and pulsatility index (PI)] were calculated. Means of cerebrovascular haemodynamic measures were compared by ethnicity, with the introduction of explanatory variables to a regression model to determine which variable could best account for ethnic differences. RESULTS: Cerebrovascular resistance (RI) was $12.9 \times 10^3 (0.9-24.8, P = 0.04)$ greater in South Asians than Europeans. Systolic, diastolic and mean MCA velocities were also higher in South Asians (mean velocity $41.4 +/- 8.0$ cm/s vs $38.0 +/- 8.0$ cm/s, respectively, $P = 0.001$). Low frequency gain, a measure of autoregulation, was worse in South Asians compared with Europeans ($0.50 +/- 0.01$ cm/s mm/Hg vs $0.45 +/- 0.01$ cm/s mm/Hg, $P = 0.01$). RI positively correlated with HbA(1c) ($r = 0.184; P < 0.01$). Adjustment for BP could not explain the higher RI in South Asians, but adjustment for HbA(1c) abolished the ethnic difference in RI ($5.8 \times 10^3 (6.5$ to $18.1, P = 0.4$). CONCLUSIONS: Cerebrovascular resistance and autoregulation are worse in South Asians than in Europeans, despite equivalent resting BP. The greater hyperglycaemia in South Asians accounts for their adverse cerebrovascular resistance. This could explain excess stroke in South Asians but requires testing in longitudinal studies.


(6) BLAHA MJ, NASIR K, BLUMENTHAL RS. Statin therapy for healthy men identified as "increased risk". JAMA. 2012 Apr. 11, vol. 307, n° 14, pp.1489-1490


BACKGROUND: Although there is consistent evidence that higher levels of education are associated with better health and reduced disease risk, there is little evidence on whether this is true throughout the lifecourse. This study examines whether additional higher educational qualifications acquired later on in adulthood are associated with a reduction in coronary heart disease (CHD) risk over and above qualifications from earlier on in life. METHODS: The National Child Development Study 1958 British birth cohort was analysed, with data at birth, age 7 (1965), age 23 (1981), 42 (2000) and age 44 years (2002). The effect of highest academic and vocational qualifications obtained by the age of 23 years, and after the age of 23 years on 10-year risk of developing CHD was estimated. RESULTS: CHD risk among women who left school without any qualifications but went on to obtain some qualifications was lower (0.1% risk) compared with their peers who left school without any qualifications (0.14% risk). Among men, the effect of additional higher qualifications on CHD risk was also negative but restricted to those who left school without any qualifications. CONCLUSIONS: Men and women who leave school without any qualifications may be able to 'catch up' to some extent with more qualified people in terms of lowered CHD risk, if they obtain qualifications later on in life. However, there are important limitations to these observed associations which limit any causal interpretation of the results.


All attempts at treating strokes by pharmacologically reducing the human brain's vulnerability to ischaemia have failed, leaving stroke as a leading cause of death, disability and massive socioeconomic loss worldwide. Over decades, research has failed to translate over 1,000 experimental treatments from discovery in cells and rodents to use in humans, a scientific crisis that gave rise to the prevailing belief that pharmacological neuroprotection is not feasible or practicable in higher-order brains. To provide a strategy for advancing stroke therapy, we used higher-order gyrencephalic non-human primates, which bear genetic, anatomical and behavioural similarities to humans and tested neuroprotection by PSD-95 inhibitors—promising compounds that uncouple postsynaptic density protein PSD-95 from neurotoxic signalling pathways. Here we show that stroke damage can be prevented in non-human primates in which a PSD-95 inhibitor is administered after stroke onset in clinically relevant situations. This treatment reduced infarct volumes as gauged by magnetic resonance imaging and histology, preserved the capacity of ischaemic cells to maintain gene transcription in genome-wide screens of ischaemic brain tissue, and significantly preserved neurological function in neurobehavioural assays. The degree of tissue neuroprotection by magnetic resonance imaging corresponded strongly to the preservation of neurological function, supporting the intuitive but unproven dictum that integrity of brain tissue can reflect functional outcome. Our findings establish that tissue neuroprotection and improved functional outcome after stroke is unequivocally achievable in gyrencephalic non-human primates treated with PSD-95 inhibitors. Efforts must ensue to translate these findings to humans


Randomized clinical trials (RCTs) are usually the preferred strategy with which to generate evidence of comparative effectiveness, but conducting an RCT is not always feasible. Though observational studies and RCTs often provide comparable estimates, the questioning of observational analyses has recently intensified because of randomized-observational discrepancies regarding the effect of postmenopausal hormone replacement therapy on coronary heart disease. Reanalyses of observational data that excluded prevalent users of hormone replacement therapy led to attenuated discrepancies, which begs the question of whether exclusion of prevalent users should be generally recommended. In the current study, the authors evaluated the effect of excluding prevalent users of statins in a meta-analysis of observational studies of persons with cardiovascular disease. The pooled, multivariate-adjusted mortality hazard ratio for statin use was 0.77 (95% confidence interval (CI): 0.65, 0.91) in 4 studies that compared incident users with nonusers, 0.70 (95% CI: 0.64, 0.78) in 13 studies that compared a combination of prevalent and incident users with nonusers, and 0.54 (95% CI: 0.45, 0.66) in 13 studies that compared prevalent users with nonusers. The corresponding hazard ratio from 18 RCTs was 0.84 (95% CI: 0.77, 0.91). It appears that the greater the proportion of prevalent statin users in observational studies, the larger the discrepancy between observational and randomized estimates


BACKGROUND: Few studies have examined the possible effects of reproductive factors on cardiovascular disease (CVD) risks in Asian women. METHODS: A cohort of 267,400 female textile workers in Shanghai, China, was administered a questionnaire at enrolment (1989-91) and followed for mortality through 2000. Relative risks (hazard ratios) for ischaemic heart disease (IHD), ischaemic stroke and haemorrhagic stroke were calculated using Cox proportional hazards modelling, adjusting for relevant co-variates. RESULTS: Risks were not consistently associated with age at menopause, parity, stillbirths, miscarriages or duration of lactation. An increasing trend in IHD mortality risk, but not stroke, was observed with decreasing age at menarche. There was no evidence of increased CVD mortality risk by oral or injectable contraceptive use or induced abortions. As expected, greater mortality rates from CVD and increased CVD risks were also observed with smoking. CONCLUSIONS: Use of steroid contraceptives, induced abortions and reduced parity from China’s one-child-per-family policy has not had an adverse effect on risk of CVD mortality in this cohort

(14) GREENLAND P. Should the resting electrocardiogram be ordered as a routine risk assessment test in healthy asymptomatic adults? JAMA. 2012 Apr. 11, vol. 307, n° 14, pp.1530-1531


BACKGROUND: A high circulating concentration of interleukin 6 is associated with increased risk of coronary heart disease. Blockade of the interleukin-6 receptor (IL6R) with a monoclonal antibody (tocilizumab) licensed for treatment of rheumatoid arthritis reduces systemic and articular inflammation. However, whether IL6R blockade also reduces risk of coronary heart disease is unknown. METHODS: Applying the mendelian randomisation principle, we used single nucleotide polymorphisms (SNPs) in the gene IL6R to evaluate the likely efficacy and safety of IL6R inhibition for primary prevention of coronary heart disease. We compared genetic findings with the effects of tocilizumab reported in randomised trials in patients with rheumatoid arthritis. FINDINGS: In 40 studies including up to 133,449 individuals, an IL6R SNP (rs7529229) marking a non-synonymous IL6R variant (rs8192284; p.Asp358Ala) was associated with increased circulating log interleukin-6 concentration (increase per allele 9.45%, 95% CI 8.34-10.57) as well as reduced C-reactive protein (decrease per allele 8.35%, 95% CI 7.31-9.38) and fibrinogen concentrations (decrease per allele 0.85%, 95% CI 0.60-1.10). This pattern of effects was consistent with IL6R blockade from infusions of tocilizumab (4-8 mg/kg every 4 weeks) in patients with rheumatoid arthritis studied in randomised trials. In 25,458 coronary heart disease cases and 100,740 controls, the IL6R rs7529229 SNP was associated with a decreased odds of coronary heart disease events (per allele odds ratio 0.95, 95% CI 0.93-0.97, p=1.53x10(-5)). INTERPRETATION: On the basis of genetic evidence in human beings, IL6R signalling seems to have a causal role in development of coronary heart disease. IL6R blockade could provide a novel therapeutic approach to prevention of coronary heart disease that warrants testing in suitably powered randomised trials. Genetic studies in populations could be used more widely to help to validate and prioritise novel drug targets or to repurpose existing agents and targets for new therapeutic uses. FUNDING: UK Medical Research Council; British Heart Foundation; Rosetrees Trust; US National Heart, Lung, and Blood Institute; Du Pont Pharma; Chest, Heart and Stroke Scotland; Wellcome Trust; Coronary Thrombosis Trust; Northwick Park Institute for Medical Research; UCLH/UCL Comprehensive Medical Research Centre; US National Institute on Aging;

BACKGROUND: Guidelines for coronary heart disease (CHD) prevention recommend using multifactorial risk prediction algorithms, particularly the Framingham risk score. We sought to examine whether adding information on job strain to the Framingham model improves its predictive power in a low-risk working population. METHODS: Our analyses are based on data from the prospective Whitehall II cohort study, UK. Job strain among 5533 adults (mean age 48.9 years, 1666 women) was ascertained in Phases 1 (1985-88), 2 (1989-90) and 3 (1991-93). Variables comprising the Framingham score (blood lipids, blood pressure, diabetes and smoking) were measured at Phase 3. In men and women who were CHD free at baseline, CHD mortality and non-fatal myocardial infarction (MI) were ascertained from 5-yearly screenings and linkage to mortality and hospital records until Phase 7 (2002-04). RESULTS: A total of 160 coronary deaths and non-fatal MIs occurred during the mean follow-up period of 11.3 years. The addition of indicators of job strain to the Framingham score increased the C-statistics from 0.725 [95% confidence intervals (95% CIs): 0.575-0.854] to only 0.726 (0.577-0.855), corresponding to a net reclassification improvement of 0.7% (95% CIs: -4.2 to 5.6%). The findings were similar after inclusion of definite angina in the CHD outcome (352 total cases) and when using alternative operational definitions for job strain. CONCLUSION: In this middle-aged low-risk working population, job strain was associated with an increased risk of CHD. However, when compared with the Framingham algorithm, adding job strain did not improve the model's predictive performance.


BACKGROUND: Admission rates among patients presenting to emergency departments with possible acute coronary syndromes are high, although for most of these patients, the symptoms are ultimately found not to have a cardiac cause. Coronary computed tomographic angiography (CCTA) has a very high negative predictive value for the detection of coronary disease, but its usefulness in determining whether discharge of patients from the emergency department is safe is not well established. METHODS: We randomly assigned low-to-intermediate-risk patients presenting with possible acute coronary syndromes, in a 2:1 ratio, to undergo CCTA or to receive traditional care. Patients were enrolled at five centers in the United States. Patients older than 30 years of age with a Thrombolysis in Myocardial Infarction risk score of 0 to 2 and signs or symptoms warranting admission or testing were eligible. The primary outcome was safety, assessed in the subgroup of patients with a negative CCTA examination, with safety defined as...
the absence of myocardial infarction and cardiac death during the first 30 days after presentation.

RESULTS: We enrolled 1370 subjects: 908 in the CCTA group and 462 in the group receiving traditional care. The baseline characteristics were similar in the two groups. Of 640 patients with a negative CCTA examination, none died or had a myocardial infarction within 30 days (0%; 95% confidence interval [CI], 0 to 0.57). As compared with patients receiving traditional care, patients in the CCTA group had a higher rate of discharge from the emergency department (49.6% vs. 22.7%; difference, 26.8 percentage points; 95% CI, 21.4 to 32.2), a shorter length of stay (median, 18.0 hours vs. 24.8 hours; P<0.001), and a higher rate of detection of coronary disease (9.0% vs. 3.5%; difference, 5.6 percentage points; 95% CI, 0 to 11.2). There was one serious adverse event in each group. CONCLUSIONS: A CCTA-based strategy for low-to-intermediate-risk patients presenting with a possible acute coronary syndrome appears to allow the safe, expedited discharge from the emergency department of many patients who would otherwise be admitted. (Funded by the Commonwealth of Pennsylvania Department of Health and the American College of Radiology Imaging Network Foundation; ClinicalTrials.gov number, NCT00933400.)


BACKGROUND: Thrombin potently activates platelets through the protease-activated receptor PAR-1. Vorapaxar is a novel antiplatelet agent that selectively inhibits the cellular actions of thrombin through antagonism of PAR-1. METHODS: We randomly assigned 26,449 patients who had a history of myocardial infarction, ischemic stroke, or peripheral arterial disease to receive vorapaxar (2.5 mg daily) or matching placebo and followed them for a median of 30 months. The primary efficacy end point was the composite of death from cardiovascular causes, myocardial infarction, or stroke. After 2 years, the data and safety monitoring board recommended discontinuation of the study treatment in patients with a history of stroke owing to the risk of intracranial hemorrhage. RESULTS: At 3 years, the primary end point had occurred in 1028 patients (9.3%) in the vorapaxar group and in 1176 patients (10.5%) in the placebo group (hazard ratio for the vorapaxar group, 0.87; 95% confidence interval [CI], 0.80 to 0.94; P<0.001). Cardiovascular death, myocardial infarction, stroke, or recurrent ischemia leading to revascularization occurred in 1259 patients (11.2%) in the vorapaxar group and 1417 patients (12.4%) in the placebo group (hazard ratio, 0.88; 95% CI, 0.82 to 0.95; P=0.001). Moderate or severe bleeding occurred in 4.2% of patients who received vorapaxar and 2.5% of those who received placebo (hazard ratio, 1.66; 95% CI, 1.43 to 1.93; P<0.001). There was an increase in the rate of intracranial hemorrhage in the vorapaxar group (1.0%, vs. 0.5% in the placebo group; P<0.001). CONCLUSIONS: Inhibition of PAR-1 with vorapaxar reduced the risk of cardiovascular death or ischemic events in patients with stable atherosclerosis who were receiving standard therapy. However, it increased the risk of moderate or severe bleeding, including intracranial hemorrhage. (Funded by Merck; TRA 2P-TIMI 50 ClinicalTrials.gov number, NCT00526474.)


BACKGROUND: Intravenous alteplase is the only approved treatment for acute ischemic stroke. Tenecteplase, a genetically engineered mutant tissue plasminogen activator, is an alternative thrombolytic agent. METHODS: In this phase 2B trial, we randomly assigned 75 patients to receive alteplase (0.9 mg per kilogram of body weight) or tenecteplase (0.1 mg per kilogram or 0.25 mg per kilogram) less than 6 hours after the onset of ischemic stroke. To favor the selection of patients most likely to benefit from thrombolytic therapy, the eligibility criteria were a perfusion lesion at least 20% greater than the infarct core on computed tomographic (CT) perfusion imaging at baseline and an associated vessel occlusion on CT angiography. The coprimary end points
were the proportion of the perfusion lesion that was reperfused at 24 hours on perfusion-weighted magnetic resonance imaging and the extent of clinical improvement at 24 hours as assessed on the National Institutes of Health Stroke Scale (NIHSS, a 42-point scale on which higher scores indicate more severe neurologic deficits). RESULTS: The three treatment groups each comprised 25 patients. The mean (±SD) NIHSS score at baseline for all patients was 14.4±2.6, and the time to treatment was 2.9±0.8 hours. Together, the two tenecteplase groups had greater reperfusion (P=0.004) and clinical improvement (P<0.001) at 24 hours than the alteplase group. There were no significant between-group differences in intracranial bleeding or other serious adverse events. The higher dose of tenecteplase (0.25 mg per kilogram) was superior to the lower dose and to alteplase for all efficacy outcomes, including absence of serious disability at 90 days (in 72% of patients, vs. 40% with alteplase; P=0.02). CONCLUSIONS: Tenecteplase was associated with significantly better reperfusion and clinical outcomes than alteplase in patients with stroke who were selected on the basis of CT perfusion imaging. (Funded by the Australian National Health and Medical Research Council; Australia New Zealand Clinical Trials Registry number, ACTRN12608000466347.)

(21) REDBERG RF, KATZ MH. Healthy men should not take statins. JAMA. 2012 Apr. 11, vol. 307, no 14, pp.1491-1492


BACKGROUND: Persistent inflammation has been proposed to contribute to various stages in the pathogenesis of cardiovascular disease. Interleukin-6 receptor (IL6R) signalling propagates downstream inflammation cascades. To assess whether this pathway is causally relevant to coronary heart disease, we studied a functional genetic variant known to affect IL6R signalling. METHODS: In a collaborative meta-analysis, we studied Asp358Ala (rs2228145) in IL6R in relation to a panel of conventional risk factors and inflammation biomarkers in 125,222 participants. We also compared the frequency of Asp358Ala in 51,441 patients with coronary heart disease and in 136,226 controls. To gain insight into possible mechanisms, we assessed Asp358Ala in relation to localised gene expression and to postlipopolysaccharide stimulation of interleukin 6. FINDINGS: The minor allele frequency of Asp358Ala was 39%. Asp358Ala was not associated with lipid concentrations, blood pressure, adiposity, dysglycaemia, or smoking (p value for association per minor allele >/=0.04 for each). By contrast, for every copy of 358Ala inherited, mean concentration of IL6R increased by 34.3% (95% CI 30.4-38.2) and of interleukin 6 by 14.6% (10.7-18.4), and mean concentration of C-reactive protein was reduced by 7.5% (5.9-9.1) and of fibrinogen by 1.0% (0.7-1.3). For every copy of 358Ala inherited, risk of coronary heart disease was reduced by 3.4% (1.8-5.0). Asp358Ala was not related to IL6R mRNA levels or interleukin-6 production in monocytes. INTERPRETATION: Large-scale human genetic and biomarker data are consistent with a causal association between IL6R-related pathways and coronary heart disease. FUNDING: British Heart Foundation; UK Medical Research Council; UK National Institute of Health Research, Cambridge Biomedical Research Centre; BUPA Foundation


Maladies liées à l'alcool


OBJECTIVES: Two-year alcohol use trajectories were documented among residents in a project-based Housing First program. Project-based Housing First provides immediate, low-barrier, nonabstinence-based, permanent supportive housing to chronically homeless individuals within a single housing project. The study aim was to address concerns that nonabstinence-based housing may enable alcohol use. METHODS: A 2-year, within-subjects analysis was conducted among 95 chronically homeless individuals with alcohol problems who were allocated to project-based Housing First. Alcohol variables were assessed through self-report. Data on intervention exposure were extracted from agency records. RESULTS: Multilevel growth models indicated significant within-subjects decreases across alcohol use outcomes over the study period. Intervention exposure, represented by months spent in housing, consistently predicted additional decreases in alcohol use outcomes. CONCLUSIONS: Findings did not support the enabling hypothesis. Although the project-based Housing First program did not require abstinence or treatment attendance, participants decreased their alcohol use and alcohol-related problems as a function of time and intervention exposure


BACKGROUND: High cardiovascular diseases (CVD) mortality among the middle aged is a major cause of reduced life expectancy in Russia, especially among men. Hazardous alcohol consumption is suspected to be a powerful contributing factor. METHODS: All men (1099) and women (519) aged 30-70 years who died between 1 January 2008 and 31 August 2009 from CVD in the city of Arkhangelsk, north-west Russia, were included. CVD mortality was stratified by age, gender and diagnosis. For the cases diagnosed by forensic pathologists, the blood alcohol concentration (BAC) was determined. The forensic autopsy rate was 72% for men and 62% for women. RESULTS: Age-standardized CVD mortality rate (all age groups) in men was higher than in women. The largest male-female ratio (4.3) was observed in the age group of 50-59 years. Alcoholic and unspecified cardiomyopathies were the most dominant of CVD mortalities in women, and second in men aged <50 years; they accounted for 50 and 25% of deaths, respectively. About one-third of men and women who died from CVD aged <60 years had consumed alcohol shortly before death. This occurred most frequently among the diagnostic groups 'other acute or subacute cardiac ischaemia', 'atherosclerotic heart disease' and 'cardiomyopathies'. Alcohol was more likely to be found at autopsy in men than in women (odds ratio 1.55; 95% confidence interval 1.14-2.10). No difference was found for those who died from myocardial infarction, cerebrovascular diseases and cardiomyopathies. Of the deceased, <1% had a BAC of \( \geq 4 \text{ g/l} \). CONCLUSIONS: A high proportion of subjects who died from CVD in Arkhangelsk consumed alcohol shortly before death. It was highest among males aged 50-59 years. The largest gender difference in mortality, highest absolute number of premature CVD deaths, and the highest proportion of alcohol-positive autopsies occurred among them. Since associations with alcohol consumption varied considerably between the types of CVD diagnoses, this observation should be taken into account when planning future research. Our study does not provide evidence that cardiovascular deaths are misclassified cases of acute alcohol poisoning.
1,218 >/= 5 years). Health facility and health worker readiness was variable: chloroquine was available at only 5% of facilities, 73% stocked recommended artesunate and sulfadoxine/pyrimethamine (AS+SP), 51% had the capacity to perform parasitological diagnosis, 53% of health workers had received in-service training on ACTs, 24% were trained in the use of malaria Rapid Diagnostic Tests, and 19% had received a supervisory visit including malaria case-management. At all health facilities 46% of febrile patients were parasitologically tested and 35% of patients were both, tested and treated according to test result. At facilities where AS+SP and malaria diagnostics were available 66% of febrile patients were tested and 51% were both, tested and treated according to test result. Among test positive patients 64% were treated with AS+SP but 24% were treated with artemether monotherapy. Among test negative patients only 17% of patients were treated for malaria. The majority of ACT dispensing and counseling practices were suboptimal. CONCLUSIONS: Five years following change of the policy from chloroquine to ACTs and 3 years before the end of the new malaria strategic plan chloroquine was successfully phased out from public facilities in Sudan, however, an important gap remained in the availability of ACTs, diagnostic capacities and coverage with malaria case-management activities. The national scale-up of diagnostics, using the findings of this survey as well as future qualitative research, should present an opportunity not only to expand existing testing capacities but also to implement effective support interventions to bridge the health systems gaps and support corrective case-management measures, including the discontinuation of artemether monotherapy treatment


Evolving resistance to artemisinin-based compounds threatens to derail attempts to control malaria. Resistance has been confirmed in western Cambodia and has recently emerged in western Thailand, but is absent from neighboring Laos. Artemisinin resistance results in reduced parasite clearance rates (CRs) after treatment. We used a two-phase strategy to identify genome region(s) underlying this ongoing selective event. Geographical differentiation and haplotype structure at 6969 polymorphic single-nucleotide polymorphisms (SNPs) in 91 parasites from Cambodia, Thailand, and Laos identified 33 genome regions under strong selection. We screened SNPs and microsatellites within these regions in 715 parasites from Thailand, identifying a selective sweep on chromosome 13 that shows strong association (P = 10(-6) to 10(-12)) with slow CRs, illustrating the efficacy of targeted association for identifying the genetic basis of adaptive traits

(3) LEVINE HD. **Medical experiences with American troops in the Pacific; with remarks on the diagnostic value of sternal puncture in malaria and on the innocuousness of hookworm infection.** N Engl J Med. 1946 Dec. 26, vol. 235, n° 26, pp.933-938


Burkitt's lymphoma is a highly aggressive B-cell non-Hodgkin lymphoma and is the fastest growing human tumour. The disease is associated with Epstein-Barr virus and was one of the first tumours shown to have a chromosomal translocation that activates an oncogene (c-MYC). Burkitt's lymphoma is the most common childhood cancer in areas where malaria is holoendemic. The incidence is very high in immunosuppressed patients in non-endemic areas, especially when associated with HIV infection. Outcome with intensive chemotherapy has improved and is now excellent in children, but the prognosis is poor in elderly adults. The success of intensive treatment relies on good supportive care. The therapy offered in oncology units in low-income countries is not as aggressive as in centres in high-income countries and outcomes are less
successful. Adjuvant monoclonal antibody therapy with rituximab shows promise for improved outcomes and reduced toxic effects in the future.


BACKGROUND: Pyronaridine-artesunate is an artemisinin-based combination therapy under evaluation for the treatment of Plasmodium falciparum and P. vivax malaria. METHODS: We conducted a phase 3, open-label, multicenter, noninferiority trial that included 1271 patients between 3 and 60 years of age from Asia (81.3%) or Africa (18.7%) with microscopically confirmed, uncomplicated P. falciparum malaria. Patients underwent randomization for treatment with a fixed-dose combination of 180 mg of pyronaridine and 60 mg of artesunate or with 250 mg of mefloquine plus 100 mg of artesunate. Doses were calculated according to body weight and administered once daily for 3 days. RESULTS: Pyronaridine-artesunate was noninferior to mefloquine plus artesunate for the primary outcome: adequate clinical and parasitologic response in the per-protocol population on day 28, corrected for reinfection with the use of polymerase-chain-reaction (PCR) genotyping. For this outcome, efficacy in the group receiving pyronaridine-artesunate was 99.2% (743 of 749 patients; 95% confidence interval [CI], 98.3 to 99.7) and that in the group receiving mefloquine plus artesunate was 97.8% (360 of 368 patients; 95% CI, 95.8 to 99.1), with a treatment difference of 1.4 percentage points (95% CI, 0.0 to 3.5; P=0.05). In the intention-to-treat population, efficacy on day 42 in the group receiving pyronaridine-artesunate was 83.1% (705 of 848 patients; 95% CI, 80.4 to 85.6) and that in the group receiving mefloquine plus artesunate was 83.9% (355 of 423 patients; 95% CI, 80.1 to 87.3). In Cambodia, where there were 211 study patients, the median parasite clearance time was prolonged for both treatments: 64 hours versus 16.0 to 38.9 hours in other countries (P<0.001, on the basis of Kaplan-Meier estimates). Kaplan-Meier estimates of the recrudescence rate in the intention-to-treat population in Cambodia until day 42 were higher with pyronaridine-artesunate than with mefloquine plus artesunate (10.2% [95% CI, 5.4 to 18.6] vs. 0%; P=0.04 as calculated with the log-rank test), but similar for the other countries combined (4.7% [95% CI, 3.3 to 6.7] and 2.8% [95% CI, 1.5 to 5.3], respectively; P=0.24). Elevated levels of aminotransferases were observed in those receiving pyronaridine-artesunate. Two patients receiving mefloquine plus artesunate had seizures. CONCLUSIONS: Fixed-dose pyronaridine-artesunate was efficacious in the treatment of uncomplicated P. falciparum malaria. In Cambodia, extended parasite clearance times were suggestive of in vivo resistance to artemisinin. (Funded by Shin Poong Pharmaceutical Company and the Medicines for Malaria Venture; ClinicalTrials.gov number, NCT00403260.)

(6) WALTON GA. **Incidence of malaria in tropical Africa.** Nature. 1948 July 17, vol. 162, n° 4107, p.114
Pathologies liées à l’obésité


Although low- and middle-income countries still bear the burden of major infectious diseases, chronic noncommunicable diseases are becoming increasingly common due to rapid demographic, epidemiologic, and nutritional transitions. However, information is generally scant in these countries regarding chronic disease incidence, social determinants, and risk factors. The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) aims to contribute relevant information with respect to the development and progression of clinical and subclinical chronic diseases, particularly cardiovascular diseases and diabetes. In this report, the authors delineate the study's objectives, principal methodological features, and timeline. At baseline, ELSA-Brasil enrolled 15,105 civil servants from 5 universities and 1 research institute. The baseline examination (2008-2010) included detailed interviews, clinical and anthropometric examinations, an oral glucose tolerance test, overnight urine collection, a 12-lead resting electrocardiogram, measurement of carotid intima-media thickness, echocardiography, measurement of pulse wave velocity, hepatic ultrasonography, retinal fundus photography, and an analysis of heart rate variability. Long-term biologic sample storage will allow investigation of biomarkers that may predict cardiovascular diseases and diabetes. Annual telephone surveillance, initiated in 2009, will continue for the duration of the study. A follow-up examination is scheduled for 2012-2013


As with other instrumental variable (IV) analyses, Mendelian randomization (MR) studies rest on strong assumptions. These assumptions are not routinely systematically evaluated in MR applications, although such evaluation could add to the credibility of MR analyses. In this article, the authors present several methods that are useful for evaluating the validity of an MR study. They apply these methods to a recent MR study that used fat mass and obesity-associated (FTO) genotype as an IV to estimate the effect of obesity on mental disorder. These approaches to evaluating assumptions for valid IV analyses are not fail-safe, in that there are situations where the approaches might either fail to identify a biased IV or inappropriately suggest that a valid IV is biased. Therefore, the authors describe the assumptions upon which the IV assessments rely. The methods they describe are relevant to any IV analysis, regardless of whether it is based on a genetic IV or other possible sources of exogenous variation. Methods that assess the IV assumptions are generally not conclusive, but routinely applying such methods is nonetheless likely to improve the scientific contributions of MR studies.

Many studies have found cross-sectional associations between characteristics of the neighborhood built environment and physical activity (PA) behavior. However, most are based on self-reported PA, which is known to result in overestimation of PA and differential misclassification by demographic and biological characteristics. Cardiorespiratory fitness (CRF) is an objective marker of PA because it is primarily determined by PA. Furthermore, it is causally related to long-term health outcomes. Therefore, analyses of the association between CRF and built environment could strengthen arguments for the importance of built environment influences on health. We examined the association between neighborhood walkability and CRF and body-mass index (BMI). This cross-sectional analysis included 16,543 adults (5017 women, 11,526 men) aged 18-90 years with home addresses in Texas who had a comprehensive clinical examination between 1987 and 2005. Outcomes included CRF from total duration on a maximal exercise treadmill test and measured BMI. Three neighborhood walkability factors emerged from principal components analyses of block-group measures derived from the U.S. Census. In multilevel adjusted analyses, the neighborhood walkability factors were significantly associated with CRF and BMI among men and women in the expected direction. An interaction between one of the neighborhood factors and age was also observed. The interaction suggested that living in neighborhoods with older homes and with residents traveling shorter distances to work was more strongly positively associated with CRF among younger adults and more strongly negatively associated with BMI among older adults. In conclusion, neighborhood characteristics hypothesized to support more PA and less driving were associated with higher levels of CRF and lower BMI. Demonstration of an association between built environment characteristics and CRF is a significant advance over past studies based on self-reported PA. Nevertheless, stronger causal evidence depends on more robust study designs and sophisticated measures of the environment, behavior, and their physiological consequences.


BACKGROUND: Adults with type 2 diabetes mellitus often have limitations in mobility that increase with age. An intensive lifestyle intervention that produces weight loss and improves fitness could slow the loss of mobility in such patients. METHODS: We randomly assigned 5145 overweight or obese adults between the ages of 45 and 74 years with type 2 diabetes to either an intensive lifestyle intervention or a diabetes support-and-education program; 5016 participants contributed data. We used hidden Markov models to characterize disability states and mixed-effects ordinal logistic regression to estimate the probability of functional decline. The primary outcome was self-reported limitation in mobility, with annual assessments for 4 years. RESULTS: At year 4, among 2514 adults in the lifestyle-intervention group, 517 (20.6%) had severe disability and 969 (38.5%) had good mobility; the numbers among 2502 participants in the support group were 656 (26.2%) and 798 (31.9%), respectively. The lifestyle-intervention group had a relative reduction of 48% in the risk of loss of mobility, as compared with the support group (odds ratio,
0.52; 95% confidence interval, 0.44 to 0.63; P<0.001). Both weight loss and improved fitness (as assessed on treadmill testing) were significant mediators of this effect (P<0.001 for both variables). Adverse events that were related to the lifestyle intervention included a slightly higher frequency of musculoskeletal symptoms at year 1. CONCLUSIONS: Weight loss and improved fitness slowed the decline in mobility in overweight adults with type 2 diabetes. (Funded by the Department of Health and Human Services and others; ClinicalTrials.gov number, NCT00017953.)


BACKGROUND: Social disparities in obesity are often more marked among women than men, possibly due to social factors. Taking a life-history perspective, we hypothesized that childhood infections could be relevant via sex-specific effects of immune system activation on sexual development and, hence, body shape. METHODS: We used multivariable linear regression to assess the sex-specific, adjusted associations of 'childhood' pathogens [0 (n = 1002), 1 (n = 2199), 2 (n = 3442) or 3 (n = 4833) of HSV1, CMV and hepatitis A antibodies] and 'adult' pathogens [0 (n = 5836), 1 (n = 3018) or >/= 2 (n = 720) of HSV2, HHV8 and hepatitis B or C] with waist-hip ratio (WHR) and body mass index (BMI) standard deviations (SDs) using NHANES III (1988-94). As validation, we assessed associations with height. RESULTS: 'Childhood' pathogens were positively associated with WHR among women [0.18 SD, 95% confidence interval (95% CI) 0.04-0.32 for 3, compared with 0], but not men (-0.04 SD, 95% CI -0.15 to 0.08), adjusted for age, education, race/ethnicity, smoking and alcohol. Further adjustments for leg length barely changed the estimates. There were no such sex-specific associations for BMI or for adult pathogens. 'Childhood', but not 'adult', pathogens were negatively associated with height, adjusted for age, sex, education and race/ethnicity. CONCLUSIONS: These observations are consistent with the lifecourse hypothesis that early exposure to infections makes women vulnerable to central obesity. This hypothesis potentially sheds new light on the developmental origins of obesity, and is consistent with the generally higher levels of central obesity among women than men in developing populations


Most diseases, injuries, and other health conditions experienced by working people are multifactorial, especially as the workforce ages. Evidence supporting the role of work and personal risk factors in the health of working people is frequently underused in developing interventions. Achieving a longer, healthy working life requires a comprehensive preventive approach. To help develop such an approach, we evaluated the influence of both occupational and personal risk factors on workforce health. We present 32 examples illustrating 4 combinatorial models of occupational hazards and personal risk factors (genetics, age, gender, chronic disease, obesity, smoking, alcohol use, prescription drug use). Models that address occupational and personal risk factors and their interactions can improve our understanding of health hazards and guide research and interventions


BACKGROUND: While substantive epidemiological literature suggests that alcohol drinking and obesity are potential risk factors of colorectal cancer (CRC), the possible interaction between the two has not been adequately explored. We used a case-control study to examine if alcohol drinking is associated with an increased risk of CRC and if such risk differs in people with and without obesity. METHODS: Newly diagnosed CRC cases were identified between 1999 and 2003 in Newfoundland and Labrador (NL). Cases were frequency-matched by age and sex with controls selected using random digit dialing. Cases (702) and controls (717) completed self-administered questionnaires assessing health and lifestyle variables. Estimates of alcohol intake included types of beverage, years of drinking, and average number of alcohol drinks per day. Odds ratios were estimated to investigate the associations of alcohol independently and when stratified by obesity status on the risk of CRC. RESULTS: Among obese participants (BMI \geq 30), alcohol was associated with higher risk of CRC (OR: 2.2; 95% CI: 1.2-4.0) relative to the non-alcohol category. Among obese individuals, 3 or more different types of drinks were associated with a 3.4-fold higher risk of CRC relative to non-drinkers. The risk of CRC also increased with drinking years and drinks daily among obese participants. However, no increased risk was observed in people without obesity. CONCLUSION: The effect of alcohol of drinking on CRC seems to be modified by obesity.
immunization, to evaluate whether immune-response variables predicted HIV-1 infection through 42 months of follow-up. RESULTS: Of six primary variables, two correlated significantly with infection risk: the binding of IgG antibodies to variable regions 1 and 2 (V1V2) of HIV-1 envelope proteins (Env) correlated inversely with the rate of HIV-1 infection (estimated odds ratio, 0.57 per 1-SD increase; \( P=0.02; q=0.08 \)), and the binding of plasma IgA antibodies to Env correlated directly with the rate of infection (estimated odds ratio, 1.54 per 1-SD increase; \( P=0.03; q=0.08 \)). Neither low levels of V1V2 antibodies nor high levels of Env-specific IgA antibodies were associated with higher rates of infection than were found in the placebo group. Secondary analyses suggested that Env-specific IgA antibodies may mitigate the effects of potentially protective antibodies. CONCLUSIONS: This immune-correlates study generated the hypotheses that V1V2 antibodies may have contributed to protection against HIV-1 infection, whereas high levels of Env-specific IgA antibodies may have mitigated the effects of protective antibodies. Vaccines that are designed to induce higher levels of V1V2 antibodies and lower levels of Env-specific IgA antibodies than are induced by the RV144 vaccine may have improved efficacy against HIV-1 infection.


(14) LONG ER. Tuberculosis in Germany. Science. 1948 May 7, vol. 107, n° 2784, p.460


(20) Politique de l’OMS pour les activités conjointes de lutte contre la tuberculose et le VIH
L’Organisation Mondiale de la Santé (OMS) vient de publier un document complicant ses recommandations existantes sur la tuberculose associée au VIH. Destinée aux directeurs de programmes, aux responsables de la mise en œuvre ainsi qu’aux autres partenaires intervenant dans ce champ, cette publication met à jour un précédent document de travail publié en 2004 intitulé « politique actuelle de collaboration pour les activités de lutte contre la tuberculose et le VIH ». Les activités conjointes tuberculose/VIH recommandées sont regroupées selon trois objectifs. Le premier concerne la mise en place et le renforcement des mécanismes de collaboration pour la prestation de services intégrés tuberculose et VIH, en coordonnant au mieux
les activités dans ce domaine. Le second est de réduire la charge de la tuberculose chez les individus vivant avec le VIH et d’organiser le plus rapidement possible le traitement antirétroviral. L’OMS recommande, par exemple, de lutter contre la transmission de l’infection tuberculeuse dans les établissements collectifs et les lieux de soins. Le dernier porte sur la réduction de la charge du VIH chez les personnes touchées par la tuberculose (ou présumées tuberculeuses), en intensifiant, entre autres, le dépistage du VIH chez ces dernières.

Guide
Annexes en anglais