



Bulletin de veille

« Focus sur 12 pathologies graves »

Février 2010

Service de Documentation

Le Service Documentation de l'EHESP édite **mensuellement** un bulletin de veille. Celui-ci signale les **articles récents**, parus dans des revues scientifiques de renommée internationale, autour de **12 pathologies graves**, ainsi que sur la **pandémie grippale**. Ce bulletin signale également des **rapports officiels et institutionnels** disponibles en texte intégral.

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Bulletin de veille – Février 2010 « Focus sur 12 pathologies graves »

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

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

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

- American journal of epidemiology
- American journal of public health
- BMC public health
- BMJ (Clinical research ed.) - British medical journal
- International journal of epidemiology
- JAMA : the journal of the American Medical Association
- Lancet
- Nature
- Risk analysis : an official publication of the Society for Risk Analysis
- Science
- Social science & medicine
- The New England journal of medicine

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Articles scientifiques**Bronchite chronique obstructive**[sommaire](#)

- (1) FUHRMAN C, ROCHE N, VERGNENEGRE A, CHOUAID C, *et al.* [**Chronic bronchitis: prevalence and quality of life. Analysis of data from the French Health Interview Survey 2002-2003**]. *Rev Mal Respir.* 2009 Sept., vol. 26, n° 7, pp.759-768

INTRODUCTION: Chronic bronchitis is associated with an increased risk of COPD and health-related quality of life (HRQoL) impairment. The objectives of the study were to estimate the prevalence of chronic bronchitis and to describe its relations with quality of life. **METHODS:** The French Health Interview Survey was conducted in 2003 in a representative sample of households. Data were collected during an interviewer's visits to the home. Respiratory symptoms and HRQoL (SF-36) were assessed in 9,050 adults aged 45 years and older using a self-administered questionnaire. **RESULTS:** The prevalence of chronic bronchitis was estimated at 3.5%. Chronic bronchitis was associated with an impaired physical component summary score after adjusting for sex, age and dyspnoea. It was associated with a reduced mental component summary score (MCS) among men. In women, this association was only significant in the absence of dyspnoea. **CONCLUSION:** The prevalence of chronic bronchitis was 3.5% among adults aged 45 years and older. Chronic bronchitis was associated with impairment in health-related quality of life

- (2) HASSANEIN SE, NARSAVAGE GL. **The dose effect of pulmonary rehabilitation on physical activity, perceived exertion, and quality of life.** *J Cardiopulm Rehabil Prev.* 2009 July, vol. 29, n° 4, pp.255-260

PURPOSE: Pulmonary rehabilitation (PR) programs have been shown to improve functional status, exercise performance, and quality of life (QOL) and decrease perception of exertion in individuals with chronic obstructive pulmonary disease. The purpose of this study was to identify the dose effect of PR on the outcome variables of activity level, perceived exertion, and physical and mental QOL. **METHODS:** The study used a retrospective explanatory design. The sample (N = 104) included records of individuals diagnosed with chronic bronchitis and emphysema who attended a PR program from 2000 to 2005 at a Midwest inner-city, academic medical center. Participants attended rehabilitation sessions 2 to 3 days per week for approximately 90 minutes each day; maximum duration of the program was 3 months (24 sessions). The PR dose was calculated by multiplying the number of PR sessions with the number of weeks attended. **RESULTS:** There were 32 men and 72 women, with a mean age of 59.9 years +/- 10.2 years. All patients were retired or unemployed, and 99% used oxygen during exercise. A higher PR dose was significantly related to improvement in activity level measured by maximum metabolic equivalent (MET) level achieved. A nonsignificant but minimally clinically important difference was found on the Medical Outcomes Study Short-Form 36 (SF-36) outcomes of mental and physical QOL. **CONCLUSIONS:** The findings of the current study support a significant relationship between PR dose and activity level (maximum MET level achieved). Physical and mental QOL improved clinically after PR. Optimal program outcomes were related to greater patient participation in supervised PR

- (3) HUKKINEN M, KORHONEN T, BROMS U, KOSKENVUO M, *et al.* **Long-term smoking behavior patterns predicting self-reported chronic bronchitis.** *COPD.* 2009 Aug., vol. 6, n° 4, pp.242-249

We examined the effects of long-term smoking patterns on self-reported symptoms of chronic bronchitis within the Finnish adult twin cohort including 21, 609 individuals responding to questionnaires in 1975 and 1981, of which 11,015 respondents participated also in 1990. We also explored the association between smoking and bronchitis among discordant twin pairs. Among those without chronic bronchitis at baseline we examined incidence of chronic bronchitis in 1981

both by 1975 smoking status, but also based on subgroups formed according to change in smoking behaviors between 1975 and 1981. We conducted similar analyses in the longitudinal data including three consecutive measurements of smoking status. Logistic regressions demonstrated that among current smokers, the risk of chronic bronchitis increased about 1.5-fold by each amount category of daily cigarettes. When analyzing change of smoking status between 1975 and 1981, daily moderate and heavy smokers, smoking increasers and decreasers, as well as re-current smokers demonstrated elevated risks. In the analysis among discordant twin pairs the smoking co-twins had a 14-fold likelihood for chronic bronchitis compared to their never-smoking co-twins. Panel analyses showed that, not only moderate and heavy, but also former and light smokers, had significant risks for chronic bronchitis. Those with late smoking initiation, leisure time physical activity or over 10 years of smoking cessation were less likely to have chronic bronchitis. We conclude that in long term evaluation no safe level of smoking exists. Abstinence from tobacco seems to be the public health message justified by these results in prevention of chronic bronchitis

- (4) JIVCU C, GOTFRIED M. **Gemifloxacin use in the treatment of acute bacterial exacerbation of chronic bronchitis.** Int J Chron Obstruct Pulmon Dis. 2009, vol. 4, pp.291-300
<http://www.ncbi.nlm.nih.gov/pubmed/19684863>

The newest generation of fluoroquinolones have proven efficacy against bacterial organisms associated with acute exacerbation of chronic bronchitis (AECB). Gemifloxacin, as one of the quinolones in this class, exhibits many of the pharmacokinetic and pharmacodynamic characteristics of the class with a few notable differences. Against *Streptococcus pneumoniae* it has a lower minimal inhibitory concentration (MIC) than the other respiratory fluoroquinolones and it has activity against both bacterial DNA gyrase and topoisomerase IV. The increased activity of gemifloxacin against both enzymes may be associated with decreased rates of resistance. Clinically, gemifloxacin has been shown to have positive effects on length of hospitalization and increased success at long-term follow-up in AECB patients. These associations were observed in noninferiority comparison studies. Although an advantage with the use of gemifloxacin in AECB is suggested, there are no comparison data available to conclude that gemifloxacin is superior to the other respiratory fluoroquinolones. Gemifloxacin is generally well tolerated, but is associated with a characteristic rash and gastrointestinal upset as its most common observed side effects

- (5) PAHWA P, KARUNANAYAKE CP. **Modeling of longitudinal polytomous outcome from complex survey data--application to investigate an association between mental distress and non-malignant respiratory diseases.** BMC Med Res Methodol. 2009, vol. 9, p.84
<http://dx.doi.org/10.1186/1471-2288-9-84>

BACKGROUND: The data from longitudinal complex surveys based on multi-stage sampling designs contain cross-sectional dependencies among units due to clustered nature of the data and within-subject dependencies due to repeated measurements. Special statistical methods are required to analyze longitudinal complex survey data. **METHODS:** Statistics Canada's longitudinal National Population Health Survey (NPHS) dataset from the first five cycles (1994/1995 to 2002/2003) was used to investigate the effects of demographic, social, life-style, and health-related factors on the longitudinal changes of mental distress scores among the NPHS participants who self-reported physician diagnosed respiratory diseases, specifically asthma and chronic bronchitis. The NPHS longitudinal sample includes 17,276 persons of all ages. In this report, participants 15 years and older ($n = 14,713$) were considered for statistical analysis. Mental distress, an ordinal outcome variable (categories: no/low, moderate, and high) was examined. Ordered logistic regression models based on the weighted generalized estimating equations approach were fitted to investigate the association between respiratory diseases and mental distress adjusting for other covariates of interest. Variance estimates of regression coefficients were computed by using bootstrap methods. The final model was used to predict the probabilities of prevalence of no/low, moderate or high mental distress scores. **RESULTS:** Accounting for design effects does not vary the significance of the coefficients of the model. Participants suffering with chronic bronchitis were significantly at a higher risk ($OR_{adj} = 1.37$; 95% CI: 1.12-1.66) of reporting high levels of mental distress compared to those who did not self-report

chronic bronchitis. There was no significant association between asthma and mental distress. There was a significant interaction between sex and self-perceived general health status indicating a dose-response relationship. Among females, the risk of mental distress increases with increasing deteriorating (from excellent to very poor) self-perceived general health.

CONCLUSIONS: A positive association was observed between the physician diagnosed self-reported chronic bronchitis and an increased prevalence of mental distress when adjusted for important covariates. Variance estimates of regression coefficients obtained from the sandwich estimator (i.e. not accounting for design effects) were similar to bootstrap variance estimates (i.e. accounting for design effects). Even though these two sets of variance estimates are similar, it is more appropriate to use bootstrap variance estimates

- (6) ZHANG J, XU JF, LIU YB, XIAO ZK, *et al.* **Population pharmacokinetics of oral levofloxacin 500 mg once-daily dosage in community-acquired lower respiratory tract infections: results of a prospective multicenter study in China.** *J Infect Chemother.* 2009 Oct., vol. 15, n° 5, pp.293-300
<http://dx.doi.org/10.1007/s10156-009-0714-8>

This study aimed to explore the pharmacokinetic features of levofloxacin (LVFX) in Chinese patients with infections and to confirm oral LVFX 500 mg once daily as an optimal treatment regimen based on pharmacokinetic-pharmacodynamic (PK-PD) analysis. A total of 1052 plasma samples from 164 Chinese adult patients with community acquired lower respiratory tract infections (CALRTIs) and 18 healthy volunteers were used for population PK analysis. LVFX 500-mg tablets were given once daily. A nonlinear mixed effects model (NONMEM) program was used for population PK model-building and a two-compartment model with first-order absorption process was established. Creatinine clearance (CL(cr)) and body weight were identified as intrinsic factors which significantly affected oral clearance (CL(t)/F) and the apparent volume of distribution of the central compartment (V1/F), respectively. The final model is described as follows: $CL(t)/F (l/h) = (8.97 + 0.917 \times (CL(cr) (ml/min) - 100.92) \times 60/1000) \times \exp(\eta_{CL(t)/F})$. $V1/F (l) = (85.3 + 1.22 \times (\text{weight (kg)} - 60.75)) \times \exp(\eta_{V1/F})$. $Q/F (l/h) = 0.351$. $V2/F (l) = 6.81$. $k(a) (h^{-1}) = 1.44 \times \exp(\eta_{ka})$. Based on the population PK model, mean C(max) and AUC(0-24h) in CALRTI patients were estimated as 5.13 microg/ml and 58.98 microg.h/ml, respectively. A subgroup analysis showed that patients with mild renal dysfunction ($50 \text{ ml/min} < \text{or} = CL(cr) < 80 \text{ ml/min}$) had 34% higher AUC(0-24h) values compared to patients with normal renal function ($CL(cr) > \text{or} = 80 \text{ ml/min}$). Postmodeling simulation using final population PK estimates also showed that C(max) and AUC(0-24h) increased markedly in patients with severe renal dysfunction. The results indicate that LVFX dosage adjustment should be individualized on the basis of the CL(cr), especially in those with CL(cr) less than 50 ml/min. None of the PK parameters had any correlation with the occurrence of adverse events. PK-PD analysis indicated that, in patients treated with LVFX 500 mg once daily, the AUC(0-24h)/MIC ratio exceeded the target for those major CALRTI pathogens isolated. In addition, the C(max)/MIC ratio reached 5 for *Streptococcus pneumoniae*, indicating that the emergence of LVFX-resistant *S. pneumoniae* could be prevented during the therapy with this dosage regimen. These results demonstrate that oral LVFX 500 mg once daily has favorable PK parameters and PK-PD features in patients with CALRTIs, and the results strongly support this dosage regimen for the treatment of CALRTI

- (7) ZHU G, AGUSTI A, GULSVIK A, BAKKE P, *et al.* **CTLA4 gene polymorphisms are associated with chronic bronchitis.** *Eur Respir J.* 2009 Sept., vol. 34, n° 3, pp.598-604
<http://dx.doi.org/10.1183/09031936.00141808>

Chronic obstructive pulmonary disease (COPD) is characterised by chronic and progressive dyspnoea, cough and sputum production. T-lymphocytes may play a key role in the pathogenesis of COPD and chronic bronchitis. Cytotoxic T-lymphocyte antigen (CTLA) 4 is a potential candidate gene because it modulates T-cell activation. Genetic association between nine CTLA4 single nucleotide polymorphisms (SNPs) and chronic bronchitis was assessed in 606 pedigrees (1,896 individuals) from the International COPD Genetics Network (ICGN) population. We then replicated the associations in 342 COPD subjects with chronic bronchitis and 511 COPD subjects without chronic bronchitis from Bergen, Norway. Family-based association tests were used to analyse the

ICGN cohort, and a logistic regression model was used for the Bergen cohort. Six CTLA4 SNPs were significantly associated with chronic bronchitis in the ICGN cohort ($0.0079 < \text{or} = p < \text{or} = 0.0432$), with three being replicated with the same directionality of association in the Bergen cohort ($0.0325 < \text{or} = p < \text{or} = 0.0408$). One of these replicated SNPs (rs231775) encodes the Thr to Ala substitution at amino acid position 17. Haplotype analyses supported the results of single SNP analyses. Thus, CTLA4 is likely to be a genetic determinant of chronic bronchitis among COPD cases

Cancer du poumon

[sommaire](#)

- (1) BAGNARDI V, RANDI G, LUBIN J, CONSONNI D, *et al.* **Alcohol consumption and lung cancer risk in the Environment and Genetics in Lung Cancer Etiology (EAGLE) study.** Am J Epidemiol. 2010 Jan. 1, vol. 171, n° 1, pp.36-44
<http://dx.doi.org/10.1093/aje/kwp332> (Accès réservé EHESP)

The authors investigated the relation between alcohol consumption and lung cancer risk in the Environment and Genetics in Lung Cancer Etiology (EAGLE) Study, a population-based case-control study. Between 2002 and 2005, 2,100 patients with primary lung cancer were recruited from 13 hospitals within the Lombardy region of Italy and were frequency-matched on sex, area of residence, and age to 2,120 randomly selected controls. Alcohol consumption during adulthood was assessed in 1,855 cases and 2,065 controls. Data on lifetime tobacco smoking, diet, education, and anthropometric measures were collected. Adjusted odds ratios and 95% confidence intervals for categories of mean daily ethanol intake were calculated using unconditional logistic regression. Overall, both nondrinkers (odds ratio = 1.42, 95% confidence interval: 1.03, 2.01) and very heavy drinkers (≥ 60 g/day; odds ratio = 1.44, 95% confidence interval: 1.01, 2.07) were at significantly greater risk than very light drinkers (0.1-4.9 g/day). The alcohol effect was modified by smoking behavior, with no excess risk being observed in never smokers. In summary, heavy alcohol consumption was a risk factor for lung cancer among smokers in this study. Although residual confounding by tobacco smoking cannot be ruled out, this finding may reflect interplay between alcohol and smoking, emphasizing the need for preventive measures

- (2) BALLATORI E, FATIGONI S, ROILA F. **Treatment of lung cancer.** N Engl J Med. 2009 Dec. 17, vol. 361, n° 25, pp.2485-2487
<http://dx.doi.org/10.1056/NEJMc0909634> (Accès réservé EHESP)
- (3) CARLSTEN C, BURKE W. **Re: "Invited commentary: genes, environment, and hybrid vigor".** Am J Epidemiol. 2010 Jan. 1, vol. 171, n° 1, p.133
<http://dx.doi.org/10.1093/aje/kwp397> (Accès réservé EHESP)
- (4) CHUNG RY, SCHOOLING CM, COWLING BJ, LEUNG GM. **How does socioeconomic development affect risk of mortality? An age-period-cohort analysis from a recently transitioned population in China.** Am J Epidemiol. 2010 Feb. 1, vol. 171, n° 3, pp.345-356
<http://dx.doi.org/10.1093/aje/kwp378> (Accès réservé EHESP)

During the 20th century, the Hong Kong Chinese population experienced 2 abrupt but temporally distinct macroenvironmental changes: The transition from essentially preindustrial living conditions to a rapidly developing economy through mass migration in the late 1940s was followed by the emergence of an infant and childhood adiposity epidemic in the 1960s. The authors aimed to delineate the effects of these 2 aspects of economic development on mortality, thus providing a sentinel for other rapidly developing economies. Sex-specific Poisson models were used to estimate effects of age, calendar period, and birth cohort on Hong Kong adult mortality between 1976 and 2005. All-cause and cause-specific mortality, including mortality from ischemic heart

disease (IHD), cardiovascular disease excluding IHD, lung cancer, other cancers, and respiratory disease, were considered. Male mortality from IHD and female mortality from other cancers increased with birth into a more economically developed environment. Cardiovascular disease mortality increased with birth after the start of the infant and childhood adiposity epidemic, particularly for men. Macroenvironmental changes associated with economic development had sex-specific effects over the life course, probably originating in early life. The full population health consequences of these changes are unlikely to manifest until persons who have spent their early lives in such environments reach an age at which they become vulnerable to chronic diseases

- (5) CONSONNI D, DE MS, LUBIN JH, WACHOLDER S, *et al.* **Lung cancer and occupation in a population-based case-control study.** Am J Epidemiol. 2010 Feb. 1, vol. 171, n° 3, pp.323-333 <http://dx.doi.org/10.1093/aje/kwp391> (Accès réservé EHESP)

The authors examined the relation between occupation and lung cancer in the large, population-based Environment And Genetics in Lung cancer Etiology (EAGLE) case-control study. In 2002-2005 in the Lombardy region of northern Italy, 2,100 incident lung cancer cases and 2,120 randomly selected population controls were enrolled. Lifetime occupational histories (industry and job title) were coded by using standard international classifications and were translated into occupations known (list A) or suspected (list B) to be associated with lung cancer. Smoking-adjusted odds ratios and 95% confidence intervals were calculated with logistic regression. For men, an increased risk was found for list A (177 exposed cases and 100 controls; odds ratio = 1.74, 95% confidence interval: 1.27, 2.38) and most occupations therein. No overall excess was found for list B with the exception of filling station attendants and bus and truck drivers (men) and launderers and dry cleaners (women). The authors estimated that 4.9% (95% confidence interval: 2.0, 7.8) of lung cancers in men were attributable to occupation. Among those in other occupations, risk excesses were found for metal workers, barbers and hairdressers, and other motor vehicle drivers. These results indicate that past exposure to occupational carcinogens remains an important determinant of lung cancer occurrence

- (6) LANGHOLZ B, RICHARDSON DB. **Fitting general relative risk models for survival time and matched case-control analysis.** Am J Epidemiol. 2010 Feb. 1, vol. 171, n° 3, pp.377-383 <http://dx.doi.org/10.1093/aje/kwp403> (Accès réservé EHESP)

Cox proportional hazards regression analysis of survival data and conditional logistic regression analysis of matched case-control data are methods that are widely used by epidemiologists. Standard statistical software packages accommodate only log-linear model forms, which imply exponential exposure-response functions and multiplicative interactions. In this paper, the authors describe methods for fitting non-log-linear Cox and conditional logistic regression models. The authors use data from a study of lung cancer mortality among Colorado Plateau uranium miners (1950-1982) to illustrate these methods for fitting general relative risk models to matched case-control data, counter-matched data with weights, d:m matching, and full cohort Cox regression using the SAS statistical package (SAS Institute Inc., Cary, North Carolina)

- (7) MCMAHON GT, BLAKE MA, WU CL. **Case records of the Massachusetts General Hospital. Case 1-2010. A 75-year-old man with hypertension, hyperglycemia, and edema.** N Engl J Med. 2010 Jan. 14, vol. 362, n° 2, pp.156-166 <http://dx.doi.org/10.1056/NEJMcp0905546> (Accès réservé EHESP)

- (8) RAINE R, WONG W, SCHOLLES S, ASHTON C, *et al.* **Social variations in access to hospital care for patients with colorectal, breast, and lung cancer between 1999 and 2006: retrospective analysis of hospital episode statistics.** BMJ. 2010, vol. 340, p.b5479 <http://www.ncbi.nlm.nih.gov/pubmed/20075152> (Accès réservé EHESP)

OBJECTIVES: To determine the extent to which type of hospital admission (emergency compared with elective) and surgical procedure varied by socioeconomic circumstances, age, sex, and year of admission for colorectal, breast, and lung cancer. **DESIGN:** Repeated cross sectional study with data from individual patients, 1 April 1999 to 31 March 2006. **SETTING:** Hospital episode statistics (HES) dataset. **PARTICIPANTS:** 564 821 patients aged 50 and over admitted with a diagnosis of colorectal, breast, or lung cancer. **MAIN OUTCOME MEASURES:** Proportion of patients admitted as emergencies, and the proportion receiving the recommended surgical treatment. **RESULTS:** Patients from deprived areas, older people, and women were more likely to be admitted as emergencies. For example, the adjusted odds ratio for patients with breast cancer in the least compared with most deprived fifth of deprivation was 0.63 (95% confidence interval 0.60 to 0.66) and the adjusted odds ratio for patients with lung cancer aged 80-89 compared with those aged 50-59 was 3.13 (2.93 to 3.34). There were some improvements in disparities between age groups but not for patients living in deprived areas over time. Patients from deprived areas were less likely to receive preferred procedures for rectal, breast, and lung cancer. These findings did not improve with time. For example, 67.4% (3529/5237) of patients in the most deprived fifth of deprivation had anterior resection for rectal cancer compared with 75.5% (4497/5959) of patients in the least deprived fifth (1.34, 1.22 to 1.47). Over half (54.0%, 11 256/20 849) of patients in the most deprived fifth of deprivation had breast conserving surgery compared with 63.7% (18 445/28 960) of patients in the least deprived fifth (1.21, 1.16 to 1.26). Men were less likely than women to undergo anterior resection and lung cancer resection and older people were less likely to receive breast conserving surgery and lung cancer resection. For example, the adjusted odds ratio for lung cancer patients aged 80-89 compared with those aged 50-59 was 0.52 (0.46 to 0.59). **Conclusions** Despite the implementation of the NHS Cancer Plan, social factors still strongly influence access to and the provision of care

- (9) SERUGA B, AMIR E, TANNOCK I. **Treatment of lung cancer.** N Engl J Med. 2009 Dec. 17, vol. 361, n° 25, pp.2485-2487
<http://www.ncbi.nlm.nih.gov/pubmed/20050212> (Accès réservé EHESP)
- (10) TAKANO T. **Treatment of lung cancer.** N Engl J Med. 2009 Dec. 17, vol. 361, n° 25, pp.2485-2486
<http://www.ncbi.nlm.nih.gov/pubmed/20050213> (Accès réservé EHESP)
- (11) TAKKOUICHE B, REGUEIRA-MENDEZ C, MONTES-MARTINEZ A. **Risk of cancer among hairdressers and related workers: a meta-analysis.** Int J Epidemiol. 2009 Dec., vol. 38, n° 6, pp.1512-1531
<http://dx.doi.org/10.1093/ije/dyp283> (Accès réservé EHESP)

BACKGROUND: Hairdressers and allied occupations represent a large and fast growing group of professionals. The fact that these professionals are chronically exposed to a large number of chemicals present in their work environment, including potential carcinogens contained in hair dyes, makes it necessary to carry out a systematic evaluation of the risk of cancer in this group. **METHODS:** We retrieved studies by systematically searching Medline and other computerized databases, and by manually examining the references of the original articles and monographs retrieved. We also contacted international researchers working on this or similar topics to complete our search. We included 247 studies reporting relative risk (RR) estimates of hairdresser occupation and cancer of different sites. **RESULTS:** Study-specific RRs were weighted by the inverse of their variance to obtain fixed and random effects pooled estimates. The pooled RR of occupational exposure as a hairdresser was 1.27 (95% CI 1.15-1.41) for lung cancer, 1.52 [95% confidence interval (CI) 1.11-2.08] for larynx cancer, 1.30 (95% CI 1.20-1.42) for bladder cancer and 1.62 (95% CI 1.22-2.14) for multiple myeloma. Data for other anatomic sites showed increases of smaller magnitude. The results restricted to those studies carried out before the ban of two major carcinogens from hair dyes in the mid-1970s were similar to the general results. **CONCLUSIONS:** Hairdressers have a higher risk of cancer than the general population.

Improvement of the ventilation system in the hairdresser salons and implementation of hygiene measures aimed at mitigating exposure to potential carcinogens at work may reduce the risk

- (12) WANG J, QIU JH. **Treatment of lung cancer**. N Engl J Med. 2009 Dec. 17, vol. 361, n° 25, p.2486
<http://www.ncbi.nlm.nih.gov/pubmed/20050214> (Accès réservé EHESP)

Diabète

[sommaire](#)

- (1) ABBOUD H, HENRICH WL. **Clinical practice. Stage IV chronic kidney disease**. N Engl J Med. 2010 Jan. 7, vol. 362, n° 1, pp.56-65
<http://dx.doi.org/10.1056/NEJMcp0906797> (Accès réservé EHESP)
- (2) BLOOMGARDEN Z, STELL L, JOVANOVIC L. **Treatment for mild gestational diabetes**. N Engl J Med. 2010 Jan. 28, vol. 362, n° 4, pp.366-367
<http://www.ncbi.nlm.nih.gov/pubmed/20112447> (Accès réservé EHESP)
- (3) BONDS DE, MILLER ME, BERGENSTAL RM, BUSE JB, *et al.* **The association between symptomatic, severe hypoglycaemia and mortality in type 2 diabetes: retrospective epidemiological analysis of the ACCORD study**. BMJ. 2010, vol. 340, p.b4909
<http://www.ncbi.nlm.nih.gov/pubmed/20061358> (Accès réservé EHESP)

OBJECTIVE: To determine whether there is a link between hypoglycaemia and mortality among participants in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. **DESIGN:** Retrospective epidemiological analysis of data from the ACCORD trial. Setting Diabetes clinics, research clinics, and primary care clinics. **PARTICIPANTS:** Patients were eligible for the ACCORD study if they had type 2 diabetes, a glycated haemoglobin (haemoglobin A(1C)) concentration of 7.5% or more during screening, and were aged 40-79 years with established cardiovascular disease or 55-79 years with evidence of subclinical disease or two additional cardiovascular risk factors. Intervention Intensive (haemoglobin A(1C) <6.0%) or standard (haemoglobin A(1C) 7.0-7.9%) glucose control. **OUTCOME MEASURES:** Symptomatic, severe hypoglycaemia, manifest as either blood glucose concentration of less than 2.8 mmol/l (<50 mg/dl) or symptoms that resolved with treatment and that required either the assistance of another person or medical assistance, and all cause and cause specific mortality, including a specific assessment for involvement of hypoglycaemia. **RESULTS:** 10 194 of the 10 251 participants enrolled in the ACCORD study who had at least one assessment for hypoglycaemia during regular follow-up for vital status were included in this analysis. Unadjusted annual mortality among patients in the intensive glucose control arm was 2.8% in those who had one or more episodes of hypoglycaemia requiring any assistance compared with 1.2% for those with no episodes (53 deaths per 1924 person years and 201 deaths per 16 315 person years, respectively; adjusted hazard ratio (HR) 1.41, 95% CI 1.03 to 1.93). A similar pattern was seen among participants in the standard glucose control arm (3.7% (21 deaths per 564 person years) v 1.0% (176 deaths per 17 297 person years); adjusted HR 2.30, 95% CI 1.46 to 3.65). On the other hand, among participants with at least one hypoglycaemic episode requiring any assistance, a non-significantly lower risk of death was seen in those in the intensive arm compared with those in the standard arm (adjusted HR 0.74, 95% 0.46 to 1.23). A significantly lower risk was observed in the intensive arm compared with the standard arm in participants who had experienced at least one hypoglycaemic episode requiring medical assistance (adjusted HR 0.55, 95% CI 0.31 to 0.99). Of the 451 deaths that occurred in ACCORD up to the time when the intensive treatment arm was closed, one death was adjudicated as definitely related to hypoglycaemia. **CONCLUSION:** Symptomatic, severe hypoglycaemia was associated with an increased risk of death within each study arm. However, among participants who experienced at least one episode of hypoglycaemia,

the risk of death was lower in such participants in the intensive arm than in the standard arm. Symptomatic, severe hypoglycaemia does not appear to account for the difference in mortality between the two study arms up to the time when the ACCORD intensive glycaemia arm was discontinued. TRIAL REGISTRATION: NCT00000620

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<http://dx.doi.org/3;10.1001/jama.2009.1930> (Accès réservé EHESP)
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<http://www.ncbi.nlm.nih.gov/pubmed/20044400> (Accès réservé EHESP)
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<http://dx.doi.org/10.1001/jama.2009.2026> (Accès réservé EHESP)
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<http://dx.doi.org/10.1126/science.326.5959.1478> (Accès réservé EHESP)
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<http://dx.doi.org/10.1056/NEJMcibr0911499> (Accès réservé EHESP)
- (13) HE C, ZHANG C, HUNTER DJ, HANKINSON SE, *et al.* **Age at menarche and risk of type 2 diabetes: results from 2 large prospective cohort studies.** Am J Epidemiol. 2010 Feb. 1, vol. 171, n° 3, pp.334-344
<http://dx.doi.org/10.1093/aje/kwp372> (Accès réservé EHESP)

The authors investigated the association between age at menarche and risk of type 2 diabetes mellitus (T2DM) among 101,415 women from the Nurses' Health Study (NHS) aged 34-59 years

(1980-2006) and 100,547 women from Nurses' Health Study II (NHS II) aged 26-46 years (1991-2005). During 2,430,274 and 1,373,875 person-years of follow-up, respectively, 7,963 and 2,739 incident cases of T2DM were documented. Young age at menarche was associated with increased risk of T2DM after adjustment for potential confounders, including body figure at age 10 years and body mass index (BMI; weight (kg)/height (m)²) at age 18 years. Relative risks of T2DM across age-at-menarche categories (< or =11, 12, 13, 14, and > or =15 years) were 1.18 (95% confidence interval (CI): 1.10, 1.27), 1.09 (95% CI: 1.02, 1.17), 1.00 (referent), 0.92 (95% CI: 0.83, 1.01), and 0.95 (95% CI: 0.84, 1.06), respectively, in the NHS (P for trend < 0.0001) and 1.40 (95% CI: 1.24, 1.57), 1.13 (95% CI: 1.00, 1.27), 1.00 (referent), 0.98 (95% CI: 0.82, 1.18), and 0.96 (95% CI: 0.78, 1.19), respectively, in NHS II (P for trend < 0.0001). Associations were substantially attenuated after additional control for updated time-varying BMI. These data suggest that early menarche is associated with increased risk of T2DM in adulthood. The association may be largely mediated through excessive adult adiposity. The association was stronger among younger women, supporting a role for sex hormones in younger onset of T2DM, in addition to BMI

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<http://dx.doi.org/10.1038/nature08625> (Accès payant)

Effects of susceptibility variants may depend on from which parent they are inherited. Although many associations between sequence variants and human traits have been discovered through genome-wide associations, the impact of parental origin has largely been ignored. Here we show that for 38,167 Icelanders genotyped using single nucleotide polymorphism (SNP) chips, the parental origin of most alleles can be determined. For this we used a combination of genealogy and long-range phasing. We then focused on SNPs that associate with diseases and are within 500 kilobases of known imprinted genes. Seven independent SNP associations were examined. Five-one with breast cancer, one with basal-cell carcinoma and three with type 2 diabetes-have parental-origin-specific associations. These variants are located in two genomic regions, 11p15 and 7q32, each harbouring a cluster of imprinted genes. Furthermore, we observed a novel association between the SNP rs2334499 at 11p15 and type 2 diabetes. Here the allele that confers risk when paternally inherited is protective when maternally transmitted. We identified a differentially methylated CTCF-binding site at 11p15 and demonstrated correlation of rs2334499 with decreased methylation of that site

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<http://www.ncbi.nlm.nih.gov/pubmed/20044398> (Accès réservé EHESP)

- (16) MATY SC, JAMES SA, KAPLAN GA. **Life-course socioeconomic position and incidence of diabetes mellitus among blacks and whites: the Alameda County Study, 1965-1999.** Am J Public Health. 2010 Jan., vol. 100, n° 1, pp.137-145
<http://dx.doi.org/10.2105/AJPH.2008.133892> (Accès réservé EHESP)

OBJECTIVES: We examined associations between several life-course socioeconomic position (SEP) measures (childhood SEP, education, income, occupation) and diabetes incidence from 1965 to 1999 in a sample of 5422 diabetes-free Black and White participants in the Alameda County Study. **METHODS:** Race-specific Cox proportional hazard models estimated diabetes risk associated with each SEP measure. Demographic confounders (age, gender, marital status) and potential pathway components (physical inactivity, body composition, smoking, alcohol consumption, hypertension, depression, access to health care) were included as covariates. **RESULTS:** Diabetes incidence was twice as high for Blacks as for Whites. Diabetes risk factors independently increased risk, but effect sizes were greater among Whites. Low childhood SEP elevated risk for both racial groups. Protective effects were suggested for low education and blue-

collar occupation among Blacks, but these factors increased risk for Whites. Income was protective for Whites but not Blacks. Covariate adjustment had negligible effects on associations between each SEP measure and diabetes incidence for both racial groups. CONCLUSIONS: These findings suggest an important role for life-course SEP measures in determining risk of diabetes, regardless of race and after adjustment for factors that may confound or mediate these associations

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<http://dx.doi.org/10.1056/NEJMicm0810147> (Accès réservé EHESP)

- (18) MILLER ME, BONDS DE, GERSTEIN HC, SEAQUIST ER, *et al.* **The effects of baseline characteristics, glycaemia treatment approach, and glycated haemoglobin concentration on the risk of severe hypoglycaemia: post hoc epidemiological analysis of the ACCORD study.** BMJ. 2010, vol. 340, p.b5444
<http://www.ncbi.nlm.nih.gov/pubmed/20061360> (Accès réservé EHESP)

OBJECTIVES: To investigate potential determinants of severe hypoglycaemia, including baseline characteristics, in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial and the association of severe hypoglycaemia with levels of glycated haemoglobin (haemoglobin A(1C)) achieved during therapy. DESIGN: Post hoc epidemiological analysis of a double 2x2 factorial, randomised, controlled trial. SETTING: Diabetes clinics, research clinics, and primary care clinics. PARTICIPANTS: 10 209 of the 10 251 participants enrolled in the ACCORD study with type 2 diabetes, a haemoglobin A(1C) concentration of 7.5% or more during screening, and aged 40-79 years with established cardiovascular disease or 55-79 years with evidence of significant atherosclerosis, albuminuria, left ventricular hypertrophy, or two or more additional risk factors for cardiovascular disease (dyslipidaemia, hypertension, current smoker, or obese). Interventions Intensive (haemoglobin A(1C) <6.0%) or standard (haemoglobin A(1C) 7.0-7.9%) glucose control. MAIN OUTCOME MEASURES: Severe hypoglycaemia was defined as episodes of "low blood glucose" requiring the assistance of another person and documentation of either a plasma glucose less than 2.8 mmol/l (<50 mg/dl) or symptoms that promptly resolved with oral carbohydrate, intravenous glucose, or glucagon. RESULTS: The annual incidence of hypoglycaemia was 3.14% in the intensive treatment group and 1.03% in the standard glycaemia group. We found significantly increased risks for hypoglycaemia among women (P=0.0300), African-Americans (P<0.0001 compared with non-Hispanic whites), those with less than a high school education (P<0.0500 compared with college graduates), aged participants (P<0.0001 per 1 year increase), and those who used insulin at trial entry (P<0.0001). For every 1% unit decline in the haemoglobin A(1C) concentration from baseline to 4 month visit, there was a 28% (95% CI 19% to 37%) and 14% (4% to 23%) reduced risk of hypoglycaemia requiring medical assistance in the standard and intensive groups, respectively. In both treatment groups, the risk of hypoglycaemia requiring medical assistance increased with each 1% unit increment in the average updated haemoglobin A(1C) concentration (standard arm: hazard ratio 1.76, 95% CI 1.50 to 2.06; intensive arm: hazard ratio 1.15, 95% CI 1.02 to 1.21). CONCLUSIONS: A greater drop in haemoglobin A(1C) concentration from baseline to the 4 month visit was not associated with an increased risk for hypoglycaemia. Patients with poorer glycaemic control had a greater risk of hypoglycaemia, irrespective of treatment group. Identification of baseline subgroups with increased risk for severe hypoglycaemia can provide guidance to clinicians attempting to modify patient therapy on the basis of individual risk. TRIAL REGISTRATION: ClinicalTrials.gov number NCT00000620

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<http://www.ncbi.nlm.nih.gov/pubmed/20050388> (Accès réservé EHESP)

- (20) NYWEIDE DJ, WEEKS WB, GOTTLIEB DJ, CASALINO LP, *et al.* **Relationship of primary care physicians' patient caseload with measurement of quality and cost performance.** JAMA. 2009 Dec. 9, vol. 302, n° 22, pp.2444-2450
<http://dx.doi.org/10.1001/jama.2009.1810> (Accès réservé EHESP)

CONTEXT: Sufficient numbers of patients are necessary to generate statistically reliable measurements of physicians' quality and cost performance. OBJECTIVE: To determine whether primary care physicians in the same physician practice collectively see enough Medicare patients annually to detect meaningful differences between practices in ambulatory quality and cost measures. DESIGN, SETTING, AND PATIENTS: Primary care physicians in the United States were linked to their physician practices using the Healthcare Organization Services database maintained by IMS Health. Patients who visited primary care physicians in the 2005 Medicare Part B 20% sample were used to estimate Medicare caseloads per practice. Caseloads necessary to detect 10% relative differences in costs and quality were calculated using national mean ambulatory Medicare spending, rates of mammography for women 66 to 69 years, and hemoglobin A(1c) testing for 66- to 75-year-olds with diabetes, preventable hospitalization rate, and 30-day readmission rate after discharge for congestive heart failure (CHF). MAIN OUTCOME MEASURES: Percentage of primary care physician practices with a sufficient number of eligible patients to detect a 10% relative difference in each performance measure. RESULTS: Primary care physician practices had annual median caseloads of 260 Medicare patients (interquartile range [IQR], 135-500), 25 women eligible for mammography (IQR, 10-50), 30 patients with diabetes eligible for hemoglobin A(1c) testing (IQR, 15-55), and 0 patients hospitalized for CHF. For ambulatory costs, mammography rate, and hemoglobin A(1c) testing rate, the percentage of primary care physician practices with sufficient caseloads to detect 10% relative differences in performance ranged from less than 10% of practices with fewer than 11 primary care physicians to 100% of practices with more than 50 primary care physicians. None of the primary care physician practices had sufficient caseloads to detect 10% relative differences in preventable hospitalization or 30-day readmission after discharge for CHF. CONCLUSION: Relatively few primary care physician practices are large enough to reliably measure 10% relative differences in common measures of quality and cost performance among fee-for-service Medicare patients

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<http://dx.doi.org/10.1056/NEJMra0903074> (Accès réservé EHESP)

- (22) ROSENGREN AH, JOKUBKA R, TOJJAR D, GRANHALL C, *et al.* **Overexpression of alpha2A-adrenergic receptors contributes to type 2 diabetes.** Science. 2010 Jan. 8, vol. 327, n° 5962, pp.217-220
<http://dx.doi.org/10.1126/science.1176827> (Accès réservé EHESP)

Several common genetic variations have been associated with type 2 diabetes, but the exact disease mechanisms are still poorly elucidated. Using congenic strains from the diabetic Goto-Kakizaki rat, we identified a 1.4-megabase genomic locus that was linked to impaired insulin granule docking at the plasma membrane and reduced beta cell exocytosis. In this locus, Adra2a, encoding the alpha2A-adrenergic receptor [alpha(2A)AR], was significantly overexpressed. Alpha(2A)AR mediates adrenergic suppression of insulin secretion. Pharmacological receptor antagonism, silencing of receptor expression, or blockade of downstream effectors rescued insulin secretion in congenic islets. Furthermore, we identified a single-nucleotide polymorphism in the human ADRA2A gene for which risk allele carriers exhibited overexpression of alpha(2A)AR, reduced insulin secretion, and increased type 2 diabetes risk. Human pancreatic islets from risk allele carriers exhibited reduced granule docking and secreted less insulin in response to glucose; both effects were counteracted by pharmacological alpha(2A)AR antagonists

- (23) SCHRODER K, ZHOU R, TSCHOPP J. **The NLRP3 inflammasome: a sensor for metabolic danger?** Science. 2010 Jan. 15, vol. 327, n° 5963, pp.296-300
<http://dx.doi.org/327/10.1126/science.1184003> (Accès réservé EHESP)

Interleukin-1beta (IL-1beta), reactive oxygen species (ROS), and thioredoxin-interacting protein (TXNIP) are all implicated in the pathogenesis of type 2 diabetes mellitus (T2DM). Here we review mechanisms directing IL-1beta production and its pathogenic role in islet dysfunction during chronic hyperglycemia. In doing so, we integrate previously disparate disease-driving mechanisms for IL-1beta, ROS, and TXNIP in T2DM into one unifying model in which the NLRP3 inflammasome plays a central role. The NLRP3 inflammasome also drives IL-1beta maturation and secretion in another disease of metabolic dysregulation, gout. Thus, we propose that the NLRP3 inflammasome contributes to the pathogenesis of T2DM and gout by functioning as a sensor for metabolic stress

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<http://www.ncbi.nlm.nih.gov/pubmed/20050387> (Accès réservé EHESP)

- (25) STEFAN N, SCHICK F, HARING HU. **Sex hormone-binding globulin and risk of type 2 diabetes.** N Engl J Med. 2009 Dec. 31, vol. 361, n° 27, pp.2675-2676
<http://dx.doi.org/10.1056/NEJMc0910143> (Accès réservé EHESP)

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<http://www.ncbi.nlm.nih.gov/pubmed/20044397> (Accès réservé EHESP)

- (27) TALMUD PJ, HINGORANI AD, COOPER JA, MARMOT MG, *et al.* **Utility of genetic and non-genetic risk factors in prediction of type 2 diabetes: Whitehall II prospective cohort study.** BMJ. 2010, vol. 340, p.b4838
<http://www.ncbi.nlm.nih.gov/pubmed/20075150> (Accès réservé EHESP)

OBJECTIVES: To assess the performance of a panel of common single nucleotide polymorphisms (genotypes) associated with type 2 diabetes in distinguishing incident cases of future type 2 diabetes (discrimination), and to examine the effect of adding genetic information to previously validated non-genetic (phenotype based) models developed to estimate the absolute risk of type 2 diabetes. **DESIGN:** Workplace based prospective cohort study with three 5 yearly medical screenings. **PARTICIPANTS:** 5535 initially healthy people (mean age 49 years; 33% women), of whom 302 developed new onset type 2 diabetes over 10 years. **OUTCOME MEASURES:** Non-genetic variables included in two established risk models-the Cambridge type 2 diabetes risk score (age, sex, drug treatment, family history of type 2 diabetes, body mass index, smoking status) and the Framingham offspring study type 2 diabetes risk score (age, sex, parental history of type 2 diabetes, body mass index, high density lipoprotein cholesterol, triglycerides, fasting glucose)-and 20 single nucleotide polymorphisms associated with susceptibility to type 2 diabetes. Cases of incident type 2 diabetes were defined on the basis of a standard oral glucose tolerance test, self report of a doctor's diagnosis, or the use of anti-diabetic drugs. **RESULTS:** A genetic score based on the number of risk alleles carried (range 0-40; area under receiver operating characteristics curve 0.54, 95% confidence interval 0.50 to 0.58) and a genetic risk function in which carriage of risk alleles was weighted according to the summary odds ratios of their effect from meta-analyses of genetic studies (area under receiver operating characteristics curve 0.55, 0.51 to 0.59) did not effectively discriminate cases of diabetes. The Cambridge risk score (area under curve 0.72, 0.69 to 0.76) and the Framingham offspring risk score (area under curve 0.78, 0.75 to 0.82) led to better discrimination of cases than did genotype based tests. Adding genetic information to phenotype based risk models did not improve

discrimination and provided only a small improvement in model calibration and a modest net reclassification improvement of about 5% when added to the Cambridge risk score but not when added to the Framingham offspring risk score. **CONCLUSION:** The phenotype based risk models provided greater discrimination for type 2 diabetes than did models based on 20 common independently inherited diabetes risk alleles. The addition of genotypes to phenotype based risk models produced only minimal improvement in accuracy of risk estimation assessed by recalibration and, at best, a minor net reclassification improvement. The major translational application of the currently known common, small effect genetic variants influencing susceptibility to type 2 diabetes is likely to come from the insight they provide on causes of disease and potential therapeutic targets

- (28) TOMLINSON G, DETSKY AS. **Composite end points in randomized trials: there is no free lunch.** JAMA. 2010 Jan. 20, vol. 303, n° 3, pp.267-268
<http://dx.doi.org/10.1001/jama.2009.2017> (Accès réservé EHESP)
- (29) UNGER EF, THOMPSON AM, BLANK MJ, TEMPLE R. **Erythropoiesis-stimulating agents--time for a reevaluation.** N Engl J Med. 2010 Jan. 21, vol. 362, n° 3, pp.189-192
<http://dx.doi.org/10.1056/NEJMp0912328> (Accès réservé EHESP)
- (30) WALTERS BN. **Treatment for mild gestational diabetes.** N Engl J Med. 2010 Jan. 28, vol. 362, n° 4, pp.365-366
<http://dx.doi.org/10.1056/NEJMc0910810> (Accès réservé EHESP)

Dépression

[sommaire](#)

- (1) DESANTO IJ, CULLEN MR, CANTLEY L, SLADE MD, *et al.* **Effects of externally rated job demand and control on depression diagnosis claims in an industrial cohort.** Am J Epidemiol. 2010 Feb. 1, vol. 171, n° 3, pp.303-311
<http://dx.doi.org/10.1093/aje/kwp359> (Accès réservé EHESP)

This study examined whether externally rated job demand and control were associated with depression diagnosis claims in a heavy industrial cohort. The retrospective cohort sample consisted of 7,566 hourly workers aged 18-64 years who were actively employed at 11 US plants between January 1, 1996, and December 31, 2003, and free of depression diagnosis claims during an initial 2-year run-in period. Logistic regression analysis was used to model the effect of tertiles of demand and control exposure on depression diagnosis claims. Demand had a significant positive association with depression diagnosis claims in bivariate models and models adjusted for demographic (age, gender, race, education, job grade, tenure) and lifestyle (smoking status, body mass index, cholesterol level) variables (high demand odds ratio = 1.39, 95% confidence interval: 1.04, 1.86). Control was associated with greater risk of depression diagnosis at moderate levels in unadjusted models only (odds ratio = 1.47, 95% confidence interval: 1.12, 1.93), while low control, contrary to expectation, was not associated with depression. The effects of the externally rated demand exposure were lost with adjustment for location. This may reflect differences in measurement or classification of exposure, differences in depression diagnosis by location, or other location-specific factors

- (2) FLETCHER J. **The effects of intimate partner violence on health in young adulthood in the United States.** Soc Sci Med. 2010 Jan., vol. 70, n° 1, pp.130-135
<http://dx.doi.org/10.1016/j.socscimed.2009.09.030> (Accès réservé EHESP)

This paper uses data on a national sample of adolescents from the United States followed through the transition into young adulthood to examine the association between intimate partner violence

(IPV) and health outcomes, including depressive symptoms, self reported health status, and health care utilization. Researchers have shown an important IPV-health link in a number of settings but have often been limited by using cross-sectional data, convenience samples, and the inability to control for important risk factors and confounders. The findings from this study suggests that these limitations likely inflate the estimated link between IPV and health by as much as 60% but also show that IPV has important health impacts on a number of outcomes. The results also show no differential impact of IPV by gender or previous exposure to child abuse. The health effects of IPV are also typically larger for current exposure than previous exposure, but each exposure type is shown to reduce health

- (3) FOURNIER JC, DERUBEIS RJ, HOLLON SD, DIMIDJIAN S, *et al.* **Antidepressant drug effects and depression severity: a patient-level meta-analysis.** JAMA. 2010 Jan. 6, vol. 303, n° 1, pp.47-53

<http://dx.doi.org/10.1001/jama.2009.1943> (Accès réservé EHESP)

CONTEXT: Antidepressant medications represent the best established treatment for major depressive disorder, but there is little evidence that they have a specific pharmacological effect relative to pill placebo for patients with less severe depression. OBJECTIVE: To estimate the relative benefit of medication vs placebo across a wide range of initial symptom severity in patients diagnosed with depression. DATA SOURCES: PubMed, PsycINFO, and the Cochrane Library databases were searched from January 1980 through March 2009, along with references from meta-analyses and reviews. STUDY SELECTION: Randomized placebo-controlled trials of antidepressants approved by the Food and Drug Administration in the treatment of major or minor depressive disorder were selected. Studies were included if their authors provided the requisite original data, they comprised adult outpatients, they included a medication vs placebo comparison for at least 6 weeks, they did not exclude patients on the basis of a placebo washout period, and they used the Hamilton Depression Rating Scale (HDRS). Data from 6 studies (718 patients) were included. DATA EXTRACTION: Individual patient-level data were obtained from study authors. RESULTS: Medication vs placebo differences varied substantially as a function of baseline severity. Among patients with HDRS scores below 23, Cohen d effect sizes for the difference between medication and placebo were estimated to be less than 0.20 (a standard definition of a small effect). Estimates of the magnitude of the superiority of medication over placebo increased with increases in baseline depression severity and crossed the threshold defined by the National Institute for Clinical Excellence for a clinically significant difference at a baseline HDRS score of 25. CONCLUSIONS: The magnitude of benefit of antidepressant medication compared with placebo increases with severity of depression symptoms and may be minimal or nonexistent, on average, in patients with mild or moderate symptoms. For patients with very severe depression, the benefit of medications over placebo is substantial

- (4) GORDON SC, LANDA D. **Disclosure of the genetic risk of Alzheimer's disease.** N Engl J Med. 2010 Jan. 14, vol. 362, n° 2, pp.181-182

<http://dx.doi.org/10.1056/NEJMc096300> (Accès réservé EHESP)

- (5) KLINE A, FALCA-DODSON M, SUSSNER B, CICCONE DS, *et al.* **Effects of repeated deployment to Iraq and Afghanistan on the health of New Jersey Army National Guard troops: implications for military readiness.** Am J Public Health. 2010 Feb., vol. 100, n° 2, pp.276-283

<http://dx.doi.org/10.2105/AJPH.2009.162925> (Accès réservé EHESP)

OBJECTIVES: We assessed the effects of prior military service in Iraq or Afghanistan on the health of New Jersey Army National Guard members preparing for deployment to Iraq.

METHODS: We analyzed anonymous, self-administered predeployment surveys from 2543 National Guard members deployed to Iraq in 2008. We used bivariate and multivariate analyses to measure the effects of prior service in Afghanistan (Operation Enduring Freedom [OEF]) or Iraq

(Operation Iraqi Freedom [OIF]) on mental and physical health. RESULTS: Nearly 25% of respondents reported at least 1 previous OEF or OIF deployment. Previously deployed soldiers were more than 3 times as likely as soldiers with no previous deployments to screen positive for posttraumatic stress disorder (adjusted odds ratio [AOR]=3.69; 95% confidence interval [CI]=2.59, 5.24) and major depression (AOR=3.07; 95% CI=1.81, 5.19), more than twice as likely to report chronic pain (AOR=2.20; 95% CI=1.78, 2.72) and more than 90% more likely to score below the general population norm on physical functioning (AOR=1.94; 95% CI=1.51, 2.48). CONCLUSIONS: Repeated OEF and OIF deployments may adversely affect the military readiness of New Jersey National Guard combat soldiers

- (6) KUEHN BM. **No easy answers for physicians caring for pregnant women with depression.** JAMA. 2009 Dec. 9, vol. 302, n° 22, pp.2413-4, 2420
<http://dx.doi.org/10.1001/jama.2009.1762> (Accès réservé EHESP)

- (7) MANSFIELD AJ, KAUFMAN JS, MARSHALL SW, GAYNES BN, *et al.* **Deployment and the use of mental health services among U.S. Army wives.** N Engl J Med. 2010 Jan. 14, vol. 362, n° 2, pp.101-109
<http://dx.doi.org/10.1056/NEJMoa0900177> (Accès réservé EHESP)

BACKGROUND: Military operations in Iraq and Afghanistan have involved the frequent and extended deployment of military personnel, many of whom are married. The effect of deployment on mental health in military spouses is largely unstudied. METHODS: We examined electronic medical-record data for outpatient care received between 2003 and 2006 by 250,626 wives of active-duty U.S. Army soldiers. After adjustment for the sociodemographic characteristics and the mental health history of the wives, as well as the number of deployments of the personnel, we compared mental health diagnoses according to the number of months of deployment in Operation Iraqi Freedom in the Iraq-Kuwait region and Operation Enduring Freedom in Afghanistan during the same period. RESULTS: The deployment of spouses and the length of deployment were associated with mental health diagnoses. In adjusted analyses, as compared with wives of personnel who were not deployed, women whose husbands were deployed for 1 to 11 months received more diagnoses of depressive disorders (27.4 excess cases per 1000 women; 95% confidence interval [CI], 22.4 to 32.3), sleep disorders (11.6 excess cases per 1000; 95% CI, 8.3 to 14.8), anxiety (15.7 excess cases per 1000; 95% CI, 11.8 to 19.6), and acute stress reaction and adjustment disorders (12.0 excess cases per 1000; 95% CI, 8.6 to 15.4). Deployment for more than 11 months was associated with 39.3 excess cases of depressive disorders (95% CI, 33.2 to 45.4), 23.5 excess cases of sleep disorders (95% CI, 19.4 to 27.6), 18.7 excess cases of anxiety (95% CI, 13.9 to 23.5), and 16.4 excess cases of acute stress reaction and adjustment disorders (95% CI, 12.2 to 20.6). CONCLUSIONS: Prolonged deployment was associated with more mental health diagnoses among U.S. Army wives, and these findings may have relevance for prevention and treatment efforts

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<http://dx.doi.org/10.1016/j.socscimed.2009.09.035> (Accès réservé EHESP)

This cross-sectional study aimed to investigate the influence of socio-contextual variables on depressive symptoms in 158 adolescent survivors of the 2004 terrorist attack in Beslan, Russia, based on an ecological perspective. Participants were assessed 18 months after the traumatic event. Adolescents aged 14-17 years completed self-reported measures assessing depressive symptoms, social support, sense of community, and collectivism. The results of path analyses indicated that for both boys and girls, the endorsement of collectivistic values was related to increased family support, which in turn was associated with lower rates of depressive symptoms. In the male group, collectivism and sense of community were positively associated with peer

support, which in turn was negatively related to depressive symptomatology. The findings suggest that social support and community connectedness may serve as protective resources in adolescents' psychological responses to terror-related stressors, and that gender differences as well as cultural values should be taken into consideration when implementing interventions with youths exposed to terrorism

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<http://dx.doi.org/10.1001/jama.2009.1919> (Accès réservé EHESP)
- (10) WELLS TS, LEARDMANN CA, FORTUNA SO, SMITH B, *et al.* **A prospective study of depression following combat deployment in support of the wars in Iraq and Afghanistan .** Am J Public Health. 2010 Jan., vol. 100, n° 1, pp.90-99
<http://dx.doi.org/10.2105/AJPH.2008.155432> (Accès réservé EHESP)

OBJECTIVE: We investigated relations between deployment and new-onset depression among US service members recently deployed to the wars in Iraq and Afghanistan. **METHODS:** We included 40 219 Millennium Cohort Study participants who completed baseline and follow-up questionnaires and met inclusion criteria. Participants were identified with depression if they met the Primary Care Evaluation of Mental Disorders Patient Health Questionnaire criteria for depression at follow-up, but not at baseline. **RESULTS:** Deployed men and women with combat exposures had the highest onset of depression, followed by those not deployed and those deployed without combat exposures. Combat-deployed men and women were at increased risk for new-onset depression compared with nondeployed men and women (men: adjusted odds ratio [AOR]=1.32; 95% confidence interval [CI]=1.13, 1.54; women: AOR=2.13; 95% CI=1.70, 2.65). Conversely, deployment without combat exposures led to decreased risk for new-onset depression compared with those who did not deploy (men: AOR=0.66; 95% CI=0.53, 0.83; women: AOR=0.65; 95% CI=0.47, 0.89). **CONCLUSIONS:** Deployment with combat exposures is a risk factor for new-onset depression among US service members. Post-deployment screening may be beneficial for US service members exposed to combat

Grippe A

[sommaire](#)

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[http://dx.doi.org/10.1016/S0140-6736\(09\)61971-1](http://dx.doi.org/10.1016/S0140-6736(09)61971-1) (Accès réservé EHESP)
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<http://dx.doi.org/10.1038/nature08722> (Accès payant)

The M2 protein of influenza A virus is a membrane-spanning tetrameric proton channel targeted by the antiviral drugs amantadine and rimantadine. Resistance to these drugs has compromised their effectiveness against many influenza strains, including pandemic H1N1. A recent crystal structure of M2(22-46) showed electron densities attributed to a single amantadine in the amino-terminal half of the pore, indicating a physical occlusion mechanism for inhibition. However, a solution NMR structure of M2(18-60) showed four rimantadines bound to the carboxy-terminal lipid-facing surface of the helices, suggesting an allosteric mechanism. Here we show by solid-state NMR spectroscopy that two amantadine-binding sites exist in M2 in phospholipid bilayers. The high-affinity site, occupied by a single amantadine, is located in the N-terminal channel lumen, surrounded by residues mutated in amantadine-resistant viruses. Quantification of the protein-amantadine distances resulted in a 0.3 Å-resolution structure of the high-affinity binding site. The second, low-affinity, site was observed on the C-terminal protein surface, but only when the drug reaches high concentrations in the bilayer. The orientation and dynamics of the drug are distinct in the two sites, as shown by ²H NMR. These results indicate that amantadine physically occludes the M2 channel, thus paving the way for developing new antiviral drugs against influenza viruses. The study demonstrates the ability of solid-state NMR to elucidate small-molecule interactions with membrane proteins and determine high-resolution structures of their complexes

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<http://dx.doi.org/10.1056/NEJMoa0905498> (Accès réservé EHESP)

BACKGROUND: As of June 11, 2009, a total of 17,855 probable or confirmed cases of 2009 pandemic influenza A (H1N1) had been reported in the United States. Risk factors for transmission remain largely uncharacterized. We characterize the risk factors and describe the transmission of the virus within households. **METHODS:** Probable and confirmed cases of infection with the 2009 H1N1 virus in the United States were reported to the Centers for Disease Control and Prevention with the use of a standardized case form. We investigated transmission of infection in 216 households—including 216 index patients and their 600 household contacts—in which the index patient was the first case patient and complete information on symptoms and age was available for all household members. **RESULTS:** An acute respiratory illness developed in 78 of 600 household contacts (13%). In 156 households (72% of the 216 households), an acute respiratory illness developed in none of the household contacts; in 46 households (21%), illness developed in one contact; and in 14 households (6%), illness developed in more than one contact. The proportion of household contacts in whom acute respiratory illness developed decreased with the size of the household, from 28% in two-member households to 9% in six-member households. Household contacts 18 years of age or younger were twice as susceptible as those 19 to 50 years of age (relative susceptibility, 1.96; Bayesian 95% credible interval, 1.05 to 3.78; P=0.005), and household contacts older than 50 years of age were less susceptible than those who were 19 to 50 years of age (relative susceptibility, 0.17; 95% credible interval, 0.02 to 0.92; P=0.03). Infectivity did not vary with age. The mean time between the onset of symptoms in a case patient and the onset of symptoms in the household contacts infected by that patient was 2.6 days (95%

credible interval, 2.2 to 3.5). **CONCLUSIONS:** The transmissibility of the 2009 H1N1 influenza virus in households is lower than that seen in past pandemics. Most transmissions occur soon before or after the onset of symptoms in a case patient

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<http://dx.doi.org/10.1056/NEJMoa0907650> (Accès réservé EHESP)

BACKGROUND: The 2009 pandemic influenza A (H1N1) virus has emerged to cause the first pandemic of the 21st century. Development of effective vaccines is a public health priority. **METHODS:** We conducted a single-center study, involving 176 adults, 18 to 50 years of age, to test the monovalent influenza A/California/2009 (H1N1) surface-antigen vaccine, in both MF59-adjuvanted and nonadjuvanted forms. Subjects were randomly assigned to receive two intramuscular injections of vaccine containing 7.5 microg of hemagglutinin on day 0 in each arm or one injection on day 0 and the other on day 7, 14, or 21; or two 3.75-microg doses of MF59-adjuvanted vaccine, or 7.5 or 15 microg of nonadjuvanted vaccine, administered 21 days apart. Antibody responses were measured by means of hemagglutination-inhibition assay and a microneutralization assay on days 0, 14, 21, and 42 after injection of the first dose. **RESULTS:** The most frequent local and systemic reactions were pain at the injection site and muscle aches, noted in 70% and 42% of subjects, respectively; reactions were more common with the MF59-adjuvanted vaccine than with nonadjuvanted vaccine. Three subjects reported fever, with a temperature of 38 degrees C or higher, after either dose. Antibody titers, expressed as geometric means, were higher at day 21 among subjects who had received one dose of MF59-adjuvanted vaccine than among those who had received one dose of nonadjuvanted vaccine ($P < 0.001$ by the microneutralization assay). By day 21, hemagglutination-inhibition and microneutralization antibody titers of 1:40 or more were seen in 77 to 96% and 92 to 100% of subjects receiving MF59-adjuvanted vaccine, respectively, and in 63 to 72% and 67 to 76% of those receiving nonadjuvanted vaccine, respectively. By day 42, after two doses of vaccine, hemagglutination-inhibition and microneutralization antibody titers of 1:40 or more were seen in 92 to 100% and 100% of recipients of MF59-adjuvanted vaccine, respectively, and in 74 to 79% and 78 to 83% of recipients of nonadjuvanted vaccine, respectively. **CONCLUSIONS:** Monovalent 2009 influenza A (H1N1) MF59-adjuvanted vaccine generates antibody responses likely to be associated with protection after a single dose is administered. (ClinicalTrials.gov number, NCT00943358)

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<http://dx.doi.org/10.1056/NEJMoa0907413> (Accès réservé EHESP)

BACKGROUND: A novel 2009 influenza A (H1N1) virus is responsible for the first influenza pandemic in 41 years. A safe and effective vaccine is needed. A randomized, observer-blind, parallel-group trial evaluating two doses of an inactivated, split-virus 2009 H1N1 vaccine in healthy adults between the ages of 18 and 64 years is ongoing at a single site in Australia. METHODS: We evaluated the immunogenicity and safety of the vaccine after each of two scheduled doses, administered 21 days apart. A total of 240 subjects, equally divided into two age groups (<50 years and ≥50 years), were enrolled and underwent randomization to receive either 15 microg or 30 microg of hemagglutinin antigen by intramuscular injection. We measured antibody titers using hemagglutination-inhibition and microneutralization assays at baseline and 21 days after vaccination. The coprimary immunogenicity end points were the proportion of subjects with antibody titers of 1:40 or more on hemagglutination-inhibition assay, the proportion of subjects with either seroconversion or a significant increase in antibody titer, and the factor increase in the geometric mean titer. RESULTS: By day 21 after the first dose, antibody titers of 1:40 or more were observed in 114 of 120 subjects (95.0%) who received the 15-microg dose and in 106 of 119 subjects (89.1%) who received the 30-microg dose. A similar result was observed after the second dose of vaccine. No deaths, serious adverse events, or adverse events of special interest were reported. Local discomfort (e.g., injection-site tenderness or pain) was reported by 56.3% of subjects, and systemic symptoms (e.g., headache) by 53.8% of subjects after each dose. Nearly all events were mild to moderate in intensity. CONCLUSIONS: A single 15-microg dose of 2009 H1N1 vaccine was immunogenic in adults, with mild-to-moderate vaccine-associated reactions. (ClinicalTrials.gov number, NCT00938639)

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<http://dx.doi.org/10.1126/science.1178258> (Accès réservé EHESP)

Rapid antigenic evolution in the influenza A virus hemagglutinin precludes effective vaccination

with existing vaccines. To understand this phenomenon, we passaged virus in mice immunized with influenza vaccine. Neutralizing antibodies selected mutants with single-amino acid hemagglutinin substitutions that increased virus binding to cell surface glycan receptors. Passaging these high-avidity binding mutants in naive mice, but not immune mice, selected for additional hemagglutinin substitutions that decreased cellular receptor binding avidity. Analyzing a panel of monoclonal antibody hemagglutinin escape mutants revealed a positive correlation between receptor binding avidity and escape from polyclonal antibodies. We propose that in response to variation in neutralizing antibody pressure between individuals, influenza A virus evolves by adjusting receptor binding avidity via amino acid substitutions throughout the hemagglutinin globular domain, many of which simultaneously alter antigenicity

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<http://dx.doi.org/10.1038/nature08760> (Accès payant)

Influenza A virus, being responsible for seasonal epidemics and reoccurring pandemics, represents a worldwide threat to public health. High mutation rates facilitate the generation of viral escape mutants, rendering vaccines and drugs directed against virus-encoded targets potentially ineffective. In contrast, targeting host cell determinants temporarily dispensable for the host but crucial for virus replication could prevent viral escape. Here we report the discovery of 287 human host cell genes influencing influenza A virus replication in a genome-wide RNA interference (RNAi) screen. Using an independent assay we confirmed 168 hits (59%) inhibiting either the endemic H1N1 (119 hits) or the current pandemic swine-origin (121 hits) influenza A virus strains, with an overlap of 60%. Notably, a subset of these common hits was also essential for replication of a highly pathogenic avian H5N1 strain. In-depth analyses of several factors provided insights into their infection stage relevance. Notably, SON DNA binding protein (SON) was found to be important for normal trafficking of influenza virions to late endosomes early in infection. We also show that a small molecule inhibitor of CDC-like kinase 1 (CLK1) reduces influenza virus replication by more than two orders of magnitude, an effect connected with impaired splicing of the viral M2 messenger RNA. Furthermore, influenza-virus-infected p27^(-/-) (cyclin-dependent kinase inhibitor 1B; Cdkn1b) mice accumulated significantly lower viral titres in the lung, providing in vivo evidence for the importance of this gene. Thus, our results highlight the potency of genome-wide RNAi screening for the dissection of virus-host interactions and the identification of drug targets for a broad range of influenza viruses

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[http://dx.doi.org/10.1016/S0140-6736\(10\)60154-7](http://dx.doi.org/10.1016/S0140-6736(10)60154-7) (Accès réservé EHESP)
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<http://dx.doi.org/10.1056/NEJMc0910448> (Accès réservé EHESP)

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<http://dx.doi.org/10.1056/NEJMoa0906089> (Accès réservé EHESP)

BACKGROUND: In April 2009, an outbreak of novel swine-origin influenza A (2009 H1N1 influenza) occurred at a high school in Queens, New York. We describe the outbreak and characterize the clinical and epidemiologic aspects of this novel virus. **METHODS:** The New York City Department of Health and Mental Hygiene characterized the outbreak through laboratory confirmation of the presence of the 2009 H1N1 virus in nasopharyngeal and oropharyngeal specimens and through information obtained from an online survey. Detailed information on exposure and the onset of symptoms was used to estimate the incubation period, generation time, and within-school reproductive number associated with 2009 H1N1 influenza, with the use of established techniques. **RESULTS:** From April 24 through May 8, infection with the 2009 H1N1 virus was confirmed in 124 high-school students and employees. In responses to the online questionnaire, more than 800 students and employees (35% of student respondents and 10% of employee respondents) reported having an influenza-like illness during this period. No persons with confirmed 2009 H1N1 influenza or with influenza-like illness had severe symptoms. A linkage with travel to Mexico was identified. The estimated median incubation period for confirmed 2009 H1N1 influenza was 1.4 days (95% confidence interval [CI], 1.0 to 1.8), with symptoms developing in 95% of cases by 2.2 days (95% CI, 1.7 to 2.6). The estimated median generation time was 2.7 days (95% CI, 2.0 to 3.5). We estimate that the within-school reproductive number was 3.3. **CONCLUSIONS:** The findings from this investigation suggest that 2009 H1N1 influenza in the high school was widespread but did not cause severe illness. The reasons for the rapid and extensive spread of influenza-like illnesses are unknown. The natural history and transmission of the 2009 H1N1 influenza virus appear to be similar to those of previously observed circulating pandemic and inter-pandemic influenza viruses

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<http://dx.doi.org/10.1056/NEJMoa0907673> (Accès réservé EHESP)

BACKGROUND: While the Northern Hemisphere experiences the effects of the 2009 pandemic influenza A (H1N1) virus, data from the recent influenza season in the Southern Hemisphere can provide important information on the burden of disease in children. **METHODS:** We conducted a retrospective case series involving children with acute infection of the lower respiratory tract or fever in whom 2009 H1N1 influenza was diagnosed on reverse-transcriptase polymerase-chain-reaction assay and who were admitted to one of six pediatric hospitals serving a catchment area of 1.2 million children. We compared rates of admission and death with those among age-matched children who had been infected with seasonal influenza strains in previous years. **RESULTS:** Between May and July 2009, a total of 251 children were hospitalized with 2009 H1N1 influenza. Rates of hospitalization were double those for seasonal influenza in 2008. Of the children who were hospitalized, 47 (19%) were admitted to an intensive care unit, 42 (17%) required mechanical ventilation, and 13 (5%) died. The overall rate of death was 1.1 per 100,000 children, as compared with 0.1 per 100,000 children for seasonal influenza in 2007. (No pediatric deaths associated with seasonal influenza were reported in 2008.) Most deaths were caused by refractory hypoxemia in infants under 1 year of age (death rate, 7.6 per 100,000). **CONCLUSIONS:** Pandemic 2009 H1N1 influenza was associated with pediatric death rates that were 10 times the rates for seasonal influenza in previous years

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<http://dx.doi.org/10.1056/NEJMoa0910444> (Accès réservé EHESP)

BACKGROUND: Like previous epidemic and pandemic diseases, 2009 pandemic influenza A (H1N1) may pose an increased risk of severe illness in pregnant women. **METHODS:** Statewide surveillance for patients who were hospitalized with or died from 2009 H1N1 influenza was initiated by the California Department of Public Health. We reviewed demographic and clinical data reported from April 23 through August 11, 2009, for all H1N1-infected, reproductive-age women who were hospitalized or died--nonpregnant women, pregnant women, and postpartum women (those who had delivered < or = 2 weeks previously). **RESULTS:** Data were reported for 94 pregnant women, 8 postpartum women, and 137 nonpregnant women of reproductive age who were hospitalized with 2009 H1N1 influenza. Rapid antigen tests were falsely negative in 38% of the patients tested (58 of 153). Most pregnant patients (89 of 94 [95%]) were in the second or third trimester, and approximately one third (32 of 93 [34%]) had established risk factors for complications from influenza other than pregnancy. As compared with early antiviral treatment (administered < or = 2 days after symptom onset) in pregnant women, later treatment was associated with admission to an intensive care unit (ICU) or death (relative risk, 4.3). In all, 18 pregnant women and 4 postpartum women (total, 22 of 102 [22%]) required intensive care, and 8 (8%) died. Six deliveries occurred in the ICU, including four emergency cesarean deliveries. The 2009 H1N1 influenza-specific maternal mortality ratio (the number of maternal deaths per 100,000 live births) was 4.3. **CONCLUSIONS:** 2009 H1N1 influenza can cause severe illness and death in pregnant and postpartum women; regardless of the results of rapid antigen testing, prompt evaluation and antiviral treatment of influenza-like illness should be considered in such women. The high cause-specific maternal mortality rate suggests that 2009 H1N1 influenza may increase the 2009 maternal mortality ratio in the United States

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<http://www.ncbi.nlm.nih.gov/pubmed/20071427> (Accès réservé EHESP)
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[http://dx.doi.org/10.1016/S0140-6736\(09\)61927-9](http://dx.doi.org/10.1016/S0140-6736(09)61927-9) (Accès réservé EHESP)

Mass gatherings of people challenge public health capacities at host locations and the visitors' places of origin. Hajj--the yearly pilgrimage by Muslims to Saudi Arabia--is one of the largest, most culturally and geographically diverse mass gatherings in the world. With the 2009 pandemic influenza A H1N1 and upcoming Hajj, the Saudi Arabian Ministry of Health (MoH) convened a preparedness consultation in June, 2009. Consultants from global public health agencies met in their official capacities with their Saudi Arabian counterparts. The MoH aimed to pool and share public health knowledge about mass gatherings, and review the country's preparedness plans, focusing on the prevention and control of pandemic influenza. This process resulted in several

practical recommendations, many to be put into practice before the start of Hajj and the rest during Hajj. These preparedness plans should ensure the optimum provision of health services for pilgrims to Saudi Arabia, and minimum disease transmission on their return home. Review of the implementation of these recommendations and their effect will not only inform future mass gatherings in Saudi Arabia, but will also strengthen preparedness efforts in other settings

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BACKGROUND: Knowledge of the age-specific prevalence of immunity from, and incidence of infection with, 2009 pandemic influenza A H1N1 virus is essential for modelling the future burden of disease and the effectiveness of interventions such as vaccination. **METHODS:** In this cross-sectional serological survey, we obtained 1403 serum samples taken in 2008 (before the first wave of H1N1 infection) and 1954 serum samples taken in August and September, 2009 (after the first wave of infection) as part of the annual collection for the Health Protection Agency seroepidemiology programme from patients accessing health care in England. Antibody titres were measured by use of haemagglutination inhibition and microneutralisation assays. We calculated the proportion of samples with antibodies to pandemic H1N1 virus in 2008 by age group and compared the proportion of samples with haemagglutination inhibition titre 1:32 or more (deemed a protective response) before the first wave of infection with the proportion after the first wave. **FINDINGS:** In the baseline serum samples from 2008, haemagglutination inhibition and microneutralisation antibody titres increased significantly with age (F test $p < 0.0001$). The proportion of samples with haemagglutination inhibition titre 1:32 or more ranged from 1.8% (three of 171; 95% CI 0.6-5.0) in children aged 0-4 years to 31.3% (52 of 166; 24.8-38.7) in adults aged 80 years or older. In London and the West Midlands, the difference in the proportion of samples with haemagglutination inhibition titre equal to or above 1:32 between baseline and September, 2009, was 21.3% (95% CI 8.8-40.3) for children younger than 5 years of age, 42.0% (26.3-58.2) for 5-14-year-olds, and 20.6% (1.6-42.4) for 15-24-year-olds, with no difference between baseline and September in older age groups. In other regions, only children younger than 15 years showed a significant increase from baseline (6.3%, 1.8-12.9). **INTERPRETATION:** Around one child in every three was infected with 2009 pandemic H1N1 in the first wave of infection in regions with a high incidence, ten times more than estimated from clinical surveillance. Pre-existing antibody in older age groups protects against infection. Children have an important role in transmission of influenza and would be a key target group for vaccination both for their protection and for the protection of others through herd immunity. **FUNDING:** National Institute for Health Research Health Technology Assessment Programme

- (35) NEUZIL KM. **Pandemic influenza vaccine policy--considering the early evidence.** *N Engl J Med.* 2009 Dec. 17, vol. 361, n° 25, p.e59 <http://dx.doi.org/10.1056/NEJMe0908224> (Accès réservé EHESP)

- (36) NOLAN T, MCVERNON J, SKELJO M, RICHMOND P, *et al.* **Immunogenicity of a monovalent 2009 influenza A(H1N1) vaccine in infants and children: a randomized trial.** *JAMA.* 2010 Jan. 6, vol. 303, n° 1, pp.37-46 <http://dx.doi.org/10.1001/jama.2009.1911> (Accès réservé EHESP)

CONTEXT: In the ongoing influenza pandemic, a safe and effective vaccine against 2009 influenza A(H1N1) is needed for infants and children. **OBJECTIVE:** To assess the immunogenicity and safety of a 2009 influenza A(H1N1) vaccine in children. **DESIGN, SETTING, AND PARTICIPANTS:** Randomized, observer-blind, age-stratified, parallel group study assessing 2 doses of an inactivated, split-virus 2009 influenza A(H1N1) vaccine in 370 healthy infants and children aged 6 months to less than 9 years living in Australia. **INTERVENTION:** Intramuscular

injection of 15 microg or 30 microg of hemagglutinin antigen dose of monovalent, unadjuvanted 2009 influenza A(H1N1) vaccine in a 2-dose regimen, administered 21 days apart. MAIN OUTCOME MEASURES: Hemagglutination inhibition assay to estimate the proportion of participants with antibody titers of 1:40 or greater, seroconversion, or a significant antibody titer increase, and factor increase in geometric mean titer. Assessments of solicited adverse events during 7 days and unsolicited adverse events for 21 days after each vaccination. RESULTS: Following the first dose of vaccine, antibody titers of 1:40 or greater were observed in 161 of 174 infants and children in the 15-microg group (92.5%; 95% confidence interval [CI], 87.6%-95.6%) and in 168 of 172 infants and children in the 30-microg group (97.7%; 95% CI, 94.2%-99.1%). Corresponding seroconversion rates were 86.8% (95% CI, 80.9%-91.0%) and 94.2% (95% CI, 89.6%-96.8%), and factor increases in geometric mean titer were 13.6 (95% CI, 11.8-15.6) and 18.3 (95% CI, 15.7-21.4). All participants demonstrated antibody titers of 1:40 or greater after the second vaccine dose. Immune responses were robust regardless of age, baseline serostatus, or seasonal influenza vaccination status. The majority of adverse events were mild to moderate in severity. CONCLUSION: One 15-microg dose of vaccine was immunogenic in infants and children starting at 6 months of age and vaccine-associated reactions were mild to moderate in severity. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00940108

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[http://dx.doi.org/10.1016/S0140-6736\(09\)62194-2](http://dx.doi.org/10.1016/S0140-6736(09)62194-2) (Accès réservé EHESP)

- (39) SOUMPASIS I, BUTLER F. **Development and application of a stochastic epidemic model for the transmission of Salmonella Typhimurium at the farm level of the pork production chain.** Risk Anal. 2009 Nov., vol. 29, n° 11, pp.1521-1533
<http://dx.doi.org/10.1111/j.1539-6924.2009.01274.x> (Accès payant)

In previous work a deterministic model for the compartment level was built, taking into account the two different syndromes with which Salmonella Typhimurium appears at pig farms. Based on this model, a stochastic one was built in this work that simulated different compartmental sizes, taking into account compartments of 200 to 400 pigs. Multiple scenarios of starting conditions of infection (SCI) ranging from 0.25 to 100% were tested for each population size. The effect of each of these two factors on the probability of disease extinctions and the prevalence of each of the classes of the model and the risk groups of pigs were estimated. The results showed that the compartment population had an inverse effect on the probability of disease extinction. On the other hand, low SCI resulted in high levels of early extinctions reaching 45%, while higher SCI led to high levels of late extinctions. Early extinctions resulted in the absence of the pathogen from the compartment, while late extinctions did not assure it. This effect shows that reducing the population of the compartment combined with appropriate cleaning and good farming practices could have a positive effect in the reduction of the risk of introducing S. Typhimurium into the slaughtering procedure. On the other hand, the profile of seroprevalence at slaughter age allows for risk characterization of the farm, given the relative stability and the small variation for higher SCI

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<http://dx.doi.org/10.1056/NEJMopv0911052> (Accès réservé EHESP)

- (41) UYEKI TM, SHARMA A, BRANDA JA. **Case records of the Massachusetts General Hospital. Case 40-2009. A 29-year-old man with Fever and respiratory failure.** N Engl J Med. 2009 Dec. 24, vol. 361, n° 26, pp.2558-2569
<http://dx.doi.org/10.1056/NEJMcp0905545> (Accès réservé EHESP)
- (42) WATSON R. **Council of Europe launches investigation into H1N1 pandemic.** BMJ. 2010, vol. 340, p.c641
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<http://www.ncbi.nlm.nih.gov/pubmed/20064849> (Accès réservé EHESP)
- (46) WRIGHT PF, KIRKLAND KB, MODLIN JF. **When to consider the use of antibiotics in the treatment of 2009 H1N1 influenza-associated pneumonia.** N Engl J Med. 2009 Dec. 10, vol. 361, n° 24, p.e112
<http://dx.doi.org/10.1056/NEJMopv0910749> (Accès réservé EHESP)
- (47) YANG Y, SUGIMOTO JD, HALLORAN ME, BASTA NE, *et al.* **The transmissibility and control of pandemic influenza A (H1N1) virus.** Science. 2009 Oct. 30, vol. 326, n° 5953, pp.729-733
<http://dx.doi.org/10.1126/science.1177373> (Accès réservé EHESP)
- Pandemic influenza A (H1N1) 2009 (pandemic H1N1) is spreading throughout the planet. It has become the dominant strain in the Southern Hemisphere, where the influenza season has now ended. Here, on the basis of reported case clusters in the United States, we estimated the household secondary attack rate for pandemic H1N1 to be 27.3% [95% confidence interval (CI) from 12.2% to 50.5%]. From a school outbreak, we estimated that a typical schoolchild infects 2.4 (95% CI from 1.8 to 3.2) other children within the school. We estimated the basic reproductive number, R₀, to range from 1.3 to 1.7 and the generation interval to range from 2.6 to 3.2 days. We used a simulation model to evaluate the effectiveness of vaccination strategies in the United States for fall 2009. If a vaccine were available soon enough, vaccination of children, followed by adults, reaching 70% overall coverage, in addition to high-risk and essential workforce groups, could mitigate a severe epidemic
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<http://www.ncbi.nlm.nih.gov/pubmed/20044393> (Accès réservé EHESP)

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<http://dx.doi.org/10.1001/jama.2009.1790> (Accès réservé EHESP)
- (2) GORDON SC, LANDA D. **Disclosure of the genetic risk of Alzheimer's disease.** N Engl J Med. 2010 Jan. 14, vol. 362, n° 2, pp.181-182
<http://dx.doi.org/10.1056/NEJMc096300> (Accès réservé EHESP)
- (3) GREEN RC, SCHNEIDER LS, AMATO DA, BEELEN AP, *et al.* **Effect of tarenflurbil on cognitive decline and activities of daily living in patients with mild Alzheimer disease: a randomized controlled trial.** JAMA. 2009 Dec. 16, vol. 302, n° 23, pp.2557-2564
<http://dx.doi.org/10.1001/jama.2009.1866> (Accès réservé EHESP)

CONTEXT: Amyloid-beta peptide (Abeta(42)) has been implicated in the pathogenesis of Alzheimer disease (AD). Tarenflurbil, a selective Abeta(42)-lowering agent, demonstrated encouraging results on cognitive and functional outcomes among mildly affected patients in an earlier phase 2 trial. OBJECTIVE: To determine the efficacy, safety, and tolerability of tarenflurbil. DESIGN, SETTING, AND PATIENTS: A multicenter, randomized, double-blind, placebo-controlled trial enrolling patients with mild AD was conducted at 133 trial sites in the United States between February 21, 2005, and April 30, 2008. Concomitant treatment with cholinesterase inhibitors or memantine was permitted. INTERVENTION: Tarenflurbil, 800 mg, or placebo, administered twice a day. MAIN OUTCOME MEASURES: Co-primary efficacy end points were the change from baseline to month 18 in total score on the subscale of the Alzheimer Disease Assessment Scale-Cognitive Subscale (ADAS-Cog, 80-point version) and Alzheimer Disease Cooperative Studies-activities of daily living (ADCS-ADL) scale. Additional prespecified slope analyses explored the possibility of disease modification. RESULTS: Of the 1684 participants randomized, 1649 were included in the analysis, and 1046 completed the trial. Tarenflurbil had no beneficial effect on the co-primary outcomes (difference in change from baseline to month 18 vs placebo, based on least squares means: 0.1 for ADAS-Cog; 95% CI, -0.9 to 1.1; P = .86 and -0.5 for ADCS-ADL; 95% CI, -1.9 to 0.9; P = .48) using an intent-to-treat analysis. No significant differences occurred in the secondary outcomes. The ADAS-Cog score decreased by 7.1 points over 18 months. The tarenflurbil group had a small increase in frequency of dizziness, anemia, and infections. CONCLUSION: Tarenflurbil did not slow cognitive decline or the loss of activities of daily living in patients with mild AD. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00105547

- (4) KANG JE, LIM MM, BATEMAN RJ, LEE JJ, *et al.* **Amyloid-beta dynamics are regulated by orexin and the sleep-wake cycle.** Science. 2009 Nov. 13, vol. 326, n° 5955, pp.1005-1007
<http://dx.doi.org/10.1126/science.1180962> (Accès réservé EHESP)

Amyloid-beta (Abeta) accumulation in the brain extracellular space is a hallmark of Alzheimer's disease. The factors regulating this process are only partly understood. Abeta aggregation is a concentration-dependent process that is likely responsive to changes in brain interstitial fluid (ISF) levels of Abeta. Using in vivo microdialysis in mice, we found that the amount of ISF Abeta correlated with wakefulness. The amount of ISF Abeta also significantly increased during acute sleep deprivation and during orexin infusion, but decreased with infusion of a dual orexin receptor antagonist. Chronic sleep restriction significantly increased, and a dual orexin receptor antagonist decreased, Abeta plaque formation in amyloid precursor protein transgenic mice. Thus, the sleep-wake cycle and orexin may play a role in the pathogenesis of Alzheimer's disease

- (5) LI NC, LEE A, WHITMER RA, KIVIPELTO M, *et al.* **Use of angiotensin receptor blockers and risk of dementia in a predominantly male population: prospective cohort analysis.** BMJ.

2010, vol. 340, p.b5465

<http://www.ncbi.nlm.nih.gov/pubmed/20068258> (Accès réservé EHESP)

OBJECTIVE: To investigate whether angiotensin receptor blockers protect against Alzheimer's disease and dementia or reduce the progression of both diseases. **DESIGN:** Prospective cohort analysis. **SETTING:** Administrative database of the US Veteran Affairs, 2002-6. Population 819 491 predominantly male participants (98%) aged 65 or more with cardiovascular disease. **MAIN OUTCOME MEASURES:** Time to incident Alzheimer's disease or dementia in three cohorts (angiotensin receptor blockers, lisinopril, and other cardiovascular drugs, the "cardiovascular comparator") over a four year period (fiscal years 2003-6) using Cox proportional hazard models with adjustments for age, diabetes, stroke, and cardiovascular disease. Disease progression was the time to admission to a nursing home or death among participants with pre-existing Alzheimer's disease or dementia. **RESULTS:** Hazard rates for incident dementia in the angiotensin receptor blocker group were 0.76 (95% confidence interval 0.69 to 0.84) compared with the cardiovascular comparator and 0.81 (0.73 to 0.90) compared with the lisinopril group. Compared with the cardiovascular comparator, angiotensin receptor blockers in patients with pre-existing Alzheimer's disease were associated with a significantly lower risk of admission to a nursing home (0.51, 0.36 to 0.72) and death (0.83, 0.71 to 0.97). Angiotensin receptor blockers exhibited a dose-response as well as additive effects in combination with angiotensin converting enzyme inhibitors. This combination compared with angiotensin converting enzyme inhibitors alone was associated with a reduced risk of incident dementia (0.54, 0.51 to 0.57) and admission to a nursing home (0.33, 0.22 to 0.49). Minor differences were shown in mean systolic and diastolic blood pressures between the groups. Similar results were observed for Alzheimer's disease. **CONCLUSIONS:** Angiotensin receptor blockers are associated with a significant reduction in the incidence and progression of Alzheimer's disease and dementia compared with angiotensin converting enzyme inhibitors or other cardiovascular drugs in a predominantly male population

- (6) LIEB W, BEISER AS, VASAN RS, TAN ZS, *et al.* **Association of plasma leptin levels with incident Alzheimer disease and MRI measures of brain aging.** JAMA. 2009 Dec. 16, vol. 302, n° 23, pp.2565-2572
<http://dx.doi.org/10.1001/jama.2009.1836> (Accès réservé EHESP)

CONTEXT: The adipokine leptin facilitates long-term potentiation and synaptic plasticity in the hippocampus, promotes beta-amyloid clearance, and improves memory function in animal models of aging and Alzheimer disease (AD). **OBJECTIVE:** To relate baseline circulating leptin concentrations in a community-based sample of individuals without dementia to incident dementia and AD during follow-up and magnetic resonance imaging (MRI) measures of brain aging in survivors. **DESIGN, SETTING, AND PARTICIPANTS:** Prospective study of plasma leptin concentrations measured in 785 persons without dementia (mean [SD] age, 79 [5] years; 62% female), who were in the Framingham original cohort at the 22nd examination cycle (1990-1994). A subsample of 198 dementia-free survivors underwent volumetric brain MRI between 1999 and 2005, approximately 7.7 years after leptin was assayed. Two measures of brain aging, total cerebral brain volume and temporal horn volume (which is inversely related to hippocampal volume) were assessed. **MAIN OUTCOME MEASURE:** Incidence of dementia and AD during follow-up until December 31, 2007. **RESULTS:** During a median follow-up of 8.3 years (range, 0-15.5 years), 111 participants developed incident dementia; 89 had AD. Higher leptin levels were associated with a lower risk of incident dementia and AD in multivariable models (hazard ratio per 1-SD increment in log leptin was 0.68 [95% confidence interval, 0.54-0.87] for all-cause dementia and 0.60 [95% confidence interval, 0.46-0.79] for AD). This corresponds to an absolute AD risk over a 12-year follow-up of 25% for persons in the lowest quartile (first quartile) vs 6% for persons in the fourth quartile of sex-specific leptin levels. In addition, a 1-SD elevation in plasma leptin level was associated with higher total cerebral brain volume and lower temporal horn volume, although the association of leptin level with temporal horn volume did not reach statistical significance. **CONCLUSION:** Circulating leptin was associated with a reduced incidence of dementia and AD and with cerebral brain volume in asymptomatic older adults

- (7) MONTINE TJ, LARSON EB. **Late-life dementias: does this unyielding global challenge require a broader view?** JAMA. 2009 Dec. 16, vol. 302, n° 23, pp.2593-2594
<http://dx.doi.org/10.1001/jama.2009.1863> (Accès réservé EHESP)
- (8) QUERFURTH HW, LAFERLA FM. **Alzheimer's disease.** N Engl J Med. 2010 Jan. 28, vol. 362, n° 4, pp.329-344
<http://dx.doi.org/10.1056/NEJMra0909142> (Accès réservé EHESP)
- (9) SANDERS AE, WANG C, KATZ M, DERBY CA, *et al.* **Association of a functional polymorphism in the cholesteryl ester transfer protein (CETP) gene with memory decline and incidence of dementia.** JAMA. 2010 Jan. 13, vol. 303, n° 2, pp.150-158
<http://dx.doi.org/10.1001/jama.2009.1988> (Accès réservé EHESP)

CONTEXT: Polymorphisms in the cholesteryl ester transfer protein (CETP) gene have been associated with exceptional longevity and lower cardiovascular risk, but associations with memory decline and dementia risk are unclear. OBJECTIVE: To test the hypothesis that a single-nucleotide polymorphism (SNP) at CETP codon 405 (isoleucine to valine V405; SNP rs5882) is associated with a lower rate of memory decline and lower risk of incident dementia, including Alzheimer disease (AD). DESIGN, SETTING, AND PARTICIPANTS: Prospective cohort study comprising 608 community-dwelling adults without dementia aged 70 years or older from the Einstein Aging Study with CETP genotype available. Fifteen participants with prevalent dementia were excluded, and 70 without follow-up--63 lost to follow-up and 7 new to the study--were excluded from the Cox proportional hazards model, which included 523 participants in the analysis. Standardized neuropsychological and neurological measures were administered annually from 1994-2009. Linear mixed-effects models adjusted for sex, education, race, medical comorbidities, and apolipoprotein (APOE) epsilon4 examined associations of V405 genotype with longitudinal performance on cognitive tests of episodic memory (Free and Cued Selective Reminding Test [FCSRT], possible scores of 0-48), attention (Digit Span), and psychomotor speed (Digit Symbol Substitution). The V405 genotype was the main predictor of incident dementia or AD in similarly adjusted Cox proportional hazards models with age as the time scale. MAIN OUTCOME MEASURES: Memory decline and incident dementia. RESULTS: Valine allele frequency was 43.5%. A total of 40 cases of incident dementia occurred during follow-up (mean [(SD), 4.3 [3.1] years). Compared with isoleucine homozygotes, valine homozygotes had significantly slower memory decline on the FCSRT (0.43 points per year of age for isoleucine; 95% confidence interval [CI], -0.58 to -0.29 vs 0.21 points per year of age for valine; 95% CI, -0.39 to -0.04; difference in linear age slope, 0.22; 95% CI, 0.02 to 0.41; P = .03) and no significant differences on the Digit Span or Digit Symbol Substitution tests. Valine homozygotes also had lower risk of dementia (hazard ratio, 0.28; 95% CI, 0.10-0.85; P = .02) and AD (hazard ratio, 0.31; 95% CI, 0.10-0.95; P = .04). CONCLUSION: This preliminary report suggests that CETP V405 valine homozygosity is associated with slower memory decline and lower incident dementia and AD risk

Maladies cardio-vasculaires

[sommaire](#)

- (1) BARRY M. **Dabigatran versus warfarin in patients with atrial fibrillation.** N Engl J Med. 2009 Dec. 31, vol. 361, n° 27, p.2674
<http://www.ncbi.nlm.nih.gov/pubmed/20050385> (Accès réservé EHESP)
- (2) BHATT DL, LINCOFF AM, GIBSON CM, STONE GW, *et al.* **Intravenous platelet blockade with cangrelor during PCI.** N Engl J Med. 2009 Dec. 10, vol. 361, n° 24, pp.2330-2341
<http://dx.doi.org/10.1056/NEJMoa0908629> (Accès réservé EHESP)

BACKGROUND: Intravenous cangrelor, a rapid-acting, reversible adenosine diphosphate (ADP) receptor antagonist, might reduce ischemic events during percutaneous coronary intervention (PCI). **METHODS:** In this double-blind, placebo-controlled study, we randomly assigned 5362 patients who had not been treated with clopidogrel to receive either cangrelor or placebo at the time of PCI, followed by 600 mg of clopidogrel. The primary end point was a composite of death, myocardial infarction, or ischemia-driven revascularization at 48 hours. Enrollment was stopped when an interim analysis concluded that the trial would be unlikely to show superiority for the primary end point. **RESULTS:** The primary end point occurred in 185 of 2654 patients receiving cangrelor (7.0%) and in 210 of 2641 patients receiving placebo (8.0%) (odds ratio in the cangrelor group, 0.87; 95% confidence interval [CI], 0.71 to 1.07; P=0.17) (modified intention-to-treat population adjusted for missing data). In the cangrelor group, as compared with the placebo group, two prespecified secondary end points were significantly reduced at 48 hours: the rate of stent thrombosis, from 0.6% to 0.2% (odds ratio, 0.31; 95% CI, 0.11 to 0.85; P=0.02), and the rate of death from any cause, from 0.7% to 0.2% (odds ratio, 0.33; 95% CI, 0.13 to 0.83; P=0.02). There was no significant difference in the rate of blood transfusion (1.0% in the cangrelor group and 0.6% in the placebo group, P=0.13), though major bleeding on one scale was increased in the cangrelor group, from 3.5% to 5.5% (P<0.001), because of more groin hematomas. **CONCLUSIONS:** The use of periprocedural cangrelor during PCI was not superior to placebo in reducing the primary end point. The prespecified secondary end points of stent thrombosis and death were lower in the cangrelor group, with no significant increase in the rate of transfusion. Further study of intravenous ADP blockade with cangrelor may be warranted. (ClinicalTrials.gov number, NCT00385138.)

- (3) BRESSLER J, FOLSOM AR, COUPER DJ, VOLCIK KA, *et al.* **Genetic variants identified in a European genome-wide association study that were found to predict incident coronary heart disease in the atherosclerosis risk in communities study.** Am J Epidemiol. 2010 Jan. 1, vol. 171, n° 1, pp.14-23
<http://dx.doi.org/10.1093/aje/kwp377> (Accès réservé EHESP)

In 2007, the Wellcome Trust Case Control Consortium (WTCCC) performed a genome-wide association study in 2,000 British coronary heart disease (CHD) cases and 3,000 controls after genotyping 469,557 single nucleotide polymorphisms (SNPs). Seven variants associated with CHD were initially identified, and 5 SNPs were later found in replication studies. In the current study, the authors aimed to determine whether the 12 SNPs reported by the WTCCC predicted incident CHD through 2004 in a biracial, prospective cohort study (Atherosclerosis Risk in Communities) comprising 15,792 persons aged 45-64 years who had been selected by probability sampling from 4 different US communities in 1987-1989. Cox proportional hazards models with adjustment for age and gender were used to estimate CHD hazard rate ratios (HRRs) over a 17-year period (1,362 cases in whites and 397 cases in African Americans) under an additive genetic model. The results showed that 3 SNPs in whites (rs599839, rs1333049, and rs501120; HRRs were 1.10 (P = 0.044), 1.14 (P < 0.001), and 1.14 (P = 0.030), respectively) and 1 SNP in African Americans (rs7250581; HRR = 1.60, P = 0.05) were significantly associated with incident CHD. This study demonstrates that genetic variants revealed in a case-control genome-wide association study enriched for early disease onset may play a role in the genetic etiology of CHD in the general population

- (4) BUCKLAND G, GONZALEZ CA, AGUDO A, VILARDELL M, *et al.* **Adherence to the Mediterranean diet and risk of coronary heart disease in the Spanish EPIC Cohort Study.** Am J Epidemiol. 2009 Dec. 15, vol. 170, n° 12, pp.1518-1529
<http://dx.doi.org/10.1093/aje/kwp282> (Accès réservé EHESP)

No known cohort study has investigated whether the Mediterranean diet can reduce incident coronary heart disease (CHD) events in a Mediterranean population. This study examined the relation between Mediterranean diet adherence and risk of incident CHD events in the 5 Spanish centers of the European Prospective Investigation into Cancer and Nutrition. Analysis included

41,078 participants aged 29-69 years, recruited in 1992-1996 and followed up until December 2004 (mean follow-up: 10.4 years). Confirmed incident fatal and nonfatal CHD events were analyzed according to Mediterranean diet adherence, measured by using an 18-unit relative Mediterranean diet score. A total of 609 participants (79% male) had a fatal or nonfatal confirmed acute myocardial infarction (n = 468) or unstable angina requiring revascularization (n = 141). After stratification by center and age and adjustment for recognized CHD risk factors, high compared with low relative Mediterranean diet score was associated with a significant reduction in CHD risk (hazard ratio = 0.60, 95% confidence interval: 0.47, 0.77). A 1-unit increase in relative Mediterranean diet score was associated with a 6% reduced risk of CHD (95% confidence interval: 0.91, 0.97), with similar risk reductions by sex. Mediterranean diet adherence was associated with a significantly reduced CHD risk in this Mediterranean country, supporting its role in primary prevention of CHD in healthy populations

- (5) CATTANEO M. **Ticagrelor versus clopidogrel in acute coronary syndromes**. N Engl J Med. 2009 Dec. 10, vol. 361, n° 24, pp.2386-2388
<http://www.ncbi.nlm.nih.gov/pubmed/20050197> (Accès réservé EHESP)
- (6) CLARKE R, PEDEN JF, HOPEWELL JC, KYRIAKOU T, *et al.* **Genetic variants associated with Lp(a) lipoprotein level and coronary disease**. N Engl J Med. 2009 Dec. 24, vol. 361, n° 26, pp.2518-2528
<http://dx.doi.org/10.1056/NEJMoa0902604> (Accès réservé EHESP)

BACKGROUND: An increased level of Lp(a) lipoprotein has been identified as a risk factor for coronary artery disease that is highly heritable. The genetic determinants of the Lp(a) lipoprotein level and their relevance for the risk of coronary disease are incompletely understood.
METHODS: We used a novel gene chip containing 48,742 single-nucleotide polymorphisms (SNPs) in 2100 candidate genes to test for associations in 3145 case subjects with coronary disease and 3352 control subjects. Replication was tested in three independent populations involving 4846 additional case subjects with coronary disease and 4594 control subjects.
RESULTS: Three chromosomal regions (6q26-27, 9p21, and 1p13) were strongly associated with the risk of coronary disease. The LPA locus on 6q26-27 encoding Lp(a) lipoprotein had the strongest association. We identified a common variant (rs10455872) at the LPA locus with an odds ratio for coronary disease of 1.70 (95% confidence interval [CI], 1.49 to 1.95) and another independent variant (rs3798220) with an odds ratio of 1.92 (95% CI, 1.48 to 2.49). Both variants were strongly associated with an increased level of Lp(a) lipoprotein, a reduced copy number in LPA (which determines the number of kringle IV-type 2 repeats), and a small Lp(a) lipoprotein size. Replication studies confirmed the effects of both variants on the Lp(a) lipoprotein level and the risk of coronary disease. A meta-analysis showed that with a genotype score involving both LPA SNPs, the odds ratios for coronary disease were 1.51 (95% CI, 1.38 to 1.66) for one variant and 2.57 (95% CI, 1.80 to 3.67) for two or more variants. After adjustment for the Lp(a) lipoprotein level, the association between the LPA genotype score and the risk of coronary disease was abolished.
CONCLUSIONS: We identified two LPA variants that were strongly associated with both an increased level of Lp(a) lipoprotein and an increased risk of coronary disease. Our findings provide support for a causal role of Lp(a) lipoprotein in coronary disease

- (7) COUGHLIN SS. **Invited commentary: genetic variants and individual- and societal-level risk factors**. Am J Epidemiol. 2010 Jan. 1, vol. 171, n° 1, pp.24-26
<http://dx.doi.org/10.1093/aje/kwp379> (Accès réservé EHESP)

Over the past decade, leading epidemiologists have noted the importance of social factors in studying and understanding the distribution and determinants of disease in human populations; but to what extent are epidemiologic studies integrating genetic information and other biologic variables with information about individual-level risk factors and group-level or societal factors related to the broader residential, behavioral, or cultural context? There remains a need to

consider ways to integrate genetic information with social and contextual information in epidemiologic studies, partly to combat the overemphasis on the importance of genetic factors as determinants of disease in human populations. Even in genome-wide association studies of coronary heart disease and other common complex diseases, only a small proportion of heritability is explained by the genetic variants identified to date. It is possible that familial clustering due to genetic factors has been overestimated and that important environmental or social influences (acting alone or in combination with genetic variants) have been overlooked. The accompanying article by Bressler et al. (Am J Epidemiol. 2010;171(1):14-23) highlights some of these important issues

- (8) DE PM, SHARGALL Y. **Images in clinical medicine. Vanishing mediastinal mass.** N Engl J Med. 2009 Dec. 31, vol. 361, n° 27, p.2653
<http://dx.doi.org/10.1056/NEJMicm0809572> (Accès réservé EHESP)
- (9) EDWARDS JL. **Hormonal therapy for prostate cancer in men with heart disease.** JAMA. 2010 Jan. 6, vol. 303, n° 1, p.32
<http://dx.doi.org/10.1001/jama.2009.1930> (Accès réservé EHESP)
- (10) FARZANEH-FAR R, LIN J, EPEL ES, HARRIS WS, *et al.* **Association of marine omega-3 fatty acid levels with telomeric aging in patients with coronary heart disease.** JAMA. 2010 Jan. 20, vol. 303, n° 3, pp.250-257
<http://dx.doi.org/10.1001/jama.2009.2008> (Accès réservé EHESP)

CONTEXT: Increased dietary intake of marine omega-3 fatty acids is associated with prolonged survival in patients with coronary heart disease. However, the mechanisms underlying this protective effect are poorly understood. OBJECTIVE: To investigate the association of omega-3 fatty acid blood levels with temporal changes in telomere length, an emerging marker of biological age. DESIGN, SETTING, AND PARTICIPANTS: Prospective cohort study of 608 ambulatory outpatients in California with stable coronary artery disease recruited from the Heart and Soul Study between September 2000 and December 2002 and followed up to January 2009 (median, 6.0 years; range, 5.0-8.1 years). MAIN OUTCOME MEASURES: We measured leukocyte telomere length at baseline and again after 5 years of follow-up. Multivariable linear and logistic regression models were used to investigate the association of baseline levels of omega-3 fatty acids (docosahexaenoic acid [DHA] and eicosapentaenoic acid [EPA]) with subsequent change in telomere length. RESULTS: Individuals in the lowest quartile of DHA+EPA experienced the fastest rate of telomere shortening (0.13 telomere-to-single-copy gene ratio [T/S] units over 5 years; 95% confidence interval [CI], 0.09-0.17), whereas those in the highest quartile experienced the slowest rate of telomere shortening (0.05 T/S units over 5 years; 95% CI, 0.02-0.08; $P < .001$ for linear trend across quartiles). Levels of DHA+EPA were associated with less telomere shortening before (unadjusted beta coefficient $\times 10^{-3}$) = 0.06; 95% CI, 0.02-0.10) and after (adjusted beta coefficient $\times 10^{-3}$) = 0.05; 95% CI, 0.01-0.08) sequential adjustment for established risk factors and potential confounders. Each 1-SD increase in DHA+EPA levels was associated with a 32% reduction in the odds of telomere shortening (adjusted odds ratio, 0.68; 95% CI, 0.47-0.98). CONCLUSION: Among this cohort of patients with coronary artery disease, there was an inverse relationship between baseline blood levels of marine omega-3 fatty acids and the rate of telomere shortening over 5 years

- (11) KATHIRESAN S. **Lp(a) lipoprotein redux--from curious molecule to causal risk factor.** N Engl J Med. 2009 Dec. 24, vol. 361, n° 26, pp.2573-2574
<http://dx.doi.org/10.1056/NEJMe0910792> (Accès réservé EHESP)

- (12) KNOPMAN DS. **Invited commentary: Albuminuria and microvascular disease of the brain--a shared pathophysiology.** Am J Epidemiol. 2010 Feb. 1, vol. 171, n° 3, pp.287-289
<http://dx.doi.org/10.1093/aje/kwp429> (Accès réservé EHESP)

This commentary considers the implications of the association between albuminuria and cognitive decline described by Jassal et al. in this issue of the Journal (Am J Epidemiol. 2010;171(3):290-291). The authors report that men with albuminuria had a greater likelihood than men without albuminuria of experiencing declines in cognitive function over a 6.6-year period. Albuminuria is the result of endothelial damage in the kidney, which, in turn, is the result of microvascular disease. If one of the key mechanisms of brain microvascular disease is leakage of serum proteins into the brain extracellular space, in a fashion parallel to albuminuria that occurs in nephrosclerosis, several facets of cerebrovascular disease and cognitive decline are explained. First, brain microvascular disease would not be recognized by traditional clinical features of cerebrovascular disease because brain microvascular disease occurs gradually and insidiously. Second, the extravasation of serum proteins as a result of brain microvascular disease would account for the perivascular distribution of white matter hyperintensities on magnetic resonance imaging. Albuminuria might be a useful screening test for generalized microvascular disease and, if detected, might reasonably prompt brain imaging and more intensive therapeutic efforts to forestall further endothelial dysfunction in the kidney, brain, and elsewhere

- (13) MCMURRAY JJ. **Clinical practice. Systolic heart failure.** N Engl J Med. 2010 Jan. 21, vol. 362, n° 3, pp.228-238
<http://dx.doi.org/10.1056/NEJMcp0909392> (Accès réservé EHESP)

- (14) MITCHELL AR. **Coronary calcium screening.** N Engl J Med. 2009 Dec. 17, vol. 361, n° 25, pp.2490-2491
<http://dx.doi.org/10.1056/NEJMc0909481> (Accès réservé EHESP)

- (15) MITKA M. **Researchers hope measuring performance will improve stroke care and prevention.** JAMA. 2010 Jan. 6, vol. 303, n° 1, pp.17-18
<http://dx.doi.org/10.1001/jama.2009.1862> (Accès réservé EHESP)

- (16) MITKA M. **Task force: nontraditional markers add little to heart risk assessment.** JAMA. 2009 Nov. 25, vol. 302, n° 20, pp.2192-2193
<http://dx.doi.org/10.1001/jama.2009.1678> (Accès réservé EHESP)

- (17) NEWMAN TB, PLETCHER MJ. **Coronary calcium screening.** N Engl J Med. 2009 Dec. 17, vol. 361, n° 25, pp.2491-2492
<http://www.ncbi.nlm.nih.gov/pubmed/20050217> (Accès réservé EHESP)

- (18) OMLAND T, DE LEMOS JA, SABATINE MS, CHRISTOPHI CA, *et al.* **A sensitive cardiac troponin T assay in stable coronary artery disease.** N Engl J Med. 2009 Dec. 24, vol. 361, n° 26, pp.2538-2547
<http://dx.doi.org/10.1056/NEJMoa0805299> (Accès réservé EHESP)

BACKGROUND: In most patients with stable coronary artery disease, plasma cardiac troponin T levels are below the limit of detection for the conventional assay. The distribution and determinants of very low circulating troponin T levels, as well as their association with cardiovascular events, in such patients are unknown. METHODS: We used a new, high-sensitivity assay to determine the concentration of cardiac troponin T in plasma samples from 3679 patients with stable coronary artery disease and preserved left ventricular function. Results of the assay

were analyzed in relation to the incidence of cardiovascular events during a median follow-up period of 5.2 years. RESULTS: With the highly sensitive assay, concentrations of cardiac troponin T were at or above the limit of detection (0.001 microg per liter) in 3593 patients (97.7%) and at or above the 99th percentile for apparently healthy subjects (0.0133 microg per liter) in 407 patients (11.1%). After adjustment for other independent prognostic indicators, there was a strong and graded increase in the cumulative incidence of cardiovascular death (adjusted hazard ratio per unit increase in the natural logarithm of the troponin T level, 2.09; 95% confidence interval [CI], 1.60 to 2.74; P<0.001) and of heart failure (adjusted hazard ratio, 2.20; 95% CI, 1.66 to 2.90; P<0.001) in this study group. Increased risk associated with higher levels of troponin T was evident well below the limit of detection of conventional cardiac troponin T assays and below the 99th percentile of values in a healthy population. There was no association between troponin T levels as measured with the highly sensitive assay and the incidence of myocardial infarction (adjusted hazard ratio, 1.16; 95% CI, 0.97 to 1.40; P=0.11). CONCLUSIONS: After adjustment for other independent prognostic indicators, cardiac troponin T concentrations as measured with a highly sensitive assay were significantly associated with the incidence of cardiovascular death and heart failure but not with myocardial infarction in patients with stable coronary artery disease

- (19) POLLER L, JESPERSEN J, IBRAHIM S. **Dabigatran versus warfarin in patients with atrial fibrillation.** N Engl J Med. 2009 Dec. 31, vol. 361, n° 27, pp.2673-2674
<http://www.ncbi.nlm.nih.gov/pubmed/20050386> (Accès réservé EHESP)

- (20) SHIMIZU Y, KODAMA K, NISHI N, KASAGI F, *et al.* **Radiation exposure and circulatory disease risk: Hiroshima and Nagasaki atomic bomb survivor data, 1950-2003.** BMJ. 2010, vol. 340, p.b5349

<http://www.ncbi.nlm.nih.gov/pubmed/20075151> (Accès réservé EHESP)

OBJECTIVE: To investigate the degree to which ionising radiation confers risk of mortality from heart disease and stroke. DESIGN: Prospective cohort study with more than 50 years of follow-up. SETTING: Atomic bomb survivors in Hiroshima and Nagasaki, Japan. PARTICIPANTS: 86 611 Life Span Study cohort members with individually estimated radiation doses from 0 to >3 Gy (86% received <0.2 Gy). MAIN OUTCOME MEASURES: Mortality from stroke or heart disease as the underlying cause of death and dose-response relations with atomic bomb radiation. RESULTS: About 9600 participants died of stroke and 8400 died of heart disease between 1950 and 2003. For stroke, the estimated excess relative risk per gray was 9% (95% confidence interval 1% to 17%, P=0.02) on the basis of a linear dose-response model, but an indication of possible upward curvature suggested relatively little risk at low doses. For heart disease, the estimated excess relative risk per gray was 14% (6% to 23%, P<0.001); a linear model provided the best fit, suggesting excess risk even at lower doses. However, the dose-response effect over the restricted dose range of 0 to 0.5 Gy was not significant. Prospective data on smoking, alcohol intake, education, occupation, obesity, and diabetes had almost no impact on the radiation risk estimates for either stroke or heart disease, and misdiagnosis of cancers as circulatory diseases could not account for the associations seen. CONCLUSION: Doses above 0.5 Gy are associated with an elevated risk of both stroke and heart disease, but the degree of risk at lower doses is unclear. Stroke and heart disease together account for about one third as many radiation associated excess deaths as do cancers among atomic bomb survivors

- (21) TAUBMAN SL, ROBINS JM, MITTLEMAN MA, HERNAN MA. **Intervening on risk factors for coronary heart disease: an application of the parametric g-formula.** Int J Epidemiol. 2009 Dec., vol. 38, n° 6, pp.1599-1611
<http://dx.doi.org/10.1093/ije/dyp192> (Accès réservé EHESP)

Estimating the population risk of disease under hypothetical interventions--such as the population risk of coronary heart disease (CHD) were everyone to quit smoking and start exercising or to start exercising if diagnosed with diabetes--may not be possible using standard analytic techniques. The parametric g-formula, which appropriately adjusts for time-varying confounders

affected by prior exposures, is especially well suited to estimating effects when the intervention involves multiple factors (joint interventions) or when the intervention involves decisions that depend on the value of evolving time-dependent factors (dynamic interventions). We describe the parametric g-formula, and use it to estimate the effect of various hypothetical lifestyle interventions on the risk of CHD using data from the Nurses' Health Study. Over the period 1982-2002, the 20-year risk of CHD in this cohort was 3.50%. Under a joint intervention of no smoking, increased exercise, improved diet, moderate alcohol consumption and reduced body mass index, the estimated risk was 1.89% (95% confidence interval: 1.46-2.41). We discuss whether the assumptions required for the validity of the parametric g-formula hold in the Nurses' Health Study data. This work represents the first large-scale application of the parametric g-formula in an epidemiologic cohort study

- (22) WATANABE M, OKAMURA T, KOKUBO Y, HIGASHIYAMA A, *et al.* **Elevated serum creatine kinase predicts first-ever myocardial infarction: a 12-year population-based cohort study in Japan, the Suita study.** *Int J Epidemiol.* 2009 Dec., vol. 38, n° 6, pp.1571-1579
<http://dx.doi.org/10.1093/ije/dyp212> (Accès réservé EHESP)

BACKGROUND: In myocardial infarction (MI), it is well known that serum creatine kinase (s-CK) increases after onset, but it is unclear whether s-CK elevates before MI onset. The present analysis examined whether elevated s-CK levels predicted first-ever MI or stroke. **METHODS:** This study was a population-based cohort study in a Japanese urban area. Study subjects were comprised of 5026 initially healthy Japanese (2370 men and 2656 women, mean age: 54.5 years) without a history of MI or stroke. They were followed-up for 11.8 years on average, and 103 MIs (definite: 45; probable: 58) and 168 strokes (definite: 126; probable: 42) were observed. There was no subject who developed MI just at baseline (the follow-up period among those with definite MI was, at earliest, 0.20 years). **RESULTS:** The adjusted hazard ratio for definite MI was 4.18 (95% confidence interval 1.66-10.53) with s-CK levels of ≥ 200 IU/l, compared with the reference category (s-CK levels of ≤ 99 IU/l), whereas no relationship was observed between s-CK levels and the risk for stroke. With regard to definite MI, an interaction between s-CK levels and dyslipidaemia was observed. Among subjects with hypercholesterolaemia, the hazard ratio linearly elevated with increased s-CK levels. On the other hand, no linear elevation was observed among subjects without hypercholesterolaemia (P for interaction = 0.011). **CONCLUSIONS:** The present study suggested that screening for elevated s-CK levels in initially healthy Japanese subjects was useful to predict first-ever MI in the future, especially in subjects with dyslipidaemia

Maladies liées à l'alcool

[sommaire](#)

- (1) GMEL G, KUNTSCHE E, WICKI M, LABHART F. **Measuring alcohol-related consequences in school surveys: alcohol-attributable consequences or consequences with students' alcohol attribution.** *Am J Epidemiol.* 2010 Jan. 1, vol. 171, n° 1, pp.93-104
<http://dx.doi.org/10.1093/aje/kwp331> (Accès réservé EHESP)

In alcohol epidemiology surveys, there is a tradition of measuring alcohol-related consequences using respondents' attribution of alcohol as the cause. The authors aimed to compare the prevalence and frequency of self-attributed consequences to consequences without self-attribution using alcohol-attributable fractions (AAF). In 2007, a total of 7,174 Swiss school students aged 13-16 years reported the numbers of 6 alcohol-related adverse consequences (e.g., fights, injuries) they had incurred in the past 12 months. Consequences were measured with and without attribution of alcohol as the cause. The alcohol-use measures were frequency and volume of drinking in the past 12 months and number of risky single-occasion (≥ 5 drinks) drinking episodes in the past 30 days. Attributable fractions were derived from logistic (≥ 1 incident) and Poisson (number of incidents) regression analyses. Although relative risk estimates were higher when alcohol-attributed consequences were compared with nonattributed consequences, the use of AAFs resulted in more alcohol-related consequences (10,422 self-attributed consequences vs. 24,520 nonattributed consequences determined by means of AAFs).

The likelihood of underreporting was higher among drinkers with intermediate frequencies than among either rare drinkers or frequent drinkers. Therefore, the extent of alcohol-related adverse consequences among adolescents may be underestimated when using self-attributed consequences, because of differential attribution processes, especially among infrequent drinkers

- (2) O'DOWD A. **Earlier help could reduce current "unsustainable" burden on NHS of alcohol.** BMJ. 2010, vol. 340, p.c80
<http://www.ncbi.nlm.nih.gov/pubmed/20053836> (Accès réservé EHESP)
- (3) SHERIDAN RL, GOLDSTEIN MA, STODDARD FJ, JR., WALKER TG. **Case records of the Massachusetts General Hospital. Case 41-2009. A 16-year-old boy with hypothermia and frostbite.** N Engl J Med. 2009 Dec. 31, vol. 361, n° 27, pp.2654-2662
<http://dx.doi.org/10.1056/NEJMcpc0910088> (Accès réservé EHESP)

Paludisme

[sommaire](#)

- (1) GRAHAM IA, BESSER K, BLUMER S, BRANIGAN CA, *et al.* **The genetic map of *Artemisia annua* L. identifies loci affecting yield of the antimalarial drug artemisinin.** Science. 2010 Jan. 15, vol. 327, n° 5963, pp.328-331
<http://dx.doi.org/10.1126/science.1182612> (Accès réservé EHESP)

Artemisinin is a plant natural product produced by *Artemisia annua* and the active ingredient in the most effective treatment for malaria. Efforts to eradicate malaria are increasing demand for an affordable, high-quality, robust supply of artemisinin. We performed deep sequencing on the transcriptome of *A. annua* to identify genes and markers for fast-track breeding. Extensive genetic variation enabled us to build a detailed genetic map with nine linkage groups. Replicated field trials resulted in a quantitative trait loci (QTL) map that accounts for a significant amount of the variation in key traits controlling artemisinin yield. Enrichment for positive QTLs in parents of new high-yielding hybrids confirms that the knowledge and tools to convert *A. annua* into a robust crop are now available

- (2) HOULIHAN CF, PATEL S, PRICE DA, VALAPPIL M, *et al.* **A/H1N1 flu pandemic. Life threatening infections labelled swine flu.** BMJ. 2010, vol. 340, p.c137
<http://www.ncbi.nlm.nih.gov/pubmed/20071428> (Accès réservé EHESP)
- (3) LOUICHAROEN C, PATIN E, PAUL R, NUCHPRAYOON I, *et al.* **Positively selected G6PD-Mahidol mutation reduces *Plasmodium vivax* density in Southeast Asians.** Science. 2009 Dec. 11, vol. 326, n° 5959, pp.1546-1549
<http://dx.doi.org/10.1126/science.1178849> (Accès réservé EHESP)

Glucose-6-phosphate dehydrogenase (G6PD) deficiency--the most common known enzymopathy--is associated with neonatal jaundice and hemolytic anemia usually after exposure to certain infections, foods, or medications. Although G6PD-deficient alleles appear to confer a protective effect against malaria, the link with clinical protection from *Plasmodium* infection remains unclear. We investigated the effect of a common G6PD deficiency variant in Southeast Asia--the G6PD-Mahidol(487A) variant--on human survival related to *vivax* and *falciparum* malaria. Our results show that strong and recent positive selection has targeted the Mahidol variant over the past 1500 years. We found that the G6PD-Mahidol(487A) variant reduces *vivax*, but not *falciparum*, parasite density in humans, which indicates that *Plasmodium vivax* has been a driving force behind the strong selective advantage conferred by this mutation

- (4) MILHOUS WK, WEINA PJ. **Plant science. The botanical solution for malaria.** Science. 2010 Jan. 15, vol. 327, n° 5963, pp.279-280
<http://dx.doi.org/10.1126/science.1184780> (Accès réservé EHESP)

Pathologies liées à l'obésité

[sommaire](#)

- (1) BODELON C, DOHERTY JA, CHEN C, ROSSING MA, *et al.* **Use of nonsteroidal antiinflammatory drugs and risk of endometrial cancer.** Am J Epidemiol. 2009 Dec. 15, vol. 170, n° 12, pp.1512-1517
<http://dx.doi.org/10.1093/aje/kwp321> (Accès réservé EHESP)

Results of 3 previous studies suggest that use of aspirin is related to a reduced risk of endometrial cancer, at least in obese women (body mass index, ≥ 30 kg/m²). Using data obtained in a population-based, case-control study in western Washington State, the authors examined this question. Between 2003 and 2005, 410 women diagnosed with invasive endometrial cancer and 356 controls were interviewed regarding the use of aspirin and other nonsteroidal antiinflammatory drugs (NSAIDs). A history of use of NSAIDs was not associated with the risk of endometrial cancer (odds ratio = 1.04, 95% confidence interval: 0.76, 1.42). The lack of association was also present specifically for use of aspirin (odds ratio = 1.06, 95% confidence interval: 0.73, 1.53). NSAID use was unrelated to risk of endometrial cancer in both obese and nonobese women. Results from this study suggest that the use of aspirin or other NSAIDs has little or no influence on the risk of endometrial cancer

- (2) CHANG HJ. **Scientists probe brain's role in obesity.** JAMA. 2010 Jan. 6, vol. 303, n° 1, p.19
<http://dx.doi.org/10.1001/jama.2009.1861> (Accès réservé EHESP)
- (3) CHAUFAN C, HONG GH, FOX P. **Taxing "sin foods" - obesity prevention and public health policy.** N Engl J Med. 2009 Dec. 10, vol. 361, n° 24, p.e113
<http://dx.doi.org/10.1056/NEJMopv0909847> (Accès réservé EHESP)
- (4) CHOW CK, LOCK K, TEO K, SUBRAMANIAN SV, *et al.* **Environmental and societal influences acting on cardiovascular risk factors and disease at a population level: a review.** Int J Epidemiol. 2009 Dec., vol. 38, n° 6, pp.1580-1594
<http://dx.doi.org/10.1093/ije/dyn258> (Accès réservé EHESP)

It has long been known that cardiovascular disease (CVD) rates vary considerably among populations, across space and through time. It is now apparent that most of the attributable risk for myocardial infarction 'within' populations from across the world can be ascribed to the varying levels of a limited number of risk factors among individuals in a population. Individual risk factors (e.g. blood pressure) can be modified with resulting health gains. Yet, the persistence of large international variations in cardiovascular risk factors and resulting CVD incidence and mortality indicates that there are additional factors that apply to 'populations' that are important to understand as part of a comprehensive approach to CVD control. This article reviews the evidence on why certain populations are more at risk than others

- (5) CHUNG RY, SCHOOLING CM, COWLING BJ, LEUNG GM. **How does socioeconomic development affect risk of mortality? An age-period-cohort analysis from a recently transitioned population in China.** Am J Epidemiol. 2010 Feb. 1, vol. 171, n° 3, pp.345-356
<http://dx.doi.org/10.1093/aje/kwp378> (Accès réservé EHESP)

During the 20th century, the Hong Kong Chinese population experienced 2 abrupt but temporally distinct macroenvironmental changes: The transition from essentially preindustrial living conditions

to a rapidly developing economy through mass migration in the late 1940s was followed by the emergence of an infant and childhood adiposity epidemic in the 1960s. The authors aimed to delineate the effects of these 2 aspects of economic development on mortality, thus providing a sentinel for other rapidly developing economies. Sex-specific Poisson models were used to estimate effects of age, calendar period, and birth cohort on Hong Kong adult mortality between 1976 and 2005. All-cause and cause-specific mortality, including mortality from ischemic heart disease (IHD), cardiovascular disease excluding IHD, lung cancer, other cancers, and respiratory disease, were considered. Male mortality from IHD and female mortality from other cancers increased with birth into a more economically developed environment. Cardiovascular disease mortality increased with birth after the start of the infant and childhood adiposity epidemic, particularly for men. Macroenvironmental changes associated with economic development had sex-specific effects over the life course, probably originating in early life. The full population health consequences of these changes are unlikely to manifest until persons who have spent their early lives in such environments reach an age at which they become vulnerable to chronic diseases

- (6) FARLEY TA, BAKER ET, FUTRELL L, RICE JC. **The ubiquity of energy-dense snack foods: a national multicity study.** Am J Public Health. 2010 Feb., vol. 100, n° 2, pp.306-311
<http://dx.doi.org/10.2105/AJPH.2009.178681> (Accès réservé EHESP)

OBJECTIVES: We assessed the availability and accessibility of energy-dense snacks in retail stores whose primary merchandise was not food and whether these varied by store type, region, or socioeconomic factors. METHODS: We conducted systematic observations of 1082 retail stores in 19 US cities and determined the availability and accessibility of 6 categories of energy-dense snack foods. RESULTS: Snack food was available in 41% of the stores; the most common forms were candy (33%), sweetened beverages (20%), and salty snacks (17%). These foods were often within arm's reach of the cash register queue. We observed snack foods in 96% of pharmacies, 94% of gasoline stations, 22% of furniture stores, 16% of apparel stores, and 29% to 65% of other types of stores. Availability varied somewhat by region but not by the racial or socioeconomic characteristics of nearby census tracts. CONCLUSIONS: Energy-dense snack foods and beverages, implicated as contributors to the obesity epidemic, are widely available in retail stores whose primary business is not food. The ubiquity of these products may contribute to excess energy consumption in the United States

- (7) FLEGAL KM, CARROLL MD, OGDEN CL, CURTIN LR. **Prevalence and trends in obesity among US adults, 1999-2008.** JAMA. 2010 Jan. 20, vol. 303, n° 3, pp.235-241
<http://dx.doi.org/10.1001/jama.2009.2014> (Accès réservé EHESP)

CONTEXT: The prevalence of obesity increased in the United States between 1976-1980 and 1988-1994 and again between 1988-1994 and 1999-2000. OBJECTIVE: To examine trends in obesity from 1999 through 2008 and the current prevalence of obesity and overweight for 2007-2008. DESIGN, SETTING, AND PARTICIPANTS: Analysis of height and weight measurements from 5555 adult men and women aged 20 years or older obtained in 2007-2008 as part of the National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of the US population. Data from the NHANES obtained in 2007-2008 were compared with results obtained from 1999 through 2006. MAIN OUTCOME MEASURE: Estimates of the prevalence of overweight and obesity in adults. Overweight was defined as a body mass index (BMI) of 25.0 to 29.9. Obesity was defined as a BMI of 30.0 or higher. RESULTS: In 2007-2008, the age-adjusted prevalence of obesity was 33.8% (95% confidence interval [CI], 31.6%-36.0%) overall, 32.2% (95% CI, 29.5%-35.0%) among men, and 35.5% (95% CI, 33.2%-37.7%) among women. The corresponding prevalence estimates for overweight and obesity combined (BMI > or = 25) were 68.0% (95% CI, 66.3%-69.8%), 72.3% (95% CI, 70.4%-74.1%), and 64.1% (95% CI, 61.3%-66.9%). Obesity prevalence varied by age group and by racial and ethnic group for both men and women. Over the 10-year period, obesity showed no significant trend among women (adjusted odds ratio [AOR] for 2007-2008 vs 1999-2000, 1.12 [95% CI, 0.89-1.32]). For men, there was a significant linear trend (AOR for 2007-2008 vs 1999-2000, 1.32 [95% CI, 1.12-1.58]); however, the

3 most recent data points did not differ significantly from each other. CONCLUSIONS: In 2007-2008, the prevalence of obesity was 32.2% among adult men and 35.5% among adult women. The increases in the prevalence of obesity previously observed do not appear to be continuing at the same rate over the past 10 years, particularly for women and possibly for men

- (8) FORD AL, BERGH C, SODERSTEN P, SABIN MA, *et al.* **Treatment of childhood obesity by retraining eating behaviour: randomised controlled trial.** BMJ. 2010, vol. 340, p.b5388
<http://www.ncbi.nlm.nih.gov/pubmed/20051465> (Accès réservé EHESP)

OBJECTIVE: To determine whether modifying eating behaviour with use of a feedback device facilitates weight loss in obese adolescents. DESIGN: Randomised controlled trial with 12 month intervention. SETTING: Hospital based obesity clinic. PARTICIPANTS: 106 newly referred obese young people aged 9-17. INTERVENTIONS: A computerised device, Mandometer, providing real time feedback to participants during meals to slow down speed of eating and reduce total intake; standard lifestyle modification therapy. MAIN OUTCOME MEASURES: Change in body mass index (BMI) standard deviation score (SDS) over 12 months with assessment 18 months after the start of the intervention. Secondary outcomes were body fat SDS, metabolic status, quality of life evaluation, change in portion size, and eating speed. RESULTS: Using the last available data on all participants (n=106), those in the Mandometer group had significantly lower mean BMI SDS at 12 months compared with standard care (baseline adjusted mean difference 0.24, 95% confidence interval 0.11 to 0.36). Similar results were obtained when analyses included only the 91 who attended per protocol (baseline adjusted mean difference 0.27, 0.14 to 0.41; P<0.001), with the difference maintained at 18 months (0.27, 0.11 to 0.43; P=0.001) (n=87). The mean meal size in the Mandometer group fell by 45 g (7 to 84 g). Mean body fat SDS adjusted for baseline levels was significantly lower at 12 months (0.24, 0.10 to 0.39; P=0.001). Those in the Mandometer group also had greater improvement in concentration of high density lipoprotein cholesterol (P=0.043). CONCLUSIONS: Retraining eating behaviour with a feedback device is a useful adjunct to standard lifestyle modification in treating obesity among adolescents. TRIAL REGISTRATION: ClinicalTrials.gov NCT00407420

- (9) GAZIANO JM. **Fifth phase of the epidemiologic transition: the age of obesity and inactivity.** JAMA. 2010 Jan. 20, vol. 303, n° 3, pp.275-276
<http://dx.doi.org/10.1001/jama.2009.2025> (Accès réservé EHESP)
- (10) GIBBONS A. **Human evolution. What's for dinner? Researchers seek our ancestors' answers.** Science. 2009 Dec. 11, vol. 326, n° 5959, pp.1478-1479
<http://dx.doi.org/10.1126/science.326.5959.1478> (Accès réservé EHESP)
- (11) KAPLAN MG. **Taxing sugar-sweetened beverages.** N Engl J Med. 2010 Jan. 28, vol. 362, n° 4, p.368
<http://dx.doi.org/10.1056/NEJMc0911234> (Accès réservé EHESP)
- (12) KATAN MB, LUDWIG DS. **Extra calories cause weight gain--but how much?** JAMA. 2010 Jan. 6, vol. 303, n° 1, pp.65-66
<http://dx.doi.org/10.1001/jama.2009.1912> (Accès réservé EHESP)
- (13) KEANE M. **Taxing sugar-sweetened beverages.** N Engl J Med. 2010 Jan. 28, vol. 362, n° 4, pp.368-369
<http://www.ncbi.nlm.nih.gov/pubmed/20112448> (Accès réservé EHESP)

- (14) PIRKOLA J, VAARASMAKI M, LA-KORPELA M, BLOIGU A, *et al.* **Low-grade, systemic inflammation in adolescents: association with early-life factors, gender, and lifestyle.** *Am J Epidemiol.* 2010 Jan. 1, vol. 171, n° 1, pp.72-82
<http://dx.doi.org/10.1093/aje/kwp320> (Accès réservé EHESP)

Low-grade, systemic inflammation is related to increased risk of cardiovascular disease in adults. The proinflammatory state tracks from adolescence to adulthood. Identifying correlates of inflammation in adolescents could provide opportunities to prevent cardiovascular disease in adulthood. However, population-based data on correlates of inflammation in adolescence are limited. Therefore, the authors studied the associations of early-life factors, gender, and lifestyle with inflammation (measured by high-sensitivity C-reactive protein and leukocyte count) at age 16 years (2001-2002) in the prospective, population-based Northern Finland Birth Cohort 1986 Study (n = 5,240). In females, being born small for gestational age and current use of oral contraceptives were associated with the proinflammatory state. The association of birth size with inflammation was not observed in males. In logistic regression analyses, oral contraceptive use (odds ratio (OR) = 2.83), abdominal obesity (OR = 5.17), and smoking (OR = 2.72) were associated with elevation of both inflammation markers in females; abdominal obesity (OR = 5.72) and smoking (OR = 2.02) were associated in males. Thus, females appear more susceptible to the adverse effects of being born small for gestational age than males. Given the widespread use of oral contraceptives and the potential pathophysiologic consequences of the proinflammatory state, the association of oral contraceptive use with inflammation in adolescence may have public health implications

- (15) PRABHAKARAN D, ROY A. **Commentary: Societal influences on cardiovascular disease: time to assess and act.** *Int J Epidemiol.* 2009 Dec., vol. 38, n° 6, pp.1595-1598
<http://dx.doi.org/10.1093/ije/dyp295> (Accès réservé EHESP)
- (16) RINALDI MJ. **Taxing sugar-sweetened beverages.** *N Engl J Med.* 2010 Jan. 28, vol. 362, n° 4, p.369
<http://www.ncbi.nlm.nih.gov/pubmed/20112449> (Accès réservé EHESP)
- (17) SEO JA, KIM BG, CHO H, KIM HS, *et al.* **The cutoff values of visceral fat area and waist circumference for identifying subjects at risk for metabolic syndrome in elderly Korean: Ansan Geriatric (AGE) cohort study.** *BMC Public Health.* 2009, vol. 9, p.443
<http://dx.doi.org/10.1186/1471-2458-9-443> (Accès libre)

BACKGROUND: In Korea, the cutoff values of waist circumference (WC) for the identification of metabolic syndrome (MetS) were suggested to be 90 cm for men and 85 cm for women based on the analysis mainly in middle-aged adults. As aging is associated with increased fat, especially abdominal visceral fat, the cutoff value of WC may differ according to age. In addition, the usefulness of visceral abdominal fat area (VFA) to predict MetS in the elderly has not been studied yet. We aimed to suggest WC and VFA criteria and to compare the predictability of WC and VFA to identify people at risk for MetS. **METHODS:** A total of 689 elderly subjects aged ≥ 63 years (308 men, 381 women) were chosen in this cross-sectional study from an ongoing, prospective, population-based study, the Ansan Geriatric (AGE) cohort study. VFA was measured by single slice abdominal computed tomography scanning. The metabolic risk factors except WC (plasma glucose, blood pressure, serum triglycerides and HDL cholesterol levels) were defined using modified NCEP-ATP III criteria. We estimated the accuracy of VFA and WC for identifying at least two of these factors by receiver operating characteristic (ROC) curve analysis. **RESULTS:** Two hundred three of 308 men and 280 of 381 women had ≥ 2 metabolic risk factors. The area under the ROC curve (AUC) value for VFA to predict the presence of ≥ 2 metabolic risk factors was not significantly different from that for WC (men, 0.735 and 0.750; women, 0.715 and 0.682; AUC values for VFA and WC, respectively). The optimal cutoff points for VFA and WC for predicting the presence of ≥ 2 metabolic risk factors were 92.6 cm² and

86.5 cm for men and 88.9 cm² and 86.5 cm for women. **CONCLUSION:** WC had comparable power with VFA to identify elderly people who are at risk for MetS. Elderly Korean men and women had very similar cutoff points for both VFA and WC measurements for estimating the risk of MetS. Age-specific cutoff point for WC might be considered to identify subjects at risk for MetS

- (18) SHARMA P. **Clinical practice. Barrett's esophagus.** N Engl J Med. 2009 Dec. 24, vol. 361, n° 26, pp.2548-2556
<http://dx.doi.org/10.1056/NEJMcp0902173> (Accès réservé EHESP)

- (19) SIEGEL JM, PRELIP ML, ERAUSQUIN JT, KIM SA. **A worksite obesity intervention: results from a group-randomized trial.** Am J Public Health. 2010 Feb., vol. 100, n° 2, pp.327-333
<http://dx.doi.org/10.2105/AJPH.2008.154153> (Accès réservé EHESP)

OBJECTIVES: We used a participatory process to develop an obesity intervention appropriate for elementary school personnel. **METHODS:** A randomized controlled trial included 16 school worksites (8 intervention, 8 control). Intervention schools formed committees to develop and implement health promotion activities for employees. Anthropometric and self-report data were collected at baseline and postintervention (2 years later). The primary outcome measures were body mass index (BMI), waist-hip ratio, physical activity, and fruit and vegetable consumption. **RESULTS:** After adjustment for age, ethnicity, and job classification, employees in intervention schools reduced their BMI by an average of 0.04 kg/m², and those in control schools increased their BMI by an average of 0.37 kg/m². Comparisons for waist-hip ratio, weekly physical activity minutes, and fruit and vegetable consumption were not significant. **CONCLUSIONS:** The participatory process appeared to be an effective means for stimulating change. The intervention may have slowed and perhaps reversed the tendency of adults to gain weight progressively with age

- (20) SULAIMAN R, LABIB M. **Diagnosis of diabetes. First define impaired fasting glycaemia.** BMJ. 2009, vol. 339, p.b5642
<http://www.ncbi.nlm.nih.gov/pubmed/20044397> (Accès réservé EHESP)

- (21) TSAI AC. **Indirect costs of structural interventions.** JAMA. 2009 Dec. 23, vol. 302, n° 24, pp.2661-2662
<http://dx.doi.org/10.1001/jama.2009.1888> (Accès réservé EHESP)

- (22) ZIMMERMAN FJ, BELL JF. **Associations of television content type and obesity in children.** Am J Public Health. 2010 Feb., vol. 100, n° 2, pp.334-340
<http://dx.doi.org/10.2105/AJPH.2008.155119> (Accès réservé EHESP)

OBJECTIVES: We tested the associations of content types of children's television viewing with subsequent body mass index (BMI) to assess the plausibility of different causal pathways. **METHODS:** We used time-use diary data from the Panel Survey of Income Dynamics to measure television viewing categorized by format and educational and commercial content. Analyses were stratified by age because children younger than 7 years are less able to understand the persuasive intent of advertising. BMI z scores in 2002 were regressed on television viewing, sociodemographic variables, mother's BMI, and BMI in 1997 (for older children only). **RESULTS:** Among children aged 0 to 6 years in 1997, commercial viewing in 1997 was significantly associated with BMI z scores in 2002 in fully adjusted regressions. Among children older than 6 years, commercial viewing in 2002 was associated with 2002 BMI. These results were robust after adjustment for exercise and eating while watching television. **CONCLUSIONS:** The evidence does not support the contention that television viewing contributes to obesity because it is a sedentary activity. Television advertising, rather than viewing per se, is associated with obesity

- (1) **Mortality of HIV-infected patients starting potent antiretroviral therapy: comparison with the general population in nine industrialized countries.** *Int J Epidemiol.* 2009 Dec., vol. 38, n° 6, pp.1624-1633

<http://dx.doi.org/10.1093/ije/dyp306> (Accès réservé EHESP)

BACKGROUND: Mortality in HIV-infected patients has declined substantially with combination antiretroviral therapy (ART), but it is unclear whether it has reached that of the general population. We compared mortality in patients starting ART in nine countries of Europe and North America with the corresponding general population, taking into account their response to ART. **METHODS:** Eligible patients were enrolled in prospective cohort studies participating in the ART Cohort Collaboration. We calculated the ratio of observed to expected deaths from all causes [standardized mortality ratio (SMR)], measuring time from 6 months after starting ART, according to risk group, clinical stage at the start of ART and CD4 cell count and viral load at 6 months. Expected numbers of deaths were obtained from age-, sex- and country-specific mortality rates. **RESULTS:** Among 29 935 eligible patients, 1134 deaths were recorded in 131 510 person-years of follow-up. The median age was 37 years, 8162 (27%) patients were females, 4400 (15%) were injecting drug users (IDUs) and 6738 (23%) had AIDS when starting ART. At 6 months, 23 539 patients (79%) had viral load measurements ≤ 500 copies/ml. The lowest SMR, 1.05 [95% confidence interval (CI) 0.82-1.35] was found for men who have sex with men (MSM) who started ART free of AIDS, reached a CD4 cell count of ≥ 350 cells/microL and suppressed viral replication to ≤ 500 copies/ml by the sixth month. In contrast, the SMR was 73.7 (95% CI 46.4-116.9) in IDUs who failed to suppress viral replication and had CD4 cell counts < 50 cells/microL at 6 months. The percentage of patients with SMRs < 2 was 46% for MSM, 42% for heterosexually infected patients and 0% for patients with a history of injection drug use. Corresponding percentages for SMRs > 10 were 4, 14 and 47%. **CONCLUSIONS:** In industrialized countries, the mortality experience of HIV-infected patients who start ART and survive the first 6 months continues to be higher than in the general population, but for many patients excess mortality is moderate and comparable with patients having other chronic conditions. Much of the excess mortality might be prevented by earlier diagnosis of HIV followed by timely initiation of ART

- (2) BAILOR MH, SUN X, AL-HASHIMI HM. **Topology links RNA secondary structure with global conformation, dynamics, and adaptation.** *Science.* 2010 Jan. 8, vol. 327, n° 5962, pp.202-206
<http://dx.doi.org/10.1126/science.1181085> (Accès réservé EHESP)

Thermodynamic rules that link RNA sequences to secondary structure are well established, but the link between secondary structure and three-dimensional global conformation remains poorly understood. We constructed comprehensive three-dimensional maps depicting the orientation of A-form helices across RNA junctions in the Protein Data Bank and rationalized our findings with modeling and nuclear magnetic resonance spectroscopy. We show that the secondary structures of junctions encode readily computable topological constraints that accurately predict the three-dimensional orientation of helices across all two-way junctions. Our results suggest that RNA global conformation is largely defined by topological constraints encoded at the secondary structural level and that tertiary contacts and intermolecular interactions serve to stabilize specific conformers within the topologically allowed ensemble

- (3) COHEN J. **AIDS vaccine research. HIV natural resistance field finally overcomes resistance.** *Science.* 2009 Dec. 11, vol. 326, n° 5959, pp.1476-1477
<http://dx.doi.org/10.1126/science.326.5959.1476> (Accès réservé EHESP)

- (4) COLE SR, JACOBSON LP, TIEN PC, KINGSLEY L, *et al.* **Using marginal structural measurement-error models to estimate the long-term effect of antiretroviral therapy on**

incident AIDS or death. Am J Epidemiol. 2010 Jan. 1, vol. 171, n° 1, pp.113-122
<http://dx.doi.org/10.1093/aje/kwp329> (Accès réservé EHESP)

To estimate the net effect of imperfectly measured highly active antiretroviral therapy on incident acquired immunodeficiency syndrome or death, the authors combined inverse probability-of-treatment-and-censoring weighted estimation of a marginal structural Cox model with regression-calibration methods. Between 1995 and 2007, 950 human immunodeficiency virus-positive men and women were followed in 2 US cohort studies. During 4,054 person-years, 374 initiated highly active antiretroviral therapy, 211 developed acquired immunodeficiency syndrome or died, and 173 dropped out. Accounting for measured confounders and determinants of dropout, the weighted hazard ratio for acquired immunodeficiency syndrome or death comparing use of highly active antiretroviral therapy in the prior 2 years with no therapy was 0.36 (95% confidence limits: 0.21, 0.61). This association was relatively constant over follow-up ($P = 0.19$) and stronger than crude or adjusted hazard ratios of 0.75 and 0.95, respectively. Accounting for measurement error in reported exposure using external validation data on 331 men and women provided a hazard ratio of 0.17, with bias shifted from the hazard ratio to the estimate of precision as seen by the 2.5-fold wider confidence limits (95% confidence limits: 0.06, 0.43). Marginal structural measurement-error models can simultaneously account for 3 major sources of bias in epidemiologic research: validated exposure measurement error, measured selection bias, and measured time-fixed and time-varying confounding

- (5) SELLIER P, LAFUENTE-LAFUENTE C, BERGMANN JF. **Interleukin-2 therapy in patients with HIV infection.** N Engl J Med. 2010 Jan. 21, vol. 362, n° 3, pp.270-271
<http://dx.doi.org/10.1056/NEJMc0910951> (Accès réservé EHESP)

Tuberculose

[sommaire](#)

- (1) AGARWAL N, BISHAI WR. **Microbiology. Subversion from the sidelines.** Science. 2010 Jan. 22, vol. 327, n° 5964, pp.417-418
<http://dx.doi.org/10.1126/science.1185569> (Accès réservé EHESP)
- (2) BOULLE A, ELEY B. **Commentary: Reducing HIV-associated tuberculosis in children.** Int J Epidemiol. 2009 Dec., vol. 38, n° 6, pp.1621-1623
<http://dx.doi.org/10.1093/ije/dyp301> (Accès réservé EHESP)
- (3) EDMONDS A, LUSIAMA J, NAPRAVNIK S, KITETELE F, *et al.* **Anti-retroviral therapy reduces incident tuberculosis in HIV-infected children.** Int J Epidemiol. 2009 Dec., vol. 38, n° 6, pp.1612-1621
<http://dx.doi.org/10.1093/ije/dyp208> (Accès réservé EHESP)

BACKGROUND: We aimed to estimate the effect of anti-retroviral therapy (ART) on incident tuberculosis (TB) in a cohort of HIV-infected children. **METHODS:** We analysed data from ART-naive, TB disease-free children enrolled between December 2004 and April 2008 into an HIV care program in Kinshasa, Democratic Republic of Congo. To estimate the effect of ART on TB incidence while accounting for time-dependent confounders affected by exposure, a Cox proportional hazards marginal structural model was used. **RESULTS:** 364 children contributed 596.0 person-years of follow-up. At baseline, the median age was 6.9 years; 163 (44.8%) were in HIV clinical stage 3 or 4. During follow-up, 242 (66.5%) children initiated ART and 81 (22.3%) developed TB. At TB diagnosis, 41 (50.6%) were receiving ART. The TB incidence rate in those receiving ART was 10.2 per 100 person-years [95% confidence interval (CI) 7.4-13.9] compared with 20.4 per 100 person-years (95% CI 14.6-27.8) in those receiving only primary HIV care. TB incidence decreased with time on ART, from 18.9 per 100 person-years in the first 6 months to 5.3

per 100 person-years after 12 months of ART. The model-estimated TB hazard ratio for ART was 0.51 (95% CI 0.27-0.94). **CONCLUSIONS:** For HIV-infected children in TB-endemic areas, ART reduces the hazard of developing TB by 50%

- (4) FENNER L, EGGER M, GAGNEUX S. **Annie Darwin's death, the evolution of tuberculosis and the need for systems epidemiology.** *Int J Epidemiol.* 2009 Dec., vol. 38, n° 6, pp.1425-1428
<http://dx.doi.org/10.1093/ije/dyp367> (Accès réservé EHESP)
- (5) FULLERTON DG, GORDON SB, CALVERLEY PM. **Chronic obstructive pulmonary disease in non-smokers.** *Lancet.* 2009 Dec. 12, vol. 374, n° 9706, pp.1964-1965
[http://dx.doi.org/10.1016/S0140-6736\(09\)62116-4](http://dx.doi.org/10.1016/S0140-6736(09)62116-4) (Accès réservé EHESP)
- (6) HOPKINSON NS, POLKEY MI. **Chronic obstructive pulmonary disease in non-smokers.** *Lancet.* 2009 Dec. 12, vol. 374, n° 9706, pp.1964-1966
[http://dx.doi.org/10.1016/S0140-6736\(09\)62115-2](http://dx.doi.org/10.1016/S0140-6736(09)62115-2) (Accès réservé EHESP)
- (7) JEE SH, GOLUB JE, JO J, PARK IS, *et al.* **Smoking and risk of tuberculosis incidence, mortality, and recurrence in South Korean men and women.** *Am J Epidemiol.* 2009 Dec. 15, vol. 170, n° 12, pp.1478-1485
<http://dx.doi.org/10.1093/aje/kwp308> (Accès réservé EHESP)

The authors explored the association of cigarette smoking with tuberculosis incidence, recurrence, and mortality. A 14-year prospective cohort study (1992-2006) was carried out in 1,294,504 South Koreans. Participants were grouped by smoking history, and the authors assessed tuberculosis incidence, mortality, and recurrence risk for each group. Unadjusted and adjusted Cox proportional hazards models were used to investigate the association between smoking history and the 3 outcomes of interest, adjusting for age and alcohol use. Compared with never smokers, current smokers had increased mortality from tuberculosis among both men (adjusted hazard ratio (HR) = 1.6, 95% confidence interval (CI): 1.3, 2.0) and women (HR = 1.6, 95% CI: 1.0, 2.4). Current male smokers had greater risk of incident tuberculosis than former smokers (HR = 1.4, 95% CI: 1.3, 1.5), and risk among current smokers increased with number of cigarettes smoked daily. In females, cigarette smoking was not associated with incident tuberculosis. There was interaction between smoking and sex for incidence (P = 0.00047). The effect of smoking was generally reduced with adjustment for body mass index. Among men, the highest alcohol consumption category (> or =100 g/day) was associated with risk of incident tuberculosis (HR = 1.5, 95% CI: 1.3, 1.7). This study provides longitudinal evidence that smoking increases risk of incident tuberculosis, mortality from tuberculosis, and tuberculosis recurrence

- (8) PAVORD ID, YOUSAF N, BIRRING SS. **Chronic obstructive pulmonary disease in non-smokers.** *Lancet.* 2009 Dec. 12, vol. 374, n° 9706, pp.1964-1966
[http://dx.doi.org/10.1016/S0140-6736\(09\)62114-0](http://dx.doi.org/10.1016/S0140-6736(09)62114-0) (Accès réservé EHESP)
- (9) VOLKMAN HE, POZOS TC, ZHENG J, DAVIS JM, *et al.* **Tuberculous granuloma induction via interaction of a bacterial secreted protein with host epithelium.** *Science.* 2010 Jan. 22, vol. 327, n° 5964, pp.466-469
<http://dx.doi.org/10.1126/science.1179663> (Accès réservé EHESP)

Granulomas, organized aggregates of immune cells, are a hallmark of tuberculosis and have traditionally been thought to restrict mycobacterial growth. However, analysis of *Mycobacterium marinum* in zebrafish has shown that the early granuloma facilitates mycobacterial growth;

uninfected macrophages are recruited to the granuloma where they are productively infected by *M. marinum*. Here, we identified the molecular mechanism by which mycobacteria induce granulomas: The bacterial secreted protein 6-kD early secreted antigenic target (ESAT-6), which has long been implicated in virulence, induced matrix metalloproteinase-9 (MMP9) in epithelial cells neighboring infected macrophages. MMP9 enhanced recruitment of macrophages, which contributed to nascent granuloma maturation and bacterial growth. Disruption of MMP9 function attenuated granuloma formation and bacterial growth. Thus, interception of epithelial MMP9 production could hold promise as a host-targeting tuberculosis therapy

Rapports et dossiers en ligne**Nouvelle publication :****Point de mire sur la prévention – Pleins feux sur les programmes et la recherche**

« Nouvelle publication en ligne de CATIE destinée aux personnes qui travaillent sur les stratégies de prévention contre le VIH et l'hépatite C. En mettant l'accent sur la recherche et son intégration pratique dans la planification et la prestation de services de première ligne, Point de mire sur la prévention a pour but de vous aider à comprendre et finalement à utiliser les connaissances résultant de la recherche accomplie sur la prévention du VIH et de l'hépatite C. »

<http://www.catie.ca/Fre/Prevention/PointDeMire/PointdeMireIndex.shtml> (Accès libre)

Recherche en santé[sommaire](#)

Self-reported health assessments in the 2002 World Health. Survey: how do they correlate with education? SV Subramanian et al. Bulletin de l'organisation mondiale de la santé, Volume 88, février 2010, 81-160

<http://dx.doi.org/10.2471/BLT.09.067058> (Accès libre)

Cancer du poumon[sommaire](#)**Journée mondiale contre le cancer – 4 février 2010**

Fiches repères sur le site de l'OMS et de l'INCA :

http://www.who.int/mediacentre/events/annual/world_cancer_day/fr/index.html

<http://www.e-cancer.fr/la-sante-publique/3940-journee-mondiale-contre-le-cancer>

« Cancer en Europe : la bataille continue » (Europa) :

http://ec.europa.eu/news/environment/100204_fr.htm

Deuxième rapport d'étape du Comité national de suivi pour la radiothérapie

[Commentaire sur le site de l'Inca](#)

[Le rapport](#) (Accès libre)

Source-specific effects of micronutrients in lung cancer prevention. *Lung Cancer* Volume 67, Issue 3, March 2010, Pages 275-281

<http://dx.doi.org/10.1016/j.lungcan.2009.11.010> (Accès réservé EHESP)

Characteristics of never smoker lung cancer including environmental and occupational risk factors. *Lung Cancer* Volume 67, Issue 2, February 2010, Pages 144-150

<http://dx.doi.org/10.1016/j.lungcan.2009.04.005> (Accès réservé EHESP)

Therapeutic indications in oncology: Emerging features and regulatory dynamics. *European Journal of Cancer*, Volume 46, Issue 3, February 2010, Pages 471-475

<http://dx.doi.org/10.1016/j.ejca.2009.11.021> (Accès réservé EHESP)

Childhood cancer mortality in Europe, 1970–2007. *European Journal of Cancer*. Volume 46, Issue 2, January 2010, Pages 384-394

<http://dx.doi.org/10.1016/j.ejca.2009.09.011> (Accès réservé EHESP)

Diabète[sommaire](#)

The weight of affluence. Bulletin de l'organisation mondiale de la santé, Volume 88, février 2010, 81-160
<http://www.who.int/bulletin/volumes/88/2/10-020210.pdf> (**Accès libre**)

Scientists shed light on insulin activity

“A British-Czech team of scientists has discovered how insulin interacts with cells in the human body. Published in the journal *Proceedings of the National Academy of Science (PNAS)*, the findings could give a major boost to researchers hoping to develop viable treatments to fight type I diabetes” (Europa)
http://ec.europa.eu/research/headlines/news/article_10_02_08_en.html

Dépression[sommaire](#)

Mesurer statistiquement la dépression : Enjeux et limites. Thomas MORIN, Direction de la recherche, des études, de l'évaluation et des statistiques. DREES, SERIE SOURCES ET METHODES, n° 9 – janvier 2010
<http://www.sante.gouv.fr/drees/seriesource-method/pdf/seriesource-method09.pdf> (**Accès libre**)

Maladie d'Alzheimer[sommaire](#)**2e anniversaire du plan Alzheimer 2008-2012.**

Présidence de la République, 1er février 2010

http://www.elysee.fr/download/?mode=press&filename=10-02-01_Dossier_de_presse_Alzheimer.pdf

Site officiel dédié au plan Alzheimer : <http://www.plan-alzheimer.gouv.fr/>

(**Accès libre**)

Maladie d'Alzheimer : annoncer et accompagner le diagnostic. HAS-Actualités & Pratiques - N° 16 - Février 2010, Focus

http://www.has-sante.fr/portail/jcms/c_912573/maladie-dalzheimer-annoncer-et-accompagner-le-diagnostic (**Accès libre**)

Maladies cardio-vasculaires[sommaire](#)

Cardiovascular risk factor trends and potential for reducing coronary heart disease mortality in the United States of America, Simon Capewell et al., Bulletin de l'organisation mondiale de la santé, Volume 88, février 2010, 81-160

<http://dx.doi.org/10.2471/BLT.08.057885> (**Accès libre**)

The Rho exchange factor Arhgef1 mediates the effects of angiotensin II on vascular tone and blood pressure, Nature Medicine 16, 183 - 190 (2010).

<http://dx.doi.org/10.1038/nm.2079> (**Accès payant**)

Des Nantais (INSERM 915) montrent le rôle d'une nouvelle protéine dans l'hypertension artérielle, l'Arhgef1, impliquée dans le système rénine-angiotensine-aldostérone (SRAA).

Maladies liées à l'alcool[sommaire](#)

Is low dose alcohol exposure during pregnancy harmful? Swedish National Institute of Public Health (SNIPH). Site de l'OMS. 2009. En ligne le 15 janvier 2010

http://www.euro.who.int/HEN/Syntheses/short/20100115_1 (**Accès libre**)

Paludisme[sommaire](#)**The Relationship between Anti-merozoite Antibodies and Incidence of Plasmodium falciparum Malaria: A Systematic Review and Meta-analysis.** PLoS Medicine, janvier 2010.

Une méta-analyse de 33 études conforte la notion que les anticorps de la classe IgG naturellement élaborés contre le mérozoïte de *Plasmodium falciparum* peuvent avoir un effet protecteur contre la maladie clinique. Certains antigènes de mérozoïte mériteraient sans doute d'être inclus dans un candidat vaccin contre le paludisme.

<http://dx.doi.org/10.1371/journal.pmed.1000218> ([Accès libre](#))

Pathologies liées à l'obésité[sommaire](#)**Obésité - Pose et ablation de ballon intragastrique.** Rapport d'évaluation technologique, novembre 2009. Haute Autorité de Santé. (Mis en ligne le 22 janvier 2010)

http://www.has-sante.fr/portail/upload/docs/application/pdf/2010-01/rapport_ballon_intragastrique.pdf

([Accès libre](#))

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