Bulletin de veille

« Focus sur 12 pathologies graves »

Janvier 2011

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Bulletin de veille – Janvier 2011
« 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

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- 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 issus de l'interrogation de la base Medline (interrogée le 7/01/2011)

Rapports , dossiers en ligne et articles supplémentaires

Articles scientifiques

Bronchite chronique obstructive

sommaire

(1) METEL'SKAIA VA, ALESHKIN BA, VOROPAEVA EA, KARAULOV AV, *et al.* **[Colonization resistance and immunological reactivity of children's oropharyngeal mucosa in health and bronchopulmonary pathology]**. Vestn Ross Akad Med Nauk. 2010, n° 7, pp.10-15
http://www.ncbi.nlm.nih.gov/pubmed/20795396

The study group was comprised of 27 practically healthy children, 51 patients with acute bronchitis, 15 with chronic bronchitis and 11 with pneumonia. It was shown that changes of microbiocoenosis in back of the throat (BOT) were related to increased mucosal contamination with normal microflora and opportunistic microorganisms. The highest degree of contamination was observed in children with acute bronchitis. Normocoenosis was detected only in 13 practically healthy children. The disorders of microbiocoenosis took the form of disbiosis and acute inflammatory processes in patients with acute and chronic bronchitis and pneumonia. However, the large amount of normal flora together with the high Ig level ensured marked colonization resistance as evidenced by the values of natural colonization coefficient of nasopharyngeal epithelium (NCCNE) and balance coefficient (BC). These data suggested development of compensated secondary immunodeficiencies. In patients with acute bronchitis and pneumonia, local synthesis of Ig prevailed. It is shown that BC can be used to screen children for disorders of mucosal immunity. The presence of increased saliva IgE levels in patients with acute and chronic bronchitis supports the generally accepted concept of bronchi as a "shock organ" in allergic condition. It was demonstrated that IgE levels in saliva increase earlier than in serum and may be used as a prognostic criterion in patients with bronchopulmonary pathology

(2) YAKOOT M, SALEM A, OMAR AM. **Clinical efficacy of farcosolvin syrup (ambroxol-theophylline-guaiphenesin mixture) in the treatment of acute exacerbation of chronic bronchitis**. Int J Chron Obstruct Pulmon Dis. 2010, vol. 5, pp.251-256
http://www.ncbi.nlm.nih.gov/pubmed/20714379

BACKGROUND: Acute exacerbations of chronic bronchitis (AECB) are defined as recurrent attacks of worsening bronchial inflammation that are marked by an increase in the volume of daily sputum produced, a change in color of the expectorated sputum, and worsening dyspnea. Farcosolvin (Pharco Pharmaceuticals, Alexandria, Egypt) is a mixture of ambroxol (15 mg); theophylline (50 mg); and guaiphenesin (30 mg), per 5 mL syrup. OBJECTIVE: To test the clinical efficacy of Farcosolvin in the treatment of AECB in a randomized, single-blinded, controlled study design. PATIENTS AND METHODS: One hundred patients with AECB were randomized to either Farcosolvin or guaiphenesin treatment groups, in addition to the standard medical treatment for their cases. Baseline clinical symptomatolgy of breathlessness, cough, and sputum severity scoring were compared before and after 3 and 7 days of treatment in both groups and the differences compared between groups. Changes in perceived improvement were also compared between groups using the Clinical Global Impression of Improvement or Change Scale (CGIC). RESULTS: There were statistically significant improvements in breathlessness and cough scores in both groups (pretreatment versus posttreatment at day 3 and at day 7; $P < 0.05$). There were highly statistically significant differences between groups in improvement in breathlessness and cough scores, after 3 and 7 days treatment, in favor of the Farcosolvin treatment group ($P < 0.001$). Out of 50 patients, 48 (96%) in the Farcosolvin-treated group rated their improvement on the CGIC scale as "much" and "very much" improved, while only 41 patients (82%) reported such a degree of improvement in the control group. The difference was statistically significant ($P < 0.05$). CONCLUSION: We concluded from our study that Farcosolvin syrup might be safe and effective in improving symptoms in cases of acute exacerbation of chronic bronchitis

(3) SANCHEZ-MARTELES M, MOLINA MA, BERMEJO SE, RUIZ LF, *et al.* **[Prognostic value of NT-proBNP in chronic pulmonary disease exacerbation]**. Med Clin (Barc). 2010 Oct. 2, vol.

135, n° 10, pp.441-446
http://dx.doi.org/10.1016/j.medcli.2009.11.047

BACKGROUND AND OBJECTIVE: Brain natriuretic peptide (BNP) is produced and released mainly from ventricles. BNP has been shown to be useful in diagnosis and prognosis in heart failure and some pulmonary conditions. The aim of this study is to analyse whether NT-proBNP has a prognostic value in chronic pulmonary patients without overt heart failure. PATIENT AND METHOD: We conducted an observational and prospective study. We included 192 patients admitted to the Internal Medicine Departments of Hospital Clinico "Lozano Blesa" (Zaragoza, Spain) and "Virgen de la Luz" (Cuenca, Spain) with acute exacerbation of pulmonary disease. Blood samples were taken to determine NT-proBNP concentrations. All patients were followed for 6 months after admission. RESULTS: 6,3% of patients died, 22,9% were prescribed with home oxygen-therapy, 18,2% received a diuretic prescription and 21,9% were re-admitted at least once during the follow-up period. Mean NT-proBNP was 1180pg/ml. A concentration above 500pg/ml and 350pg/ml of NT-proBNP was useful to predict mortality and diuretic prescription respectively. CONCLUSIONS: Among patients with acute exacerbations of chronic pulmonary disease, NT-proBNP could be a prognostic factor to identify those at risk of death or worst clinical development

(4) HAMARI A, TOLJAMO T, NIEMINEN P, KINNULA VL. **High frequency of chronic cough and sputum production with lowered exercise capacity in young smokers**. Ann Med. 2010 Oct., vol. 42, n° 7, pp.512-520
http://dx.doi.org/10.3109/07853890.2010.505933

OBJECTIVES: The aim was to evaluate how cigarette smoking is associated with respiratory symptoms, fitness, and anthropometric measures in young smokers. METHODS: The prevalence of smoking was investigated in a cohort of young military draftees (n = 1130; 98% between 18-21 years of age) in Northern Finland. The associations of smoking with respiratory symptoms, physical fitness (12-min running test), education, and anthropometric measures were analysed using a self-reported questionnaire with high response rate (80%). RESULTS: Almost half (46.5%) of the young males were daily smokers, 17.4% being occasional smokers. The prevalence of self-reported chronic cough and sputum production was high in daily smokers (40.7%) and occasional smokers (26.9%) compared to non-smokers (12%). These symptoms were significantly associated with the smoking history. Aerobic fitness was worse in regular smokers compared to non-smokers (P < 0.001). Smokers had a higher body mass index than non-smokers (P = 0.035). In the regular smokers, the more active the subjects were in sports, the less they smoked when evaluated by pack year history (P < 0.001). Smokers had a lower educational level than occasional smokers or, especially, non-smokers (P < 0.001). CONCLUSIONS: The frequency of young smokers with chronic cough and sputum production was very high, posing a serious risk to their future health

Cancer du poumon

sommaire

(1) KIRBY T. **Canada accused of hypocrisy over asbestos exports**. Lancet. 2010 Dec. 11, vol. 376, n° 9757, pp.1973-1974
http://www.ncbi.nlm.nih.gov/pubmed/21171229 (**accès réservé EHESP**)

(2) ICHIHARA E, MATSUOKA J, KIURA K. **Early palliative care in non-small-cell lung cancer**. N Engl J Med. 2010 Dec. 2, vol. 363, n° 23, pp.2263-2265
http://dx.doi.org/10.1056/NEJMc1010529#SA1 (**collection papier de la bibliothèque**)

(3) MACREA MM, HOROWITZ M, SHISHIR O. **Early palliative care in non-small-cell lung cancer**. N Engl J Med. 2010 Dec. 2, vol. 363, n° 23, pp.2263-2265
http://dx.doi.org/10.1056/NEJMc1010529#SA2 (**collection papier de la bibliothèque**)

(4) PEREZ MF, SIEGEL MD. **Early palliative care in non-small-cell lung cancer**. N Engl J Med. 2010 Dec. 2, vol. 363, n° 23, pp.2264-2265
http://dx.doi.org/10.1056/NEJMc1010529#SA3 (**collection papier de la bibliothèque**)

(5) VORDERMARK D. **Early palliative care in non-small-cell lung cancer**. N Engl J Med. 2010 Dec. 2, vol. 363, n° 23, pp.2264-2265
http://dx.doi.org/10.1056/NEJMc1010529#SA4 (**collection papier de la bibliothèque**)

(6) FELDSER DM, KOSTOVA KK, WINSLOW MM, TAYLOR SE, *et al.* **Stage-specific sensitivity to p53 restoration during lung cancer progression**. Nature. 2010 Nov. 25, vol. 468, n° 7323, pp.572-575
http://dx.doi.org/10.1038/nature09535 (**accès payant**)

Tumorigenesis is a multistep process that results from the sequential accumulation of mutations in key oncogene and tumour suppressor pathways. Personalized cancer therapy that is based on targeting these underlying genetic abnormalities presupposes that sustained inactivation of tumour suppressors and activation of oncogenes is essential in advanced cancers. Mutations in the p53 tumour-suppressor pathway are common in human cancer and significant efforts towards pharmaceutical reactivation of defective p53 pathways are underway. Here we show that restoration of p53 in established murine lung tumours leads to significant but incomplete tumour cell loss specifically in malignant adenocarcinomas, but not in adenomas. We define amplification of MAPK signalling as a critical determinant of malignant progression and also a stimulator of Arf tumour-suppressor expression. The response to p53 restoration in this context is critically dependent on the expression of Arf. We propose that p53 not only limits malignant progression by suppressing the acquisition of alterations that lead to tumour progression, but also, in the context of p53 restoration, responds to increased oncogenic signalling to mediate tumour regression. Our observations also underscore that the p53 pathway is not engaged by low levels of oncogene activity that are sufficient for early stages of lung tumour development. These data suggest that restoration of pathways important in tumour progression, as opposed to initiation, may lead to incomplete tumour regression due to the stage-heterogeneity of tumour cell populations

(7) JUNTTILA MR, KARNEZIS AN, GARCIA D, MADRILES F, *et al.* **Selective activation of p53-mediated tumour suppression in high-grade tumours**. Nature. 2010 Nov. 25, vol. 468, n° 7323, pp.567-571
http://dx.doi.org/10.1038/nature09526 (**accès payant**)

Non-small cell lung carcinoma (NSCLC) is the leading cause of cancer-related death worldwide, with an overall 5-year survival rate of only 10-15%. Deregulation of the Ras pathway is a frequent hallmark of NSCLC, often through mutations that directly activate Kras. p53 is also frequently inactivated in NSCLC and, because oncogenic Ras can be a potent trigger of p53 (ref. 3), it seems likely that oncogenic Ras signalling has a major and persistent role in driving the selection against p53. Hence, pharmacological restoration of p53 is an appealing therapeutic strategy for treating this disease. Here we model the probable therapeutic impact of p53 restoration in a spontaneously evolving mouse model of NSCLC initiated by sporadic oncogenic activation of endogenous Kras. Surprisingly, p53 restoration failed to induce significant regression of established tumours, although it did result in a significant decrease in the relative proportion of high-grade tumours. This is due to selective activation of p53 only in the more aggressive tumour cells within each tumour. Such selective activation of p53 correlates with marked upregulation in Ras signal intensity and induction of the oncogenic signalling sensor p19(ARF)( )(ref. 6). Our data indicate that p53-mediated tumour suppression is triggered only when oncogenic Ras signal flux exceeds a critical threshold. Importantly, the failure of low-level oncogenic Kras to engage p53 reveals inherent limits in the capacity of p53 to restrain early tumour evolution and in the efficacy of therapeutic p53 restoration to eradicate cancers

(8) IANNETTONI MD. **Staging strategies for lung cancer**. JAMA. 2010 Nov. 24, vol. 304, n° 20, pp.2296-2297
http://dx.doi.org/10.1001/jama.2010.1723 (**accès réservé EHESP**)

(9) ANNEMA JT, VAN MEERBEECK JP, RINTOUL RC, DOOMS C, *et al.* **Mediastinoscopy vs endosonography for mediastinal nodal staging of lung cancer: a randomized trial**. JAMA. 2010 Nov. 24, vol. 304, n° 20, pp.2245-2252
http://dx.doi.org/10.1001/jama.2010.1705 (**accès réservé EHESP**)

CONTEXT: Mediastinal nodal staging is recommended for patients with resectable non-small cell lung cancer (NSCLC). Surgical staging has limitations, which results in the performance of unnecessary thoracotomies. Current guidelines acknowledge minimally invasive endosonography followed by surgical staging (if no nodal metastases are found by endosonography) as an alternative to immediate surgical staging. OBJECTIVE: To compare the 2 recommended lung cancer staging strategies. DESIGN, SETTING, AND PATIENTS: Randomized controlled multicenter trial (Ghent, Leiden, Leuven, Papworth) conducted between February 2007 and April 2009 in 241 patients with resectable (suspected) NSCLC in whom mediastinal staging was indicated based on computed or positron emission tomography. INTERVENTION: Either surgical staging or endosonography (combined transesophageal and endobronchial ultrasound [EUS-FNA and EBUS-TBNA]) followed by surgical staging in case no nodal metastases were found at endosonography. Thoracotomy with lymph node dissection was performed when there was no evidence of mediastinal tumor spread. MAIN OUTCOME MEASURES: The primary outcome was sensitivity for mediastinal nodal (N2/N3) metastases. The reference standard was surgical pathological staging. Secondary outcomes were rates of unnecessary thoracotomy and complications. RESULTS: Two hundred forty-one patients were randomized, 118 to surgical staging and 123 to endosonography, of whom 65 also underwent surgical staging. Nodal metastases were found in 41 patients (35%; 95% confidence interval [CI], 27%-44%) by surgical staging vs 56 patients (46%; 95% CI, 37%-54%) by endosonography (P = .11) and in 62 patients (50%; 95% CI, 42%-59%) by endosonography followed by surgical staging (P = .02). This corresponded to sensitivities of 79% (41/52; 95% CI, 66%-88%) vs 85% (56/66; 95% CI, 74%-92%) (P = .47) and 94% (62/66; 95% CI, 85%-98%) (P = .02). Thoracotomy was unnecessary in 21 patients (18%; 95% CI, 12%-26%) in the mediastinoscopy group vs 9 (7%; 95% CI, 4%-13%) in the endosonography group (P = .02). The complication rate was similar in both groups. CONCLUSIONS: Among patients with (suspected) NSCLC, a staging strategy combining endosonography and surgical staging compared with surgical staging alone resulted in greater sensitivity for mediastinal nodal metastases and fewer unnecessary thoracotomies. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00432640

(10) COLGAN R, ZANER CI. **A piece of my mind. A modern family**. JAMA. 2010 Nov. 24, vol. 304, n° 20, pp.2221-2222
http://dx.doi.org/10.1001/jama.2010.1709 (**accès réservé EHESP**)

(11) KAMEROW D. **Screening for early detection of lung cancer**. BMJ. 2010, vol. 341, p.c6544
http://www.ncbi.nlm.nih.gov/pubmed/21084372

(12) PANDEY JP. **Genomewide association studies and assessment of risk of disease**. N Engl J Med. 2010 Nov. 18, vol. 363, n° 21, pp.2076-2077
http://dx.doi.org/10.1056/NEJMc1010310#SA1 (**collection papier de la bibliothèque**)

(13) MARSHALL E. **Cancer screening. The promise and pitfalls of a cancer breakthrough**. Science. 2010 Nov. 12, vol. 330, n° 6006, pp.900-901
http://dx.doi.org/330/60010.1126/science.330.6006.900-b (**accès réservé EHESP**)

(14) YACHIDA S, JONES S, BOZIC I, ANTAL T, *et al.* **Distant metastasis occurs late during the genetic evolution of pancreatic cancer**. Nature. 2010 Oct. 28, vol. 467, n° 7319, pp.1114-1117
http://dx.doi.org/10.1038/nature09515 (**accès payant**)

Metastasis, the dissemination and growth of neoplastic cells in an organ distinct from that in which they originated, is the most common cause of death in cancer patients. This is particularly true for pancreatic cancers, where most patients are diagnosed with metastatic disease and few show a sustained response to chemotherapy or radiation therapy. Whether the dismal prognosis of patients with pancreatic cancer compared to patients with other types of cancer is a result of late diagnosis or early dissemination of disease to distant organs is not known. Here we rely on data generated by sequencing the genomes of seven pancreatic cancer metastases to evaluate the clonal relationships among primary and metastatic cancers. We find that clonal populations that give rise to distant metastases are represented within the primary carcinoma, but these clones are genetically evolved from the original parental, non-metastatic clone. Thus, genetic heterogeneity of metastases reflects that within the primary carcinoma. A quantitative analysis of the timing of the genetic evolution of pancreatic cancer was performed, indicating at least a decade between the occurrence of the initiating mutation and the birth of the parental, non-metastatic founder cell. At least five more years are required for the acquisition of metastatic ability and patients die an average of two years thereafter. These data provide novel insights into the genetic features underlying pancreatic cancer progression and define a broad time window of opportunity for early detection to prevent deaths from metastatic disease

(15) CAMPBELL PJ, YACHIDA S, MUDIE LJ, STEPHENS PJ, *et al.* **The patterns and dynamics of genomic instability in metastatic pancreatic cancer**. Nature. 2010 Oct. 28, vol. 467, n° 7319, pp.1109-1113
http://dx.doi.org/10.1038/nature09460 (**accès payant**)

Pancreatic cancer is an aggressive malignancy with a five-year mortality of 97-98%, usually due to widespread metastatic disease. Previous studies indicate that this disease has a complex genomic landscape, with frequent copy number changes and point mutations, but genomic rearrangements have not been characterized in detail. Despite the clinical importance of metastasis, there remain fundamental questions about the clonal structures of metastatic tumours, including phylogenetic relationships among metastases, the scale of ongoing parallel evolution in metastatic and primary sites, and how the tumour disseminates. Here we harness advances in DNA sequencing to annotate genomic rearrangements in 13 patients with pancreatic cancer and explore clonal relationships among metastases. We find that pancreatic cancer acquires rearrangements indicative of telomere dysfunction and abnormal cell-cycle control, namely dysregulated G1-to-S-phase transition with intact G2-M checkpoint. These initiate amplification of cancer genes and occur predominantly in early cancer development rather than the later stages of the disease. Genomic instability frequently persists after cancer dissemination, resulting in ongoing, parallel and even convergent evolution among different metastases. We find evidence that there is genetic heterogeneity among metastasis-initiating cells, that seeding metastasis may require driver mutations beyond those required for primary tumours, and that phylogenetic trees across metastases show organ-specific branches. These data attest to the richness of genetic variation in cancer, brought about by the tandem forces of genomic instability and evolutionary selection

(16) MOOLGAVKAR SH, TURIM J, ALEXANDER DD, LAU EC, *et al.* **Potency factors for risk assessment at Libby, Montana**. Risk Anal. 2010 Aug., vol. 30, n° 8, pp.1240-1248
http://dx.doi.org/R10.1111/j.1539-6924.2010.01411.x (**accès payant**)

We reanalyzed the Libby vermiculite miners' cohort assembled by Sullivan to estimate potency factors for lung cancer, mesothelioma, nonmalignant respiratory disease (NMRD), and all-cause mortality associated with exposure to Libby fibers. Our principal statistical tool for analyses of lung cancer, NMRD, and total mortality in the cohort was the time-dependent proportional hazards model. For mesothelioma, we used an extension of the Peto formula. For a cumulative exposure to Libby fiber of 100 f/mL-yr, our estimates of relative risk (RR) are as follows: lung cancer, RR = 1.12, 95% confidence interval (CI) =[1.06, 1.17]; NMRD, RR = 1.14, 95% CI =[1.09, 1.18]; total

mortality, RR = 1.06, 95% CI =[1.04, 1.08]. These estimates were virtually identical when analyses were restricted to the subcohort of workers who were employed for at least one year. For mesothelioma, our estimate of potency is K(M) = 0.5 x 10(-8), 95% CI =[0.3 x 10(-8), 0.8 x 10(-8)]. Finally, we estimated the mortality ratios standardized against the U.S. population for lung cancer, NMRD, and total mortality and obtained estimates that were in good agreement with those reported by Sullivan. The estimated potency factors form the basis for a quantitative risk assessment at Libby

(17) KREUZER M, SCHNELZER M, TSCHENSE A, WALSH L, *et al.* **Cohort profile: the German uranium miners cohort study (WISMUT cohort), 1946-2003**. Int J Epidemiol. 2010 Aug., vol. 39, n° 4, pp.980-987
http://dx.doi.org/10.1093/ije/dyp216

Dengue

sommaire

(1) ENSERINK M. **Infectious diseases. Australia to test 'mosquito vaccine' against human disease**. Science. 2010 Dec. 10, vol. 330, n° 6010, pp.1460-1461
http://dx.doi.org/330/6010.1126/science.330.6010.1460 (**accès réservé EHESP**)

(2) ENSERINK M. **Science and society. GM mosquito trial alarms opponents, strains ties in Gates-funded project**. Science. 2010 Nov. 19, vol. 330, n° 6007, pp.1030-1031
http://dx.doi.org/330/6010.1126/science.330.6007.1030 (**accès réservé EHESP**)

(3) WILBAR CL, JR. **Control of dengue in Hawaii**. Am J Public Health. 1947 June, vol. 37, n° 6, pp.663-674
http://www.ncbi.nlm.nih.gov/pubmed/20242031 (**accès réservé EHESP**)

(4) KARAMCHANDANI PV. **Dengue group of fevers in India**. Lancet. 1946 Jan. 19, vol. 1, p.92
http://www.ncbi.nlm.nih.gov/pubmed/21011278 (**accès réservé EHESP**)

Diabète

sommaire

(1) LONNROTH K, RAVIGLIONE MC. **Here is diabetes in The Lancet's tuberculosis series!** Lancet. 2010 Dec. 11, vol. 376, n° 9757, pp.1987-1988
http://dx.doi.org/10.1016/S0140-6736(10)62262-3 (**accès réservé EHESP**)

(2) GIULIARI G. **Images in clinical medicine. Intravitreal triamcinolone for diabetic macular edema**. N Engl J Med. 2010 Dec. 9, vol. 363, n° 24, p.2351
http://dx.doi.org/10.1056/NEJMicm1003140 (**collection papier de la bibliothèque**)

(3) MCCARTHY MI. **Genomics, type 2 diabetes, and obesity**. N Engl J Med. 2010 Dec. 9, vol. 363, n° 24, pp.2339-2350
http://dx.doi.org/10.1056/NEJMra0906948 (**collection papier de la bibliothèque**)

(4) BENKIMOUN P. **French doctors demand to know why drug stayed on the market for so long**. BMJ. 2010, vol. 341, p.c6882
http://www.ncbi.nlm.nih.gov/pubmed/21131340 (**accès réservé EHESP**)

(5) BASS J, TAKAHASHI JS. **Circadian integration of metabolism and energetics**. Science. 2010 Dec. 3, vol. 330, n° 6009, pp.1349-1354
http://dx.doi.org/330/6010.1126/science.1195027 (**accès réservé EHESP**)

Circadian clocks align behavioral and biochemical processes with the day/night cycle. Nearly all vertebrate cells possess self-sustained clocks that couple endogenous rhythms with changes in cellular environment. Genetic disruption of clock genes in mice perturbs metabolic functions of specific tissues at distinct phases of the sleep/wake cycle. Circadian desynchrony, a characteristic of shift work and sleep disruption in humans, also leads to metabolic pathologies. Here, we review advances in understanding the interrelationship among circadian disruption, sleep deprivation, obesity, and diabetes and implications for rational therapeutics for these conditions

(6) BITTON S, ROTH J. **Addressing food insecurity: freedom from want, freedom from fear**. JAMA. 2010 Dec. 1, vol. 304, n° 21, pp.2405-2406
http://dx.doi.org/10.1001/jama.2010.1747 (**accès réservé EHESP**)

(7) MORITA H, NAGAI R. **Retinopathy progression in type 2 diabetes**. N Engl J Med. 2010 Nov. 25, vol. 363, n° 22, pp.2171-2174
http://dx.doi.org/10.1056/NEJMc1009236#SA1 (**collection papier de la bibliothèque**)

(8) LIEW G, WANG JJ, MITCHELL P. **Retinopathy progression in type 2 diabetes**. N Engl J Med. 2010 Nov. 25, vol. 363, n° 22, pp.2171-2172
http://dx.doi.org/10.1056/NEJMc1009236#SA2 (**collection papier de la bibliothèque**)

(9) BAUM SJ. **Retinopathy progression in type 2 diabetes**. N Engl J Med. 2010 Nov. 25, vol. 363, n° 22, pp.2172-2174
http://dx.doi.org/10.1056/NEJMc1009236#SA3 (**collection papier de la bibliothèque**)

(10) GIRAL P, ROSENBAUM D. **Retinopathy progression in type 2 diabetes**. N Engl J Med. 2010 Nov. 25, vol. 363, n° 22, pp.2172-2174
http://dx.doi.org/10.1056/NEJMc1009236#SA4 (**collection papier de la bibliothèque**)

(11) RIND DM. **Retinopathy progression in type 2 diabetes**. N Engl J Med. 2010 Nov. 25, vol. 363, n° 22, pp.2172-2173
http://dx.doi.org/10.1056/NEJMc1009236#SA5 (**collection papier de la bibliothèque**)

(12) SIGAL RJ, KENNY GP. **Combined aerobic and resistance exercise for patients with type 2 diabetes**. JAMA. 2010 Nov. 24, vol. 304, n° 20, pp.2298-2299
http://dx.doi.org/10.1001/jama.2010.1719 (**accès réservé EHESP**)

(13) CHURCH TS, BLAIR SN, COCREHAM S, JOHANNSEN N, *et al.* **Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: a randomized controlled trial**. JAMA. 2010 Nov. 24, vol. 304, n° 20, pp.2253-2262
http://dx.doi.org/10.1001/jama.2010.1710 (**accès réservé EHESP**)

CONTEXT: Exercise guidelines for individuals with diabetes include both aerobic and resistance training although few studies have directly examined this exercise combination. OBJECTIVE: To examine the benefits of aerobic training alone, resistance training alone, and a combination of both on hemoglobin A(1c) (HbA(1c)) in individuals with type 2 diabetes. DESIGN, SETTING, AND PARTICIPANTS: A randomized controlled trial in which 262 sedentary men and women in Louisiana with type 2 diabetes and HbA(1c) levels of 6.5% or higher were enrolled in the 9-month

exercise program between April 2007 and August 2009. INTERVENTION: Forty-one participants were assigned to the nonexercise control group, 73 to resistance training 3 days a week, 72 to aerobic exercise in which they expended 12 kcal/kg per week; and 76 to combined aerobic and resistance training in which they expended 10 kcal/kg per week and engaged in resistance training twice a week. Main Outcome Change in HbA(1c) level. Secondary outcomes included measures of anthropometry and fitness. RESULTS: The study included 63.0% women and 47.3% nonwhite participants who were a mean (SD) age of 55.8 years (8.7 years) with a baseline HbA(1c) level of 7.7% (1.0%). Compared with the control group, the absolute mean change in HbA(1c) in the combination training exercise group was -0.34% (95% confidence interval [CI], -0.64% to -0.03%; P = .03). The mean changes in HbA(1c) were not statistically significant in either the resistance training (-0.16%; 95% CI, -0.46% to 0.15%; P = .32) or the aerobic (-0.24%; 95% CI, -0.55% to 0.07%; P = .14) groups compared with the control group. Only the combination exercise group improved maximum oxygen consumption (mean, 1.0 mL/kg per min; 95% CI, 0.5-1.5, P < .05) compared with the control group. All exercise groups reduced waist circumference from -1.9 to -2.8 cm compared with the control group. The resistance training group lost a mean of -1.4 kg fat mass (95% CI, -2.0 to -0.7 kg; P < .05) and combination training group lost a mean of -1.7 (-2.3 to -1.1 kg; P < .05) compared with the control group. CONCLUSIONS: Among patients with type 2 diabetes mellitus, a combination of aerobic and resistance training compared with the nonexercise control group improved HbA(1c) levels. This was not achieved by aerobic or resistance training alone. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00458133

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http://dx.doi.org/10.1056/NEJMoa1004809 (**collection papier de la bibliothèque**)

BACKGROUND: Early exposure to complex dietary proteins may increase the risk of beta-cell autoimmunity and type 1 diabetes in children with genetic susceptibility. We tested the hypothesis

that supplementing breast milk with highly hydrolyzed milk formula would decrease the cumulative incidence of diabetes-associated autoantibodies in such children. METHODS: In this double-blind, randomized trial, we assigned 230 infants with HLA-conferred susceptibility to type 1 diabetes and at least one family member with type 1 diabetes to receive either a casein hydrolysate formula or a conventional, cow's-milk-based formula (control) whenever breast milk was not available during the first 6 to 8 months of life. Autoantibodies to insulin, glutamic acid decarboxylase (GAD), the insulinoma-associated 2 molecule (IA-2), and zinc transporter 8 were analyzed with the use of radiobinding assays, and islet-cell antibodies were analyzed with the use of immunofluorescence, during a median observation period of 10 years (mean, 7.5). The children were monitored for incident type 1 diabetes until they were 10 years of age. RESULTS: The unadjusted hazard ratio for positivity for one or more autoantibodies in the casein hydrolysate group, as compared with the control group, was 0.54 (95% confidence interval [CI], 0.29 to 0.95), and the hazard ratio adjusted for an observed difference in the duration of exposure to the study formula was 0.51 (95% CI, 0.28 to 0.91). The unadjusted hazard ratio for positivity for two or more autoantibodies was 0.52 (95% CI, 0.21 to 1.17), and the adjusted hazard ratio was 0.47 (95% CI, 0.19 to 1.07). The rate of reported adverse events was similar in the two groups. CONCLUSIONS: Dietary intervention during infancy appears to have a long-lasting effect on markers of beta-cell autoimmunity--markers that may reflect an autoimmune process leading to type 1 diabetes. (ClinicalTrials.gov number, NCT00570102.)

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http://dx.doi.org/10.1016/S0140-6736(10)61304-9 (**accès réservé EHESP**)

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http://dx.doi.org/10.1016/S0140-6736(10)61032-X (**accès réservé EHESP**)

BACKGROUND: Despite treatment with renin-angiotensin-aldosterone system (RAAS) inhibitors, patients with diabetes have increased risk of progressive renal failure that correlates with albuminuria. We aimed to assess whether paricalcitol could be used to reduce albuminuria in patients with diabetic nephropathy. METHODS: In this multinational, placebo-controlled, double-blind trial, we enrolled patients with type 2 diabetes and albuminuria who were receiving angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. Patients were assigned (1:1:1) by computer-generated randomisation sequence to receive 24 weeks' treatment with placebo,1 mug/day paricalcitol, or 2 mug/day paricalcitol. The primary endpoint was the percentage change in geometric mean urinary albumin-to-creatinine ratio (UACR) from baseline to last measurement during treatment for the combined paricalcitol groups versus the placebo group. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00421733. FINDINGS: Between February, 2007, and October, 2008, 281 patients were enrolled and assigned to receive placebo(n=93), 1 mug paricalcitol (n=93), or 2 mug paricalcitol (n=95); 88 patients on placebo, 92 on 1 mug paricalcitol, and 92 on2 mug paricalcitol received at least one dose of study drug, and had UACR data at baseline and at least one timepoint during treatment, and so were included in the primary analysis. Change in UACR was: -3% (from 61 to 60 mg/mmol;95% CI -16 to 13) in the placebo group; -16% (from 62 to 51 mg/mmol; -24 to -9) in the combined paricalcitol groups, with a between-group difference versus placebo of -15% (95% CI -28 to 1; p=0.071); -14% (from 63 to 54 mg/mmol; -24 to -1) in the 1 mug paricalcitol group, with a between-group difference versus placebo of -11%(95% CI -27 to 8; p=0.23); and -20% (from 61 to 49 mg/mmol; -30 to -8) in the 2 mug paricalcitol group, with a between-group difference versus placebo of -18% (95% CI -32 to 0; p=0.053). Patients on 2 mug paricalcitol showed a nearly, sustained reduction in UACR, ranging from -18% to -28% (p=0.014 vs placebo).

Incidence of hypercalcaemia,adverse events, and serious adverse events was similar between groups receiving paricalcitol versus placebo. INTERPRETATION: Addition of 2 mug/day paricalcitol to RAAS inhibition safely lowers residual albuminuria in patients with diabetic nephropathy, and could be a novel approach to lower residual renal risk in diabetes. FUNDING: Abbott

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http://dx.doi.org/10.1038/nature09491 (**accès payant**)

The global prevalence of obesity is increasing across most ages in both sexes. This is contributing to the early emergence of type 2 diabetes and its related epidemic. Having either parent obese is an independent risk factor for childhood obesity. Although the detrimental impacts of diet-induced maternal obesity on adiposity and metabolism in offspring are well established, the extent of any contribution of obese fathers is unclear, particularly the role of non-genetic factors in the causal pathway. Here we show that paternal high-fat-diet (HFD) exposure programs beta-cell 'dysfunction' in rat F(1) female offspring. Chronic HFD consumption in Sprague-Dawley fathers induced increased body weight, adiposity, impaired glucose tolerance and insulin sensitivity. Relative to controls, their female offspring had an early onset of impaired insulin secretion and glucose tolerance that worsened with time, and normal adiposity. Paternal HFD altered the expression of 642 pancreatic islet genes in adult female offspring ($P < 0.01$); genes belonged to 13 functional clusters, including cation and ATP binding, cytoskeleton and intracellular transport. Broader pathway analysis of 2,492 genes differentially expressed ($P < 0.05$) demonstrated involvement of calcium-,

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(30) LEVIN G, KESTENBAUM B, IDA CHEN YD, JACOBS DR, JR., *et al.* **Glucose, insulin, and incident hypertension in the multi-ethnic study of atherosclerosis**. Am J Epidemiol. 2010 Nov. 15, vol. 172, n° 10, pp.1144-1154
http://dx.doi.org/10.1093/aje/kwq266 (**accès réservé EHESP**)

Diabetes mellitus and hypertension commonly coexist, but the nature of this link is not well understood. The authors tested whether diabetes and higher concentrations of fasting serum

glucose and insulin are associated with increased risk of developing incident hypertension in the community-based Multi-Ethnic Study of Atherosclerosis. At baseline, 3,513 participants were free of hypertension, defined as systolic blood pressure >/=140 mm Hg, diastolic blood pressure >/=90 mm Hg, or use of antihypertensive medications to treat high blood pressure. Of these, 965 participants (27%) developed incident hypertension over 4.7 years' median follow-up between 2002 and 2007. Compared with participants with normal baseline fasting glucose, those with impaired fasting glucose and diabetes had adjusted relative risks of hypertension of 1.16 (95% confidence interval (CI): 0.96, 1.40) and 1.41 (95% CI: 1.17, 1.71), respectively (P = 0.0015). The adjusted relative risk of incident hypertension was 1.08 (95% CI: 1.04, 1.13) for each mmol/L higher glucose (P < 0.0001) and 1.15 (95% CI: 1.05, 1.25) for each doubling of insulin (P = 0.0016). Further adjustment for serum cystatin C, urinary albumin/creatinine ratio, and arterial elasticity measured by tonometry substantially reduced the magnitudes of these associations. In conclusion, diabetes and higher concentrations of glucose and insulin may contribute to the development of hypertension, in part through kidney disease and arterial stiffness

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http://dx.doi.org/10.1016/j.socscimed.2010.08.008 (**accès réservé EHESP**)

As health care systems seek to provide patient-centered care as a cornerstone of quality, the link between patient-centeredness and patient outcomes is a concern. Past research reveals inconsistent findings regarding the impact of patient-centeredness on patient outcomes, and few studies have investigated the factors that moderate this relationship. Most studies have used self-rated outcomes on a cross-sectional basis, even though most patient care is inherently longitudinal. The current study extends past research by examining the theoretical and empirical relationships between patients' perceptions of autonomy support and autonomy preferences with regard to their health outcomes. We hypothesized that autonomy preferences moderate the positive relationships between perceived autonomy support and patient-physician relationships, and on self-rated and objective health outcomes such that the relationships are more positive when patient autonomy preferences are high. Data were collected 3 times over a one-year period from a sample of 614 patients with type 2 diabetes in Taiwan. The results revealed strong support for the hypothesized relationships between perceived autonomy support and patient trust, satisfaction, and mental health-related quality of life (HRQoL) after adjusting for baseline scores; however, the direct link between autonomy support and patients' glycemic control was not significant. Specifically, patients with high decisional preference experienced a greater increase in subsequent trust and satisfaction than patients with low decisional preference. Further, patients with high information preference had a higher level of satisfaction over time than patients with low information preference. In addition, it was found that perceived autonomy support improved both physical and mental HRQoL but only if combined with high levels of information preference. This study provides evidence of a contingency perspective of the relationship between patient autonomy support and outcomes. By recognizing the uniqueness of each patient's autonomy preferences, healthcare practitioners can increase the efficiency of patient-centered care and improve patient outcomes

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http://dx.doi.org/10.1093/aje/kwq267 (**accès réservé EHESP**)

This study examined prepregnancy cardiometabolic risk factors and gestational diabetes mellitus (GDM) in subsequent pregnancies. The authors selected 1,164 women without diabetes before pregnancy who delivered 1,809 livebirths between 5 consecutive examinations from 1985 to 2006 in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. The authors measured prepregnancy cardiometabolic risk factors and performed multivariate repeated-measures logistic regression to compute the odds of GDM adjusted for race, age, parity, birth order, and other covariates. Impaired fasting glucose (100-125 vs. <90 mg/dL), elevated fasting

insulin (>15-20 and >20 vs. <10 muU/mL), and low levels of high-density lipoprotein cholesterol (<40 vs. >50 mg/dL) before pregnancy were directly associated with GDM: The odds ratios = 4.74 (95% confidence interval (CI): 2.14, 10.51) for fasting glucose, 2.19 (95% CI: 1.15, 4.17) for middle insulin levels and 2.36 (95% CI: 1.20, 4.63) for highest insulin levels, and 3.07 (95% CI: 1.62, 5.84) for low levels of high-density lipoprotein cholesterol among women with a negative family history of diabetes; all P < 0.01. Among overweight women, 26.7% with 1 or more cardiometabolic risk factors developed GDM versus 7.4% with none. Metabolic impairment exists before GDM pregnancy in nondiabetic women. Interconceptual metabolic screening could be included in routine health assessments to identify high-risk women for GDM in a subsequent pregnancy and to potentially minimize fetal exposure to metabolic abnormalities that program future disease

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http://dx.doi.org/10.1016/j.socscimed.2010.08.022 (**accès réservé EHESP**)

The attempts of social network members to regulate individuals' health behaviors, or health-related social control, is one mechanism by which social relationships influence health. Little is known, however, about whether this process varies in married versus unmarried individuals managing a chronic illness in which health behaviors are a key component. Researchers have proposed that social control attempts may have dual effects on recipients' well-being, such that improved health behaviors may occur at the cost of increased emotional distress. The current study accordingly sought to examine marital status differences in the sources, frequency, and responses to health-related social control in an ethnically diverse sample of 1477 patients with type 2 diabetes from southern California, USA. Results from two-way ANCOVAs revealed that married individuals reported their spouses most frequently as sources of social control, with unmarried women naming children and unmarried men naming friends/neighbors most frequently as sources of social control. Married men reported receiving social control most often, whereas unmarried men reported receiving social control least often. Regression analyses that examined behavioral and emotional responses to social control revealed that social control using persuasion was associated with better dietary behavior among married patients. Results also revealed a complex pattern of emotional responses, such that social control was associated with both appreciation and hostility, with the effect for appreciation most pronounced among women. Findings from this study highlight the importance of marital status and gender differences in social network members' involvement in the management of a chronic illness

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Dépression

sommaire

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http://dx.doi.org/10.1016/S0140-6736(10)61886-7 (**accès réservé EHESP**)

(2) PATEL V, WEISS HA, CHOWDHARY N, NAIK S, *et al.* **Effectiveness of an intervention led by lay health counsellors for depressive and anxiety disorders in primary care in Goa, India (MANAS): a cluster randomised controlled trial**. Lancet. 2010 Dec. 18, vol. 376, n° 9758, pp.2086-2095
http://dx.doi.org/10.1016/S0140-6736(10)61508-5 (**accès réservé EHESP**)

BACKGROUND: Depression and anxiety disorders are common mental disorders worldwide. The MANAS trial aimed to test the effectiveness of an intervention led by lay health counsellors in primary care settings to improve outcomes of people with these disorders. METHODS: In this cluster randomised trial, primary care facilities in Goa, India, were assigned (1:1) by computer-generated randomised sequence to intervention or control (enhanced usual care) groups. All adults who screened positive for common mental disorders were eligible. The collaborative stepped-care intervention offered case management and psychosocial interventions, provided by a trained lay health counsellor, supplemented by antidepressant drugs by the primary care physician and supervision by a mental health specialist. The research assessor was masked. The primary outcome was recovery from common mental disorders as defined by the International Statistical Classification of Diseases and Related Health Problems-10th revision (ICD-10) at 6 months. This study is registered with ClinicalTrials.gov, number NCT00446407. FINDINGS: 24 study clusters, with an equal proportion of public and private facilities, were randomised equally between groups. 1160 of 1360 (85%) patients in the intervention group and 1269 of 1436 (88%) in the control group completed the outcome assessment. Patients with ICD-10-confirmed common mental disorders in the intervention group were more likely to have recovered at 6 months than were those in the control group (n=620 [65.0%] vs 553 [52.9%]; risk ratio 1.22, 95% CI 1.00-1.47; risk difference=12.1%, 95% CI 1.6%-22.5%). The intervention had strong evidence of an effect in public facility attenders (369 [65.9%] vs 267 [42.5%], risk ratio 1.55, 95% CI 1.02-2.35) but no evidence for an effect in private facility attenders (251 [64.1%] vs 286 [65.9%], risk ratio 0.95, 0.74-1.22). There were three deaths and four suicide attempts in the collaborative stepped-care group and six deaths and six suicide attempts in the enhanced usual care group. None of the deaths were from suicide. INTERPRETATION: A trained lay counsellor-led collaborative care intervention can lead to an improvement in recovery from CMD among patients attending public primary care facilities. FUNDING: The Wellcome Trust

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http://dx.doi.org/10.1001/jama.2010.1769 (**accès réservé EHESP**)

CONTEXT: Most smokers with mental illness do not receive tobacco cessation treatment. OBJECTIVE: To determine whether integrating smoking cessation treatment into mental health care for veterans with posttraumatic stress disorder (PTSD) improves long-term smoking abstinence rates. DESIGN, SETTING, AND PATIENTS: A randomized controlled trial of 943 smokers with military-related PTSD who were recruited from outpatient PTSD clinics at 10 Veterans Affairs medical centers and followed up for 18 to 48 months between November 2004 and July 2009. INTERVENTION: Smoking cessation treatment integrated within mental health care for PTSD delivered by mental health clinicians (integrated care [IC]) vs referral to Veterans Affairs smoking cessation clinics (SCC). Patients received smoking cessation treatment within 3 months of study enrollment. MAIN OUTCOME MEASURES: Smoking outcomes included 12-month bioverified prolonged abstinence (primary outcome) and 7- and 30-day point prevalence abstinence assessed at 3-month intervals. Amount of smoking cessation medications and counseling sessions delivered were tested as mediators of outcome. Posttraumatic stress disorder and depression were repeatedly assessed using the PTSD Checklist and Patient Health Questionnaire 9, respectively, to determine if IC participation or quitting smoking worsened psychiatric status. RESULTS: Integrated care was better than SCC on prolonged abstinence (8.9% vs 4.5%; adjusted odds ratio, 2.26; 95% confidence interval [CI], 1.30-3.91; P = .004). Differences between IC vs SCC were largest at 6 months for 7-day point prevalence abstinence (78/472 [16.5%] vs 34/471 [7.2%], P < .001) and remained significant at 18 months (86/472 [18.2%] vs 51/471 [10.8%], P < .001). Number of counseling sessions received and days of cessation medication used explained 39.1% of the treatment effect. Between baseline and 18 months, psychiatric status did not differ between treatment conditions. Posttraumatic stress disorder symptoms for quitters and nonquitters improved. Nonquitters worsened slightly on the Patient Health Questionnaire 9 relative to quitters (differences ranged between 0.4 and 2.1, P = .03), whose scores did not change over time. CONCLUSION: Among smokers with military-related PTSD, integrating smoking cessation treatment into mental health care compared with referral to specialized cessation treatment resulted in greater prolonged abstinence. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00118534

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http://www.ncbi.nlm.nih.gov/pubmed/21098617 (**accès réservé EHESP**)

OBJECTIVES: To determine, using longitudinal analyses, if retirement is followed by a change in the risk of incident chronic diseases, depressive symptoms, and fatigue. Design Prospective study with repeat measures from 7 years before to 7 years after retirement. SETTING: Large French occupational cohort (the GAZEL study), 1989-2007. Participants 11 246 men and 2858 women. MAIN OUTCOME MEASURES: Respiratory disease, diabetes, coronary heart disease and stroke, mental fatigue, and physical fatigue, measured annually by self report over the 15 year observation period; depressive symptoms measured at four time points. RESULTS: The average number of repeat measurements per participant was 12.1. Repeated measures logistic regression

with generalised estimating equations showed that the cumulative prevalence of self reported respiratory disease, diabetes, and coronary heart disease and stroke increased with age, with no break in the trend around retirement. In contrast, retirement was associated with a substantial decrease in the prevalence of both mental fatigue (odds ratio for fatigue one year after versus one year before retirement 0.19, 95% confidence interval 0.18 to 0.21) and physical fatigue (0.27, 0.26 to 0.30). A major decrease was also observed in depressive symptoms (0.60, 0.53 to 0.67). The decrease in fatigue around retirement was more pronounced among people with a chronic disease before retirement. CONCLUSIONS: Longitudinal modelling of repeat data showed that retirement did not change the risk of major chronic diseases but was associated with a substantial reduction in mental and physical fatigue and depressive symptoms, particularly among people with chronic diseases

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(10) CHERTOW GM, LEVIN NW, BECK GJ, DEPNER TA, *et al.* **In-center hemodialysis six times per week versus three times per week**. N Engl J Med. 2010 Dec. 9, vol. 363, n° 24, pp.2287-2300
http://dx.doi.org/10.1056/NEJMoa1001593 (**collection papier de la bibliothèque**)

BACKGROUND: In this randomized clinical trial, we aimed to determine whether increasing the frequency of in-center hemodialysis would result in beneficial changes in left ventricular mass, self-reported physical health, and other intermediate outcomes among patients undergoing maintenance hemodialysis. METHODS: Patients were randomly assigned to undergo hemodialysis six times per week (frequent hemodialysis, 125 patients) or three times per week (conventional hemodialysis, 120 patients) for 12 months. The two coprimary composite outcomes were death or change (from baseline to 12 months) in left ventricular mass, as assessed by cardiac magnetic resonance imaging, and death or change in the physical-health composite score of the RAND 36-item health survey. Secondary outcomes included cognitive performance; self-reported depression; laboratory markers of nutrition, mineral metabolism, and anemia; blood pressure; and rates of hospitalization and of interventions related to vascular access. RESULTS: Patients in the frequent-hemodialysis group averaged 5.2 sessions per week; the weekly standard Kt/V(urea) (the product of the urea clearance and the duration of the dialysis session normalized to the volume of distribution of urea) was significantly higher in the frequent-hemodialysis group than in the conventional-hemodialysis group (3.54+/-0.56 vs. 2.49+/-0.27). Frequent hemodialysis was associated with significant benefits with respect to both coprimary composite outcomes (hazard ratio for death or increase in left ventricular mass, 0.61; 95% confidence interval [CI], 0.46 to 0.82; hazard ratio for death or a decrease in the physical-health composite score, 0.70; 95% CI, 0.53 to 0.92). Patients randomly assigned to frequent hemodialysis were more likely to undergo interventions related to vascular access than were patients assigned to conventional hemodialysis (hazard ratio, 1.71; 95% CI, 1.08 to 2.73). Frequent hemodialysis was associated with improved control of hypertension and hyperphosphatemia. There were no significant effects of frequent hemodialysis on cognitive performance, self-reported depression, serum albumin concentration, or use of erythropoiesis-stimulating agents. CONCLUSIONS: Frequent hemodialysis, as compared with conventional hemodialysis, was associated with favorable results with respect to the composite outcomes of death or change in left ventricular mass and death or change in a physical-health composite score but prompted more frequent interventions related to vascular access. (Funded by the National Institute of Diabetes and Digestive and Kidney Diseases and others; ClinicalTrials.gov number, NCT00264758.)

(11) TURNER EH. **Reboxetine in depression. All the relevant data?** BMJ. 2010, vol. 341, p.c6487
http://www.ncbi.nlm.nih.gov/pubmed/21081614 (**accès réservé EHESP**)

(12) KRISHNADAS R. **Reboxetine in depression. NICE guidance differs, so where next?** BMJ. 2010, vol. 341, p.c6484
http://www.ncbi.nlm.nih.gov/pubmed/21081613 (**accès réservé EHESP**)

(13) BOLTON JM, ROBINSON J. **Population-attributable fractions of Axis I and Axis II mental disorders for suicide attempts: findings from a representative sample of the adult, noninstitutionalized US population**. Am J Public Health. 2010 Dec., vol. 100, n° 12, pp.2473-2480
http://dx.doi.org/10.2105/AJPH.2010.192252 (**accès réservé EHESP**)

OBJECTIVES: We aimed to determine the percentage of suicide attempts attributable to individual Axis I and Axis II mental disorders by studying population-attributable fractions (PAFs) in a nationally representative sample. METHODS: Data were from the National Epidemiologic Survey on Alcohol and Related Conditions Wave 2 (NESARC; 2004-2005), a large (N = 34 653) survey of mental illness in the United States. We used multivariate logistic regression to compare individuals with and without a history of suicide attempt across Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Axis I disorders (anxiety, mood, psychotic, alcohol, and drug disorders) and all 10 Axis II personality disorders. PAFs were calculated for each disorder. RESULTS: Of the 25 disorders we examined in the model, 4 disorders had notably high PAF values: major depressive disorder (PAF = 26.6%; 95% confidence interval [CI] = 20.1, 33.2), borderline personality disorder (PAF = 18.1%; 95% CI = 13.4, 23.5), nicotine dependence (PAF = 8.4%; 95% CI = 3.4, 13.7), and posttraumatic stress disorder (PAF = 6.3%; 95% CI = 3.2, 10.0). CONCLUSIONS: Our results provide new insight into the relationships between mental disorders and suicide attempts in the general population. Although many mental illnesses were associated with an increased likelihood of suicide attempt, elevated rates of suicide attempts were mostly attributed to the presence of 4 disorders

(14) MAGUEN S, REN L, BOSCH JO, MARMAR CR, *et al.* **Gender differences in mental health diagnoses among Iraq and Afghanistan veterans enrolled in veterans affairs health care**. Am J Public Health. 2010 Dec., vol. 100, n° 12, pp.2450-2456
http://dx.doi.org/10.2105/AJPH.2009.166165 (**accès réservé EHESP**)

OBJECTIVES: We examined gender differences in sociodemographic, military service, and mental health characteristics among Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) veterans. We evaluated associations between these sociodemographic and service characteristics and depression and posttraumatic stress disorder (PTSD) diagnoses. METHODS: In a retrospective, cross-sectional study, we used univariate descriptive statistics and log binominal regression analyses of Department of Veterans Affairs (VA) administrative data on 329 049 OEF and OIF veterans seeking VA health care from April 1, 2002, through March 31, 2008. RESULTS: Female veterans were younger and more likely to be Black and to receive depression diagnoses than were male veterans, who were more frequently diagnosed with PTSD and alcohol use disorders. Older age was associated with a higher prevalence of PTSD and depression diagnoses among women but not among men. CONCLUSIONS: Consideration of gender differences among OEF and OIF veterans seeking health care at the VA will facilitate more targeted prevention and treatment services for these newly returning veterans

(15) HOSSAIN M, ZIMMERMAN C, ABAS M, LIGHT M, *et al.* **The relationship of trauma to mental disorders among trafficked and sexually exploited girls and women**. Am J Public Health. 2010 Dec., vol. 100, n° 12, pp.2442-2449
http://dx.doi.org/10.2105/AJPH.2009.173229 (**accès réservé EHESP**)

OBJECTIVES: We explored the association between traumatic events and mental health among girls and women trafficked for sexual exploitation. METHODS: We used subscales of the Brief

Symptom Inventory and Harvard Trauma Questionnaire to interview 204 trafficked girls and women in 7 posttrafficking service settings. Multivariate logistic regression models based on interview data were fitted for depression, anxiety, and posttraumatic stress disorder (PTSD) separately and adjusted for pretrafficking abuse to determine impact of trafficking-related trauma exposures. RESULTS: Injuries and sexual violence during trafficking were associated with higher levels of PTSD, depression, and anxiety. Sexual violence was associated with higher levels of PTSD (adjusted odds ratio [AOR] = 5.6; 95% confidence interval [CI] = 1.3, 25.4). More time in trafficking was associated with higher levels of depression and anxiety (AOR = 2.2; 95% CI = 1.1, 4.5). More time since trafficking was associated with lower levels of depression and anxiety but not of PTSD. CONCLUSIONS: Our findings inform the emerging field of mental health care for trafficked persons by highlighting the importance of assessing severity and duration of trafficking-related abuses and need for adequate recovery time. Therapies for anxiety, PTSD, and mood disorders in low-resource settings should be evaluated

(16) YEUNG A, SHYU I, FISHER L, WU S, *et al.* **Culturally sensitive collaborative treatment for depressed chinese americans in primary care**. Am J Public Health. 2010 Dec., vol. 100, n° 12, pp.2397-2402
http://dx.doi.org/10.2105/AJPH.2009.184911 (**accès réservé EHESP**)

OBJECTIVES: We examined the feasibility and effectiveness of using culturally sensitive collaborative treatment (CSCT) to improve recognition, engagement, and treatment of depressed Chinese Americans in primary care. METHODS: Chinese American patients in a primary care setting (n = 4228) were screened for depression. The primary study outcome was treatment engagement rate, and the secondary outcome was treatment response. RESULTS: Of the study participants, 296 (7%) screened positive for depression, 122 (41%) of whom presented for a psychiatric assessment; 104 (85%) were confirmed with major depressive disorder, and 100 (96%) of these patients were randomized into treatment involving either care management or usual care. Patients in the care management and usual care groups did not differ in terms of their outcomes. CSCT resulted in a nearly 7-fold increase in treatment rate among depressed patients in primary care. CONCLUSIONS: CSCT is both feasible and effective in improving recognition and treatment engagement of depressed Chinese Americans. Care management may have limited effects on depressed patients treated by psychiatrists, given that these patients tend to have favorable responses in general

(17) KEYES CL, DHINGRA SS, SIMOES EJ. **Change in level of positive mental health as a predictor of future risk of mental illness**. Am J Public Health. 2010 Dec., vol. 100, n° 12, pp.2366-2371
http://dx.doi.org/10.2105/AJPH.2010.192245 (**accès réservé EHESP**)

OBJECTIVES: We sought to describe the prevalence of mental health and illness, the stability of both diagnoses over time, and whether changes in mental health level predicted mental illness in a cohort group. METHODS: In 2009, we analyzed data from the 1995 and 2005 Midlife in the United States cross-sectional surveys (n = 1723), which measured positive mental health and 12-month mental disorders of major depressive episode, panic, and generalized anxiety disorders. RESULTS: Population prevalence of any of 3 mental disorders and levels of mental health appeared stable but were dynamic at the individual level. Fifty-two percent of the 17.5% of respondents with any mental illness in 2005 were new cases; one half of those languishing in 1995 improved in 2005, and one half of those flourishing in 1995 declined in 2005. Change in mental health was strongly predictive of prevalence and incidence (operationalized as a new, not necessarily a first, episode) of mental illness in 2005. CONCLUSIONS: Gains in mental health predicted declines in mental illness, supporting the call for public mental health promotion; losses of mental health predicted increases in mental illness, supporting the call for public mental health protection

(18) MEZUK B, RAFFERTY JA, KERSHAW KN, HUDSON D, *et al.* **Reconsidering the role of social disadvantage in physical and mental health: stressful life events, health behaviors, race, and depression**. Am J Epidemiol. 2010 Dec. 1, vol. 172, n° 11, pp.1238-1249
http://dx.doi.org/10.1093/aje/kwq283 (**accès réservé EHESP**)

Prevalence of depression is associated inversely with some indicators of socioeconomic position, and the stress of social disadvantage is hypothesized to mediate this relation. Relative to whites, blacks have a higher burden of most physical health conditions but, unexpectedly, a lower burden of depression. This study evaluated an etiologic model that integrates mental and physical health to account for this counterintuitive patterning. The Baltimore Epidemiologic Catchment Area Study (Maryland, 1993-2004) was used to evaluate the interaction between stress and poor health behaviors (smoking, alcohol use, poor diet, and obesity) and risk of depression 12 years later for 341 blacks and 601 whites. At baseline, blacks engaged in more poor health behaviors and had a lower prevalence of depression compared with whites (5.9% vs. 9.2%). The interaction between health behaviors and stress was nonsignificant for whites (odds ratio (OR = 1.04, 95% confidence interval: 0.98, 1.11); for blacks, the interaction term was significant and negative (beta: -0.18, P < 0.014). For blacks, the association between median stress and depression was stronger for those who engaged in zero (OR = 1.34) relative to 1 (OR = 1.12) and >/=2 (OR = 0.94) poor health behaviors. Findings are consistent with the proposed model of mental and physical health disparities

(19) MACLEOD J. **Commentary: broken hearts and minds--depression and incident heart disease and stroke**. Int J Epidemiol. 2010 Aug., vol. 39, n° 4, pp.1025-1026
http://dx.doi.org10.1093/ije/dyq099 (**accès réservé EHESP**)

(20) NABI H, KIVIMAKI M, SUOMINEN S, KOSKENVUO M, *et al.* **Does depression predict coronary heart disease and cerebrovascular disease equally well? The Health and Social Support Prospective Cohort Study**. Int J Epidemiol. 2010 Aug., vol. 39, n° 4, pp.1016-1024
http://dx.doi.org10.1093/ije/dyq050 (**accès réservé EHESP**)

BACKGROUND: The relationship between depression and cerebrovascular disease (CBVD) continues to be debated although little research has compared the predictive power of depression for coronary heart disease (CHD) with that for CBVD within the same population. This study aimed to compare the importance of depression for CHD and CBVD within the same population of adults free of apparent cardiovascular disease. METHODS: A random sample of 23,282 adults (9507 men, 13,775 women) aged 20-54 years were followed up for 7 years. Fatal and first non-fatal CHD and CBVD events were documented by linkage to the National-hospital-discharge and mortality registers. RESULTS: Sex-age-education-adjusted hazard ratio (HR) for CHD was 1.66 [95% confidence interval (CI) 1.24-2.24] for participants with mild to severe depressive symptoms, i.e. those scoring > or =10 on the 21-item Beck Depression Inventory, and 2.04 (1.27-3.27) for those who filled antidepressant prescriptions compared with those without depression markers in 1998, i.e. at study baseline. For CBVD, the corresponding HRs were 1.01 (0.67-1.53) and 1.77 (0.95-3.29). After adjustment for behavioural and biological risk factors these associations were reduced but remained evident for CHD, the adjusted HRs being 1.47 (1.08-1.99) and 1.72 (1.06-2.77). For CBVD, the corresponding multivariable adjusted HRs were 0.87 (0.57-1.32) and 1.52 (0.81-2.84). CONCLUSIONS: Self-reported depression using a standardized questionnaire and clinical markers of mild to severe depression were associated with an increased risk for CHD. There was no clear evidence that depression is a risk factor for CBVD, but this needs further confirmation

Grippe A

sommaire

(1) MYERS LB, GOODWIN R. **Determinants of adults' intention to vaccinate against pandemic swine flu**. BMC Public Health. 2011 Jan. 6, vol. 11, n° 1, p.15
http://dx.doi.org/10.1186/1471-2458-11-15 (**accès libre**)

ABSTRACT: BACKGROUND: Vaccination is one of the cornerstones of controlling an influenza pandemic. To optimise vaccination rates in the general population, ways of identifying determinants that influence decisions to have or not to have a vaccination need to be understood. Therefore, this study aimed to predict intention to have a swine influenza vaccination in an adult population in the UK. An extension of the Theory of Planned Behaviour provided the theoretical

framework for the study. METHODS: Three hundred and sixty two adults from the UK, who were not in vaccination priority groups, completed either an online (n =306) or pen and paper (n = 56) questionnaire. Data were collected from 30th October 2009, just after swine flu vaccination became available in the UK, and concluded on 31st December 2009. The main outcome of interest was future swine flu vaccination intentions. RESULTS: The extended Theory of Planned Behaviour predicted 60% of adults' intention to have a swine flu vaccination with attitude, subjective norm, perceived control, anticipating feelings of regret (the impact of missing a vaccination opportunity), intention to have a seasonal vaccine this year, one perceived barrier: "I cannot be bothered to get a swine flu vaccination" and two perceived benefits: "vaccination decreases my chance of getting swine flu or its complications" and "if I get vaccinated for swine flu, I will decrease the frequency of having to consult my doctor," being significant predictors of intention. Black British were less likely to intend to have a vaccination compared to Asian or White respondents. CONCLUSIONS: Theoretical frameworks which identify determinants that influence decisions to have a pandemic influenza vaccination are useful. The implications of this research are discussed with a view to maximising any future pandemic influenza vaccination uptake using theoretically-driven applications

(2) ADALJA AA. **Comparing severity and outcomes for seasonal and 2009 H1N1 infections**. JAMA. 2011 Jan. 5, vol. 305, n° 1, pp.39-40
http://dx.doi.org/30510.1001/jama.2010.1888 (**accès réservé EHESP**)

(3) BULTS M, BEAUJEAN DJ, ZWART OD, KOK G, *et al.* **Perceived risk, anxiety, and behavioural responses of the general public during the early phase of the Influenza A (H1N1) pandemic in the Netherlands: results of three consecutive online surveys**. BMC Public Health. 2011 Jan. 3, vol. 11, n° 1, p.2
http://dx.doi.org/1471-2410.1186/1471-2458-11-2 (**accès libre**)

ABSTRACT: BACKGROUND: Research into risk perception and behavioural responses in case of emerging infectious diseases is still relatively new. The aim of this study was to examine perceptions and behaviours of the general public during the early phase of the Influenza A (H1N1) pandemic in the Netherlands. METHODS: Two cross-sectional and one follow-up online survey (survey 1, 30 April-4 May; survey 2, 15-19 June; survey 3, 11-20 August 2009). Adults aged 18 years and above participating in a representative Internet panel were invited (survey 1, n=456; survey 2, n=478; follow-up survey 3, n=934). Main outcome measures were 1) time trends in risk perception, feelings of anxiety, and behavioural responses (survey 1-3) and 2) factors associated with taking preventive measures and strong intention to comply with government-advised preventive measures in the future (survey 3). RESULTS: Between May and August 2009, the level of knowledge regarding Influenza A (H1N1) increased, while perceived severity of the new flu, perceived self-efficacy, and intention to comply with preventive measures decreased. The perceived reliability of information from the government decreased from May to August (62% versus 45%). Feelings of anxiety decreased from May to June, and remained stable afterwards. From June to August 2009, perceived vulnerability increased and more respondents took preventive measures (14% versus 38%). Taking preventive measures was associated with no children in the household, high anxiety, high self-efficacy, more agreement with statements on avoidance, and paying much attention to media information regarding Influenza A (H1N1). Having a strong intention to comply with government-advised preventive measures in the future was associated with higher age, high perceived severity, high anxiety, high perceived efficacy of measures, high self-efficacy, and finding governmental information to be reliable. CONCLUSIONS: Decreasing trends over time in perceived severity and anxiety are consistent with the reality: the clinical picture of influenza turned out to be mild in course of time. Although (inter)national health authorities initially overestimated the case fatality rate, the public stayed calm and remained to have a relatively high intention to comply with preventive measures

(4) SHI P, KESKINOCAK P, SWANN JL, LEE BY. **The impact of mass gatherings and holiday traveling on the course of an influenza pandemic: a computational model**. BMC Public Health. 2010 Dec. 21, vol. 10, n° 1, p.778
http://dx.doi.org/10.1186/1471-2458-10-778 (**accès libre**)

ABSTRACT: BACKGROUND: During the 2009 H1N1 influenza pandemic, concerns arose about the potential negative effects of mass public gatherings and travel on the course of the pandemic. Better understanding the potential effects of temporal changes in social mixing patterns could help public officials determine if and when to cancel large public gatherings or enforce regional travel restrictions, advisories, or surveillance during an epidemic. METHODS: We develop a computer simulation model using detailed data from the state of Georgia to explore how various changes in social mixing and contact patterns, representing mass gatherings and holiday traveling, may affect the course of an influenza pandemic.Various scenarios with different combinations of the length of the mass gatherings or traveling period (range: 0.5 to 5 days), the proportion of the population attending the mass gathering events or on travel (range: 1% to 50%), and the initial reproduction numbers R0 (1.3, 1.5, 1.8) are explored. RESULTS: Mass gatherings that occur within 10 days before the epidemic peak can result in as high as a 10% relative increase in the peak prevalence and the total attack rate, and may have even worse impacts on local communities and travelers' families. Holiday traveling can lead to a second epidemic peak under certain scenarios. Conversely, mass traveling or gatherings may have little effect when occurring much earlier or later than the epidemic peak, e.g., more than 40 days earlier or 20 days later than the peak when the initial R0 = 1.5. CONCLUSIONS: Our results suggest that monitoring, postponing, or cancelling large public gatherings may be warranted close to the epidemic peak but not earlier or later during the epidemic. Influenza activity should also be closely monitored for a potential second peak if holiday traveling occurs when prevalence is high

(5) ANDRUS JK, AGUILERA X, OLIVA O, ALDIGHIERI S. **Global health security and the International Health Regulations**. BMC Public Health. 2010, vol. 10 Suppl 1, p.S2 http://dx.doi.org/1471-2458-110.1186/1471-2458-10-S1-S2 (**accès libre**)

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

(6) KANT L, KRISHNAN SK. **Information and communication technology in disease surveillance, India: a case study**. BMC Public Health. 2010, vol. 10 Suppl 1, p.S11 http://dx.doi.org/1471-2458-1010.1186/1471-2458-10-S1-S11 (**accès libre**)

India has made appreciable progress and continues to demonstrate a strong commitment for establishing and operating a disease surveillance programme responsive to the requirements of the International Health Regulations (IHR[2005]). Within five years of its launch, India has effectively used modern information and communication technology for collection, storage, transmission and management of data related to disease surveillance and effective response. Terrestrial and/or satellite based linkages are being established within all states, districts, state-run medical colleges, infectious disease hospitals, and public health laboratories. This network enables speedy data transfer, video conferencing, training and e-learning for outbreaks and programme monitoring. A 24x7 call centre is in operation to receive disease alerts. To complement these efforts, a media scanning and verification cell functions to receive reports of early warning signals. During the 2009 H1N1 outbreak, the usefulness of the information and

communication technology (ICT) network was well appreciated. India is using ICT as part of its Integrated Disease Surveillance Project (IDSP) to help overcome the challenges in further expansion in hard-to-reach populations, to increase the involvement of the private sector, and to increase the use of other modes of communication like e-mail and voicemail

(7) SOBERS-GRANNUM N, SPRINGER K, FERDINAND E, ST JJ. **Response to the challenges of pandemic H1N1 in a small island state: the Barbadian experience**. BMC Public Health. 2010, vol. 10 Suppl 1, p.S10
http://dx.doi.org/1471-2458-1010.1186/1471-2458-10-S1-S10 (**accès libre**)

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

(8) HENTER JI, PALMKVIST-KAIJSER K, HOLZGRAEFE B, BRYCESON YT, *et al.* **Cytotoxic therapy for severe swine flu A/H1N1**. Lancet. 2010 Dec. 18, vol. 376, n° 9758, p.2116
http://dx.doi.org/10.1016/S0140-6736(10)61345-1 (**accès réservé EHESP**)

(9) QUINN SC, KUMAR S, FREIMUTH VS, MUSA D, *et al.* **Racial Disparities in Exposure, Susceptibility, and Access to Health Care in the US H1N1 Influenza Pandemic**. Am J Public Health. 2010 Dec. 16,
http://dx.doi.org/10.2105/AJPH.2009.188029 (**accès réservé EHESP**)

Objectives. We conducted the first empirical examination of disparities in H1N1 exposure, susceptibility to H1N1 complications, and access to health care during the H1N1 influenza pandemic. Methods. We conducted a nationally representative survey among a sample drawn from more than 60000 US households. We analyzed responses from 1479 adults, including significant numbers of Blacks and Hispanics. The survey asked respondents about their ability to impose social distance in response to public health recommendations, their chronic health conditions, and their access to health care. Results. Risk of exposure to H1N1 was significantly related to race and ethnicity. Spanish-speaking Hispanics were at greatest risk of exposure but were less susceptible to complications from H1N1. Disparities in access to health care remained significant for Spanish-speaking Hispanics after controlling for other demographic factors. We used measures based on prevalence of chronic conditions to determine that Blacks were the most susceptible to complications from H1N1. Conclusions. We found significant race/ethnicity-related

disparities in potential risk from H1N1 flu. Disparities in the risks of exposure, susceptibility (particularly to severe disease), and access to health care may interact to exacerbate existing health inequalities and contribute to increased morbidity and mortality in these populations. (Am J Public Health. Published online ahead of print December 16, 2010: e1-e9. doi:10.2105/AJPH.2009.188029)

(10) LIBSTER R, COVIELLO S, CAVALIERI ML, MOROSI A, *et al.* **Pediatric hospitalizations due to influenza in 2010 in Argentina**. N Engl J Med. 2010 Dec. 16, vol. 363, n° 25, pp.2472-2473
http://dx.doi.org/10.1056/NEJMc1008806 (**collection papier de la bibliothèque**)

(11) WU J, XU F, LU L, LU M, *et al.* **Safety and effectiveness of a 2009 H1N1 vaccine in Beijing** . N Engl J Med. 2010 Dec. 16, vol. 363, n° 25, pp.2416-2423
http://dx.doi.org/10.1056/NEJMoa1006736 (**collection papier de la bibliothèque**)

BACKGROUND: After the first monovalent 2009 pandemic influenza A (H1N1) vaccine became available in September 2009, Chinese officials conducted a mass vaccination program in Beijing. We evaluated the safety and effectiveness of the vaccine. METHODS: During a 5-day period in September 2009, a total of 95,244 children and adults received the PANFLU.1 vaccine (Sinovac Biotech), a monovalent split-virion vaccine of 15 mug of hemagglutinin antigen without adjuvant. We assessed adverse events after immunization through an enhanced passive-surveillance system and through active surveillance, using diary cards and telephone interviews. Active surveillance for neurologic diseases was implemented in hospitals citywide. To assess vaccine effectiveness, we compared the rates of reported laboratory-confirmed cases of 2009 H1N1 virus infection in students who received the vaccine with the rates in those who did not receive the vaccine, starting 2 weeks after the mass vaccination. RESULTS: As of December 31, 2009, adverse events were reported by 193 vaccine recipients. Through hospital-based active surveillance, 362 cases of incident neurologic diseases were identified within 10 weeks after the mass vaccination, including 27 cases of the Guillain-Barre syndrome. None of the neurologic conditions occurred among vaccine recipients. From 245 schools, 25,037 students participated in the mass vaccination and 244,091 did not. During the period from October 9 through November 15, 2009, the incidence of confirmed cases of 2009 H1N1 virus infection per 100,000 students was 35.9 (9 of 25,037) among vaccinated students and 281.4 (687 of 244,091) among unvaccinated students. Thus, the estimated vaccine effectiveness was 87.3% (95% confidence interval, 75.4 to 93.4). CONCLUSIONS: Among 95,244 children and adults in Beijing, the PANFLU.1 vaccine had a safety profile similar to those of seasonal influenza vaccines and appeared to be effective against confirmed H1N1 virus infection in school-age children. (Funded by the Beijing Municipal Health Bureau.)

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(14) ZUCCOTTI G, POGLIANI L, PARIANI E, AMENDOLA A, *et al.* **Transplacental antibody transfer following maternal immunization with a pandemic 2009 influenza A(H1N1) MF59-adjuvanted vaccine**. JAMA. 2010 Dec. 1, vol. 304, n° 21, pp.2360-2361
http://dx.doi.org/10.1001/jama.2010.1729 (**accès réservé EHESP**)

(15) HARRIS KM, MAURER J, KELLERMANN AL. **Influenza vaccine--safe, effective, and mistrusted**. N Engl J Med. 2010 Dec. 2, vol. 363, n° 23, pp.2183-2185
http://dx.doi.org/10.1056/NEJMp1012333 (**collection papier de la bibliothèque**)

Maladies d'Alzheimer

sommaire

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http://www.ncbi.nlm.nih.gov/pubmed/21081609

(3) KIM J, HOLTZMAN DM. **Medicine. Prion-like behavior of amyloid-beta**. Science. 2010 Nov. 12, vol. 330, n° 6006, pp.918-919
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(4) ATTWELL D, BUCHAN AM, CHARPAK S, LAURITZEN M, *et al.* **Glial and neuronal control of brain blood flow**. Nature. 2010 Nov. 11, vol. 468, n° 7321, pp.232-243
http://dx.doi.org/10.1038/nature09613 (**accès payant**)

Blood flow in the brain is regulated by neurons and astrocytes. Knowledge of how these cells control blood flow is crucial for understanding how neural computation is powered, for interpreting functional imaging scans of brains, and for developing treatments for neurological disorders. It is now recognized that neurotransmitter-mediated signalling has a key role in regulating cerebral blood flow, that much of this control is mediated by astrocytes, that oxygen modulates blood flow regulation, and that blood flow may be controlled by capillaries as well as by arterioles. These conceptual shifts in our understanding of cerebral blood flow control have important implications for the development of new therapeutic approaches

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http://dx.doi.org/10.1016/S0140-6736(10)61994-0 (**accès réservé EHESP**)

(7) EISELE YS, OBERMULLER U, HEILBRONNER G, BAUMANN F, *et al.* **Peripherally applied Abeta-containing inoculates induce cerebral beta-amyloidosis**. Science. 2010 Nov. 12, vol. 330, n° 6006, pp.980-982
http://dx.doi.org/science.10.1126/science.1194516 (**accès réservé EHESP**)

The intracerebral injection of beta-amyloid-containing brain extracts can induce cerebral beta-amyloidosis and associated pathologies in susceptible hosts. We found that intraperitoneal inoculation with beta-amyloid-rich extracts induced beta-amyloidosis in the brains of beta-amyloid precursor protein transgenic mice after prolonged incubation times

(8) WANG B, YANG W, WEN W, SUN J, *et al.* **Gamma-secretase gene mutations in familial acne inversa**. Science. 2010 Nov. 19, vol. 330, n° 6007, p.1065
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Acne inversa (AI), also known as hidradenitis suppurativa, is a chronic, recurrent, inflammatory disease of hair follicles that often runs in families. We studied six Chinese families with features of AI as well as additional skin lesions on back, face, nape, and waist and found independent loss-

of-function mutations in PSENEN, PSEN1, or NCSTN, the genes encoding essential components of the gamma-secretase multiprotein complex. Our results identify the gamma-secretase component genes as the culprits for a subset of familial AI, implicate the gamma-secretase-Notch pathway in the molecular pathogenesis of AI, and demonstrate that familial AI can be an allelic disorder of early-onset familial Alzheimer's disease

Maladies cardio-vasculaires

sommaire

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(7) GALAN P, KESSE-GUYOT E, CZERNICHOW S, BRIANCON S, *et al.* **Effects of B vitamins and omega 3 fatty acids on cardiovascular diseases: a randomised placebo controlled trial** . BMJ. 2010, vol. 341, p.c6273
http://www.ncbi.nlm.nih.gov/pubmed/21115589 (**accès réservé EHESP**)

OBJECTIVE: To investigate whether dietary supplementation with B vitamins or omega 3 fatty acids, or both, could prevent major cardiovascular events in patients with a history of ischaemic heart disease or stroke. DESIGN: Double blind, randomised, placebo controlled trial; factorial design. SETTING: Recruitment throughout France via a network of 417 cardiologists, neurologists, and other physicians. PARTICIPANTS: 2501 patients with a history of myocardial infarction, unstable angina, or ischaemic stroke. INTERVENTION: Daily dietary supplement containing 5-methyltetrahydrofolate (560 mug), vitamin B-6 (3 mg), and vitamin B-12 (20 mug) or placebo; and containing omega 3 fatty acids (600 mg of eicosapentanoic acid and docosahexaenoic acid at a ratio of 2:1) or placebo. Median duration of supplementation was 4.7 years. MAIN OUTCOME MEASURES: Major cardiovascular events, defined as a composite of non-fatal myocardial infarction, stroke, or death from cardiovascular disease. RESULTS: Allocation to B vitamins lowered plasma homocysteine concentrations by 19% compared with placebo, but had no significant effects on major vascular events (75 v 82 patients, hazard ratio, 0.90 (95% confidence interval 0.66 to 1.23, P=0.50)). Allocation to omega 3 fatty acids increased

plasma concentrations of omega 3 fatty acids by 37% compared with placebo, but also had no significant effect on major vascular events (81 v 76 patients, hazard ratio 1.08 (0.79 to 1.47, P=0.64)). CONCLUSION: This study does not support the routine use of dietary supplements containing B vitamins or omega 3 fatty acids for prevention of cardiovascular disease in people with a history of ischaemic heart disease or ischaemic stroke, at least when supplementation is introduced after the acute phase of the initial event. TRIAL REGISTRATION: Current Controlled Trials ISRCTN41926726

(8) ATHYROS VG, TZIOMALOS K, GOSSIOS TD, GRIVA T, *et al.* **Safety and efficacy of long-term statin treatment for cardiovascular events in patients with coronary heart disease and abnormal liver tests in the Greek Atorvastatin and Coronary Heart Disease Evaluation (GREACE) Study: a post-hoc analysis**. Lancet. 2010 Dec. 4, vol. 376, n° 9756, pp.1916-1922 http://dx.doi.org/10.1016/S0140-6736(10)61272-X (**accès réservé EHESP**)

BACKGROUND: Long-term statin treatment reduces the frequency of cardiovascular events, but safety and efficacy in patients with abnormal liver tests is unclear. We assessed whether statin therapy is safe and effective for these patients through post-hoc analysis of the Greek Atorvastatin and Coronary Heart Disease Evaluation (GREACE) study population. METHODS: GREACE was a prospective, intention-to-treat study that randomly assigned by a computer-generated randomisation list 1600 patients with coronary heart disease (aged <75 years, with serum concentrations of LDL cholesterol >2.6 mmol/L and triglycerides <4.5 mmol/L) at the Hippokration University Hospital, Thessaloniki, Greece to receive statin or usual care, which could include statins. The primary outcome of our post-hoc analysis was risk reduction for first recurrent cardiovascular event in patients treated with a statin who had moderately abnormal liver tests (defined as serum alanine aminotransferase or aspartate aminotransferase concentrations of less than three times the upper limit of normal) compared with patients with abnormal liver tests who did not receive a statin. This risk reduction was compared with that for patients treated (or not) with statin and normal liver tests. FINDINGS: Of 437 patients with moderately abnormal liver tests at baseline, which were possibly associated with non-alcoholic fatty liver disease, 227 who were treated with a statin (mainly atorvastatin 24 mg per day) had substantial improvement in liver tests (p<0.0001) whereas 210 not treated with a statin had further increases of liver enzyme concentrations. Cardiovascular events occurred in 22 (10%) of 227 patients with abnormal liver tests who received statin (3.2 events per 100 patient-years) and 63 (30%) of 210 patients with abnormal liver tests who did not receive statin (10.0 events per 100 patient-years; 68% relative risk reduction, p<0.0001). This cardiovascular disease benefit was greater (p=0.0074) than it was in patients with normal liver tests (90 [14%] events in 653 patients receiving a statin [4.6 per 100 patient-years] vs 117 [23%] in 510 patients not receiving a statin [7.6 per 100 patient-years]; 39% relative risk reduction, p<0.0001). Seven (<1%) of 880 participants who received a statin discontinued statin treatment because of liver-related adverse effects (transaminase concentrations more than three-times the upper limit of normal). INTERPRETATION: Statin treatment is safe and can improve liver tests and reduce cardiovascular morbidity in patients with mild-to-moderately abnormal liver tests that are potentially attributable to non-alcoholic fatty liver disease. FUNDING: None

(9) SZABO GT, RACZ I, KOSZEGI Z. **Elective intra-aortic balloon pump placement in high-risk percutaneous coronary intervention**. JAMA. 2010 Nov. 24, vol. 304, n° 20, pp.2241-2242 http://dx.doi.org/10.1001/jama.2010.1699 (**accès réservé EHESP**)

(10) LIN GM, CHU KM, HAN CL. **Elective intra-aortic balloon pump placement in high-risk percutaneous coronary intervention**. JAMA. 2010 Nov. 24, vol. 304, n° 20, pp.2240-2242 http://dx.doi.org/10.1001/jama.2010.1697 (**accès réservé EHESP**)

(11) ENGSTROM AE, SJAUW KD, HENRIQUES JP. **Elective intra-aortic balloon pump placement in high-risk percutaneous coronary intervention**. JAMA. 2010 Nov. 24, vol. 304, n° 20, pp.2240-2241 http://dx.doi.org/304/2010.1001/jama.2010.1698 (**accès réservé EHESP**)

(12) MISHRA NK, AHMED N, ANDERSEN G, EGIDO JA, *et al.* **Thrombolysis in very elderly people: controlled comparison of SITS International Stroke Thrombolysis Registry and Virtual International Stroke Trials Archive**. BMJ. 2010, vol. 341, p.c6046 http://www.ncbi.nlm.nih.gov/pubmed/21098614 (**accès réservé EHESP**)

OBJECTIVE: To assess effect of age on response to alteplase in acute ischaemic stroke. DESIGN: Adjusted controlled comparison of outcomes between non-randomised patients who did or did not undergo thrombolysis. Analysis used Cochran-Mantel-Haenszel test and proportional odds logistic regression analysis. SETTING: Collaboration between International Stroke Thrombolysis Registry (SITS-ISTR) and Virtual International Stroke Trials Archive (VISTA). PARTICIPANTS: 23 334 patients from SITS-ISTR (December 2002 to November 2009) who underwent thrombolysis and 6166 from VISTA neuroprotection trials (1998-2007) who did not undergo thrombolysis (as controls). Of the 29 500 patients (3472 aged >80 ("elderly," mean 84.6), data on 272 patients were missing for baseline National Institutes of Health stroke severity score, leaving 29 228 patients for analysis adjusted for age and baseline severity. MAIN OUTCOME MEASURES: Functional outcomes at 90 days measured by score on modified Rankin scale. RESULTS: Median severity at baseline was the same for patients who underwent thrombolysis and controls (median baseline stroke scale score: 12 for each group, P=0.14; n=29 228). The distribution of scores on the modified Rankin scale was better among all thrombolysis patients than controls (odds ratio 1.6, 95% confidence interval 1.5 to 1.7; Cochran-Mantel-Haenszel P<0.001). The association occurred independently among patients aged </=80 (1.6, 1.5 to 1.7; P<0.001; n=25 789) and in those aged >80 (1.4, 1.3 to 1.6; P<0.001; n=3439). Odds ratios were consistent across all 10 year age ranges above 30, and benefit was significant from age 41 to 90; dichotomised outcomes (score on modified Rankin scale 0-1 v 2-6; 0-2 v 3-6; and 6 (death) v rest) were consistent with the results of the ordinal analysis. CONCLUSIONS: Outcome in patients with acute ischaemic stroke is significantly better in those who undergo thrombolysis compared with those who do not. Increasing age is associated with poorer outcome but the association between thrombolysis treatment and improved outcome is maintained in very elderly people. Age alone should not be a barrier to treatment

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(14) SAELY CH, VONBANK A, DREXEL H. **HDL cholesterol and residual risk of first cardiovascular events**. Lancet. 2010 Nov. 20, vol. 376, n° 9754, pp.1738-1739 http://dx.doi.org/10.1016/S0140-6736(10)62131-9 (**accès réservé EHESP**)

(15) CANNON CP, SHAH S, DANSKY HM, DAVIDSON M, *et al.* **Safety of anacetrapib in patients with or at high risk for coronary heart disease**. N Engl J Med. 2010 Dec. 16, vol. 363, n° 25, pp.2406-2415 http://dx.doi.org/10.1056/NEJMoa1009744 (**collection papier de la bibliothèque**)

BACKGROUND: Anacetrapib is a cholesteryl ester transfer protein inhibitor that raises high-density lipoprotein (HDL) cholesterol and reduces low-density lipoprotein (LDL) cholesterol. METHODS: We conducted a randomized, double-blind, placebo-controlled trial to assess the efficacy and safety profile of anacetrapib in patients with coronary heart disease or at high risk for coronary heart disease. Eligible patients who were taking a statin and who had an LDL cholesterol level that was consistent with that recommended in guidelines were assigned to receive 100 mg of anacetrapib or placebo daily for 18 months. The primary end points were the percent change from baseline in LDL cholesterol at 24 weeks (HDL cholesterol level was a secondary end point) and the safety and side-effect profile of anacetrapib through 76 weeks. Cardiovascular events and deaths were prospectively adjudicated. RESULTS: A total of 1623 patients underwent randomization. By 24 weeks, the LDL cholesterol level had been reduced from 81 mg per deciliter (2.1 mmol per liter) to 45 mg per deciliter (1.2 mmol per liter) in the anacetrapib group, as compared with a reduction from 82 mg per deciliter (2.1 mmol per liter) to 77 mg per deciliter (2.0 mmol per liter) in the placebo group (P<0.001)--a 39.8% reduction with anacetrapib beyond that

seen with placebo. In addition, the HDL cholesterol level increased from 41 mg per deciliter (1.0 mmol per liter) to 101 mg per deciliter (2.6 mmol per liter) in the anacetrapib group, as compared with an increase from 40 mg per deciliter (1.0 mmol per liter) to 46 mg per deciliter (1.2 mmol per liter) in the placebo group (P<0.001)--a 138.1% increase with anacetrapib beyond that seen with placebo. Through 76 weeks, no changes were noted in blood pressure or electrolyte or aldosterone levels with anacetrapib as compared with placebo. Prespecified adjudicated cardiovascular events occurred in 16 patients treated with anacetrapib (2.0%) and 21 patients receiving placebo (2.6%) (P = 0.40). The prespecified Bayesian analysis indicated that this event distribution provided a predictive probability (confidence) of 94% that anacetrapib would not be associated with a 25% increase in cardiovascular events, as seen with torcetrapib. CONCLUSIONS: Treatment with anacetrapib had robust effects on LDL and HDL cholesterol, had an acceptable side-effect profile, and, within the limits of the power of this study, did not result in the adverse cardiovascular effects observed with torcetrapib. (Funded by Merck Research Laboratories; ClinicalTrials.gov number, NCT00685776.)

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(17) KAISER C, GALATIUS S, ERNE P, EBERLI F, *et al.* **Drug-eluting versus bare-metal stents in large coronary arteries**. N Engl J Med. 2010 Dec. 9, vol. 363, n° 24, pp.2310-2319
http://dx.doi.org/10.1056/NEJMoa1009406 (**collection papier de la bibliothèque**)

BACKGROUND: Recent data have suggested that patients with coronary disease in large arteries are at increased risk for late cardiac events after percutaneous intervention with first-generation drug-eluting stents, as compared with bare-metal stents. We sought to confirm this observation and to assess whether this increase in risk was also seen with second-generation drug-eluting stents. METHODS: We randomly assigned 2314 patients needing stents that were 3.0 mm or more in diameter to receive sirolimus-eluting, everolimus-eluting, or bare-metal stents. The primary end point was the composite of death from cardiac causes or nonfatal myocardial infarction at 2 years. Late events (occurring during months 7 to 24) and target-vessel revascularization were the main secondary end points. RESULTS: The rates of the primary end point were 2.6% among patients receiving sirolimus-eluting stents, 3.2% among those receiving everolimus-eluting stents, and 4.8% among those receiving bare-metal stents, with no significant differences between patients receiving either drug-eluting stent and those receiving bare-metal stents. There were also no significant between-group differences in the rate of late events or in the rate of death, myocardial infarction, or stent thrombosis. Rates of target-vessel revascularization for reasons unrelated to myocardial infarction were 3.7% among patients receiving sirolimus-eluting stents, 3.1% among those receiving everolimus-eluting stents, and 8.9% among those receiving bare-metal stents. The rate of target-vessel revascularization was significantly reduced among patients receiving either drug-eluting stent, as compared with a bare-metal stent, with no significant difference between the two types of drug-eluting stents. CONCLUSIONS: In patients requiring stenting of large coronary arteries, no significant differences were found among sirolimus-eluting, everolimus-eluting, and bare-metal stents with respect to the rate of death or myocardial infarction. With the two drug-eluting stents, similar reductions in rates of target-vessel revascularization were seen. (Funded by the Basel Cardiovascular Research Foundation and the Swiss National Foundation for Research; Current Controlled Trials number, ISRCTN72444640.)

(18) KIM J, HOLTZMAN DM. **Medicine. Prion-like behavior of amyloid-beta**. Science. 2010 Nov. 12, vol. 330, n° 6006, pp.918-919
http://dx.doi.org/10.1126/science.1198314 (**accès réservé EHESP**)

(19) ATTWELL D, BUCHAN AM, CHARPAK S, LAURITZEN M, *et al.* **Glial and neuronal control of brain blood flow**. Nature. 2010 Nov. 11, vol. 468, n° 7321, pp.232-243
http://dx.doi.org/10.1038/nature09613 (**accès payant**)

Blood flow in the brain is regulated by neurons and astrocytes. Knowledge of how these cells control blood flow is crucial for understanding how neural computation is powered, for interpreting functional imaging scans of brains, and for developing treatments for neurological disorders. It is now recognized that neurotransmitter-mediated signalling has a key role in regulating cerebral blood flow, that much of this control is mediated by astrocytes, that oxygen modulates blood flow regulation, and that blood flow may be controlled by capillaries as well as by arterioles. These conceptual shifts in our understanding of cerebral blood flow control have important implications for the development of new therapeutic approaches

(20) STALEY K. **Stroke: recovery inhibitors under attack**. Nature. 2010 Nov. 11, vol. 468, n° 7321, pp.176-177
http://dx.doi.org/10.1038/468176a (**accès payant**)

(21) BAIGENT C, BLACKWELL L, EMBERSON J, HOLLAND LE, *et al.* **Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials**. Lancet. 2010 Nov. 13, vol. 376, n° 9753, pp.1670-1681
http://dx.doi.org/10.1016/S0140-6736(10)61350-5 (**accès réservé EHESP**)

BACKGROUND: Lowering of LDL cholesterol with standard statin regimens reduces the risk of occlusive vascular events in a wide range of individuals. We aimed to assess the safety and efficacy of more intensive lowering of LDL cholesterol with statin therapy. METHODS: We undertook meta-analyses of individual participant data from randomised trials involving at least 1000 participants and at least 2 years' treatment duration of more versus less intensive statin regimens (five trials; 39 612 individuals; median follow-up 5.1 years) and of statin versus control (21 trials; 129 526 individuals; median follow-up 4.8 years). For each type of trial, we calculated not only the average risk reduction, but also the average risk reduction per 1.0 mmol/L LDL cholesterol reduction at 1 year after randomisation. FINDINGS: In the trials of more versus less intensive statin therapy, the weighted mean further reduction in LDL cholesterol at 1 year was 0.51 mmol/L. Compared with less intensive regimens, more intensive regimens produced a highly significant 15% (95% CI 11-18; p<0.0001) further reduction in major vascular events, consisting of separately significant reductions in coronary death or non-fatal myocardial infarction of 13% (95% CI 7-19; p<0.0001), in coronary revascularisation of 19% (95% CI 15-24; p<0.0001), and in ischaemic stroke of 16% (95% CI 5-26; p=0.005). Per 1.0 mmol/L reduction in LDL cholesterol, these further reductions in risk were similar to the proportional reductions in the trials of statin versus control. When both types of trial were combined, similar proportional reductions in major vascular events per 1.0 mmol/L LDL cholesterol reduction were found in all types of patient studied (rate ratio [RR] 0.78, 95% CI 0.76-0.80; p<0.0001), including those with LDL cholesterol lower than 2 mmol/L on the less intensive or control regimen. Across all 26 trials, all-cause mortality was reduced by 10% per 1.0 mmol/L LDL reduction (RR 0.90, 95% CI 0.87-0.93; p<0.0001), largely reflecting significant reductions in deaths due to coronary heart disease (RR 0.80, 99% CI 0.74-0.87; p<0.0001) and other cardiac causes (RR 0.89, 99% CI 0.81-0.98; p=0.002), with no significant effect on deaths due to stroke (RR 0.96, 95% CI 0.84-1.09; p=0.5) or other vascular causes (RR 0.98, 99% CI 0.81-1.18; p=0.8). No significant effects were observed on deaths due to cancer or other non-vascular causes (RR 0.97, 95% CI 0.92-1.03; p=0.3) or on cancer incidence (RR 1.00, 95% CI 0.96-1.04; p=0.9), even at low LDL cholesterol concentrations. INTERPRETATION: Further reductions in LDL cholesterol safely produce definite further reductions in the incidence of heart attack, of revascularisation, and of ischaemic stroke, with each 1.0 mmol/L reduction reducing the annual rate of these major vascular events by just over a fifth. There was no evidence of any threshold within the cholesterol range studied, suggesting that reduction of LDL cholesterol by 2-3 mmol/L would reduce risk by about 40-50%. FUNDING: UK Medical Research Council, British Heart Foundation, European Community Biomed Programme, Australian National Health and Medical Research Council, and National Heart Foundation

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http://dx.doi.org/10.1056/NEJMc1012022 (**collection papier de la bibliothèque**)

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http://dx.doi.org/10.1001/jama.2010.1624 (**accès réservé EHESP**)

(24) NALLAMOTHU BK, KRUMHOLZ HM. **Putting ad hoc PCI on pause**. JAMA. 2010 Nov. 10, vol. 304, n° 18, pp.2059-2060
http://dx.doi.org/10.1001/jama.2010.1509 (**accès réservé EHESP**)

(25) LEVENE LS, BAKER R, BANKART MJ, KHUNTI K. **Association of features of primary health care with coronary heart disease mortality**. JAMA. 2010 Nov. 10, vol. 304, n° 18, pp.2028-2034
http://dx.doi.org/10.1001/jama.2010.1636 (**accès réservé EHESP**)

CONTEXT: The goal of US health care reform is to extend access. In England, with a universal access health system, coronary heart disease (CHD) mortality rates have decreased by more than two-fifths in the last decade, but variations in rates between local populations persist. OBJECTIVE: To identify which features of populations and primary health care explain variations in CHD mortality rates between the 152 primary care trust populations in England. DESIGN, SETTING, AND PARTICIPANTS: A cross-sectional study in England of all 152 primary care trusts (total registered population, 54.3 million in 2008) using a hierarchical regression model with age-standardized CHD mortality rate as the dependent variable, and population characteristics (index of multiple deprivation, smoking, ethnicity, and registers of individuals with diabetes) and service characteristics (level of provision of primary care services, levels of detected hypertension, pay for performance data) as candidate explanatory variables. MAIN OUTCOME MEASURES: Age-standardized CHD mortality rates in 2006, 2007, and 2008. RESULTS: The mean age-standardized CHD mortality rates per 100,000 European Standard Population were 97.9 (95% confidence interval [CI], 94.9-100.9) in 2006, 93.5 (95% CI, 90.4-96.5) in 2007, and 88.4 (95% CI, 85.7-91.1) in 2008. In all 3 years, 4 population characteristics were significantly positively associated with CHD mortality (index of multiple deprivation, smoking, white ethnicity, and registers of individuals with diabetes), and 1 service characteristic (levels of detected hypertension) was significantly negatively associated with CHD mortality (adjusted r(2) = 0.66 in 2006, adjusted r(2) = 0.68 in 2007, and adjusted r(2) = 0.67 in 2008). Other service characteristics did not contribute significantly to the model. CONCLUSION: In England, variations in CHD mortality are predominantly explained by population characteristics; however, greater detection of hypertension is associated with lower CHD mortality

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http://dx.doi.org/10.1001/jama.2010.1604 (**accès réservé EHESP**)

(27) THRIFT AG, SRIKANTH V, EVANS RG. **How generalisable is INTERSTROKE?** Lancet. 2010 Nov. 6, vol. 376, n° 9752, pp.1538-1539
http://dx.doi.org/10.1016/S0140-6736(10)62025-9 (**accès réservé EHESP**)

(28) CLARKSON AN, HUANG BS, MACISAAC SE, MODY I, *et al.* **Reducing excessive GABA-mediated tonic inhibition promotes functional recovery after stroke**. Nature. 2010 Nov. 11, vol. 468, n° 7321, pp.305-309
http://dx.doi.org/10.1038/nature09511 (**accès payant**)

Stroke is a leading cause of disability, but no pharmacological therapy is currently available for promoting recovery. The brain region adjacent to stroke damage-the peri-infarct zone-is critical for rehabilitation, as it shows heightened neuroplasticity, allowing sensorimotor functions to re-map from damaged areas. Thus, understanding the neuronal properties constraining this plasticity is important for the development of new treatments. Here we show that after a stroke in mice, tonic neuronal inhibition is increased in the peri-infarct zone. This increased tonic inhibition is mediated

by extrasynaptic GABA(A) receptors and is caused by an impairment in GABA (gamma-aminobutyric acid) transporter (GAT-3/GAT-4) function. To counteract the heightened inhibition, we administered in vivo a benzodiazepine inverse agonist specific for alpha5-subunit-containing extrasynaptic GABA(A) receptors at a delay after stroke. This treatment produced an early and sustained recovery of motor function. Genetically lowering the number of alpha5- or delta-subunit-containing GABA(A) receptors responsible for tonic inhibition also proved beneficial for recovery after stroke, consistent with the therapeutic potential of diminishing extrasynaptic GABA(A) receptor function. Together, our results identify new pharmacological targets and provide the rationale for a novel strategy to promote recovery after stroke and possibly other brain injuries

(29) EISELE YS, OBERMULLER U, HEILBRONNER G, BAUMANN F, *et al.* **Peripherally applied Abeta-containing inoculates induce cerebral beta-amyloidosis**. Science. 2010 Nov. 12, vol. 330, n° 6006, pp.980-982
http://dx.doi.org/science.1194516 (**accès réservé EHESP**)

The intracerebral injection of beta-amyloid-containing brain extracts can induce cerebral beta-amyloidosis and associated pathologies in susceptible hosts. We found that intraperitoneal inoculation with beta-amyloid-rich extracts induced beta-amyloidosis in the brains of beta-amyloid precursor protein transgenic mice after prolonged incubation times

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http://dx.doi.org/10.1056/NEJMoa1007964 (**collection papier de la bibliothèque**)

BACKGROUND: Gastrointestinal complications are an important problem of antithrombotic therapy. Proton-pump inhibitors (PPIs) are believed to decrease the risk of such complications, though no randomized trial has proved this in patients receiving dual antiplatelet therapy. Recently, concerns have been raised about the potential for PPIs to blunt the efficacy of clopidogrel. METHODS: We randomly assigned patients with an indication for dual antiplatelet therapy to receive clopidogrel in combination with either omeprazole or placebo, in addition to aspirin. The primary gastrointestinal end point was a composite of overt or occult bleeding, symptomatic gastroduodenal ulcers or erosions, obstruction, or perforation. The primary cardiovascular end point was a composite of death from cardiovascular causes, nonfatal myocardial infarction, revascularization, or stroke. The trial was terminated prematurely when the sponsor lost financing. RESULTS: We planned to enroll about 5000 patients; a total of 3873 were randomly assigned and 3761 were included in analyses. In all, 51 patients had a gastrointestinal event; the event rate was 1.1% with omeprazole and 2.9% with placebo at 180 days (hazard ratio with omeprazole, 0.34, 95% confidence interval [CI], 0.18 to 0.63; P<0.001). The rate of overt upper gastrointestinal bleeding was also reduced with omeprazole as compared with placebo (hazard ratio, 0.13; 95% CI, 0.03 to 0.56; P = 0.001). A total of 109 patients had a cardiovascular event, with event rates of 4.9% with omeprazole and 5.7% with placebo (hazard ratio with omeprazole, 0.99; 95% CI, 0.68 to 1.44; P = 0.96); high-risk subgroups did not show significant heterogeneity. The two groups did not differ significantly in the rate of serious adverse events, though the risk of diarrhea was increased with omeprazole. CONCLUSIONS: Among patients receiving aspirin and clopidogrel, prophylactic use of a PPI reduced the rate of upper gastrointestinal bleeding. There was no apparent cardiovascular interaction between clopidogrel and omeprazole, but our results do not rule out a clinically meaningful difference in cardiovascular events due to use of a PPI. (Funded by Cogentus Pharmaceuticals; ClinicalTrials.gov number, NCT00557921.)

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http://dx.doi.org/10.1016/j.socscimed.2010.08.018 (**accès réservé EHESP**)

Stroke in low and middle income countries is an increasing cause of death and disability, with rates and the estimated burden considerably higher than that of high income countries. Lay explanatory models are believed to be one of the major influences on health seeking behaviour

and essential to understand for appropriate education strategies. Despite stroke being a considerable health concern in Indonesia and particularly in Aceh, no studies to date have explored lay stroke models in that context. This paper presents the findings of a qualitative study informed by both hermeneutic phenomenology and ethnography. Based in rural communities in Bener Meriah and Aceh Tengah in Central Aceh, Indonesia, data were gathered through interviews, photographs and observations with 11 persons with stroke (aged 32-69 years) and 18 of their carers. Fieldwork was conducted over nine months between 2007 and 2008. The study examined lay concepts of stroke, described as a condition resulting from a local blockage in blood from multiple causes, many of which are not recognised within the biomedical frame. The blockage is understood to be reversible and therefore the condition curable. This understanding is embedded and sustained in the specific political, cultural, religious and social context. The results illustrate similarities and differences with other cross-cultural studies and suggest areas of future research and points of consideration for stroke education strategies

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http://dx.doi.org10.1093/ije/dyq061 (**accès réservé EHESP**)

BACKGROUND: Little is known about the relationship between physical functional health and long-term risk of coronary heart disease (CHD) independently of known risk factors in a general population. METHODS: Men and women aged 40-79 years at baseline who completed a health and lifestyle questionnaire and attended a health examination during 1993-97 participating in the European Prospective Investigation into Cancer-Norfolk who were free of myocardial infarction (MI), stroke and cancer were included. Eighteen months later, physical functional health was assessed using physical component summary (PCS) scores of Short-Form 36-item questionnaire (SF-36). The incidence of CHD was ascertained by death certification and hospital record linkage up to March 2008. RESULTS: A total of 14,222 men and women were included in the study. There were 389 incident CHD (total person-years = 126,896 years). People who reported better physical functional health had significantly lower risk of CHD. Using Cox proportional hazard models adjusting for age, sex, body mass index, cholesterol, systolic blood pressure, smoking, alcohol consumption, physical activity, diabetes, family history of MI, social class and aspirin usage, it was found that men and women who were in the top quartile of SF-36 PCS had half the risk of CHD [relative risk (RR) = 0.46; 95% confidence interval (CI) = 0.32-0.65] compared with the people in the bottom quartile. The relationships remained essentially unchanged after excluding incident CHD within the first 2 years of follow-up (RR = 0.48; 95% CI = 0.33-0.70). CONCLUSIONS: Physical functional health predicts subsequent CHD risk independently of known risk factors in a general population. People with poor physical functional health may benefit from targeted preventive interventions

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http://dx.doi.org10.1093/ije/dyq050 (**accès réservé EHESP**)

BACKGROUND: The relationship between depression and cerebrovascular disease (CBVD)

continues to be debated although little research has compared the predictive power of depression for coronary heart disease (CHD) with that for CBVD within the same population. This study aimed to compare the importance of depression for CHD and CBVD within the same population of adults free of apparent cardiovascular disease. METHODS: A random sample of 23,282 adults (9507 men, 13,775 women) aged 20-54 years were followed up for 7 years. Fatal and first non-fatal CHD and CBVD events were documented by linkage to the National-hospital-discharge and mortality registers. RESULTS: Sex-age-education-adjusted hazard ratio (HR) for CHD was 1.66 [95% confidence interval (CI) 1.24-2.24] for participants with mild to severe depressive symptoms, i.e. those scoring > or =10 on the 21-item Beck Depression Inventory, and 2.04 (1.27-3.27) for those who filled antidepressant prescriptions compared with those without depression markers in 1998, i.e. at study baseline. For CBVD, the corresponding HRs were 1.01 (0.67-1.53) and 1.77 (0.95-3.29). After adjustment for behavioural and biological risk factors these associations were reduced but remained evident for CHD, the adjusted HRs being 1.47 (1.08-1.99) and 1.72 (1.06-2.77). For CBVD, the corresponding multivariable adjusted HRs were 0.87 (0.57-1.32) and 1.52 (0.81-2.84). CONCLUSIONS: Self-reported depression using a standardized questionnaire and clinical markers of mild to severe depression were associated with an increased risk for CHD. There was no clear evidence that depression is a risk factor for CBVD, but this needs further confirmation

Maladies liées à l'alcool

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http://dx.doi.org/10.1093/aje/kwq290 (**accès réservé EHESP**)

Significant controversy exists as to whether soldiers are at increased risk for suicide and suicidal behaviors compared with civilians. Furthermore, little is known about whether risk factors for suicidal behaviors in civilian populations are generalizable to soldiers. The aim of the current study is to determine whether the prevalence and correlates of past-year suicidal ideation and suicide attempts differ in Canadian soldiers when compared with Canadian civilians. The current study utilized data from the Canadian Community Health Survey Cycle 1.2-Canadian Forces Supplement in conjunction with the 2001-2002 Canadian Community Health Survey Cycle 1.2. Logistic regression interaction models were used to explore differences between correlates of suicidal ideation and suicide attempts comparing Canadian soldiers with civilians. Although there was no significant difference between the 2 samples on prevalence of past-year suicidal ideation, the prevalence of past-year suicide attempts was significantly lower in the Canadian forces sample compared with the civilian population (odds ratio = 0.41, 95% confidence interval: 0.25, 0.67). Findings suggest that suicide attempts are less common in Canadian active military personnel than in the civilian population. Possible mechanisms for these differences are discussed

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http://dx.doi.org10.1093/ije/dyq056 (**accès réservé EHESP**)

BACKGROUND: To examine whether maternal alcohol intake, including binge drinking (intake > or =5 drinks, equivalent to 60 g pure ethanol on a single occasion), is associated with autistic spectrum disorders (ASD) and infantile autism. METHODS: Participants were 80,552 children and their mothers enrolled in the Danish National Birth Cohort from 1996 to 2002. Alcohol consumption was obtained by self-report during pregnancy. Information on ASD was obtained from the Danish Central Psychiatry Register. Follow-up ended on February 2008. Data were analysed by means of Cox regression. RESULTS: In total, 401 children were diagnosed with ASD and 157 with infantile autism. No association was found between average alcohol consumption and ASD or infantile autism, respectively. For binge drinking, the adjusted hazard ratio (HR) for ASD was 0.72 [95% confidence interval (CI): 0.53-0.97] among women who binge drank once during pregnancy compared with women who did not binge drink. The corresponding HR for infantile autism was 0.61 (95% CI: 0.36-1.02). However, the HR for ASD was 0.84 (95% CI: 0.51-1.36) when restricting the analysis to first-time pregnancies conceived within 6 months of trying. No estimate was made for infantile autism due to low number of cases. No association was seen for more than one binge episode and for the timing of binge drinking. CONCLUSION: Our findings do not support that a low prenatal alcohol exposure increases the risk of ASD or infantile autism. The lower risk for women who binge drank once during pregnancy is most likely non-causal

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Paludisme

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(3) TOZAN Y, KLEIN EY, DARLEY S, PANICKER R, *et al.* **Prereferral rectal artesunate for treatment of severe childhood malaria: a cost-effectiveness analysis**. Lancet. 2010 Dec. 4, vol. 376, n° 9756, pp.1910-1915
http://dx.doi.org/10.1016/S0140-6736(10)61460-2 (**accès réservé EHESP**)

BACKGROUND: Severely ill patients with malaria with vomiting, prostration, and altered consciousness cannot be treated orally and need injections. In rural areas, access to health facilities that provide parenteral antimalarial treatment is poor. Safe and effective treatment of most severe malaria cases is delayed or not achieved. Rectal artesunate interrupts disease progression by rapidly reducing parasite density, but should be followed by further antimalarial treatment. We estimated the cost-effectiveness of community-based prereferral artesunate treatment of children suspected to have severe malaria in areas with poor access to formal health care. METHODS: We assessed the cost-effectiveness (in international dollars) of the intervention from the provider perspective. We studied a cohort of 1000 newborn babies until 5 years of age. The analysis assessed how the cost-effectiveness results changed with low (25%), moderate (50%), high (75%), and full (100%) referral compliance and intervention uptake. FINDINGS: At low intervention uptake and referral compliance (25%), the intervention was estimated to avert 19 disability-adjusted life-years (DALYs; 95% CI 16-21) and to cost I$1173 (95% CI 1050-1297) per DALY averted. Under the full uptake and compliance scenario (100%), the intervention could avert 967 DALYs (884-1050) at a cost of I$77 (73-81) per DALY averted. INTERPRETATION: Prereferral artesunate treatment is a cost-effective, life-saving intervention, which can substantially improve the management of severe childhood malaria in rural African settings in which programmes for community health workers are in place. FUNDING: The Disease Control Priorities Project; Fogarty International Center; US National Institutes of Health; and the Peter Paul Career Development Professorship, Boston University

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(9) DONDORP AM, FANELLO CI, HENDRIKSEN IC, GOMES E, *et al.* **Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial**. Lancet. 2010 Nov. 13, vol. 376, n° 9753, pp.1647-1657
http://dx.doi.org/10.1016/S0140-6736(10)61924-1 (**accès réservé EHESP**)

BACKGROUND: Severe malaria is a major cause of childhood death and often the main reason for paediatric hospital admission in sub-Saharan Africa. Quinine is still the established treatment

of choice, although evidence from Asia suggests that artesunate is associated with a lower mortality. We compared parenteral treatment with either artesunate or quinine in African children with severe malaria. METHODS: This open-label, randomised trial was undertaken in 11 centres in nine African countries. Children (<15 years) with severe falciparum malaria were randomly assigned to parenteral artesunate or parenteral quinine. Randomisation was in blocks of 20, with study numbers corresponding to treatment allocations kept inside opaque sealed paper envelopes. The trial was open label at each site, and none of the investigators or trialists, apart from for the trial statistician, had access to the summaries of treatment allocations. The primary outcome measure was in-hospital mortality, analysed by intention to treat. This trial is registered, number ISRCTN50258054. FINDINGS: 5425 children were enrolled; 2712 were assigned to artesunate and 2713 to quinine. All patients were analysed for the primary outcome. 230 (8.5%) patients assigned to artesunate treatment died compared with 297 (10.9%) assigned to quinine treatment (odds ratio [OR] stratified for study site 0.75, 95% CI 0.63-0.90; relative reduction 22.5%, 95% CI 8.1-36.9; p=0.0022). Incidence of neurological sequelae did not differ significantly between groups, but the development of coma (65/1832 [3.5%] with artesunate vs 91/1768 [5.1%] with quinine; OR 0.69 95% CI 0.49-0.95; p=0.0231), convulsions (224/2712 [8.3%] vs 273/2713 [10.1%]; OR 0.80, 0.66-0.97; p=0.0199), and deterioration of the coma score (166/2712 [6.1%] vs 208/2713 [7.7%]; OR 0.78, 0.64-0.97; p=0.0245) were all significantly less frequent in artesunate recipients than in quinine recipients. Post-treatment hypoglycaemia was also less frequent in patients assigned to artesunate than in those assigned to quinine (48/2712 [1.8%] vs 75/2713 [2.8%]; OR 0.63, 0.43-0.91; p=0.0134). Artesunate was well tolerated, with no serious drug-related adverse effects. INTERPRETATION: Artesunate substantially reduces mortality in African children with severe malaria. These data, together with a meta-analysis of all trials comparing artesunate and quinine, strongly suggest that parenteral artesunate should replace quinine as the treatment of choice for severe falciparum malaria worldwide. FUNDING: The Wellcome Trust

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http://dx.doi.org/jama.2010.1001/jama.2010.1578 (**accès réservé EHESP**)

CONTEXT: Malaria commonly infects residents of and travelers to tropical regions. The clinical features of infection are notoriously nonspecific but have not been comprehensively evaluated. OBJECTIVE: To systematically review and synthesize data related to the predictive value of clinical findings for the diagnosis of malaria in endemic areas and in travelers returning from endemic areas. Data Sources, Study Selection, and DATA EXTRACTION: The databases of MEDLINE and EMBASE (1950-July 2010) were searched to identify studies published in the English language of endemic and "imported" (acquired during travel) malaria. Additional studies were identified from reference lists. Studies were included that had patients suspected of having acute malaria (usually because of fever) and compared the presence or absence of clinical findings with blood smear confirmation. Two authors independently identified studies, appraised study quality, and extracted data on the patient population, outcome assessment, and clinical findings. Differences between reviewers were resolved by consensus. DATA SYNTHESIS: Fourteen studies for endemic malaria were identified that met review criteria. Individual symptoms are of limited diagnostic utility but presence of splenomegaly (summary likelihood ratio [LR], 3.3; 95% confidence interval [CI], 2.0-4.7) or hepatomegaly (summary LR, 2.4; 95% CI, 1.6-3.6) make malaria more likely. Combinations of findings can affect the likelihood of malaria, but their performance varies by setting. Seven studies of imported malaria were identified. The presence of fever (LR, 5.1; 95% CI, 4.9-5.3), splenomegaly (summary LR, 6.5; 95% CI, 3.9-11.0), hyperbilirubinemia (LR, 7.3; 95% CI, 5.5-9.6), or thrombocytopenia (summary LR, 5.6; 95% CI, 4.1-7.5) make malaria more likely. CONCLUSIONS: In endemic areas, the likelihood of malaria is increased by the presence of splenomegaly and hepatomegaly but individual findings are of limited utility and cannot reliably exclude malaria; combinations of findings may be useful to stratify risk in patients. In returning travelers, the clinical assessment can provide substantial

diagnostic benefit, although all patients still require laboratory testing because malaria can be rapidly fatal

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(17) FEACHEM RG, PHILLIPS AA, HWANG J, COTTER C, *et al.* **Shrinking the malaria map: progress and prospects**. Lancet. 2010 Nov. 6, vol. 376, n° 9752, pp.1566-1578
http://dx.doi.org/10.1016/S0140-6736(10)61270-6 (**accès réservé EHESP**)

In the past 150 years, roughly half of the countries in the world eliminated malaria. Nowadays, there are 99 endemic countries-67 are controlling malaria and 32 are pursuing an elimination strategy. This four-part Series presents evidence about the technical, operational, and financial dimensions of malaria elimination. The first paper in this Series reviews definitions of elimination and the state that precedes it: controlled low-endemic malaria. Feasibility assessments are described as a crucial step for a country transitioning from controlled low-endemic malaria to elimination. Characteristics of the 32 malaria-eliminating countries are presented, and contrasted with countries that pursued elimination in the past. Challenges and risks of elimination are presented, including Plasmodium vivax, resistance in the parasite and mosquito populations, and potential resurgence if investment and vigilance decrease. The benefits of elimination are outlined, specifically elimination as a regional and global public good. Priorities for the next decade are described

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http://dx.doi.org/10.1016/S0140-6736(10)61269-X (**accès réservé EHESP**)

Present elimination strategies are based on recommendations derived during the Global Malaria Eradication Program of the 1960s. However, many countries considering elimination nowadays have high intrinsic transmission potential and, without the support of a regional campaign, have to deal with the constant threat of imported cases of the disease, emphasising the need to revisit the strategies on which contemporary elimination programmes are based. To eliminate malaria, programmes need to concentrate on identification and elimination of foci of infections through both passive and active methods of case detection. This approach needs appropriate treatment of both clinical cases and asymptomatic infections, combined with targeted vector control. Draining of infectious pools entirely will not be sufficient since they could be replenished by imported malaria.

Elimination will thus additionally need identification and treatment of incoming infections before they lead to transmission, or, more realistically, embarking on regional initiatives to dry up importation at its source

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http://dx.doi.org/10.1016/S0140-6736(10)61355-4 (**accès réservé EHESP**)

The marginal costs and benefits of converting malaria programmes from a control to an elimination goal are central to strategic decisions, but empirical evidence is scarce. We present a conceptual framework to assess the economics of elimination and analyse a central component of that framework-potential short-term to medium-term financial savings. After a review that showed a dearth of existing evidence, the net present value of elimination in five sites was calculated and compared with effective control. The probability that elimination would be cost-saving over 50 years ranged from 0% to 42%, with only one site achieving cost-savings in the base case. These findings show that financial savings should not be a primary rationale for elimination, but that elimination might still be a worthy investment if total benefits are sufficient to outweigh marginal costs. Robust research into these elimination benefits is urgently needed

(21) TATEM AJ, SMITH DL, GETHING PW, KABARIA CW, *et al.* **Ranking of elimination feasibility between malaria-endemic countries**. Lancet. 2010 Nov. 6, vol. 376, n° 9752, pp.1579-1591
http://dx.doi.org/10.1016/S0140-6736(10)61301-3 (**accès réservé EHESP**)

Experience gained from the Global Malaria Eradication Program (1955-72) identified a set of shared technical and operational factors that enabled some countries to successfully eliminate malaria. Spatial data for these factors were assembled for all malaria-endemic countries and combined to provide an objective, relative ranking of countries by technical, operational, and combined elimination feasibility. The analysis was done separately for Plasmodium falciparum and Plasmodium vivax, and the limitations of the approach were discussed. The relative rankings suggested that malaria elimination would be most feasible in countries in the Americas and Asia, and least feasible in countries in central and west Africa. The results differed when feasibility was measured by technical or operational factors, highlighting the different types of challenge faced by each country. The results are not intended to be prescriptive, predictive, or to provide absolute assessments of feasibility, but they do show that spatial information is available to facilitate evidence-based assessments of the relative feasibility of malaria elimination by country that can be rapidly updated

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(24) DHINGRA N, JHA P, SHARMA VP, COHEN AA, *et al.* **Adult and child malaria mortality in India: a nationally representative mortality survey**. Lancet. 2010 Nov. 20, vol. 376, n° 9754, pp.1768-1774
http://dx.doi.org/10.1016/S0140-6736(10)60831-8 (**accès réservé EHESP**)

BACKGROUND: National malaria death rates are difficult to assess because reliably diagnosed

malaria is likely to be cured, and deaths in the community from undiagnosed malaria could be misattributed in retrospective enquiries to other febrile causes of death, or vice-versa. We aimed to estimate plausible ranges of malaria mortality in India, the most populous country where the disease remains common. METHODS: Full-time non-medical field workers interviewed families or other respondents about each of 122,000 deaths during 2001-03 in 6671 randomly selected areas of India, obtaining a half-page narrative plus answers to specific questions about the severity and course of any fevers. Each field report was sent to two of 130 trained physicians, who independently coded underlying causes, with discrepancies resolved either via anonymous reconciliation or adjudication. FINDINGS: Of all coded deaths at ages 1 month to 70 years, 2681 (3.6%) of 75,342 were attributed to malaria. Of these, 2419 (90%) were in rural areas and 2311 (86%) were not in any health-care facility. Death rates attributed to malaria correlated geographically with local malaria transmission ratesderived independently from the Indian malaria control programme. The adjudicated results show 205,000 malaria deaths per year in India before age 70 years (55,000 in early childhood, 30,000 at ages 5-14 years, 120,000 at ages 15-69 years); 1.8% cumulative probability of death from malaria before age 70 years. Plausible lower and upper bounds (on the basis of only the initial coding) were 125,000-277,000. Malaria accounted for a substantial minority of about 1.3 million unattended rural fever deaths attributed to infectious diseases in people younger than 70 years. INTERPRETATION: Despite uncertainty as to which unattended febrile deaths are from malaria, even the lower bound greatly exceeds the WHO estimate of only 15,000 malaria deaths per year in India (5000 early childhood, 10 000 thereafter). This low estimate should be reconsidered, as should the low WHO estimate of adult malaria deaths worldwide. FUNDING: US National Institutes of Health, Canadian Institute of Health Research, Li Ka Shing Knowledge Institute

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Pathologies liées à l'obésité

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Circadian clocks align behavioral and biochemical processes with the day/night cycle. Nearly all vertebrate cells possess self-sustained clocks that couple endogenous rhythms with changes in cellular environment. Genetic disruption of clock genes in mice perturbs metabolic functions of specific tissues at distinct phases of the sleep/wake cycle. Circadian desynchrony, a characteristic of shift work and sleep disruption in humans, also leads to metabolic pathologies. Here, we review advances in understanding the interrelationship among circadian disruption, sleep deprivation, obesity, and diabetes and implications for rational therapeutics for these conditions

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http://www.ncbi.nlm.nih.gov/pubmed/21109577 (**accès réservé EHESP**)

OBJECTIVES: To examine the prospective associations between body mass index (BMI), waist circumference, and fat mass in childhood and cardiovascular risk factors at age 15-16. DESIGN: Prospective cohort study. SETTING: Avon Longitudinal Study of Parents and Children. PARTICIPANTS: 5235 children aged 9-12 at start of study. Main exposures BMI, waist circumference, and fat mass determined by dual energy x ray absorptiometry, assessed at age 9-12 and at age 15-16. MAIN OUTCOME MEASURES: Systolic and diastolic blood pressure and concentrations of fasting glucose, insulin, triglycerides, low density lipoprotein cholesterol, and high density lipoprotein cholesterol assessed at age 15-16. RESULTS: In girls a 1 SD greater BMI at age 9-12 was associated with cardiovascular risk factors at age 15-16 in fully adjusted models: odds ratio 1.23 (95% confidence interval 1.10 to 1.38) for high systolic blood pressure (>/=130 mm Hg); 1.19 (1.03 to 1.38) for high concentration of low density lipoprotein cholesterol (>/=2.79 mmol/l); 1.43 (1.06 to 1.92) for high concentration of triglycerides (>/=1.7 mmol/l); 1.25 (1.08 to 1.46) for low concentration of high density lipoprotein cholesterol (<1.03 mmol/l); and 1.45 (1.22 to 1.73) for high concentration of insulin (>/=16.95 IU/l). Equivalent results in boys were 1.24 (1.13 to 1.37) for systolic blood pressure; 1.30 (1.07 to 1.59) for low density lipoprotein cholesterol; 1.96 (1.51 to 2.55) for triglycerides; 1.39 (1.22 to 1.57) for high density lipoprotein cholesterol, and 1.84 (1.56 to 2.17) for insulin. BMI was associated with high fasting glucose (>/=5.6 mmol/l) only in boys (1.18, 1.03 to 1.36). With these binary outcomes there was statistical evidence that associations differed between girls and boys for fasting glucose (P=0.03) and insulin (P<0.001). When risk factors were examined as continuous outcomes there was evidence for stronger associations of BMI with more adverse levels in boys than girls for fasting insulin, glucose, and triglyceride concentrations (all interaction P</=0.03). BMI, waist circumference, and fat mass were all strongly correlated with each other (r=0.89-0.94), and associations of the three with cardiovascular outcomes were of similar magnitude with statistical evidence of consistency in associations (all P>0.2 for heterogeneity). When waist circumference or fat mass or both were added to models including BMI they did not increase the variation in cardiovascular risk factors already explained by BMI and confounders alone. Girls who were overweight/obese at age 9-12 but were normal weight by 15-16 had similar odds of adverse levels of risk factors to those who were normal weight at both ages. In boys odds of high systolic blood pressure, high concentrations of triglycerides and insulin, and low concentrations of high density lipoprotein cholesterol remained higher in this group compared with those who were normal weight at both ages but were lower than in those who remained overweight/obese at both ages. CONCLUSIONS: Measurements of waist circumference or directly assessed fat mass in childhood do not seem to be associated with cardiovascular risk factors in adolescence any more strongly than BMI. Girls who favourably alter their overweight status between childhood and adolescence have cardiovascular risk profiles broadly similar to those who were normal weight at both time points, but boys who change from overweight to normal show risk factor profiles intermediate between those seen in boys who are normal weight at both ages or overweight at both ages

(12) LARSEN TM, DALSKOV SM, VAN BM, JEBB SA, *et al.* **Diets with high or low protein content and glycemic index for weight-loss maintenance**. N Engl J Med. 2010 Nov. 25, vol. 363, n° 22, pp.2102-2113
http://dx.doi.org/10.1056/NEJMoa1007137 (**collection papier de la bibliothèque**)

BACKGROUND: Studies of weight-control diets that are high in protein or low in glycemic index have reached varied conclusions, probably owing to the fact that the studies had insufficient power. METHODS: We enrolled overweight adults from eight European countries who had lost at least 8% of their initial body weight with a 3.3-MJ (800-kcal) low-calorie diet. Participants were randomly assigned, in a two-by-two factorial design, to one of five ad libitum diets to prevent weight regain over a 26-week period: a low-protein and low-glycemic-index diet, a low-protein and high-glycemic-index diet, a high-protein and low-glycemic-index diet, a high-protein and high-glycemic-index diet, or a control diet. RESULTS: A total of 1209 adults were screened (mean age, 41 years; body-mass index [the weight in kilograms divided by the square of the height in meters], 34), of whom 938 entered the low-calorie-diet phase of the study. A total of 773 participants who completed that phase were randomly assigned to one of the five maintenance diets; 548 completed the intervention (71%). Fewer participants in the high-protein and the low-glycemic-index groups than in the low-protein-high-glycemic-index group dropped out of the study (26.4% and 25.6%, respectively, vs. 37.4%; P=0.02 and P=0.01 for the respective comparisons). The mean initial weight loss with the low-calorie diet was 11.0 kg. In the analysis of participants who completed the study, only the low-protein-high-glycemic-index diet was associated with subsequent significant weight regain (1.67 kg; 95% confidence interval [CI], 0.48 to 2.87). In an intention-to-treat analysis, the weight regain was 0.93 kg less (95% CI, 0.31 to 1.55) in the groups assigned to a high-protein diet than in those assigned to a low-protein diet (P=0.003) and 0.95 kg less (95% CI, 0.33 to 1.57) in the groups assigned to a low-glycemic-index diet than in those assigned to a high-glycemic-index diet (P=0.003). The analysis involving participants who completed the intervention produced similar results. The groups did not differ significantly with respect to diet-related adverse events. CONCLUSIONS: In this large European study, a modest increase in protein content and a modest reduction in the glycemic index led to an improvement in study completion and maintenance of weight loss. (Funded by the European Commission; ClinicalTrials.gov number, NCT00390637.)

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http://dx.doi.org/10.1016/S0140-6736(10)61514-0 (**accès réservé EHESP**)

The obesity epidemic is spreading to low-income and middle-income countries as a result of new dietary habits and sedentary ways of life, fuelling chronic diseases and premature mortality. In this report we present an assessment of public health strategies designed to tackle behavioural risk factors for chronic diseases that are closely linked with obesity, including aspects of diet and physical inactivity, in Brazil, China, India, Mexico, Russia, and South Africa. England was included for comparative purposes. Several population-based prevention policies can be expected to generate substantial health gains while entirely or largely paying for themselves through future

reductions of health-care expenditures. These strategies include health information and communication strategies that improve population awareness about the benefits of healthy eating and physical activity; fiscal measures that increase the price of unhealthy food content or reduce the cost of healthy foods rich in fibre; and regulatory measures that improve nutritional information or restrict the marketing of unhealthy foods to children. A package of measures for the prevention of chronic diseases would deliver substantial health gains, with a very favourable cost-effectiveness profile

(18) THE NS, SUCHINDRAN C, NORTH KE, POPKIN BM, *et al.* **Association of adolescent obesity with risk of severe obesity in adulthood**. JAMA. 2010 Nov. 10, vol. 304, n° 18, pp.2042-2047 http://dx.doi.org/10.1001/jama.2010.1635 (**accès réservé EHESP**)

CONTEXT: Although the prevalence of obesity has increased in recent years, individuals who are obese early in life have not been studied over time to determine whether they develop severe obesity in adulthood, thus limiting effective interventions to reduce severe obesity incidence and its potentially life-threatening associated conditions. OBJECTIVE: To determine incidence and risk of severe obesity in adulthood by adolescent weight status. DESIGN, SETTING, AND PARTICIPANTS: A cohort of 8834 individuals aged 12 to 21 years enrolled in 1996 in wave II of the US National Longitudinal Study of Adolescent Health, followed up into adulthood (ages 18-27 years during wave III [2001-2002] and ages 24-33 years during wave IV [2007-2009]). Height and weight were obtained via anthropometry and surveys administered in study participants' homes using standardized procedures. MAIN OUTCOME MEASURES: New cases of adult-onset severe obesity were calculated by sex, race/ethnicity, and adolescent weight status. Sex-stratified, discrete time hazard models estimated the net effect of adolescent obesity (aged <20 years; body mass index [BMI] >/=95th percentile of the sex-specific BMI-for-age growth chart or BMI >/=30.0) on risk of severe obesity incidence in adulthood (aged >/=20 years; BMI >/=40.0), adjusting for race/ethnicity and age and weighted for national representation. RESULTS: In 1996, 79 (1.0%; 95% confidence interval [CI], 0.7%-1.4%) adolescents were severely obese; 60 (70.5%; 95% CI, 57.2%-83.9%) remained severely obese in adulthood. By 2009, 703 (7.9%; 95% CI, 7.4%-8.5%) non-severely obese adolescents had become severely obese in adulthood, with the highest rates for non-Hispanic black women. Obese adolescents were significantly more likely to develop severe obesity in young adulthood than normal-weight or overweight adolescents (hazard ratio, 16.0; 95% CI, 12.4-20.5). CONCLUSION: In this cohort, obesity in adolescence was significantly associated with increased risk of incident severe obesity in adulthood, with variations by sex and race/ethnicity

(19) WELLS NM, EVANS GW, BEAVIS A, ONG AD. **Early childhood poverty, cumulative risk exposure, and body mass index trajectories through young adulthood**. Am J Public Health. 2010 Dec., vol. 100, n° 12, pp.2507-2512 http://dx.doi.org/10.2105/AJPH.2009.184291 (**accès réservé EHESP**)

OBJECTIVES: We assessed whether cumulative risk exposure underlies the relation between early childhood poverty and body mass index (BMI) trajectories. METHODS: We interviewed youths and their mothers in rural upstate New York (168 boys and 158 girls) from 1995 to 2006 when the youths were aged 9, 13, and 17 years. At each interview, we calculated their BMI-for-age percentile. RESULTS: Early childhood poverty predicted BMI growth trajectories from ages 9 to 17 years (b = 3.64; SE = 1.39; P < .01). Early childhood poverty also predicted changes in cumulative risk (b = 0.31; SE = 0.08; P < .001). Cumulative risk, in turn, predicted BMI trajectories (b = 2.41; SE = 0.75; P < .01). Finally, after we controlled for cumulative risk, the effect of early childhood poverty on BMI trajectories was no longer significant, indicating that cumulative risk exposure mediated the relation between early childhood poverty and BMI trajectories (b = 2.01; SE = 0.94). CONCLUSIONS: We show for the first time that early childhood poverty leads to accelerated weight gain over the course of childhood into early adulthood. Cumulative risk exposure during childhood accounts for much of this accelerated weight gain

(20) NG SF, LIN RC, LAYBUTT DR, BARRES R, *et al.* **Chronic high-fat diet in fathers programs beta-cell dysfunction in female rat offspring**. Nature. 2010 Oct. 21, vol. 467, n° 7318, pp.963-966
http://dx.doi.org/10.1038/nature09491 (**accès payant**)

The global prevalence of obesity is increasing across most ages in both sexes. This is contributing to the early emergence of type 2 diabetes and its related epidemic. Having either parent obese is an independent risk factor for childhood obesity. Although the detrimental impacts of diet-induced maternal obesity on adiposity and metabolism in offspring are well established, the extent of any contribution of obese fathers is unclear, particularly the role of non-genetic factors in the causal pathway. Here we show that paternal high-fat-diet (HFD) exposure programs beta-cell 'dysfunction' in rat F(1) female offspring. Chronic HFD consumption in Sprague-Dawley fathers induced increased body weight, adiposity, impaired glucose tolerance and insulin sensitivity. Relative to controls, their female offspring had an early onset of impaired insulin secretion and glucose tolerance that worsened with time, and normal adiposity. Paternal HFD altered the expression of 642 pancreatic islet genes in adult female offspring (P < 0.01); genes belonged to 13 functional clusters, including cation and ATP binding, cytoskeleton and intracellular transport. Broader pathway analysis of 2,492 genes differentially expressed (P < 0.05) demonstrated involvement of calcium-,

(21) SKINNER MK. **Metabolic disorders: Fathers' nutritional legacy**. Nature. 2010 Oct. 21, vol. 467, n° 7318, pp.922-923
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(22) LEVIN G, KESTENBAUM B, IDA CHEN YD, JACOBS DR, JR., *et al.* **Glucose, insulin, and incident hypertension in the multi-ethnic study of atherosclerosis**. Am J Epidemiol. 2010 Nov. 15, vol. 172, n° 10, pp.1144-1154
http://dx.doi.org/10.1093/aje/kwq266 (**accès réservé EHESP**)

Diabetes mellitus and hypertension commonly coexist, but the nature of this link is not well understood. The authors tested whether diabetes and higher concentrations of fasting serum glucose and insulin are associated with increased risk of developing incident hypertension in the community-based Multi-Ethnic Study of Atherosclerosis. At baseline, 3,513 participants were free of hypertension, defined as systolic blood pressure >/=140 mm Hg, diastolic blood pressure >/=90 mm Hg, or use of antihypertensive medications to treat high blood pressure. Of these, 965 participants (27%) developed incident hypertension over 4.7 years' median follow-up between 2002 and 2007. Compared with participants with normal baseline fasting glucose, those with impaired fasting glucose and diabetes had adjusted relative risks of hypertension of 1.16 (95% confidence interval (CI): 0.96, 1.40) and 1.41 (95% CI: 1.17, 1.71), respectively (P = 0.0015). The adjusted relative risk of incident hypertension was 1.08 (95% CI: 1.04, 1.13) for each mmol/L higher glucose (P < 0.0001) and 1.15 (95% CI: 1.05, 1.25) for each doubling of insulin (P = 0.0016). Further adjustment for serum cystatin C, urinary albumin/creatinine ratio, and arterial elasticity measured by tonometry substantially reduced the magnitudes of these associations. In conclusion, diabetes and higher concentrations of glucose and insulin may contribute to the development of hypertension, in part through kidney disease and arterial stiffness

(23) MINET KJ, MORRIS S. **Socioeconomic variation in the impact of obesity on health-related quality of life**. Soc Sci Med. 2010 Nov., vol. 71, n° 10, pp.1864-1871
http://dx.doi.org/10.1016/j.socscimed.2010.09.001 (**accès réservé EHESP**)

There is evidence that obesity has a negative impact on health-related quality of life (HRQL). However, little attention has been paid to variations in this impact between population groups. This study investigates the relationship between HRQL and obesity, and whether or not this relationship varies by socioeconomic status (SES). Data were taken from four rounds of the Health Survey for England (2003-2006; n = 33,716) for persons aged 16 and above. Banded total annual household income is regressed against a comprehensive set of SES indicators using interval regression. We use the equivalised predicted values from this model, categorised into

quartiles, as our measure of SES. We regress EQ-5D scores against interactions between body mass index and SES categories. Obesity is negatively correlated with HRQL. The negative impact of obesity is greater in people from lower SES groups. Overweight and obese people in lower SES groups have lower HRQL than those of normal weight in the same SES group, and have lower HRQL than those in higher SES groups of the same weight. This trend is also observed after controlling for individual and household characteristics, although the statistical significance and magnitude of effects is diminished

(24) GUNDERSON EP, QUESENBERRY CP, JR., JACOBS DR, JR., FENG J, *et al.* **Longitudinal study of prepregnancy cardiometabolic risk factors and subsequent risk of gestational diabetes mellitus: The CARDIA study**. Am J Epidemiol. 2010 Nov. 15, vol. 172, n° 10, pp.1131-1143
http://dx.doi.org/10.1093/aje/kwq267 (**accès réservé EHESP**)

This study examined prepregnancy cardiometabolic risk factors and gestational diabetes mellitus (GDM) in subsequent pregnancies. The authors selected 1,164 women without diabetes before pregnancy who delivered 1,809 livebirths between 5 consecutive examinations from 1985 to 2006 in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. The authors measured prepregnancy cardiometabolic risk factors and performed multivariate repeated-measures logistic regression to compute the odds of GDM adjusted for race, age, parity, birth order, and other covariates. Impaired fasting glucose (100-125 vs. <90 mg/dL), elevated fasting insulin (>15-20 and >20 vs. <10 muU/mL), and low levels of high-density lipoprotein cholesterol (<40 vs. >50 mg/dL) before pregnancy were directly associated with GDM: The odds ratios = 4.74 (95% confidence interval (CI): 2.14, 10.51) for fasting glucose, 2.19 (95% CI: 1.15, 4.17) for middle insulin levels and 2.36 (95% CI: 1.20, 4.63) for highest insulin levels, and 3.07 (95% CI: 1.62, 5.84) for low levels of high-density lipoprotein cholesterol among women with a negative family history of diabetes; all P < 0.01. Among overweight women, 26.7% with 1 or more cardiometabolic risk factors developed GDM versus 7.4% with none. Metabolic impairment exists before GDM pregnancy in nondiabetic women. Interconceptual metabolic screening could be included in routine health assessments to identify high-risk women for GDM in a subsequent pregnancy and to potentially minimize fetal exposure to metabolic abnormalities that program future disease

(25) MOROIS S, MESRINE S, JOSSET M, CLAVEL-CHAPELON F, *et al.* **Anthropometric factors in adulthood and risk of colorectal adenomas: The French E3N-EPIC prospective cohort**. Am J Epidemiol. 2010 Nov. 15, vol. 172, n° 10, pp.1166-1180

http://dx.doi.org/10.1093/aje/kwq258 (**accès réservé EHESP**)

Anthropometric factors have been associated with colorectal cancer and adenomas but with conflicting results in women or regarding adenoma characteristics. The authors aimed to explore associations between anthropometric factors (height, weight, body mass index, waist and hip circumferences, and weight changes) and adenoma risk. They analyzed the 17,391 women of the French Etude epidemiologique des femmes de la Mutuelle Generale de l'Education Nationale (E3N)-European Prospective Investigation into Cancer and Nutrition (EPIC) cohort who underwent a colonoscopy during follow-up (1993-2002), including 1,408 who developed a first colorectal adenoma. In Cox multivariate proportional hazard regression models, obesity was associated with an increased colorectal adenoma risk (hazard ratio = 1.53, 95% confidence interval: 1.21, 1.94). This association was restricted to left colon adenomas (P(homogeneity) = 0.05 and 0.01 for colon vs. rectum and right vs. left colon, respectively), with a dose-effect relation observed from 22 kg/m(2). A high waist circumference was also associated with left colon adenoma risk (hazard ratio = 1.81, 95% confidence interval: 1.36, 2.41). Mean weight gain over 0.5 kg/year was associated with a 23% increased colorectal adenoma risk. Associations did not differ between advanced and nonadvanced adenomas. In conclusion, study findings suggest that obesity and weight gain are associated with early colorectal carcinogenesis in women, and specifically regarding the distal colon

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SIDA

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(4) COHEN J. **HIV/AIDS clinical trials. A powerful and perplexing new HIV prevention tool**. Science. 2010 Dec. 3, vol. 330, n° 6009, pp.1298-1299
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primary analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, NCT00830622. FINDINGS: Between May, 2007, and October, 2008, we randomly assigned 538 participants to the SMS intervention (n=273) or to standard care (n=265). Adherence to ART was reported in 168 of 273 patients receiving the SMS intervention compared with 132 of 265 in the control group (relative risk [RR] for non-adherence 0.81, 95% CI 0.69-0.94; p=0.006). Suppressed viral loads were reported in 156 of 273 patients in the SMS group and 128 of 265 in the control group, (RR for virologic failure 0.84, 95% CI 0.71-0.99; p=0.04). The number needed to treat (NNT) to achieve greater than 95% adherence was nine (95% CI 5.0-29.5) and the NNT to achieve viral load suppression was 11 (5.8-227.3). INTERPRETATION: Patients who received SMS support had significantly improved ART adherence and rates of viral suppression compared with the control individuals. Mobile phones might be effective tools to improve patient outcome in resource-limited settings. FUNDING: US President's Emergency Plan for AIDS Relief

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OBJECTIVES: We investigated a cluster of tuberculosis (TB) cases among persons using methamphetamines in Snohomish County, Washington, to determine the extent of the outbreak, examine whether methamphetamine use contributed to TB transmission, and implement strategies to prevent further infections. METHODS: We screened contacts to find and treat persons with TB disease or infection. We then formed a multidisciplinary team to engage substance abuse services partners and implement outreach strategies including novel methods for finding contacts and a system of incentives and enablers to promote finding, screening, and treating patients with TB and their infected contacts. RESULTS: We diagnosed and completed treatment with 10 persons with TB disease. Eight of 9 adult patients and 67% of their adult contacts reported using methamphetamines. Of the 372 contacts, 319 (85.8%) were screened, 80 (25.1%) were infected, 71 (88.8%) started treatment for latent infection, and 57 (80.3%) completed treatment for latent infection. CONCLUSIONS: Collaborative approaches integrating TB control, outreach, incentives, and enablers resulted in high rates of treatment adherence and completion among patients and infected contacts. TB control programs should collaborate with substance abuse programs to address addiction, overcome substance abuse-related barriers to treatment, treat TB, and prevent ongoing transmission

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