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

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Pathologies suivies

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

Revues surveillées

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


OBJECTIVE: To determine bronchoalveolar lavage (BAL) levels of 3 innate immunity components (human beta-defensin-2 [hBD2], mannose-binding lectin [MBL], and surfactant protein-A [SP-A]), the relationship with airway neutrophilia and infection, and cytokine production of stimulated BAL cells in children with current protracted bacterial bronchitis (PBB), children with resolved PBB (PBB well), and controls. STUDY DESIGN: BAL of 102 children (mean age 2.8 years) fulfilling predefined criteria of current PBB (n = 61), PBB well (n = 20), and controls (n = 21) was cultured (quantitative bacteriology) and viruses examined by polymerase chain reaction. hBD2, MBL, and SP-A were measured, and cytokine production by lipopolysaccharide-stimulated BAL cells was determined. RESULTS: Median hBD2 and MBL levels were significantly higher in the current PBB group (hBD2 = 164.4, IQR 0-435.5 pg/mL; MBL = 1.7, 0.4-4 ng/mL) than in the PBB well group (hBD2 = 0, IQR 0-85.2; MBL = 0.6, IQR 0.03-2.9) and controls (hBD2 = 3.6, IQR 0-126; MBL = 0.4, IQR 0.02-79). hBD2 was significantly higher in children with airway infection (n = 54; median 76.9, IQR 0-397.3) compared with those without (n = 48; 0, IQR 0-236.3), P=.04. SP-A levels and cytokine production of stimulated BAL cells were similar between groups. CONCLUSION: In children’s airways, hBD2, but not MBL and SP-A, relates to inflammation and infection. In children with PBB, mechanisms involving airway hBD2 and MBL are augmented. These pulmonary innate immunity components and the ability of BAL cells to respond to stimuli are unlikely to be deficient...
GEORGE G. New solutions in service design and delivery are necessary to combat disease burden. Int J Tuberc Lung Dis. 2012 Sept., vol. 16, n° 9, p.1139


The main aim of this study was to evaluate the prevalence of respiratory symptoms among men and women separately in areas with relatively low traffic density. Data on respiratory symptoms were collected from questionnaires in the Hordaland Health Study. A total of 16,412 individuals, 40 to 45 years, were asked to participate (response rate: 55% for men and 66% for women). Women residing in areas with the highest traffic density had increased prevalence of daily cough (18% vs 8.2%, p < .01), of cough with sputum (8.8% vs 2.8%, p < .01), and of chronic cough (11% vs 4.7%, p < .01) compared with women residing in areas with lower traffic density. The differences were most pronounced for smoking females. There were no similar findings among men. In conclusion, even within areas with relatively low environmental air pollution, respiratory symptoms was related to traffic density among smoking females


SETTING: Field sites in 12 districts in different parts of India. OBJECTIVE: To determine the nationwide population prevalence of and risk factors for asthma and chronic bronchitis (CB) in adults. DESIGN: A standardised validated questionnaire based on the International Union Against Tuberculosis and Lung Disease's 1984 questionnaire was used to assess asthma and CB prevalence. Multivariate logistic regression analyses were performed to determine the risk factor associations. Estimates standardised to the 2011 population projection estimates for India were used to calculate the national disease burden. RESULTS: A total of 85,105 men and 84,470 women from 12 urban and 11 rural sites were interviewed. One or more respiratory symptoms were present in 8.5% of individuals. The overall prevalence of asthma and CB was respectively 2.05% (adults aged >/=15 years) and 3.49% (adults aged >/=35 years). Advancing age, smoking, household environmental tobacco smoke exposure, asthma in a first-degree relative, and use of unclean cooking fuels were associated with increased odds of asthma and CB. The national burden of asthma and CB was estimated at respectively 17.23 and 14.84 million. CONCLUSION: Asthma and CB in adults pose an enormous health care burden in India. Most of the associated risk factors are preventable

TASHKIN DP, SIMMONS MS, TSENG CH. Impact of changes in regular use of marijuana and/or tobacco on chronic bronchitis. COPD. 2012 Aug., vol. 9, n° 4, pp.367-374

We sought to evaluate possible changes in the prevalence of chronic bronchitis in relation to continuing or changing smoking status for marijuana and/or tobacco. For this purpose we followed 299 participants in a longitudinal cohort study of the impact of heavy habitual use of marijuana alone or with tobacco on respiratory symptoms over a mean of 9.8 years during which subjects underwent repeated administration of a detailed drug use and respiratory questionnaire at intervals of >/=1 yr. Using logistic regression, we calculated odds ratios to assess the relationship between chronic bronchitic symptoms and smoking status for marijuana and tobacco at the first visit (current smoking versus never smoking) and at the last follow-up visit (continuing smoking versus, separately, never smoking and former smoking). We found that continuing smokers of...
either marijuana or tobacco had a significantly increased likelihood of having chronic bronchitis at follow-up compared to both never smokers and former smokers. On the other hand, former smokers of either substance were no more likely to have chronic respiratory symptoms at follow-up than never smokers. These findings demonstrate the benefit of marijuana smoking cessation in resolving pre-existing symptoms of chronic bronchitis.


OBJECTIVE: To test whether chronic bronchial inflammation may be a contributing risk factor for persistent airflow limitation in children born before 32 weeks of gestation in later life. STUDY DESIGN: Thirty-six of 160 children born before 32 completed weeks of gestation who were born between 1988 and 1992 were recruited at a median age of 11 years. Eighteen age-matched children born at term were controls; 47% of the premature infants and 61% of the term born children produced sputum of sufficient quality for interleukin (IL)-8, cell numbers, and differential counts. RESULTS: Compared with term born children, sputum from the premature group had a higher proportion of neutrophils (62% vs 3.8%; P < .001) and higher IL-8/protein values (1.93 mug/g vs 0.64 mug/g; P = .008). Forced expiratory flow 25%-75% and forced expiratory volume in 1 second/vital capacity were significantly lower (73.4 % vs 116% predicted, P = .002 and 97% vs 101%, P = .012, respectively). Lung function values and sputum indices did not correlate. IL-8/protein and neutrophil percentages correlated significantly with decreasing gestational age (Spearman rank coefficient = -0.58, P = .020 and -.70, P = .03 respectively). CONCLUSION: A significant proportion of school children born very preterm demonstrate persistent peripheral airway obstruction that is accompanied by neutrophilic lower airway inflammation.
for each quintile in each calendar year is estimated from the NHIS data. For five-year birth cohorts of white, african-american, Hispanic and all race/ethnicity groupings of males and females born between 1910 and 1984, estimates are provided for prevalence of current and ever smoking, incidence of cessation, incidence of initiation, and the distribution of smoking duration and CPD for each calendar year and each single year of age through the year 1999. We believe that we are the first to provide birth-cohort-specific estimates of smoking behaviors for the U.S. population that include distributions of duration of smoking and number of cigarettes per day. These additional elements substantively enhance the utility of these estimates for estimating lung cancer risks.


Tobacco use remains the nation's leading cause of preventable premature mortality. Lung cancer, one of the many cancers caused by tobacco use, is both the leading cause of cancer death in the United States and the leading cause of male cancer death globally. This special issue of Risk Analysis features the work of the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network (CISNET), which finds that changes in Americans' smoking behaviors that began in the mid 1950s averted nearly 800,000 U.S. lung cancer deaths in the period 1975-2000 alone. However, this figure represents only about 30% of the lung cancer deaths that could potentially have been averted during this period. Despite dramatic declines in smoking prevalence since the mid 1960s, tobacco use is still far too common; today about one in five American adults smokes cigarettes. The tobacco industry's role in promoting tobacco use is now well documented and, as noted by the President's Cancer Panel, "can no more be ignored in seeking solutions to the tobacco problem than mosquitoes can be ignored in seeking to eradicate malaria." Recent developments, including the passage of legislation granting the Food and Drug Administration broad authority to regulate tobacco products, and the entry into force of the Framework Convention on Tobacco Control, an evidence-based treaty developed by the World Health Organization, hold great promise to more swiftly end the epidemic of lung cancer and other tobacco-caused diseases that exacts such a heavy toll in human suffering in the United States and around the world.


BACKGROUND: A consortium of six research groups estimated the impact on lung cancer mortality of changes in smoking behavior that began around the publication of the Surgeon General's report (SGR). This chapter presents the results of that effort. We quantified the cumulative impact of changes in smoking behaviors on lung cancer mortality in the United States over the period 1975-2000. METHODS: The six groups used common inputs and independent models to estimate the number of U.S. lung cancer deaths averted over the period 1975-2000 as a result of changes in smoking behavior beginning in the mid fifties, and the number of deaths that could have been averted if tobacco control had completely eliminated all smoking following issuance of the first SGR on Smoking and Health in 1964. RESULTS: Approximately 795,000 deaths (550,000 men and 245,000 women) were averted over the period 1975-2000 as a result of changes in smoking behavior since in 1950s. In the year 2000 alone approximately 70,000 lung cancer deaths were averted (44,000 among men and 26,000 among women). However, these represent approximately 30% of lung cancer deaths that could have potentially been averted over
the period 1975-2000 if smoking was eliminated completely. In the 10-year period 1991-2000, this fraction increased to about 37%. CONCLUSIONS: Our results show the substantial impact of changes in smoking behavior since the 1950s. Despite a major impact of changing smoking behaviors, tobacco control effort are still needed to further reduce the burden of this disease.


To better understand the contribution of cigarette smoking, and its changing role in lung cancer, this article provides an introduction to a special issue of Risk Analysis, which considers the relationship between smoking and lung cancer death rates during the period 1975-2000 for U.S. men and women aged 30-84 years. Six models are employed, which are part of a consortium of lung cancer modelers funded by National Cancer Institute's Cancer Intervention and Surveillance Modeling Network (CISNET). Starting with birth-cohort-specific smoking histories derived from National Health Interview Surveys, three scenarios are modeled: Actual Tobacco Control (observed trends in smoking), Complete Tobacco Control (a counterfactual lower bound on smoking rates that could have been achieved had all smoking ceased after the first Surgeon General's report in 1964), and No Tobacco Control (a counterfactual upper bound on smoking rates if smoking patterns that prevailed before the first studies in the 1950s began to inform the public about the hazards of smoking). Using these three scenarios and the lung cancer models, the number and percentage of lung cancer deaths averted from 1975-2000, among all deaths that could have been averted if tobacco control efforts been immediate and perfect, can be estimated. The variability of the results across multiple models provides a measure of the robustness of the results to model assumptions and structure. The results provide not only a portrait of the achieved impact of tobacco control on lung cancer mortality, but also the bounds of what still needs to be achieved.


The Rice-MD Anderson group uses a two-stage clonal expansion (TSCE) model of lung cancer mortality calibrated to a combination of MD Anderson case-control data on smoking histories and lung cancer mortality/incidence rate data collected from prospective cohorts in order to predict risk of lung cancer. This model is used to simulate lung cancer mortality in the U.S. population under the three scenarios of CISNET lung group's smoking base case project in order to estimate the effect of tobacco control policy on lung cancer mortality rates. Simulation results show that tobacco control policies have achieved 35% of the reduction in lung cancer mortality that would have resulted from cessation of all smoking in 1965.


As a member of the Cancer Intervention and Surveillance Modeling Network (CISNET), the lung cancer (LC) group at Fred Hutchinson Cancer Research Center (FHCRC) developed a model for evaluating U.S. lung cancer mortality trends and the impact of changing tobacco consumption. Model components include a biologically based two-stage clonal expansion (TSCE) model; a smoking simulator to generate smoking histories and other cause mortality; and adjustments for period and birth cohort to improve calibration to U.S. LC mortality. The TSCE model was first calibrated to five substantial cohorts: British doctors, American Cancer Society CPS-I and CPS-II, Health Professionals' Follow-Up Study (HPFS), and Nurses' Health Study (NHS). The NHS and HPFS cohorts included the most detailed smoking histories and were chosen to represent the
effects of smoking on U.S. LC mortality. The calibrated TSCE model and smoking simulator were used to simulate U.S. LC mortality. Further adjustments were necessary to account for unknown factors. This provided excellent fits between simulated and observed U.S. LC mortality for ages 30-84 and calendar years 1975-2000. The FHCRC LC model may be used to study the effects of public health information on U.S. LC trends and the impact of tobacco control policy. For example, we estimated that over 500,000 males and 200,000 females avoided LC death between 1975 and 2000 due to increasing awareness since the mid 1950s of the harmful effects of smoking. We estimated that 1.1 million male and 0.6 million female LC deaths were avoidable if smokers quit smoking in 1965.


Publication of the Surgeon General's Report in 1964 marshaled evidence of the harm to public health caused by cigarette smoking, including lung cancer mortality, and provided an impetus for introducing control programs. The purpose of this article is to develop estimates of their effect on basic smoking exposure input parameters related to introduction of the report. Fundamental inputs used to generate exposure to cigarettes are initiation and cessation rates for men and women, as well as the distribution of the number of cigarettes smoked per day. These fundamental quantities are presented for three scenarios: actual tobacco control in the United States; no tobacco control in which the experience before 1955 was assumed to continue; and complete tobacco control in which all smoking ceased following publication of the report. These results were derived using data from National Health Interview Surveys, and they provide basic input parameters for the Smoking History Generator used by each of the lung cancer models developed by the Cancer Intervention and Surveillance Modeling Network


The relationship between smoking and lung cancer is well established and cohort studies provide estimates of risk for individual cohorts. While population trends are qualitatively consistent with smoking trends, the rates do not agree well with results from analytical studies. Four carcinogenesis models for the effect of smoking on lung cancer mortality were used to estimate lung cancer mortality rates for U.S. males: two-stage clonal expansion and multistage models using parameters estimated from two Cancer Prevention Studies (CPS I and CPS II). Calibration was essential to adjust for both shift and temporal trend. The age-period-cohort model was used for calibration. Overall, models using parameters derived from CPS I performed best, and the corresponding two-stage clonal expansion model was best overall. However, temporal calibration did significantly improve agreement with the population rates, especially the effect of age and cohort.


The age-period-cohort model is known to provide an excellent description of the temporal trends in lung cancer incidence and mortality. This analytic approach is extended to include the contribution of carcinogenesis models for smoking. Usefulness of this strategy is that it offers a way to temporally calibrate a model that is fitted to population data and it can be readily adopted for the consideration of many different models. In addition, it provides diagnostics that can suggest temporal limitations of a particular carcinogenesis model in describing population rates.
Alternative carcinogenesis models can be embedded within this framework. The two-stage clonal expansion model is implemented here. The model was used to estimate the impact of tobacco control after dissemination of knowledge of the harmful effects of cigarette smoking by comparing the observed number of lung cancer deaths to those expected if there had been no control compared to an ideal of complete control in 1965. Results indicate that 35.2% and 26.5% of lung cancer deaths that could have been avoided actually were for males and females, respectively.


The smoking history generator (SHG) developed by the National Cancer Institute simulates individual life/smoking histories that serve as inputs for the Cancer Intervention and Surveillance Modeling Network (CISNET) lung cancer models. In this chapter, we review the SHG inputs, describe its outputs, and outline the methodology behind it. As an example, we use the SHG to simulate individual life histories for individuals born between 1890 and 1984 for each of the CISNET smoking scenarios and use those simulated histories to compute the corresponding smoking prevalence over the period 1975-2000.


Past studies have examined the relationship of lung cancer to smoking using longitudinal data for select samples. This study applies the two-stage clonal expansion (TSCE) model to U.S. smoking data over a 25-year period. Smoking Base Case (SBC) data on actual smoking duration and intensity from the years 1975-2000 are applied by gender to separate TSCE models, which are then calibrated to historical trends in lung cancer death rates using regression analysis. The uncalibrated and calibrated TSCE models are also applied to SBC data for two scenarios: (1) no tobacco control and (2) complete tobacco control. The results are used to develop estimates of the number of lives saved as a result of tobacco control and how many lives would be saved if cigarette use had ceased in 1965. Predictions of lung cancer from the TSCE models with CPS-II and the CPS-I data for males and especially females are considerably below historical rates with the deviations from historical rates increasing over time. Residual trends unrelated to the smoking models were also found. Tobacco control activities saved approximately 625,000 lives between the years 1975 and 2000. An additional 2,110,000 lives would have been saved if all smoking was stopped in 1965. Tobacco control has successfully prevented lung cancer deaths, but many more lives could be saved with further reductions in smoking rates. Systematic biases were observed from TSCE models using CPS-I and CPS-II data to estimate smoking-related lung cancer deaths.


In this chapter we review the epidemiology of lung cancer incidence and mortality among never smokers/nonsmokers and describe the never smoker lung cancer risk models used by the Cancer Intervention and Surveillance Network (CISNET) modelers. Our review focuses on those influences likely to have measurable population impact on never smoker risk, such as secondhand smoke, even though the individual-level impact may be small. Occupational exposures may also contribute importantly to the population attributable risk of lung cancer. We examine the following risk factors in this chapter: age, environmental tobacco smoke, cooking fumes, ionizing radiation including radon gas, inherited genetic susceptibility, selected...
occupational exposures, preexisting lung disease, and oncogenic viruses. We also compare the prevalence of never smokers between the three CISNET smoking scenarios and present the corresponding lung cancer mortality estimates among never smokers as predicted by a typical CISNET model.


Sophisticated modeling techniques can be powerful tools to help us understand the effects of cancer control interventions on population trends in cancer incidence and mortality. Readers of journal articles are, however, rarely supplied with modeling details. Six modeling groups collaborated as part of the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network (CISNET) to investigate the contribution of U.S. tobacco-control efforts toward reducing lung cancer deaths over the period 1975-2000. The six models included in this monograph were developed independently and use distinct, complementary approaches toward modeling the natural history of lung cancer. The models used the same data for inputs, and agreed on the design of the analysis and the outcome measures. This article highlights aspects of the models that are most relevant to similarities of or differences between the results. Structured comparisons can increase the transparency of these complex models.


The natural history model underlying the MGH Lung Cancer Policy Model (LCPM) does not include the two-stage clonal expansion model employed in other CISNET lung models. We used the LCPM to predict numbers of U.S. lung cancer deaths for ages 30-84 between 1975 and 2000 under four scenarios as part of the comparative modeling analysis described in this issue. The LCPM is a comprehensive microsimulation model of lung cancer development, progression, detection, treatment, and survival. Individual-level patient histories are aggregated to estimate cohort or population-level outcomes. Lung cancer states are defined according to underlying disease variables, test results, and clinical events. By simulating detailed clinical procedures, the LCPM can predict benefits and harms attributable to a variety of patient management practices, including annual screening programs. Under the scenario of observed smoking patterns, predicted numbers of deaths from the calibrated LCPM were within 2% of observed over all years (1975-2000). The LCPM estimated that historical tobacco control policies achieved 28.6% (25.2% in men, 30.5% in women) of the potential reduction in U.S. lung cancer deaths had smoking had been eliminated entirely. The hypothetical adoption in 1975 of annual helical CT screening of all persons aged 55-74 with at least 30 pack-years of cigarette exposure to historical tobacco control would have yielded a proportion realized of 39.0% (42.0% in men, 33.3% in women). The adoption of annual screening would have prevented less than half as many lung cancer deaths as the elimination of cigarette smoking.


The purpose of this study was to develop life tables by smoking status removing lung cancer as a cause of death. These life tables are inputs to studies that compare the effectiveness of lung cancer treatments or interventions, and provide a way to quantify time until death from causes other than lung cancer. The study combined actuarial and statistical smoothing methods, as well as data from multiple sources, to develop separate life tables by smoking status, birth cohort, by single year of age, and by sex. For current smokers, separate life tables by smoking quintiles were developed based on the average number of cigarettes smoked per day by birth cohort. The end product is the creation of six non-lung-cancer life tables for males and six tables for females: five current smoker quintiles and one for never smokers. Tables for former smokers are linear combinations of the appropriate table based on the current smoker quintile before quitting smoking and the never smoker probabilities, plus added covariates for the smoking quit age and time since quitting.


The MISCAN-lung model was designed to simulate population trends in lung cancer (LC) for comprehensive surveillance of the disease, to relate past exposure to risk factors to (observed) LC incidence and mortality, and to estimate the impact of cancer-control interventions. MISCAN-lung employs the technique of stochastic microsimulation of life histories affected by risk factors. It includes the two-stage clonal expansion model for carcinogenesis and a detailed LC progression model; the latter is specifically intended for the evaluation of screenings. This article elucidates further the principles of MISCAN-lung and describes its application to a comparative study within the CISNET Lung Working Group on the impact of tobacco control on U.S. LC mortality. MISCAN-lung yields an estimate of the number of LC deaths avoided during 1975-2000. The potential number of avoidable LC deaths, had everybody quit smoking in 1965, is 2.2 million; 750,000 deaths (30%) were avoided in the United States due to actual tobacco control interventions. The model fits in the actual tobacco-control scenario, providing credibility to the estimates of other scenarios, although considering survey-reported smoking trends alone has limitations.


Radon is a known cause of human lung cancer. Previously, the authors observed a significant positive association between mean county-level residential radon concentrations and lung cancer mortality in the Cancer Prevention Study II (CPS-II), a large prospective study of nearly 1.2 million participants recruited in 1982 by the American Cancer Society. There was also a significant positive association with mortality from chronic obstructive pulmonary disease. Because it is unclear whether radon is associated with mortality from other malignant or nonmalignant disease, the authors examined the association between radon and nonrespiratory mortality in the CPS-II. Mean county-level residential radon concentrations (mean = 53.5 (standard deviation: 38.0) Bq/m(3)) were linked to participants by their zip code at enrollment. Cox proportional hazards regression models were used to estimate adjusted hazard ratios and 95% confidence intervals for all-cause (excluding lung cancer and respiratory mortality) and cause-specific mortality associated with radon concentrations. A total of 811,961 participants in 2,754 counties were analyzed, including 265,477 deaths through 2006. There were no clear associations between radon and
nonrespiratory mortality in the CPS-II. These findings suggest that residential radon is not associated with any other mortality beyond lung cancer or chronic obstructive pulmonary disease.


The authors prospectively evaluated the association of soy food intake with lung cancer risk, overall and by tumor aggressiveness, and performed a meta-analysis of published data. Included in the analysis were 71,550 women recruited into the Shanghai Women's Health Study (Shanghai, China) in 1997-2000. Usual soy food intake was assessed at baseline and reassessed during follow-up through in-person interviews. During a mean follow-up period of 9.1 years, 370 incident lung cancer cases were identified; 340 patients were lifetime never smokers. After adjustment for potential confounders, soy food intake was inversely associated with subsequent risk of lung cancer (P(trend) = 0.004); the hazard ratio for the highest quintile of intake compared with the lowest was 0.63 (95% confidence interval: 0.44, 0.90). This inverse association appeared predominately among women with later age at menopause (P(interaction) = 0.01) and for aggressive lung cancer as defined by length of survival (<12 months vs. >/=12 months; P(heterogeneity) = 0.057). Meta-analysis of 7 studies conducted among nonsmokers found a summary relative risk of 0.59 (95% confidence interval: 0.49, 0.71) for the highest categories of soy or isoflavone intake versus the lowest. This study suggests that soy food consumption may reduce lung cancer risk in nonsmoking women, particularly for aggressive tumors, and its effect may be modified by endogenous estrogens.

Dengue


OBJECTIVE: To assess the quantity and distribution of evidence from randomised controlled trials for the treatment of the major neglected tropical diseases and to identify gaps in the evidence with network analysis. DESIGN: Systematic review and network analysis. DATA SOURCES: Cochrane Central Register of Controlled Trials and PubMed from inception to 31 August 2011. STUDY SELECTION: Randomised controlled trials that examined treatment of 16 neglected tropical diseases or complications thereof published in English, French, Spanish, Portuguese, German, or Dutch. RESULTS: We identified 971 eligible randomised trials. Leishmaniasis (184 trials, 23,039 participants) and geohelminth infections; 160 trials, 46,887 participants) were the most studied, while dracunculiasis (nine trials, 798 participants) and Buruli ulcer (five trials, 337 participants) were least studied. Relative to its global burden of disease, lymphatic filariasis had the fewest trials and participants. Only 11% of trials were industry funded. Either a single trial or trials with fewer than 100 participants comprised the randomised evidence for first or second line treatments for Buruli ulcer, human African trypanosomiasis, American trypanosomiasis, cysticercosis, rabies,
echinococcosis, New World cutaneous leishmaniasis, and each of the foodborne trematode infections. Among the 10 disease categories with more than 40 trials, five lacked sufficient head to head comparisons between first or second line treatments. CONCLUSIONS: There is considerable variation in the amount of evidence from randomised controlled trials for each of the 16 major neglected tropical diseases. Even in diseases with substantial evidence, such as leishmaniasis and geohelminth infections, some recommended treatments have limited supporting data and lack head to head comparisons.


BACKGROUND: Roughly half the world's population live in dengue-endemic countries, but no vaccine is licensed. We investigated the efficacy of a recombinant, live, attenuated tetravalent dengue vaccine. METHODS: In this observer-masked, randomised, controlled, monocentre, phase 2b, proof-of-concept trial, healthy Thai schoolchildren aged 4-11 years were randomly assigned (2:1) to receive three injections of dengue vaccine or control (rabies vaccine or placebo) at months 0, 6, and 12. Randomisation was by computer-generated permuted blocks of six and participants were assigned with an interactive response system. Participants were actively followed up until month 25. All acute febrile illnesses were investigated. Dengue viraemia was confirmed by serotype-specific RT-PCR and non-structural protein 1 ELISA. The primary objective was to assess protective efficacy against virologically confirmed, symptomatic dengue, irrespective of severity or serotype, occurring 1 month or longer after the third injection (per-protocol analysis). This trial is registered at ClinicalTrials.gov, NCT00842530. FINDINGS: 4002 participants were assigned to vaccine (n=2669) or control (n=1333). 3673 were included in the primary analysis (2452 vaccine, 1221 control). 134 cases of virologically confirmed dengue occurred during the study. Efficacy was 30.2% (95% CI -13.4 to 56.6), and differed by serotype. Dengue vaccine was well tolerated, with no safety signals after 2 years of follow-up after the first dose. INTERPRETATION: These data show for the first time that a safe vaccine against dengue is possible. Ongoing large-scale phase 3 studies in various epidemiological settings will provide pivotal data for the CYD dengue vaccine candidate. FUNDING: Sanofi Pasteur


OBJECTIVE: To identify existing prediction models for the risk of development of type 2 diabetes and to externally validate them in a large independent cohort. DATA SOURCES: Systematic search of English, German, and Dutch literature in PubMed until February 2011 to identify prediction models for diabetes. DESIGN: Performance of the models was assessed in terms of discrimination (C statistic) and calibration (calibration plots and Hosmer-Lemeshow test). The validation study was a prospective cohort study, with a case cohort study in a random subcohort. SETTING: Models were applied to the Dutch cohort of the European Prospective Investigation into Cancer and Nutrition cohort study (EPIC-NL). PARTICIPANTS: 38,379 people aged 20-70
with no diabetes at baseline, 2506 of whom made up the random subcohort. OUTCOME MEASURE: Incident type 2 diabetes. RESULTS: The review identified 16 studies containing 25 prediction models. We considered 12 models as basic because they were based on variables that can be assessed non-invasively and 13 models as extended because they additionally included conventional biomarkers such as glucose concentration. During a median follow-up of 10.2 years there were 924 cases in the full EPIC-NL cohort and 79 in the random subcohort. The C statistic for the basic models ranged from 0.74 (95% confidence interval 0.73 to 0.75) to 0.84 (0.82 to 0.85) for risk at 7.5 years. For prediction models including biomarkers the C statistic ranged from 0.81 (0.80 to 0.83) to 0.93 (0.92 to 0.94). Most prediction models overestimated the observed risk of diabetes, particularly at higher observed risks. After adjustment for differences in incidence of diabetes, calibration improved considerably. CONCLUSIONS: Most basic prediction models can identify people at high risk of developing diabetes in a time frame of five to 10 years. Models including biomarkers classified cases slightly better than basic ones. Most models overestimated the actual risk of diabetes. Existing prediction models therefore perform well to identify those at high risk, but cannot sufficiently quantify actual risk of future diabetes.


OBJECTIVE: To investigate the risks of adverse pregnancy and birth outcomes for treated and untreated bipolar disorder during pregnancy. DESIGN: Population based cohort study using data from national health registers. SETTING: Sweden. PARTICIPANTS: 332,137 women with a last menstrual period anytime after 1 July 2005 and giving birth anytime before the end of 31 December 2009. Women with a record of at least two bipolar diagnoses were identified and grouped as treated (n = 320)-those who had filled a prescription for mood stabilisers (lithium, antipsychotics, or anticonvulsants) during pregnancy-or untreated (n = 554). Both groups were compared with all other women giving birth (n = 331,263). MAIN OUTCOME MEASURES: Preterm birth, mode of labour initiation, gestational diabetes, infants born small or large for gestational age, neonatal morbidity, and congenital malformations. RESULTS: Of the untreated women, 30.9% (n = 171) were induced or had a planned caesarean delivery compared with 20.7% (n = 68,533) without bipolar disorder (odds ratio 1.57, 95% confidence interval 1.30 to 1.90). The corresponding values for the treated women were 37.5% (n = 120) (2.12, 1.68 to 2.67). The risks of preterm birth in both treated and untreated women were increased by 50%. Of the untreated women, 3.9% (n = 542) had a microcephalic infant compared with 2.3% (324,844) of the women without bipolar disorder (1.68, 1.07 to 2.62). The corresponding values for the treated women were 3.3% (n = 311) (1.26, 0.67 to 2.37). Similar trends were observed for risks of infants being small for gestational age infants for weight and length. Among infants of untreated women, 4.3% (n = 24) had neonatal hypoglycaemia compared with 2.5% (n=8302) among infants of women without bipolar disorder (1.51, 1.04 to 2.43), and 3.4% (n = 11) of the treated women (1.18, 0.64 to 2.16). The analyses of variation in outcomes did not support any significant differences between treated and untreated women. CONCLUSIONS: Bipolar disorder in women during pregnancy, whether treated or not, was associated with increased risks of adverse pregnancy outcomes.


BACKGROUND: In some randomized trials comparing revascularization strategies for patients with diabetes, coronary-artery bypass grafting (CABG) has had a better outcome than percutaneous coronary intervention (PCI). We sought to discover whether aggressive medical therapy and the use of drug-eluting stents could alter the revascularization approach for patients with diabetes and multivessel coronary artery disease. METHODS: In this randomized trial, we assigned patients with diabetes and multivessel coronary artery disease to undergo either PCI with drug-eluting stents or CABG. The patients were followed for a minimum of 2 years (median among survivors, 3.8 years). All patients were prescribed currently recommended medical therapies for the control of low-density lipoprotein cholesterol, systolic blood pressure, and glycated hemoglobin. The primary outcome measure was a composite of death from any cause, nonfatal myocardial infarction, or nonfatal stroke. RESULTS: From 2005 through 2010, we enrolled 1900 patients at 140 international centers. The patients’ mean age was 63.1+/−9.1 years, 29% were women, and 83% had three-vessel disease. The primary outcome occurred more frequently in the PCI group (P<0.005), with 5-year rates of 26.6% in the PCI group and 18.7% in the CABG group. The benefit of CABG was driven by differences in rates of both myocardial infarction (P<0.001) and death from any cause (P=0.049). Stroke was more frequent in the CABG group, with 5-year rates of 2.4% in the PCI group and 5.2% in the CABG group (P=0.03). CONCLUSIONS: For patients with diabetes and advanced coronary artery disease, CABG was superior to PCI in that it significantly reduced rates of death and myocardial infarction, with a higher rate of stroke. ( Funded by the National Heart, Lung, and Blood Institute and others; FREEDOM ClinicalTrials.gov number, NCT00086450.)


Independent effects of changes in biologic risk factors on type 2 diabetes incidence remain unclear. The authors examined whether associations between changes in biologic risk factors and diabetes risk are driven by initial or attained risk factor levels. Biologic risk factors were measured at baseline and at each 5-year interval follow-up (rounds 2, 3, and 4) among 4,204 initially healthy men and women, aged 20-59 years, participating in the Dutch Doetinchem Cohort Study (1987-2007). Time-dependent Cox regression analyses were used to analyze associations between changes in waist circumference, blood pressure, and high density lipoprotein cholesterol (HDL cholesterol) and incident diabetes, adjusted for initial or attained levels; 130 diabetes cases occurred during 9 years of follow-up. Five-year increases in waist circumference and blood pressure and decreases in HDL cholesterol were positively associated with risk of diabetes after adjustment for initial levels but no longer after adjustment for attained levels: waist circumference (hazard ratio (HR) = 0.86, 95% confidence interval (CI): 0.69, 1.07), systolic blood pressure (HR = 0.96, 95% CI: 0.84, 1.10), diastolic blood pressure (HR = 0.96, 95% CI: 0.87, 1.06), and HDL cholesterol (HR = 0.91, 95% CI: 0.81, 1.01). In conclusion, the associations between changes in
biologic risk factors and risk of diabetes are mainly driven by the attained levels. Hence, not the prior changes, but the attained levels seem to be of importance with regard to diabetes risk


BACKGROUND: Type 2 diabetes (T2D) is associated with increased risk of morbidity and premature mortality. Among those at high risk, incidence can be halved through healthy changes in behaviour. Information about genetic and phenotypic risk of T2D is now widely available. Whether such information motivates behaviour change is unknown. We aim to assess the effects of communicating genetic and phenotypic risk of T2D on risk-reducing health behaviours, anxiety, and other cognitive and emotional theory-based antecedents of behaviour change. METHODS: In a parallel group, open randomised controlled trial, approximately 580 adults born between 1950 and 1975 will be recruited from the on-going population-based, observational Fenland Study (Cambridgeshire, UK). Eligible participants will have undergone clinical, anthropometric, and psychosocial measurements, been genotyped for 23 single-nucleotide polymorphisms associated with T2D, and worn a combined heart rate monitor and accelerometer (Actiheart(R)) continuously for six days and nights to assess physical activity. Participants are randomised to receive either standard lifestyle advice alone (control group), or in combination with a genetic or a phenotypic risk estimate for T2D (intervention groups). The primary outcome is objectively measured physical activity. Secondary outcomes include self-reported diet, self-reported weight, intention to be physically active and to engage in a healthy diet, anxiety, diabetes-related worry, self-rated health, and other cognitive and emotional outcomes. Follow-up occurs eight weeks post-intervention. Values at follow-up, adjusted for baseline, will be compared between randomised groups. DISCUSSION: This study will provide much needed evidence on the effects of providing information about the genetic and phenotypic risk of T2D. Importantly, it will be among the first to examine the impact of genetic risk information using a randomised controlled trial design, a population-based sample, and an objectively measured behavioural outcome. Results of this trial, along with recent evidence syntheses of similar studies, should inform policy concerning the availability and use of genetic risk information


CONTEXT: The frequency of remission of type 2 diabetes achievable with lifestyle intervention is unclear. OBJECTIVE: To examine the association of a long-term intensive weight-loss intervention with the frequency of remission from type 2 diabetes to prediabetes or normoglycemia. DESIGN, SETTING, AND PARTICIPANTS: Ancillary observational analysis of a 4-year randomized controlled trial (baseline visit, August 2001-April 2004; last follow-up, April 2008) comparing an intensive lifestyle intervention (ILI) with a diabetes support and education control condition (DSE) among 4503 US adults with body mass index of 25 or higher and type 2 diabetes. INTERVENTIONS: Participants were randomly assigned to receive the ILI, which included weekly group and individual counseling in the first 6 months followed by 3 sessions per month for the second 6 months and twice-monthly contact and regular refresher group series and campaigns in years 2 to 4 (n=2241) or the DSE, which was an offer of 3 group sessions per year on diet, physical activity, and social support (n=2262). MAIN OUTCOME MEASURES: Partial or complete remission of diabetes, defined as transition from meeting diabetes criteria to a prediabetes or non diabetic level of glycemia (fasting plasma glucose <126 mg/dL and hemoglobin A1c <6.5% with no antihyperglycemic medication). RESULTS Intensive lifestyle intervention participants lost significantly more weight than DSE participants at year 1 (net difference, -7.9%;
95% CI, -8.3% to -7.6%) and at year 4 (-3.9%; 95% CI, -4.4% to -3.5%) and had greater fitness increases at year 1 (net difference, 15.4%; 95% CI, 13.7%-17.0%) and at year 4 (6.4%; 95% CI, 4.7%-8.1%) (P < .001 for each). The ILI group was significantly more likely to experience any remission (partial or complete), with prevalences of 11.5% (95% CI, 10.1%-12.8%) during the first year and 7.3% (95% CI, 6.2%-8.4%) at year 4, compared with 2.0% for the DSE group at both time points (95% CIs, 1.4%-2.6% at year 1 and 1.5%-2.7% at year 4) (P < .001 for each). Among ILI participants, 9.2% (95% CI, 7.9%-10.4%), 6.4% (95% CI, 5.3%-7.4%), and 3.5% (95% CI, 2.7%-4.3%) had continuous, sustained remission for at least 2, at least 3, and 4 years, respectively, compared with less than 2% of DSE participants (1.7% [95% CI, 1.2%-2.3%] for at least 2 years; 1.3% [95% CI, 0.8%-1.7%] for at least 3 years; and 0.5% [95% CI, 0.2%-0.8%] for 4 years). CONCLUSIONS: In these exploratory analyses of overweight adults, an intensive lifestyle intervention was associated with a greater likelihood of partial remission of type 2 diabetes compared with diabetes support and education. However, the absolute remission rates were modest. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00017953


This study evaluated the association of arsenic exposure, as measured in urine, with diabetes prevalence, glycated hemoglobin, and insulin resistance in American Indian adults from Arizona, Oklahoma, and North and South Dakota (1989-1991). We studied 3,925 men and women 45-74 years of age with available urine arsenic measures. Diabetes was defined as a fasting glucose level of 126 mg/dL or higher, a 2-hour glucose level of 200 mg/dL or higher, a hemoglobin A1c (HbA1c) of 6.5% or higher, or diabetes treatment. Median urine arsenic concentration was 14.1 microg/L (interquartile range, 7.9-24.2). Diabetes prevalence was 49.4%. After adjustment for sociodemographic factors, diabetes risk factors, and urine creatinine, the prevalence ratio of diabetes comparing the 75th versus 25th percentiles of total arsenic concentrations was 1.14 (95% confidence interval: 1.08, 1.21). The association between arsenic and diabetes was restricted to participants with poor diabetes control (HbA1c >/=8%). Arsenic was positively associated with HbA1c levels in participants with diabetes. Arsenic was not associated with HbA1c or with insulin resistance (assessed by homeostatic model assessment to quantify insulin resistance) in participants without diabetes. Urine arsenic was associated with diabetes control in a population from rural communities in the United States with a high burden of diabetes. Prospective studies that evaluate the direction of the relation between poor diabetes control and arsenic exposure are needed.


BACKGROUND: Error in self-reported measures of obesity has been frequently described, but the effect of self-reported error on recruitment into diabetes prevention programs is not well established. The aim of this study was to examine the effect of using self-reported obesity data from the Finnish diabetes risk score (FINDRISC) on recruitment into the Greater Green Triangle Diabetes Prevention Project (GTT DPP). METHODS: The GGT DPP was a structured group-based lifestyle modification program delivered in primary health care settings in South-Eastern Australia. Between 2004-05, 850 FINDRISC forms were collected during recruitment for the GGT
DPP. Eligible individuals, at moderate to high risk of developing diabetes, were invited to undertake baseline tests, including anthropometric measurements performed by specially trained nurses. In addition to errors in calculating total risk scores, accuracy of self-reported data (height, weight, waist circumference (WC) and Body Mass Index (BMI)) from FINDRISCs was compared with baseline data, with impact on participation eligibility presented. RESULTS: Overall, calculation errors impacted on eligibility in 18 cases (2.1%). Of n = 279 GGT DPP participants with measured data, errors (total score calculation, BMI or WC) in self-report were found in n = 90 (32.3%). These errors were equally likely to result in under- or over-reported risk. Under-reporting was more common in those reporting lower risk scores (Spearman-rho = -0.226, p-value < 0.001). However, underestimation resulted in only 6% of individuals at high risk of diabetes being incorrectly categorised as moderate or low risk of diabetes. CONCLUSIONS: Overall FINDRISC was found to be an effective tool to screen and recruit participants at moderate to high risk of diabetes, accurately categorising levels of overweight and obesity using self-report data. The results could be generalisable to other diabetes prevention programs using screening tools which include self-reported levels of obesity


BACKGROUND: Noncommunicable diseases are an increasing health concern worldwide, but particularly in low- and middle-income countries. This study quantified and compared education- and wealth-based inequalities in the prevalence of five noncommunicable diseases (angina, arthritis, asthma, depression and diabetes) and comorbidity in low- and middle-income country groups. METHODS: Using 2002-04 World Health Survey data from 41 low- and middle-income countries, the prevalence estimates of angina, arthritis, asthma, depression, diabetes and comorbidity in adults aged 18 years or above are presented for wealth quintiles and five education levels, by sex and country income group. Symptom-based classification was used to determine angina, arthritis, asthma and depression rates, and diabetes diagnoses were self-reported. Socioeconomic inequalities according to wealth and education were measured absolutely, using the slope index of inequality, and relatively, using the relative index of inequality. RESULTS: Wealth and education inequalities were more pronounced in the low-income country group than the middle-income country group. Both wealth and education were inversely associated with angina, arthritis, asthma, depression and comorbidity prevalence, with strongest inequalities reported for angina, asthma and comorbidity. Diabetes prevalence was positively associated with wealth and, to a lesser extent, education. Adjustments for confounding variables tended to decrease the magnitude of the inequality. CONCLUSIONS: Noncommunicable diseases are not necessarily diseases of the wealthy, and showed unequal distribution across socioeconomic groups in low- and middle-income country groups. Disaggregated research is warranted to assess the impact of individual noncommunicable diseases according to socioeconomic indicators


(18) **JEFFREY RR.** *A multidisciplinary meeting on revascularisation in patients with diabetes and angina would be helpful.* BMJ. 2012, vol. 345, p.e6739


**BACKGROUND:** While strong and consistent evidence supports the role of lifestyle modification in the prevention and management of type 2 diabetes (T2DM), the best strategies for program implementation to support lifestyle modification within primary care remain to be determined. The objective of the study is to evaluate the implementation of an evidence-based self-management program for patients with T2DM within a newly established primary care network (PCN) environment. **METHOD:** Using a non-randomized design, participants (total N = 110 per group) will be consecutively allocated in bi-monthly blocks to either a 6-month self-management program lead by an Exercise Specialist or to usual care. Our primary outcome is self-reported physical activity and pedometer steps. **DISCUSSION:** The present study will assess whether a diabetes self-management program lead by an Exercise Specialist provided within a newly emerging model of primary care and linked to available community-based resources, can lead to positive changes in self-management behaviours for adults with T2DM. Ultimately, our work will serve as a platform upon which an emerging model of primary care can incorporate effective and efficient chronic disease management practices that are sustainable through partnerships with local community partners. **CLINICAL TRIALS REGISTRATION:** ClinicalTrials.gov identifier: NCT00991380


**BACKGROUND:** We describe the design and present the results of the first year of a population-based study of screening for type 2 diabetes in individuals at high risk of developing the disease. High risk is defined as having abdominal obesity. **METHODS:** Between 2006 and 2007, 79,142 inhabitants of two Dutch municipalities aged 40-74 years were approached to participate in screening. Eligible participants had a self-reported waist circumference of >/= 80 cm for women and >/= 94 cm for men, and no known pre-existing diabetes. Of the respondents (n = 20,578; response rate 26%), 16,135 were abdominally obese. In total, 10,609 individuals gave written informed consent for participation and were randomized into either the screening (n = 5305) or the control arm (n = 5304). Participants in the screening arm were invited to have their fasting plasma glucose (FPG) measured and were referred to their general practitioner (GP) if it was >/= 6.1 mmol/L. In addition, blood lipids were determined in the screening arm, because abdominal obesity is often associated with cardiovascular risk factors. Participants in both arms received written healthy lifestyle information. Between-group differences were analyzed with Chi-square tests and logistic regression (categorical variables) and unpaired t-tests (continuous variables). **RESULTS:** The screening attendance rate was 84.1%. Attending screening was associated with age at randomization (OR = 1.03, 95% CI 1.02-1.04), being married (OR = 1.57, 95% CI 1.33-1.83) and not-smoking currently (OR = 0.52, 95% CI 0.44-0.62). Of the individuals screened, 5.6% had hyperglycemia, and a further 11.6% had an estimated absolute cardiovascular disease risk of 5% or higher, according to the Systematic Coronary Risk Evaluation risk model. These participants were referred to their GP. **CONCLUSIONS:** Self-reported home-assessed waist circumference could feasibly detect persons at high risk of hyperglycemia or cardiovascular disease. Continuation of the large-scale RCT is warranted to test the hypothesis that targeted...
population-based screening for type 2 diabetes leads to a significant reduction in cardiovascular morbidity and mortality. TRIAL REGISTRATION: ISRCTN75983009

(21) KMIETOWICZ Z. Countries that use large amounts of high fructose corn syrup have higher rates of type 2 diabetes. BMJ. 2012, vol. 345, e7994


BACKGROUND: The Austrian diabetes disease management program (DMP) was introduced in 2007 in order to improve health care delivery for diabetics via the promotion of treatment according to guidelines. Considering the current low participation rates in the DMP and the question of further promotion of the program, it is of particular interest for health insurance providers in Austria to assess whether enrollment in the DMP leads to differences in the pattern of the provision of in- and outpatient services, as well as to the subsequent costs in order to determine overall program efficiency. METHODS: Historic cohort study comparing average annual levels of in- and outpatient health services utilization and its associated costs for patients enrolled and not enrolled in the DMP before (2006) and 2 years after (2009) the implementation of the program in Austria. Data on the use of services and data on costs were extracted from the records of the Austrian Social Insurance Institution for Business. 12,199 persons were identified as diabetes patients treated with anti-diabetic medication or anti-diabetics with insulin throughout the study period. 314 diabetics were enrolled in the DMP. RESULTS: Patients enrolled in the diabetes DMP received a more evolved pattern of outpatient care, featuring higher numbers of services provided by general practitioners and specialists (79 vs. 62), more diagnostic services (22 vs. 15) as well as more services provided by outpatient care centers (9 vs. 6) in line with increased levels of participation in medical assessments as recommended by the treatment guideline in 2009. Hospitalization was lower for DMP patients spending 3.75 days in hospital, as compared to 6.03 days for diabetes patients in regular treatment. Overall, increases in costs of care and medication throughout the study period were lower for enrolled patients (euro 718 vs. euro 1.684), resulting in overall costs of euro 5,393 p.c. for DMP patients and euro 6,416 p.c. for the control group in 2009. CONCLUSIONS: Seen from a health insurance provider's perspective, the assessment of the Austrian diabetes DMP shows promising results indicating improved quality of outpatient care as well as overall cost advantages due to the lower hospitalization rates. Due to methodological limitations of the retrospective study and to the restricted data access, further promotion of the DMP must be accompanied by prospective research and preferably controlled trials in order to
provide a solid basis for the decision of whether to include diabetes DMP into the insurer's basic benefit package


BACKGROUND: To assess the coverage of individual-based primary prevention strategies for cardiovascular disease (CVD) in Cambodia and Mongolia: specifically the early identification of hypertension and diabetes mellitus, major proximate physiological CVD risk factors, and management with pharmaceutical and lifestyle advice interventions. METHODS: Analysis of data collected in national cross-sectional STEPS surveys in 2009 (Mongolia) and 2010 (Cambodia) involving participants aged 25-64 years: 5433 in Cambodia and 4539 in Mongolia. RESULTS: Mongolia has higher prevalence of CVD risk factors than Cambodia—hypertension (36.5% versus 12.3%), diabetes (6.3% versus 3.1%), hypercholesterolemia (8.5% versus 3.2%), and overweight (52.5% versus 15.5%). The difference in tobacco smoking was less notable (32.1% versus 29.4%). Coverage with prior testing for blood glucose in the priority age group 35-64 years remains limited (16.5% in Cambodia and 21.7% in Mongolia). Coverage is higher for hypertension. A large burden of both hypertension and diabetes remains unidentified at current strategies for early identification: only 45.4% (Cambodia) to 65.8% (Mongolia) of all hypertensives and 22.8% (Mongolia) to 50.3% (Cambodia) of all diabetics in the age group 35-64 years had been previously diagnosed. Approximately half of all hypertensives and of all diabetics in both countries were untreated. 7.2% and 12.2% of total hypertensive population and 5.9% and 16.1% of total diabetic population in Cambodia and Mongolia, respectively, were untreated despite being previously diagnosed. Only 24.1% and 28.6% of all hypertensives and 15.9% and 23.9% of all diabetics in Mongolia and Cambodia, respectively were adequately controlled. Estimates suggest deficits in delivery of important advice for lifestyle interventions. CONCLUSIONS: Multifaceted strategies are required to improve early identification, initiation of treatment and improving quality of treatment for common CVD risk factors. Periodic population-based surveys including questions on medical and treatment history and the context of testing and treatment can facilitate monitoring of individual-based prevention strategies


Prioritization of obesity prevention and management policy is based on one's understanding of the health risks associated with increasing body weight. However, there is evidence that the magnitude of these health risks may be changing over time. Here, the authors analyze the theoretical drivers of these changes and then examine whether there is empirical evidence to support the theory. They conclude that, although the mortality risks associated with increasing body weight may be decreasing over time, the overall health burden appears likely to increase


The objective of this study was to assess the validity of prevalent and incident self-reported diabetes compared with multiple reference definitions and to assess the reliability (repeatability) of a self-reported diagnosis of diabetes. Data from 10,321 participants in the Atherosclerosis Risk in Communities (ARIC) Study who attended visit 4 (1996-1998) were analyzed. Prevalent self-reported diabetes was compared with reference definitions defined by fasting glucose and medication use obtained at visit 4. Incident self-reported diabetes was assessed during annual follow-up telephone calls and was compared with reference definitions defined by fasting glucose, hemoglobin A1c, and medication use obtained during an in-person visit attended by a subsample of participants (n = 1,738) in 2004-2005. The sensitivity of prevalent self-reported diabetes ranged from 58.5% to 70.8%, and specificity ranged from 95.6% to 96.8%, depending on the reference definition. Similarly, the sensitivity of incident self-reported diabetes ranged from 55.9% to 80.4%, and specificity ranged from 84.5% to 90.6%. Percent positive agreement of self-reported diabetes during 9 years of repeat assessments ranged from 92.7% to 95.4%. Both prevalent self-reported diabetes and incident self-reported diabetes were 84%-97% specific and 55%-80% sensitive as compared with reference definitions using glucose and medication criteria. Self-reported diabetes was >92% reliable over time.


Perfluorooctanoic acid (PFOA) is persistent in the human body; the general population has serum levels of approximately 4 ng/mL. It causes tumors of the liver, pancreas, and testicles in rodents. The authors studied the mortality of 5,791 workers exposed to PFOA at a DuPont chemical plant in West Virginia, using a newly developed job exposure matrix based on serum data for 1,308 workers from 1979-2004. The estimated average serum PFOA level was 350 ng/mL. The authors used 2 referent groups: other DuPont workers in the region and the US population. In comparison with other DuPont workers, cause-specific mortality was elevated for mesothelioma (standardized mortality ratio (SMR) = 2.85, 95% confidence interval (CI): 1.05, 6.20), diabetes mellitus (SMR = 1.90, 95% CI: 1.35, 2.61), and chronic renal disease (SMR = 3.11, 95% CI: 1.66, 5.32). Significant positive exposure-response trends occurred for both malignant and nonmalignant renal disease (12 and 13 deaths, respectively). PFOA is concentrated in the kidneys of rodents, and there are prior findings of elevated kidney cancer in this cohort. Multiple-cause mortality analyses tended to support the results of underlying-cause analyses. No exposure-response trend was seen for diabetes or heart disease mortality. In conclusion, the authors found evidence of positive exposure-response trends for malignant and nonmalignant renal disease. These results were limited by small numbers and restriction to mortality data, which are of limited relevance for several nonfatal outcomes of a priori interest.

(33) STEYN NP, TEMPLE NJ. **Evidence to support a food-based dietary guideline on sugar consumption in South Africa.** BMC Public Health. 2012, vol. 12, p.502

BACKGROUND: To review studies undertaken in South Africa (SA) which included sugar intake associated with dental caries, non-communicable diseases, diabetes, obesity and/or micronutrient...
dilution, since the food-based dietary guideline: "Use foods and drinks that contain sugar sparingly and not between meals" was promulgated by the Department of Health (DOH) in 2002. METHODS: Three databases (PubMed, Cochrane Library, and ScienceDirect), and SA Journal of Clinical Nutrition (SAJCN), DOH and SA Medical Research Council (SAMRC) websites were searched for SA studies on sugar intake published between 2000 and January 2012. Studies were included in the review if they evaluated the following: sugar intake and dental caries; sugar intake and non-communicable diseases; sugar and diabetes; sugar and obesity and/or sugar and micronutrient dilution. RESULTS: The initial search led to 12 articles in PubMed, 0 in Cochrane, 35 in ScienceDirect, 5 in the SAJCN and 3 reports from DOH/SAMRC. However, after reading the abstracts only 7 articles from PubMed, 4 from SAJCN and 3 reports were retained for use as being relevant to the current review. Hand searching of reference lists of SAJCN articles produced two more articles. Intake of sugar appears to be increasing steadily across the South African (SA) population. Children typically consume about 50 g per day, rising to as much as 100 g per day in adolescents. This represents about 10% of dietary energy, possibly as much as 20%. It has been firmly established that sugar plays a major role in development of dental caries. Furthermore, a few studies have shown that sugar has a diluting effect on the micronutrient content of the diet which lowers the intake of micronutrients. Data from numerous systematic reviews have shown that dietary sugar increases the risk for development of both obesity and type 2 diabetes. Risk for development of these conditions appears to be especially strong when sugar is consumed as sugar-sweetened beverages. CONCLUSION: Based on the evidence provided the current DOH food-based dietary guideline on sugar intake should remain as is.


BACKGROUND: Effective self-management of diabetes is essential for the reduction of diabetes-related complications, as global rates of diabetes escalate. METHODS: Randomised controlled trial. Adults with type 2 diabetes (n = 120), with HbA1c greater than or equal to 7.5 %, were randomly allocated (4 x 4 block randomised block design) to receive an automated, interactive telephone-delivered management intervention or usual routine care. Baseline sociodemographic, behavioural and medical history data were collected by self-administered questionnaires and biological data were obtained during hospital appointments. Health-related quality of life (HRQL) was measured using the SF-36. RESULTS: The mean age of participants was 57.4 (SD 8.3), 63% of whom were male. There were no differences in demographic, socioeconomic and behavioural variables between the study arms at baseline. Over the six-month period from baseline, participants receiving the Australian TLC (Telephone-Linked Care) Diabetes program showed a 0.8% decrease in geometric mean HbA(1c) from 8.7% to 7.9%, compared with a 0.2% HbA(1c) reduction (8.9% to 8.7%) in the usual care arm (p = 0.002). There was also a significant improvement in mental HRQL, with a mean increase of 1.9 in the intervention arm, while the usual care arm decreased by 0.8 (p = 0.007). No significant improvements in physical HRQL were observed. CONCLUSIONS: These analyses indicate the efficacy of the Australian TLC Diabetes program with clinically significant post-intervention improvements in both glycaemic control and mental HRQL. These observed improvements, if supported and maintained by an ongoing...
program such as this, could significantly reduce diabetes-related complications in the longer term. Given the accessibility and feasibility of this kind of program, it has strong potential for providing effective, ongoing support to many individuals with diabetes in the future.


Dépression


BACKGROUND: This study examines exposure to perceived discrimination and its association with depression among low-income, Latina male-to-female transgender women as well as evaluates the impact of sexual partner violence and mistreatment on depression. METHODS: A total of 220 Latina male-to-female transgender women who resided in Los Angeles, California, were recruited through community based organizations and referrals. Participants completed individual interviews using a structured questionnaire. Depressive symptoms were assessed using the Patient Health Questionnaire (PHQ-9). Perceived discrimination was assessed using a fifteen-item measure that was designed to assess the experiences of maltreatment of transgender individuals. Multinomial logistic regression was used to examine the association between perceived discrimination and depression after controlling for the presence of other variables. RESULTS: Of the sample, 35% reported significant depressive symptoms (PHQ-9 >/= 15). Additionally, one-third of the participants indicated that in the two weeks prior to the interviews they had thought either of hurting themselves or that they would be better off dead. The extent of perceived discrimination in this population was extensive. Many of the participants experienced discrimination on a daily basis (14%) or at least once or twice a week (25%) as demonstrated by a positive response to at least 7 of 15 items in the measure of perceived discrimination. Almost six out of ten participants admitted that they had been victims of sexual partner violence. Those who reported more frequent discrimination were more likely to be identified with severe depression. There was also a notable association between self-reported history of sexual partner violence and depression severity. CONCLUSIONS: A significant association between depression severity and perceived discrimination was identified. How exposure to discrimination leads to increased risk of mental health problems needs additional investigation. Models investigating the association between perceived discrimination and depression among transgender women should include sexual partner violence as a potential confounding variable.


OBJECTIVES: We examined the association between discrimination and mental health distress,
focusing specifically on the relative importance of discrimination because of particular demographic domains (i.e., race/ethnicity, socioeconomic position [SEP]). METHODS: The research team surveyed a sample of gay and bisexual men (n = 294) at a community event in New York City. Participants completed a survey on demographics, discrimination experiences in the past 12 months, attributed domains of discrimination, and mental health distress. RESULTS: In adjusted models, discrimination was associated with higher depressive (B = 0.31; P < .01) and anxious (B = 0.29; P < .01) symptoms. A statistically significant quadratic term (discrimination-squared; P < .01) fit both models, such that moderate levels of discrimination were most robustly associated with poorer mental health. Discrimination because of SEP was associated with higher discrimination scores and was predictive of higher depressive (B = 0.22; P < .01) and anxious (B = 0.50; P < .01) symptoms. No other statistically significant relationship was found between discrimination domains and distress. CONCLUSIONS: In this sample, SEP emerged as the most important domain of discrimination in its association with mental health distress. Future research should consider intersecting domains of discrimination to better understand social disparities in mental health.


BACKGROUND: Noncommunicable diseases are an increasing health concern worldwide, but particularly in low- and middle-income countries. This study quantified and compared education- and wealth-based inequalities in the prevalence of five noncommunicable diseases (angina, arthritis, asthma, depression and diabetes) and comorbidity in low- and middle-income country groups. METHODS: Using 2002-04 World Health Survey data from 41 low- and middle-income countries, the prevalence estimates of angina, arthritis, asthma, depression, diabetes and comorbidity in adults aged 18 years or above are presented for wealth quintiles and five education levels, by sex and country income group. Symptom-based classification was used to determine angina, arthritis, asthma and depression rates, and diabetes diagnoses were self-reported. Socioeconomic inequalities according to wealth and education were measured absolutely, using the slope index of inequality, and relatively, using the relative index of inequality. RESULTS: Wealth and education inequalities were more pronounced in the low-income country group than the middle-income country group. Both wealth and education were inversely associated with angina, arthritis, asthma, depression and comorbidity prevalence, with strongest inequalities reported for angina, asthma and comorbidity. Diabetes prevalence was positively associated with wealth and, to a lesser extent, education. Adjustments for confounding variables tended to decrease the magnitude of the inequality. CONCLUSIONS: Noncommunicable diseases are not necessarily diseases of the wealthy, and showed unequal distribution across socioeconomic groups in low- and middle-income country groups. Disaggregated research is warranted to assess the impact of individual noncommunicable diseases according to socioeconomic indicators.


The daily solar cycle allows organisms to synchronize their circadian rhythms and sleep-wake cycles to the correct temporal niche. Changes in day-length, shift-work, and transmeridian travel lead to mood alterations and cognitive function deficits. Sleep deprivation and circadian disruption underlie mood and cognitive disorders associated with irregular light schedules. Whether irregular
Light schedules directly affect mood and cognitive functions in the context of normal sleep and circadian rhythms remains unclear. Here we show, using an aberrant light cycle that neither changes the amount and architecture of sleep nor causes changes in the circadian timing system, that light directly regulates mood-related behaviours and cognitive functions in mice. Animals exposed to the aberrant light cycle maintain daily corticosterone rhythms, but the overall levels of corticosterone are increased. Despite normal circadian and sleep structures, these animals show increased depression-like behaviours and impaired hippocampal long-term potentiation and learning. Administration of the antidepressant drugs fluoxetine or desipramine restores learning in mice exposed to the aberrant light cycle, suggesting that the mood deficit precedes the learning impairments. To determine the retinal circuits underlying this impairment of mood and learning, we examined the behavioural consequences of this light cycle in animals that lack intrinsically photosensitive retinal ganglion cells. In these animals, the aberrant light cycle does not impair mood and learning, despite the presence of the conventional retinal ganglion cells and the ability of these animals to detect light for image formation. These findings demonstrate the ability of light to influence cognitive and mood functions directly through intrinsically photosensitive retinal ganglion cells.


BACKGROUND: The degree to which parental alcohol abuse is a risk factor for offspring mental distress is unclear, due to conflicting results of previous research. The inconsistencies in previous findings may be related to sample characteristics and lack of control of confounding or moderating factors. One such factor may be the gender of the abusing parent. Also, other factors, such as parental mental health, divorce, adolescent social network, school functioning or self-esteem, may impact the outcome. This study examines the impact of maternal and paternal alcohol abuse on adolescent mental distress, including potentially confounding, mediating or moderating effects of various variables. METHODS: Data from the Nord-Trondelag Health Study (HUNT), a Norwegian population based health survey, from 4012 offspring and their parents were analyzed. Parental alcohol abuse was measured by numerical consumption indicators and CAGE, whereas offspring mental distress was measured by SCL-5, an abbreviated instrument tapping symptoms of anxiety and depression. Statistical method was analysis of variance. RESULTS: Maternal alcohol abuse was related to offspring mental distress, whereas no effect could be shown of paternal alcohol abuse. Effects of maternal alcohol abuse was partly mediated by parental mental distress, offspring social network and school functioning. However, all effects were relatively small. CONCLUSIONS: The results indicate graver consequences for offspring of alcohol abusing mothers compared to offspring of alcohol abusing fathers. However, small effect sizes suggest that adolescent offspring of alcohol abusing parents in general manage quite well.


OBJECTIVES: We examined long-term patterns of household food insecurity in children from kindergarten through eighth grade and the association between those patterns and children's proxy-reported health status in eighth grade. METHODS: We obtained data from the Early Childhood Longitudinal Study-Kindergarten Cohort, a study that followed a nationally representative sample of students from kindergarten entry in 1998-1999 through eighth grade. We classified food insecurity according to the number of years of reported household food insecurity over 4 observation years. We estimated logistic regression models to estimate the association between cumulative food insecurity exposure and health outcomes. RESULTS: Food insecurity was generally a transient rather than a persistent condition. Persistent food insecurity over the 9-
year period was associated with lower health status in eighth grade, whereas more transient food insecurity was not significantly associated with health outcomes in most models. CONCLUSIONS: Single-year estimates substantially underestimate the share of children whose households experienced food insecurity at some point during their childhood years. Persistent food insecurity is an important public health issue for children. Policy interventions to alleviate children's persistent food insecurity may promote child health


OBJECTIVE: To compare the effectiveness of classroom based cognitive behavioural therapy with attention control and usual school provision for adolescents at high risk of depression. DESIGN: Three arm parallel cluster randomised controlled trial. SETTING: Eight UK secondary schools. PARTICIPANTS: Adolescents (n=5030) aged 12-16 years in school year groups 8-11. Year groups were randomly assigned on a 1:1:1 ratio to cognitive behavioural therapy, attention control, or usual school provision. Allocation was balanced by school, year, number of students and classes, frequency of lessons, and timetabling. Participants were not blinded to treatment allocation. INTERVENTIONS: Cognitive behavioural therapy, attention control, and usual school provision provided in classes to all eligible participants. MAIN OUTCOME MEASURES: Outcomes were collected by self completed questionnaire administered by researchers. The primary outcome was symptoms of depression assessed at 12 months by the short mood and feelings questionnaire among those identified at baseline as being at high risk of depression. Secondary outcomes included negative thinking, self worth, and anxiety. Analyses were undertaken on an intention to treat basis and accounted for the clustered nature of the design. RESULTS: 1064 (21.2%) adolescents were identified at high risk of depression: 392 in the classroom based cognitive behavioural therapy arm, 374 in the attention control arm, and 298 in the usual school provision arm. At 12 months adjusted mean scores on the short mood and feelings questionnaire did not differ for cognitive behavioural therapy versus attention control (-0.63, 95% confidence interval -1.85 to 0.58, P=0.41) or for cognitive behavioural therapy versus usual school provision (0.97, -0.20 to 2.15, P=0.12). CONCLUSION: In adolescents with depressive symptoms, outcomes were similar for attention control, usual school provision, and cognitive behavioural therapy. Classroom based cognitive behavioural therapy programmes may result in increased self awareness and reporting of depressive symptoms but should not be undertaken without further evaluation and research. TRIAL REGISTRATION: Current Controlled Trials ISRCTN19083628


OBJECTIVES: We addressed whether repeated job strain and low work social support increase the risk of major depressive disorder (MDD). METHODS: We used work characteristics from Karasek's Job Strain model, measured on 3 occasions over 10 years in a cohort of 7732 British civil servants, to predict subsequent onset of MDD with the Composite International Diagnostic Interview. RESULTS: Repeated job strain was associated with increased risk of MDD (odds ratio [OR] = 2.19; 95% confidence interval [CI] = 1.48, 3.26; high job strain on 2 of 3 occasions vs none) in a fully adjusted model. Repeated low work social support was associated with MDD (OR = 1.61; 95% CI = 1.10, 2.37; low work social support on 2 of 3 occasions vs none). Repeated job
strain remained associated with MDD after adjustment for earlier psychological distress. CONCLUSIONS: Demonstration of an increased association for repeated job strain adds to the evidence that job strain is a risk factor for depression. Recognition and alleviation of job strain through work reorganization and staff training could reduce depression in employees.


Loneliness has been shown to longitudinally predict subjective well-being. The authors used data from a longitudinal population-based study (2002-2006) of non-Hispanic white, African-American, and nonblack Latino-American persons born between 1935 and 1952 and living in Cook County, Illinois. They applied marginal structural models for time-varying exposures to examine the magnitude and persistence of the effects of loneliness on subjective well-being and of subjective well-being on loneliness. Their results indicate that, if interventions on loneliness were made 1 and 2 years prior to assessing final subjective well-being, then only the intervention 1 year prior would have an effect (standardized effect = -0.29). In contrast, increases in subjective well-being 1 year prior (standardized effect = -0.26) and 2 years prior (standardized effect = -0.13) to assessing final loneliness would both have an effect on an individual's final loneliness. These effects persist even after control is made for depressive symptoms, social support, and psychiatric conditions and medications as time-varying confounders. Results from this study indicate an asymmetrical and persistent feedback of fairly substantial magnitude between loneliness and subjective well-being. Mechanisms responsible for the asymmetry are discussed. Developing interventions for loneliness and subjective well-being could have substantial psychological and health benefits.


BACKGROUND: Many previous studies did not sufficiently control for several confounding factors that may affect the association between smoking and depression, such as socioeconomic status. We investigated the association between depression and smoking status, smoking exposure, duration of smoking cessation, and age of starting smoking while controlling for socioeconomic factors. METHODS: This study was based on a community health survey performed in Jeollanam-do, South Korea, between September and November 2009. In total, 20,084 subjects (9,118 males and 10,966 females) were included in the analysis. Information on smoking characteristics, such as smoking status, pack-years of smoking, and age of starting smoking, was collected using a standardized questionnaire. Depression was defined using the Korean CES-D score. RESULTS: The odds ratios (ORs) of depression were 1.35 (0.92-1.98) for former smokers and 1.77 (1.27-2.48) for current-smokers among males, and 2.67 (1.38-5.16) for former smokers and 3.72 (2.11-6.54) for current-smokers among females, after adjusting for other confounding factors. Compared to light smoking, heavy smoking was significantly associated with depression in males [OR = 3.97, 95% confidence interval (CI) = 1.42-11.14], but not in females (OR = 1.24, 95% CI = 0.73-2.09). No significant associations between depression and age of starting smoking and duration of smoking cessation were observed among former smokers. CONCLUSIONS: Our data demonstrate that smoking is strongly associated with depression, particularly among females. These findings suggest that depression prevention may need to be combined with smoking prevention and that different strategies may be needed for males and females.
Etudes sur le tabagisme

(1) Smoking is just as lethal for women. BMJ. 2012, vol. 345, p.e7277


BACKGROUND: In 2005, Uruguay initiated a series of comprehensive anti-smoking measures. We aimed to assess the effect of Uruguay's anti-tobacco campaign. METHODS: We did a population-based trend analysis, using neighbouring Argentina, which has not instituted such extensive anti-tobacco measures, as a control. We assessed three key endpoints in both countries: per-person consumption of cigarettes, as measured by tax records; the prevalence of tobacco use in adolescents, as measured by school-based surveys; and the prevalence of tobacco use in adults, as measured by nationwide household-based surveys. FINDINGS: During 2005-11, per-person consumption of cigarettes in Uruguay decreased by 4.3% per year (95% CI 2.4 to 6.2), whereas per-person consumption in Argentina increased by 0.6% per year (-1.2 to 2.5; p=0.002 for difference in trends). During 2003-09, the 30-day prevalence of tobacco use in Uruguayan students aged 13 years, 15 years, and 17 years decreased by an estimated 8.0% per year (4.5 to 11.6), compared with a decrease of 2.5% annually (0.5 to 4.5) in Argentinian students during 2001-09 (p=0.02 for difference in trends). From 2005 to 2011, the prevalence of current tobacco use in Uruguay decreased annually by an estimated 3.3% (2.4 to 4.1), compared with an annual decrease in Argentina of 1.7% (0.8 to 2.6; p=0.02 for difference in trends).

INTERPRETATION: Uruguay's comprehensive tobacco-control campaign has been associated with a substantial, unprecedented decrease in tobacco use. Decreases in tobacco use in other low-income and middle-income countries of the magnitude seen in Uruguay would have a substantial effect on the future global burden of tobacco-related diseases. FUNDING: J William Fulbright Foreign Scholarship Board and the US Department of State


We present methods for estimating five-year birth-cohort-specific trends in smoking behavior for individuals born between 1910 and 1984. We combine cross-sectional survey data on smoking behavior from the National Health Interview Surveys (NHIS) conducted between 1965 and 2001 into a single data set. The cumulative incidence of smoking by year of age and calendar year is constructed for each birth cohort from this data set and the effect of differential mortality on ever smoking prevalence is adjusted by modeling the ever smoking prevalence of each cohort for each survey year and back extrapolating that effect to age 30. Cumulative incidence is then scaled to match the ever smoking prevalence at age 30. Survival analyses generate the cumulative cessation among ever smokers across year of age and calendar year and are used to estimate current smoking prevalence. Data from Substance Abuse and Mental Health Services Administration (SAMHSA) National Survey on Drug Use and Health is used to divide those initiating smoking into quintiles of number of cigarettes smoked per day (CPD) and the mean CPD for each quintile in each calendar year is estimated from the NHIS data. For five-year birth cohorts of white, african-american, Hispanic and all race/ethnicity groupings of males and females born between 1910 and 1984, estimates are provided for prevalence of current and ever smoking, incidence of cessation, incidence of initiation, and the distribution of smoking duration and CPD for each calendar year and each single year of age through the year 1999. We believe that we are
the first to provide birth-cohort-specific estimates of smoking behaviors for the U.S. population that include distributions of duration of smoking and number of cigarettes per day. These additional elements substantively enhance the utility of these estimates for estimating lung cancer risks.


Tobacco use remains the nation's leading cause of preventable premature mortality. Lung cancer, one of the many cancers caused by tobacco use, is both the leading cause of cancer death in the United States and the leading cause of male cancer death globally. This special issue of Risk Analysis features the work of the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network (CISNET), which finds that changes in Americans' smoking behaviors that began in the mid 1950s averted nearly 800,000 U.S. lung cancer deaths in the period 1975-2000 alone. However, this figure represents only about 30% of the lung cancer deaths that could potentially have been averted during this period. Despite dramatic declines in smoking prevalence since the mid 1960s, tobacco use is still far too common; today about one in five American adults smokes cigarettes. The tobacco industry's role in promoting tobacco use is now well documented and, as noted by the President's Cancer Panel, "can no more be ignored in seeking solutions to the tobacco problem than mosquitoes can be ignored in seeking to eradicate malaria." Recent developments, including the passage of legislation granting the Food and Drug Administration broad authority to regulate tobacco products, and the entry into force of the Framework Convention on Tobacco Control, an evidence-based treaty developed by the World Health Organization, hold great promise to more swiftly end the epidemic of lung cancer and other tobacco-caused diseases that exacts such a heavy toll in human suffering in the United States and around the world.


BACKGROUND: A consortium of six research groups estimated the impact on lung cancer mortality of changes in smoking behavior that began around the publication of the Surgeon General's report (SGR). This chapter presents the results of that effort. We quantified the cumulative impact of changes in smoking behaviors on lung cancer mortality in the United States over the period 1975-2000. METHODS: The six groups used common inputs and independent models to estimate the number of U.S. lung cancer deaths averted over the period 1975-2000 as a result of changes in smoking behavior beginning in the mid fifties, and the number of deaths that could have been averted if tobacco control had completely eliminated all smoking following issuance of the first SGR on Smoking and Health in 1964. RESULTS: Approximately 795,000 deaths (550,000 men and 245,000 women) were averted over the period 1975-2000 as a result of changes in smoking behavior since in 1950s. In the year 2000 alone approximately 70,000 lung cancer deaths were averted (44,000 among men and 26,000 among women). However, these represent approximately 30% of lung cancer deaths that could have potentially been averted over the period 1975-2000 if smoking was eliminated completely. In the 10-year period 1991-2000, this fraction increased to about 37%. CONCLUSIONS: Our results show the substantial impact of changes in smoking behavior since the 1950s. Despite a major impact of changing smoking behaviors, tobacco control effort are still needed to further reduce the burden of this disease.

OBJECTIVES: We tested a series of self-help booklets designed to prevent postpartum smoking relapse. METHODS: We recruited 700 women in months 4 through 8 of pregnancy, who quit smoking for their pregnancy. We randomized the women to receive either (1) 10 Forever Free for Baby and Me (FFB) relapse prevention booklets, mailed until 8 months postpartum, or (2) 2 existing smoking cessation materials, as a usual care control (UCC). Assessments were completed at baseline and at 1, 8, and 12 months postpartum. RESULTS: We received baseline questionnaires from 504 women meeting inclusion criteria. We found a main effect for treatment at 8 months, with FFB yielding higher abstinence rates (69.6%) than UCC (58.5%). Treatment effect was moderated by annual household income and age. Among lower income women (< $30,000), treatment effects were found at 8 and 12 months postpartum, with respective abstinence rates of 72.2% and 72.1% for FFB and 53.6% and 50.5% for UCC. No effects were found for higher income women. CONCLUSIONS: Self-help booklets appeared to be efficacious and offered a low-cost modality for providing relapse-prevention assistance to low-income pregnant and postpartum women.


BACKGROUND: Tobacco dependence is a chronic, relapsing condition that typically requires multiple quit attempts and extended treatment. When offered the opportunity, relapsed smokers are interested in recycling back into treatment for a new, assisted quit attempt. This manuscript presents the results of a randomized controlled trial testing the efficacy of interactive voice response (IVR) in recycling low-income smokers who had previously used quitline (QL) support back to QL support for a new quit attempt. METHODS: A sample of 2985 previous QL callers were randomized to either receive IVR screening for current smoking (control group) or IVR screening plus an IVR intervention. The IVR intervention consists of automated questions to identify and address barriers to re-cycling in QL support, followed by an offer to be transferred to the QL and reinitiate treatment. Re-enrollment in QL services for both groups was documented. RESULTS: The IVR system successfully reached 715 (23.9%) former QL participants. Of those, 27% (194/715) reported to the IVR system that they had quit smoking and were therefore excluded from the study and analysis. The trial's final sample was composed of 521 current smokers. The re-enrollment rate was 3.3% for the control group and 28.2% for the intervention group (p < .001). Logistic regression results indicated an 11.2 times higher odds for re-enrollment of the intervention group than the control group (p < .001). Results did not vary by gender, race, ethnicity, or level of education, however recycled smokers were older (Mean = 45.2; SD = 11.7) than smokers who declined a new treatment cycle (Mean = 41.8; SD = 13.2); (p = 0.013). The main barriers reported for not engaging in a new treatment cycle were low self-efficacy and lack of interest in quitting. After delivering IVR messages targeting these reported barriers, 32% of the smokers reporting low self-efficacy and 4.8% of those reporting lack of interest in quitting re-engaged in a new QL treatment cycle. CONCLUSION: Proactive IVR outreach is a promising tool to engage low income, relapsed smokers back into a new cycle of treatment. Integration of IVR intervention for recycling smokers with previous QL treatment has the potential to decrease tobacco-related disparities. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT01260597


BACKGROUND: Cigarette/alcohol use and premarital sex, and their subsequent consequences on the well-being of college students, are international health promotion issues. However, little is known about the temporal relationship of these risk behaviors among Taiwanese college students. METHODS: This study utilizes data from the Taiwan Youth Project, a cohort sample of 20-year-
olds (N = 2,119) with a 2-year follow-up, to explore the relationship between adolescent cigarette/alcohol use, and subsequent premarital sex. To incorporate the Taiwanese context where the normative value of abstinence until marriage remains strong, multivariate logistic regression models included data on premarital sex attitudes, stressful life events, peer influence, as well as family and individual factors which might influence this relationship. RESULTS: The sample consists of 49% male and 51% female college students. About 16% of the sample report having had premarital sex by age 20. After excluding sexually active youth, 20% of males and 13% of females report engaging in premarital sex in the 2-year follow-up interview. Multivariate logistic regression analyses reveal adolescent alcohol use is significantly associated with a higher likelihood of engaging in premarital sex for both genders; adolescent smoking is significantly associated with premarital sexual activity among males, but not females. Our results indicate liberal premarital sexual attitudes and stressful personal events are also significantly associated with premarital sexual activity. CONCLUSIONS: These findings suggest health promotion programs for college students need to take developmental and gender perspectives into account. Future research to incorporate a broader, multi-cultural context into risk reduction materials is recommended.


OBJECTIVES: We explored young adults' perceptions of snus (spitless moist snuff packed in porous bags), dissolvable tobacco products, and electronic cigarettes and intention to try these products. METHODS: We conducted 11 focus group discussions involving a total of 66 young adults (18-26 years old) on these new tobacco products (e.g., harmfulness, potential as quit aids, intention to try) held between July and December 2010. We analyzed discussions using a thematic approach. RESULTS: Participants generally reported positive perceptions of the new products, particularly because they came in flavors. Few negative perceptions were reported. Although some participants believed these products were less harmful than cigarettes and helpful in quitting smoking, others thought the opposite, particularly regarding electronic cigarettes. Participants also commented that these products could be gateways to cigarette smoking. Half of the participants, including a mix of smokers and nonsmokers, admitted they would try these products if offered by a friend. CONCLUSIONS: Young adults perceive the new tobacco products positively and are willing to experiment with them. Eliminating flavors in these products may reduce young adults’ intentions to try these products.


To better understand the contribution of cigarette smoking, and its changing role in lung cancer, this article provides an introduction to a special issue of Risk Analysis, which considers the relationship between smoking and lung cancer death rates during the period 1975-2000 for U.S. men and women aged 30-84 years. Six models are employed, which are part of a consortium of lung cancer modelers funded by National Cancer Institute's Cancer Intervention and Surveillance Modeling Network (CISNET). Starting with birth-cohort-specific smoking histories derived from National Health Interview Surveys, three scenarios are modeled: Actual Tobacco Control (observed trends in smoking), Complete Tobacco Control (a counterfactual lower bound on the
smoking rates that could have been achieved had all smoking ceased after the first Surgeon General's report in 1964), and No Tobacco Control (a counterfactual upper bound on smoking rates if smoking patterns that prevailed before the first studies in the 1950s began to inform the public about the hazards of smoking). Using these three scenarios and the lung cancer models, the number and percentage of lung cancer deaths averted from 1975-2000, among all deaths that could have been averted if tobacco control efforts been immediate and perfect, can be estimated. The variability of the results across multiple models provides a measure of the robustness of the results to model assumptions and structure. The results provide not only a portrait of the achieved impact of tobacco control on lung cancer mortality, but also the bounds of what still needs to be achieved.


Many states have implemented smoke-free workplace laws to protect employees and customers from exposure to secondhand smoke. However, exemptions in these laws have allowed indoor tobacco smoking in hookah lounges to proliferate in recent years. To describe the amount of secondhand smoke in hookah lounges, we measured the indoor air quality of 10 hookah lounges in Oregon. Air quality measurements ranged from "unhealthy" to "hazardous" according to Environmental Protection Agency standards, indicating a potential health risk for patrons and employees.


The Rice-MD Anderson group uses a two-stage clonal expansion (TSCE) model of lung cancer mortality calibrated to a combination of MD Anderson case-control data on smoking histories and lung cancer mortality/incidence rate data collected from prospective cohorts in order to predict risk of lung cancer. This model is used to simulate lung cancer mortality in the U.S. population under the three scenarios of CISNET lung group's smoking base case project in order to estimate the effect of tobacco control policy on lung cancer mortality rates. Simulation results show that tobacco control policies have achieved 35% of the reduction in lung cancer mortality that would have resulted from cessation of all smoking in 1965.


Understanding patterns of shared and type-specific etiologies for colorectal polyps may provide insights into colorectal carcinogenesis. The authors present the first systematic comparison of risk factors by colorectal polyp type in a large colonoscopy-based case-control study of 3,764 polyp-free controls and 2,543 polyp patients, including 1,444 cases with adenomas only, 662 cases with hyperplastic polyps (HPPs) only, and 437 cases with synchronous HPPs and adenomas. Surveys were completed to obtain information on usual dietary intake and other lifestyle factors. Six lifestyle factors, including cigarette smoking, obesity, no regular use of nonsteroidal anti-inflammatory drugs, high intake of red meat, low intake of fiber, and low intake of calcium, were found to be independently associated with the risk of polyps. The risk of polyps increased...
progressively with an increasing number of adverse lifestyle factors. Compared with participants with no or only 1 risk factor, odds ratios for those with 5 to 6 risk factors were 2.72 (95% confidence interval: 1.94, 3.79) for adenoma only, 4.12 (95% confidence interval: 2.78, 6.09) for HPPs only, and 9.03 (95% confidence interval: 5.69, 14.34) for synchronous HPPs and adenomas. This study provides strong evidence that lifestyle modification is important for the prevention of colorectal polyps, especially advanced and multiple adenomas, which are established precursors of colorectal cancer.


Earlier menarche and irregular periods, among other markers of sex-hormone levels, have been associated with a higher risk of asthma and allergic diseases. This has suggested an etiologic role of sex hormones in the development of these conditions. The authors investigated the association of age at menarche, irregular periods, duration of menstruation, and acne with reported medical history of asthma and/or atopy (hay fever and/or eczema/urticaria) in a historical cohort of students born before the rise in asthma prevalence in the United Kingdom and attending university in 1948-1968. Finding consistent associations in a cohort that has experienced different life-course exposures and has different confounding structure can help to identify causal associations. In the Glasgow Alumni Cohort, irregular periods were associated with atopic asthma (multinomial odds ratio (MOR) = 2.79, 95% confidence interval (CI): 1.33, 5.83) and atopy alone (MOR = 1.40, 95% CI: 1.06, 1.84) but not with nonatopic asthma (MOR = 1.02, 95% CI: 0.45, 2.30), compared with students reporting no asthma and no atopy. The authors found no association with acne, a marker of high testosterone levels, that they hypothesized could point to polycystic ovary syndrome underpinning these associations. In summary, the authors found evidence for a potentially etiologic role of irregular menstruations with some specific asthma phenotypes, namely, atopic asthma and atopy, but not with nonatopic asthma.

(17) GORNALL J. How the new guardians of public health are investing heavily in tobacco companies. BMJ. 2012, vol. 345, p.e8023  


As a member of the Cancer Intervention and Surveillance Modeling Network (CISNET), the lung cancer (LC) group at Fred Hutchinson Cancer Research Center (FHCRC) developed a model for evaluating U.S. lung cancer mortality trends and the impact of changing tobacco consumption. Model components include a biologically based two-stage clonal expansion (TSCE) model; a smoking simulator to generate smoking histories and other cause mortality; and adjustments for period and birth cohort to improve calibration to U.S. LC mortality. The TSCE model was first calibrated to five substantial cohorts: British doctors, American Cancer Society CPS-I and CPS-II, Health Professionals' Follow-Up Study (HPFS), and Nurses' Health Study (NHS). The NHS and HPFS cohorts included the most detailed smoking histories and were chosen to represent the effects of smoking on U.S. LC mortality. The calibrated TSCE model and smoking simulator were used to simulate U.S. LC mortality. Further adjustments were necessary to account for unknown...
factors. This provided excellent fits between simulated and observed U.S. LC mortality for ages 30-84 and calendar years 1975-2000. The FHCRC LC model may be used to study the effects of public health information on U.S. LC trends and the impact of tobacco control policy. For example, we estimated that over 500,000 males and 200,000 females avoided LC death between 1975 and 2000 due to increasing awareness since the mid 1950s of the harmful effects of smoking. We estimated that 1.1 million male and 0.6 million female LC deaths were avoidable if smokers quit smoking in 1965.


Publication of the Surgeon General’s Report in 1964 marshaled evidence of the harm to public health caused by cigarette smoking, including lung cancer mortality, and provided an impetus for introducing control programs. The purpose of this article is to develop estimates of their effect on basic smoking exposure input parameters related to introduction of the report. Fundamental inputs used to generate exposure to cigarettes are initiation and cessation rates for men and women, as well as the distribution of the number of cigarettes smoked per day. These fundamental quantities are presented for three scenarios: actual tobacco control in the United States; no tobacco control in which the experience before 1955 was assumed to continue; and complete tobacco control in which all smoking ceased following publication of the report. These results were derived using data from National Health Interview Surveys, and they provide basic input parameters for the Smoking History Generator used by each of the lung cancer models developed by the Cancer Intervention and Surveillance Modeling Network.


The relationship between smoking and lung cancer is well established and cohort studies provide estimates of risk for individual cohorts. While population trends are qualitatively consistent with smoking trends, the rates do not agree well with results from analytical studies. Four carcinogenesis models for the effect of smoking on lung cancer mortality were used to estimate lung cancer mortality rates for U.S. males: two-stage clonal expansion and multistage models using parameters estimated from two Cancer Prevention Studies (CPS I and CPS II). Calibration was essential to adjust for both shift and temporal trend. The age-period-cohort model was used for calibration. Overall, models using parameters derived from CPS I performed best, and the corresponding two-stage clonal expansion model was best overall. However, temporal calibration did significantly improve agreement with the population rates, especially the effect of age and cohort.


The age-period-cohort model is known to provide an excellent description of the temporal trends in lung cancer incidence and mortality. This analytic approach is extended to include the contribution of carcinogenesis models for smoking. Usefulness of this strategy is that it offers a way to temporally calibrate a model that is fitted to population data and it can be readily adopted for the consideration of many different models. In addition, it provides diagnostics that can suggest temporal limitations of a particular carcinogenesis model in describing population rates. Alternative carcinogenesis models can be embedded within this framework. The two-stage clonal expansion model is implemented here. The model was used to estimate the impact of tobacco
control after dissemination of knowledge of the harmful effects of cigarette smoking by comparing the observed number of lung cancer deaths to those expected if there had been no control compared to an ideal of complete control in 1965. Results indicate that 35.2% and 26.5% of lung cancer deaths that could have been avoided actually were for males and females, respectively.


The smoking history generator (SHG) developed by the National Cancer Institute simulates individual life/smoking histories that serve as inputs for the Cancer Intervention and Surveillance Modeling Network (CISNET) lung cancer models. In this chapter, we review the SHG inputs, describe its outputs, and outline the methodology behind it. As an example, we use the SHG to simulate individual life histories for individuals born between 1890 and 1984 for each of the CISNET smoking scenarios and use those simulated histories to compute the corresponding smoking prevalence over the period 1975-2000


BACKGROUND: Rapid change in food intake, physical activity, and tobacco use in recent decades have contributed to the soaring rates of obesity, type 2 diabetes and cardiovascular disease (CVD) in Aboriginal populations living in Canada. The nature and influence of contextual factors on Aboriginal health behaviours are not well characterized. METHODS: To describe the contextual determinants of health behaviours associated with cardiovascular risk factors on the Six Nations reserve, including the built environment, access and affordability of healthy foods, and the use of tobacco. In this cross-sectional study, 63 adults from the Six Nations Reserve completed the modified Neighbourhood Environment Walkability Scale (NEWS), questionnaire assessing food access and availability, tobacco pricing and availability, and the Environmental Profile of Community Health (EPOCH) tool. RESULTS: The structured environment of Six Nations Reserve scored low for walkability, street connectivity, aesthetics, safety, and access to walking and cycling facilities. All participants purchased groceries off-reserve, although fresh fruits and vegetables were reported to be available and affordable both on and off-reserve. On average $151/week is spent on groceries per family. Ninety percent of individuals report tobacco use is a problem in the community. Tobacco is easily accessible for children and youth, and only three percent of community members would accept increased tobacco taxation as a strategy to reduce tobacco access. CONCLUSIONS: The built environment, access and affordability of healthy food and tobacco on the Six Nations Reserve are not perceived favourably. Modification of these contextual factors described here may reduce adverse health behaviours in the community.


The Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air) was initiated in 2004 to
investigate the relation between individual-level estimates of long-term air pollution exposure and the progression of subclinical atherosclerosis and the incidence of cardiovascular disease (CVD). MESA Air builds on a multicenter, community-based US study of CVD, supplementing that study with additional participants, outcome measurements, and state-of-the-art air pollution exposure assessments of fine particulate matter, oxides of nitrogen, and black carbon. More than 7,000 participants aged 45-84 years are being followed for over 10 years for the identification and characterization of CVD events, including acute myocardial infarction and other coronary artery disease, stroke, peripheral artery disease, and congestive heart failure; cardiac procedures; and mortality. Subcohorts undergo baseline and follow-up measurements of coronary artery calcium using computed tomography and carotid artery intima-medial wall thickness using ultrasonography. This cohort provides vast exposure heterogeneity in ranges currently experienced and permitted in most developed nations, and the air monitoring and modeling methods employed will provide individual estimates of exposure that incorporate residence-specific infiltration characteristics and participant-specific time-activity patterns. The overarching study aim is to understand and reduce uncertainty in health effect estimation regarding long-term exposure to air pollution and CVD


OBJECTIVES: We investigated whether positive mental health predicts all-cause mortality. METHODS: Data were from the Midlife in the United States (MIDUS) study (n = 3032), which at baseline in 1995 measured positive mental health (flourishing and not) and past-year mental illness (major depressive episode, panic attacks, and generalized anxiety disorders), and linked respondents with National Death Index records in a 10-year follow-up ending in 2005. Covariates were age, gender, race, education, any past-year mental illness, smoking, physical inactivity, physical diseases, and physical disease risk factors. RESULTS: A total of 6.3% of participants died during the study period. The final and fully adjusted odds ratio of mortality was 1.62 (95% confidence interval [CI] = 1.00, 2.62; P = .05) for adults who were not flourishing, relative to participants with flourishing mental health. Age, gender, race, education, smoking, physical inactivity, cardiovascular disease, and HIV/AIDS were significant predictors of death during the study period. CONCLUSIONS: The absence of positive mental health increased the probability of all-cause mortality for men and women at all ages after adjustment for known causes of death


OBJECTIVES: We assessed the prevalence and sociodemographic correlates of tobacco use among US adults. METHODS: We used data from the 2009-2010 National Adult Tobacco Survey, a national landline and cell phone survey of adults aged 18 years and older, to estimate current use of any tobacco; cigarettes; cigars, cigarillos, or small cigars; chewing tobacco, snuff, or dip; water pipes; snus; and pipes. We stratified estimates by gender, age, race/ethnicity, education, income, sexual orientation, and US state. RESULTS: National prevalence of current use was 25.2% for any tobacco; 19.5% for cigarettes; 6.6% for cigars, cigarillos, or small cigars; chewing tobacco, snuff, or dip; water pipes; snus; and pipes. We stratified estimates by gender, age, race/ethnicity, education, income, sexual orientation, and US state. RESULTS: National prevalence of current use was 25.2% for any tobacco; 19.5% for cigarettes; 6.6% for cigars, cigarillos, or small cigars; 3.4% for chewing tobacco, snuff, or dip; 1.5% for water pipes; 1.4% for snus; and 1.1% for pipes. Tobacco use was greatest among respondents who were male, younger, of non-Hispanic "other" race/ethnicity, less educated, less wealthy, and lesbian, gay, bisexual, or transgender. Prevalence ranged from 14.1% (Utah) to 37.4% (Kentucky). CONCLUSIONS: Tobacco use varies by geography and sociodemographic factors, but remains prevalent among US adults. Evidence-based prevention strategies are needed to decrease tobacco use and the health and economic burden of tobacco-related diseases

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The Institute of Medicine (IOM) released a groundbreaking report on lesbian, gay, bisexual, and transgender (LGBT) health in 2011, finding limited evidence of tobacco disparities. We examined IOM search terms and used 2 systematic reviews to identify 71 articles on LGBT tobacco use. The IOM omitted standard tobacco-related search terms. The report also omitted references to studies on LGBT tobacco use (n = 56), some with rigorous designs. The IOM report may underestimate LGBT tobacco use compared with general population use.


Past studies have examined the relationship of lung cancer to smoking using longitudinal data for select samples. This study applies the two-stage clonal expansion (TSCE) model to U.S. smoking data over a 25-year period. Smoking Base Case (SBC) data on actual smoking duration and intensity from the years 1975-2000 are applied by gender to separate TSCE models, which are then calibrated to historical trends in lung cancer death rates using regression analysis. The uncalibrated and calibrated TSCE models are also applied to SBC data for two scenarios: (1) no tobacco control and (2) complete tobacco control. The results are used to develop estimates of the number of lives saved as a result of tobacco control and how many lives would be saved if cigarette use had ceased in 1965. Predictions of lung cancer from the TSCE models with CPS-II and the CPS-I data for males and especially females are considerably below historical rates with the deviations from historical rates increasing over time. Residual trends unrelated to the smoking models were also found. Tobacco control activities saved approximately 625,000 lives between the years 1975 and 2000. An additional 2,110,000 lives would have been saved if all smoking was stopped in 1965. Tobacco control has successfully prevented lung cancer deaths, but many more lives could be saved with further reductions in smoking rates. Systematic biases were observed from TSCE models using CPS-I and CPS-II data to estimate smoking-related lung cancer deaths.
BACKGROUND: Data on prevalence, pattern of tobacco use, proportion of population dependent on nicotine and their determinants are important for developing and implementing tobacco control strategies. The aim of the study was to estimate the prevalence and determinants of tobacco use and nicotine dependency. METHODS: A cross-sectional survey among a representative sample of 18,018 individuals in the age group of >=14 years was conducted in the Union Territory of Andaman and Nicobar Islands during 2007-09. A structured questionnaire, a modified version of an instrument which was used successfully in several multi-country epidemiological studies of the World Health Organisation, was used to survey individual socio-demographic details, known co-morbid conditions, tobacco use and alcohol use. Fagerstrom Test for Nicotine Dependence (FTND) was used to estimate nicotine dependence. RESULTS: The response rate of our survey was 97% (18,018/18,554). Females (n = 8,888) were significantly younger than males (34.3 + 14.6 Vs 36.2 + 15.4 years). The prevalence of current tobacco use in any form was 48.9% (95% CI: 48.2-49.6). Tobacco chewing alone was prevalent in 40.9% (95% CI: 40.1-41.6) of the population. While one tenth of males (9.7%, 95% CI: 9.1-10.4) were nicotine dependent, it was only 3% (95% CI: 2.7-3.4) in females. Three fourth of the tobacco users initiated use of tobacco before reaching 21 years of age. Age, current use of alcohol, poor educational status, marital status, social groups, and co-morbidities were the main determinants of tobacco use and nicotine dependence in the population. CONCLUSION: The high prevalence of tobacco use especially the chewing form of tobacco in the Union Territory of Andaman and Nicobar Islands and the differences in prevalence and pattern of tobacco use and nicotine dependency observed across subgroups warrants implementation of culturally specific tobacco control activities in this population.


OBJECTIVES: We estimated the number of deaths attributable to secondhand smoke (SHS), years of potential life lost (YPLL), and value of lost productivity for different US racial/ethnic groups in 2006. METHODS: We determined the number of SHS-related deaths among nonsmokers from 2 adult and 4 infant conditions using an epidemiological approach. We estimated adult SHS exposure using detectable serum cotinine. For each death, we determined the YPLL and the value of lost productivity. Results. SHS exposure resulted in more than 42 000 deaths: more than 41 000 adults and nearly 900 infants. Blacks accounted for 13% of all deaths but 24% to 36% of infant deaths. SHS-attributable deaths resulted in a loss of nearly 600 000 YPLL and $6.6 billion of lost productivity, or $158 000 per death. The value of lost productivity per death was highest among Blacks ($238 000) and Hispanics ($193 000). CONCLUSIONS: The economic toll of SHS exposure is substantial, with communities of color having the greatest losses. Interventions need to be designed to reduce the health and economic burden of smoking on smokers and nonsmokers alike and on particularly vulnerable groups.


In this chapter we review the epidemiology of lung cancer incidence and mortality among never smokers/nonsmokers and describe the never smoker lung cancer risk models used by the Cancer Intervention and Surveillance Network (CISNET) modelers. Our review focuses on those influences likely to have measurable population impact on never smoker risk, such as
secondhand smoke, even though the individual-level impact may be small. Occupational exposures may also contribute importantly to the population attributable risk of lung cancer. We examine the following risk factors in this chapter: age, environmental tobacco smoke, cooking fumes, ionizing radiation including radon gas, inherited genetic susceptibility, selected occupational exposures, preexisting lung disease, and oncogenic viruses. We also compare the prevalence of never smokers between the three CISNET smoking scenarios and present the corresponding lung cancer mortality estimates among never smokers as predicted by a typical CISNET model.


Sophisticated modeling techniques can be powerful tools to help us understand the effects of cancer control interventions on population trends in cancer incidence and mortality. Readers of journal articles are, however, rarely supplied with modeling details. Six modeling groups collaborated as part of the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network (CISNET) to investigate the contribution of U.S. tobacco-control efforts toward reducing lung cancer deaths over the period 1975-2000. The six models included in this monograph were developed independently and use distinct, complementary approaches toward modeling the natural history of lung cancer. The models used the same data for inputs, and agreed on the design of the analysis and the outcome measures. This article highlights aspects of the models that are most relevant to similarities of or differences between the results. Structured comparisons can increase the transparency of these complex models.


The natural history model underlying the MGH Lung Cancer Policy Model (LCPM) does not include the two-stage clonal expansion model employed in other CISNET lung models. We used the LCPM to predict numbers of U.S. lung cancer deaths for ages 30-84 between 1975 and 2000 under four scenarios as part of the comparative modeling analysis described in this issue. The LCPM is a comprehensive microsimulation model of lung cancer development, progression, detection, treatment, and survival. Individual-level patient histories are aggregated to estimate cohort or population-level outcomes. Lung cancer states are defined according to underlying disease variables, test results, and clinical events. By simulating detailed clinical procedures, the LCPM can predict benefits and harms attributable to a variety of patient management practices, including annual screening programs. Under the scenario of observed smoking patterns, predicted numbers of deaths from the calibrated LCPM were within 2% of observed over all years (1975-2000). The LCPM estimated that historical tobacco control policies achieved 28.6% (25.2% in men, 30.5% in women) of the potential reduction in U.S. lung cancer deaths had smoking had been eliminated entirely. The hypothetical adoption in 1975 of annual helical CT screening of all persons aged 55-74 with at least 30 pack-years of cigarette exposure to historical tobacco control would have yielded a proportion realized of 39.0% (42.0% in men, 33.3% in women). The adoption of annual screening would have prevented less than half as many lung cancer deaths as the elimination of cigarette smoking.


OBJECTIVES: We examined changes in the relative risk of death among current and former...
smokers over recent decades in the United States. METHODS: Data from the National Health Interview Survey (NHIS) and National Health and Nutrition Examination Survey (NHANES) were linked to subsequent deaths. We calculated age-standardized death rates by gender and smoking status, and estimated multivariate discrete time logit regression models. RESULTS: The risk of death for a smoker compared with that for a never-smoker increased by 25.4% from 1987 to 2006 based on NHIS data. Analysis of NHANES data from 1971 to 2006 showed an even faster annual increase in the relative risk of death for current smokers. Former smokers also showed an increasing relative risk of death, although the increase was slower than that among current smokers and not always statistically significant. These trends were not related to increasing educational selectivity of smokers or increased smoking intensity or duration among current smokers. Smokers may have become more adversely selected on other health-related variables. CONCLUSIONS: A continuing increase in the relative risk of death for current and former smokers suggests that the contribution of smoking to national mortality patterns is not decreasing as rapidly as would be implied by the decreasing prevalence of smoking among Americans.


OBJECTIVES: We assessed support for a ban by the Food and Drug Administration on menthol in cigarettes and behavioral intentions among menthol smokers in the event of such a ban. METHODS: We surveyed 2649 never, former, and current smokers and used ordinal logistic regression to calculate weighted point estimates and predictors of support for a menthol ban among the adult population and menthol smokers only. For menthol smokers, we also calculated weighted point estimates and predictors of behavioral intentions. RESULTS: Overall, 28.2% of adults opposed, 20.0% supported, and 51.9% lacked a strong opinion about a menthol ban. Support was highest among Hispanics (36.4%), African Americans (29.0%), never smokers (26.8%), and respondents with less than a high school education (28.8%). Nearly 40% of menthol smokers said they would quit if menthol cigarettes were no longer available, 12.5% would switch to a nonmenthol brand, and 25.2% would both switch and try to quit. CONCLUSIONS: Support for a menthol ban is strongest among populations with the highest prevalence of menthol cigarette use. A menthol ban might motivate many menthol smokers to quit.


The purpose of this study was to develop life tables by smoking status removing lung cancer as a cause of death. These life tables are inputs to studies that compare the effectiveness of lung cancer treatments or interventions, and provide a way to quantify time until death from causes other than lung cancer. The study combined actuarial and statistical smoothing methods, as well as data from multiple sources, to develop separate life tables by smoking status, birth cohort, by single year of age, and by sex. For current smokers, separate life tables by smoking quintiles were developed based on the average number of cigarettes smoked per day by birth cohort. The end product is the creation of six non-lung-cancer life tables for males and six tables for females: five current smoker quintiles and one for never smokers. Tables for former smokers are linear combinations of the appropriate table based on the current smoker quintile before quitting smoking and the never smoker probabilities, plus added covariates for the smoking quit age and time since quitting.

OBJECTIVE: To investigate the impact of smoking on overall mortality and life expectancy in a large Japanese population, including some who smoked throughout adult life. DESIGN: The Life Span Study, a population-based prospective study, initiated in 1950. SETTING: Hiroshima and Nagasaki, Japan. PARTICIPANTS: Smoking status for 27,311 men and 40,662 women was obtained during 1963-92. Mortality from one year after first ascertainment of smoking status until 1 January 2008 has been analysed. MAIN OUTCOME MEASURES: Mortality from all causes in current, former, and never smokers. RESULTS: Smokers born in later decades tended to smoke more cigarettes per day than those born earlier, and to have started smoking at a younger age. Among those born during 1920-45 (median 1933) and who started smoking before age 20 years, men smoked on average 23 cigarettes/day, while women smoked 17 cigarettes/day, and, for those who continued smoking, overall mortality was more than doubled in both sexes (rate ratios versus never smokers: men 2.21 (95% confidence interval 1.97 to 2.48), women 2.61 (1.98 to 3.44)) and life expectancy was reduced by almost a decade (8 years for men, 10 years for women). Those who stopped smoking before age 35 avoided almost all of the excess risk among continuing smokers, while those who stopped smoking before age 45 avoided most of it. CONCLUSIONS: The lower smoking related hazards reported previously in Japan may have been due to earlier birth cohorts starting to smoke when older and smoking fewer cigarettes per day. In Japan, as elsewhere, those who start smoking in early adult life and continue smoking lose on average about a decade of life. Much of the risk can, however, be avoided by giving up smoking before age 35, and preferably well before age 35.


The MISCAN-lung model was designed to simulate population trends in lung cancer (LC) for comprehensive surveillance of the disease, to relate past exposure to risk factors to (observed) LC incidence and mortality, and to estimate the impact of cancer-control interventions. MISCAN-lung employs the technique of stochastic microsimulation of life histories affected by risk factors. It includes the two-stage clonal expansion model for carcinogenesis and a detailed LC progression model; the latter is specifically intended for the evaluation of screenings. This article elucidates further the principles of MISCAN-lung and describes its application to a comparative study within the CISNET Lung Working Group on the impact of tobacco control on U.S. LC mortality. MISCAN-lung yields an estimate of the number of LC deaths avoided during 1975-2000. The potential number of avoidable LC deaths, had everybody quit smoking in 1965, is 2.2 million; 750,000 deaths (30%) were avoided in the United States due to actual tobacco control interventions. The model fits in the actual tobacco-control scenario, providing credibility to the estimates of other scenarios, although considering survey-reported smoking trends alone has limitations.


An increased risk of death in persons who have suffered spousal bereavement has been described in many populations. The impact of modifying factors, such as chronic disease and material circumstances, is less well understood. The authors followed 171,120 couples 60 years of age or older in a United Kingdom primary care database between 2005 and 2010 for an average of 4 years. A total of 26,646 (15.5%) couples experienced bereavement, with mean follow up after bereavement of 2 years. In a model adjusted for age, sex, comorbid conditions at baseline, material deprivation based on area of residence, season, and smoking status, the hazard ratio for mortality in the first year after bereavement was 1.25 (95% confidence interval: 1.18, 1.33). Further adjustment for changes in comorbid conditions throughout follow up did not
alter the hazard ratio for bereavement (hazard ratio = 1.27, 95% confidence interval: 1.19, 1.35). The association was strongest in individuals with no significant chronic comorbid conditions throughout follow up (hazard ratio = 1.50, 95% confidence interval: 1.28, 1.77) and in more affluent couples (P = 0.035). In the first year after bereavement, the association between bereavement and death is not primarily mediated through worsening or new onset of chronic disease. Good health and material circumstances do not protect individuals from increased mortality rates after bereavement


BACKGROUND: Cigarette smoking has been associated with accelerated decline in lung function, increased health services use and asthma severity in patients with asthma. Previous studies have provided insight into how smoking cessation improves lung function among asthma patients, however, fail to provide measurable asthma symptom-specific outcomes after smoking cessation. The objective of this study was to measure the effect of changing smoking status on asthma symptom control and health services use in adults with asthma. METHODS: The study was conducted in eight primary care practices across Ontario, Canada participating in a community-based, participatory, and evidence-based Asthma Care Program. Patients aged 18 to 55 identified with physician-diagnosed mild to moderate asthma were recruited. In addition to receiving clinical asthma care, participants were administered a questionnaire at baseline and 12-month follow-up visits to collect information on demographics, smoking status, asthma symptoms and routine health services use. The effect of changing smoking status on asthma symptom control was compared between smoking groups using Chi-square and Fisher’s exact tests where appropriate. Mixed effect models were used to measure the impact of the change in smoking status on asthma symptom and health services use while adjusting for covariates. RESULTS: This study included 519 patients with asthma; 11% of baseline smokers quit smoking while 4% of baseline non-smokers started smoking by follow-up. Individuals who quit smoking had 80% lower odds of having tightness in the chest (Odds ratio (OR) = 0.21, 95% CI: 0.06, 0.82) and 76% lower odds of night-time symptoms (OR = 0.24, 95% CI: 0.07, 0.85) compared to smokers who continued to smoke. Compared to those who remained non-smokers, those who had not been smoking at baseline but self-reported as current smoker at follow-up had significantly higher odds of chest tightness (OR = 1.36, 95% CI: 1.10, 1.70), night-time symptoms (OR = 1.55, 95% CI: 1.09, 2.20), having an asthma attack in the last six months (OR = 1.43, 95% CI: 1.17, 1.75) and visiting a walk-in clinic for asthma (OR = 4.57, 95% CI: 1.44, 14.49). CONCLUSIONS: This study provides practitioners measurable and clinically important findings that associate smoking cessation with improved asthma control. Health practitioners and asthma programs can use powerful education messages to emphasize the benefits of smoking cessation as a priority to current smokers


OBJECTIVES: We examined migration-related changes in smoking behavior in the transnational Mexican-origin population. METHODS: We combined epidemiological surveys from Mexico (Mexican National Comorbidity Survey) and the United States (Collaborative Psychiatric Epidemiology Surveys). We compared 4 groups with increasing US contact with respect to smoking initiation, persistence, and daily cigarette consumption: Mexicans with no migrant in their family, Mexicans with a migrant in their family or previous migration experience, migrants, and US-born Mexican Americans. RESULTS: Compared with Mexicans with a migrant in their family or previous migration experience, migrants were less likely to initiate smoking (odds ratio [OR] =
0.56; 95% confidence interval [CI] = 0.38, 0.83) and less likely to be persistent smokers (OR = 0.41; 95% CI = 0.26, 0.63). Among daily smokers, the US-born smoked more cigarettes per day than did Mexicans with a migrant in their family or previous migration experience for men (7.8 vs 6.5) and women (8.6 vs 4.3). CONCLUSIONS: Evidence suggests that smoking is suppressed among migrants relative to the broader transnational Mexican-origin population. The pattern of low daily cigarette consumption among US-born Mexican Americans, noted in previous research, represents an increase relative to smokers in Mexico


Smoking has been restricted in workplaces for some time. A number of organizations with health promotion or tobacco control goals have taken the further step of implementing employment restrictions. These restrictions apply to smokers and, in some cases, to anyone testing positive on cotinine tests, which also capture users of nicotine-replacement therapy and those exposed to secondhand smoke. Such policies are defended as closely related to broader antismoking goals: first, only nonsmokers can be role models and advocates for tobacco control; second, nonsmoker and "nonnicotine" hiring policies help denormalize tobacco use, thus advancing a central aspect of tobacco control. However, these arguments are problematic: not only can hiring restrictions come into conflict with broader antismoking goals, but they also raise significant problems of their own


We compared projections from a dynamic model of US adult smoking prevalence with official estimates of prevalence from the National Health Interview Survey. Ten years after they were made, the model projections closely fit the National Health Interview Survey estimates for 2005 and 2010. We conclude that a verified model of adult smoking prevalence can assist governmental authorities in establishing aspirational but feasible targets for tobacco control. By extension, carefully crafted models can help in goal setting in multiple areas of public health


BACKGROUND: Sensation seeking tendencies tend to manifest during adolescence and are associated with both health-compromising behaviors and health-enhancing behaviors. The purpose of this study is to evaluate the relationship between sensation seeking and physical activity, a health-enhancing behavior, and between sensation seeking and experimenting with cigarettes, a health compromising-behavior, among a cohort of Mexican origin adolescents residing in the United States with different levels of acculturation. METHODS: In 2009, 1,154 Mexican origin youth (50.5% girls, mean age 14.3 years (SD = 1.04)) provided data on smoking behavior, physical activity, linguistic acculturation, and sensation seeking. We conducted Pearson's chi² tests to examine the associations between categorical demographic
characteristics (i.e. gender, age, country of birth and parental educational attainment) and both cigarette experimentation and physical activity and Student’s t-tests to examine mean differences on the continuous variables (i.e. sensation seeking subscale) by the behaviors. We examined mean differences in the demographic characteristics, acculturation, and both behaviors for each of the sensation seeking subscales using analysis of variance (ANOVA). To examine relationships between the sensation seeking subscales, gender, and both behaviors, at different levels of acculturation we completed unconditional logistic regression analyses stratified by level of acculturation. RESULTS: Overall, 23.3% had experimented with cigarettes and 29.0% reported being physically active for at least 60 minutes/day on at least 5 days/week. Experimenting with cigarettes and being physically active were more prevalent among boys than girls. Among girls, higher levels of sensation seeking tendencies were associated with higher levels of acculturation and experimentation with cigarettes, but not with physical activity. Among boys, higher levels of sensation seeking tendencies were associated with higher levels of acculturation, experimenting with cigarettes and being physically active. CONCLUSIONS: Our results suggest that interventions designed to prevent smoking among Mexican origin youth may need to address social aspects associated with acculturation, paying close attention to gendered manifestations of sensation seeking.


BACKGROUND: Many previous studies did not sufficiently control for several confounding factors that may affect the association between smoking and depression, such as socioeconomic status. We investigated the association between depression and smoking status, smoking exposure, duration of smoking cessation, and age of starting smoking while controlling for socioeconomic factors. METHODS: This study was based on a community health survey performed in Jeollanam-do, South Korea, between September and November 2009. In total, 20,084 subjects (9,118 males and 10,966 females) were included in the analysis. Information on smoking characteristics, such as smoking status, pack-years of smoking, and age of starting smoking, was collected using a standardized questionnaire. Depression was defined using the Korean CES-D score. RESULTS: The odds ratios (ORs) of depression were 1.35 (0.92-1.98) for former smokers and 1.77 (1.27-2.48) for current-smokers among males, and 2.67 (1.38-5.16) for former smokers and 3.72 (2.11-6.54) for current-smokers among females, after adjusting for other confounding factors. Compared to light smoking, heavy smoking was significantly associated with depression in males [OR = 3.97, 95% confidence interval (CI) = 1.42-11.14], but not in females (OR = 1.24, 95% CI = 0.73-2.09). No significant associations between depression and age of starting smoking and duration of smoking cessation were observed among former smokers. CONCLUSIONS: Our data demonstrate that smoking is strongly associated with depression, particularly among females. These findings suggest that depression prevention may need to be combined with smoking prevention and that different strategies may be needed for males and females.


China ambitiously promised to provide safe, effective, and affordable health care services to all citizens. However, the national strategies for enhancing health remain patchy, and the policy frameworks to empower and inspire individuals and communities to pursue a healthy lifestyle are largely fragmented. The incoherency is well epitomized by China's failure to implement key parts of the Framework Convention on Tobacco Control treaty. We seek to advance constructive debate on the health care reform and national health development in China.
Grippe A


BACKGROUND: Around the globe, school closures were used sporadically to mitigate the 2009 H1N1 influenza pandemic. However, such closures can detrimentally impact economic and social life. METHODS: Here, we couple a decision analytic approach with a mathematical model of influenza transmission to estimate the impact of school closures in terms of epidemiological and cost effectiveness. Our method assumes that the transmissibility and the severity of the disease are uncertain, and evaluates several closure and reopening strategies that cover a range of thresholds in school-aged prevalence (SAP) and closure durations. RESULTS: Assuming a willingness to pay per quality adjusted life-year (QALY) threshold equal to the US per capita GDP ($46,000), we found that the cost effectiveness of these strategies is highly dependent on the severity and on a willingness to pay per QALY. For severe pandemics, the preferred strategy couples the earliest closure trigger (0.5% SAP) with the longest duration closure (24 weeks) considered. For milder pandemics, the preferred strategies also involve the earliest closure trigger, but are shorter duration (12 weeks for low transmission rates and variable length for high transmission rates). CONCLUSIONS: These findings highlight the importance of obtaining early estimates of pandemic severity and provide guidance to public health decision-makers for effectively tailoring school closures strategies in response to a newly emergent influenza pandemic


OBJECTIVE: To assess the risk of epileptic seizures in people with and without epilepsy after vaccination with a monovalent AS03 adjuvanted pandemic A/H1N1 influenza vaccine (Pandemrix; Glaxo SmithKline, Sweden). DESIGN: Register based self controlled case series. SETTING: Three Swedish counties (source population 750 000). PARTICIPANTS: 373 398 people (age 0-106, median 41.2) who were vaccinated. Vaccinated people with epileptic seizures, diagnosed as inpatients or outpatients, at any time from 90 days before until 90 days after any dose of vaccine. MAIN OUTCOME MEASURES: Endpoints were admission to hospital or outpatient hospital care with epileptic seizures as the main diagnosis. The effect estimate of relative incidence was calculated as the incidence of epileptic seizures in period after exposure relative to the incidence of epileptic seizures in two control periods, one before and one after vaccination. RESULTS: 859 people experienced epileptic seizures during the study period. There was no increased risk of seizures in people with previously diagnosed epilepsy (relative incidence 1.01, 95% confidence interval 0.74 to 1.39) and a non-significant decrease in risk for people without epilepsy (0.67, 0.27 to 1.65) during the day 1-7 risk period (where day 1 is the day of vaccination). In a second risk period (day 8-30), there was a non-significant increased risk of seizures in people without epilepsy (1.11, 0.73 to 1.70) but no increase in risk for those with epilepsy (1.00, 0.83 to 1.21). CONCLUSIONS: This study found no evidence of an increase in risk of presentation to hospital with epileptic seizures after vaccination with a monovalent AS03 adjuvanted pandemic H1N1 influenza vaccine
The influenza viruses cause annual epidemics of respiratory disease and occasional pandemics, which constitute a major public-health issue. The segmented negative-stranded RNAs are associated with the polymerase complex and nucleoprotein (NP), forming ribonucleoproteins (RNPs), which are responsible for virus transcription and replication. We describe the structure of native RNPs derived from virions. They show a double-helical conformation in which two NP strands of opposite polarity are associated with each other along the helix. Both strands are connected by a short loop at one end of the particle and interact with the polymerase complex at the other end. This structure will be relevant for unraveling the mechanisms of nuclear import of parental virus RNPs, their transcription and replication, and the encapsidation of progeny RNPs into virions.

Bacterial coinfection complicated nearly all influenza deaths in the 1918 influenza pandemic and up to 34% of 2009 pandemic influenza A(H1N1) infections managed in intensive care units worldwide. More than 65,000 deaths attributable to influenza and pneumonia occur annually in the United States. Data from 683 critically ill patients with 2009 pandemic influenza A(H1N1) infection admitted to 35 intensive care units in the United States reveal that bacterial coinfection commonly occurs within the first 6 days of influenza infection, presents similarly to influenza infection occurring alone, and is associated with an increased risk of death. Pathogens that colonize the nasopharynx, including Staphylococcus aureus, Streptococcus pneumoniae, and Streptococcus pyogenes, are most commonly isolated. Complex viral, bacterial, and host factors contribute to the pathogenesis of coinfection. Reductions in morbidity and mortality are dependent on prevention with available vaccines as well as early diagnosis and treatment.
CROWCROFT NS, ROSELLA LC. The potential effect of temporary immunity as a result of bias associated with healthy users and social determinants on observations of influenza vaccine effectiveness; could unmeasured confounding explain observed links between seasonal influenza vaccine and pandemic H1N1 infection? BMC Public Health. 2012, vol. 12, p.458

BACKGROUND: Five observational studies from Canada found an association between seasonal influenza vaccine receipt and increased risk of pandemic influenza H1N1 2009 infection. This association remains unexplained. Although uncontrolled confounding has been suggested as a possible explanation, the nature of such confounding has not been identified. Observational studies of influenza vaccination can be affected by confounding due to healthy users and the influence of social determinants on health. The purpose of this study was to investigate the influence that these two potential confounders may have in combination with temporary immunity, using stratified tables. The hypothesis is that respiratory virus infections may activate a temporary immunity that provides short-term non-specific protection against influenza and that the relationship with being a healthy user or having a social determinant may result in confounding.

METHODS: We simulated the effect of confounding on vaccine effectiveness assuming that this could result from both social determinants and healthy user effects as they both influence the risk of seasonal influenza and non-influenza respiratory virus infections as well as the likelihood of being vaccinated. We then examined what impact this may have had on measurement of seasonal influenza vaccine effectiveness against pandemic influenza. RESULTS: In this simulation, failure to adjust for healthy users and social determinants would result in an erroneously increased risk of pandemic influenza infection associated with seasonal influenza vaccination. The effect sizes were not however large. CONCLUSIONS: We found that unmeasured healthy user effects and social determinants could result in an apparent association between seasonal influenza vaccine and pandemic influenza infection by virtue of being related to temporary immunity. Adjustment for social determinants of health and the healthy user effects are required in order to improve the quality of observational studies of influenza vaccine effectiveness.


Background During the 2009 influenza A (H1N1) pandemic, pregnant women were at risk for severe influenza illness. This concern was complicated by questions about vaccine safety in pregnant women that were raised by anecdotal reports of fetal deaths after vaccination. Methods We explored the safety of influenza vaccination of pregnant women by linking Norwegian national registries and medical consultation data to determine influenza diagnosis, vaccination status, birth outcomes, and background information for pregnant women before, during, and after the pandemic. We used Cox regression models to estimate hazard ratios for fetal death, with the gestational day as the time metric and vaccination and pandemic exposure as time-dependent exposure variables. Results There were 117,347 eligible pregnancies in Norway from 2009 through 2010. Fetal mortality was 4.9 deaths per 1000 births. During the pandemic, 54% of pregnant women in their second or third trimester were vaccinated. Vaccination during pregnancy substantially reduced the risk of an influenza diagnosis (adjusted hazard ratio, 0.30; 95% confidence interval [CI], 0.25 to 0.34). Among pregnant women with a clinical diagnosis of influenza, the risk of fetal death was increased (adjusted hazard ratio, 1.91; 95% CI, 1.07 to 3.41). The risk of fetal death was reduced with vaccination during pregnancy, although this reduction was not significant (adjusted hazard ratio, 0.88; 95% CI, 0.66 to 1.17). Conclusions Pandemic influenza virus infection in pregnancy was associated with an increased risk of fetal death. Vaccination during pregnancy reduced the risk of an influenza diagnosis. Vaccination itself was not associated with increased fetal mortality and may have reduced the risk of influenza-related fetal death during the pandemic. (Funded by the Norwegian Institute of Public Health.)

BACKGROUND: The risk of influenza infection depends on biological characteristics, individual or collective behaviors and the environmental context. The Cohorts for Pandemic Influenza (CoPanFlu) France study was set up in 2009 after the identification of the novel swine-origin A/H1N1 pandemic influenza virus. This cohort of 601 households (1450 subjects) representative for the general population aims at using an integrative approach to study the risk and characteristics of influenza infection as a complex combination of data collected from questionnaires regarding sociodemographic, medical, behavioral characteristics of subjects and indoor environment, using biological samples or environmental databases. METHODS/DESIGN: Households were included between December 2009 and July 2010. The design of this study relies on systematic follow-up visits between influenza seasons and additional visits during influenza seasons, when an influenza-like illness is detected in a household via an active surveillance system. During systematic visits, a nurse collects individual and environmental data on questionnaires and obtains blood samples from all members of the household. When an influenza-like illness is detected, a nurse visits the household three times during the 12 following days, and collects data on questionnaires regarding exposure and symptoms, and biological samples (including nasal swabs) from all subjects in the household. The end of the follow-up period is expected in fall 2012. DISCUSSION: The large amount of data collected throughout the follow-up will permit a multidisciplinary study of influenza infections. Additional data is being collected and analyzed in this ongoing cohort. The longitudinal analysis of these households will permit integrative analyses of complex phenomena such as individual, collective and environmental risk factors of infection, routes of transmission, or determinants of the immune response to infection or vaccination


Influenza virus ribonucleoprotein complexes (RNP) are central to the viral life cycle and in adaptation to new host species. RNP are composed of the viral genome, viral polymerase, and many copies of the viral nucleoprotein. In vitro cell expression of all RNP protein components with four of the eight influenza virus gene segments enabled structural determination of native influenza virus RNPs by means of cryogenic electron microscopy (cryo-EM). The cryo-EM structure reveals the architecture and organization of the native RNP, defining the attributes of its largely helical structure and how polymerase interacts with nucleoprotein and the viral genome. Observations of branched-RNP structures in negative-stain electron microscopy and their putative identification as replication intermediates suggest a mechanism for viral replication by a second polymerase on the RNP template


ABSTRACT: The disproportionate effects of the 2009 H1N1 pandemic on many Canadian Aboriginal communities have drawn attention to the vulnerability of these communities in terms of health outcomes in the face of emerging and reemerging infectious diseases. Exploring the particular challenges facing these communities is essential to improving public health planning. In alignment with the objectives of the Pandemic Influenza Outbreak Research Modelling (Pan-InfORM) team, a Canadian public health workshop was held at the Centre for Disease Modelling (CDM) to: (i) evaluate post-pandemic research findings; (ii) identify existing gaps in knowledge that have yet to be addressed through ongoing research and collaborative activities; and (iii) build
upon existing partnerships within the research community to forge new collaborative links with Aboriginal health organizations. The workshop achieved its objectives in identifying main research findings and emerging information post pandemic, and highlighting key challenges that pose significant impediments to the health protection and promotion of Canadian Aboriginal populations. The health challenges faced by Canadian indigenous populations are unique and complex, and can only be addressed through active engagement with affected communities. The academic research community will need to develop a new interdisciplinary framework, building upon concepts from 'Communities of Practice', to ensure that the research priorities are identified and targeted, and the outcomes are translated into the context of community health to improve policy and practice.


Outbreaks of contagious diseases underscore the ever-looming threat of new epidemics. Compared to other disasters that inflict physical damage to infrastructure systems, epidemics can have more devastating and prolonged impacts on the population. This article investigates the interdependent economic and productivity risks resulting from epidemic-induced workforce absenteeism. In particular, we develop a dynamic input-output model capable of generating sector-disaggregated economic losses based on different magnitudes of workforce disruptions. An ex post analysis of the 2009 H1N1 pandemic in the national capital region (NCR) reveals the distribution of consequences across different economic sectors. Consequences are categorized into two metrics: (i) economic loss, which measures the magnitude of monetary losses incurred in each sector, and (ii) inoperability, which measures the normalized monetary losses incurred in each sector relative to the total economic output of that sector. For a simulated mild pandemic scenario in NCR, two distinct rankings are generated using the economic loss and inoperability metrics. Results indicate that the majority of the critical sectors ranked according to the economic loss metric comprise of sectors that contribute the most to the NCR's gross domestic product (e.g., federal government enterprises). In contrast, the majority of the critical sectors generated by the inoperability metric include sectors that are involved with epidemic management (e.g., hospitals). Hence, prioritizing sectors for recovery necessitates consideration of the balance between economic loss, inoperability, and other objectives. Although applied specifically to the NCR, the proposed methodology can be customized for other regions.


We have provided a detailed evaluation of how collaboration between an Ontario public health unit and its primary care providers facilitated an optimal response to the 2009 H1N1 influenza pandemic. Family health teams (integrated, interdisciplinary teams that provide a range of care options) provided flu assessment centers, with public health as a partner providing infection control advice, funding, coordination, antiviral medication, clinical care guidelines, supplemental nurse staffing, and arrangement of communication strategies with the public. The family health team structure offers a new capacity for timely, coordinated, and comprehensive response to public health emergencies, in partnership with public health, and provides a promising new direction for healthcare organization.
Maladie d'Alzheimer


BACKGROUND: Homozygous loss-of-function mutations in TREM2, encoding the triggering receptor expressed on myeloid cells 2 protein, have previously been associated with an autosomal recessive form of early-onset dementia. METHODS: We used genome, exome, and Sanger sequencing to analyze the genetic variability in TREM2 in a series of 1092 patients with Alzheimer's disease and 1107 controls (the discovery set). We then performed a meta-analysis on imputed data for the TREM2 variant rs75932628 (predicted to cause a R47H substitution) from three genomewide association studies of Alzheimer's disease and tested for the association of the variant with disease. We genotyped the R47H variant in an additional 1887 cases and 4061 controls. We then assayed the expression of TREM2 across different regions of the human brain and identified genes that are differentially expressed in a mouse model of Alzheimer's disease and in control mice. RESULTS: We found significantly more variants in exon 2 of TREM2 in patients with Alzheimer's disease than in controls in the discovery set (P=0.02). There were 22 variant alleles in 1092 patients with Alzheimer's disease and 5 variant alleles in 1107 controls (P<0.001). The most commonly associated variant, rs75932628 (encoding R47H), showed highly significant association with Alzheimer's disease (P<0.001). Meta-analysis of rs75932628 genotypes imputed from genomewide association studies confirmed this association (P=0.002), as did direct genotyping of an additional series of 1887 patients with Alzheimer's disease and 4061 controls (P<0.001). Trem2 expression differed between control mice and a mouse model of Alzheimer's disease. CONCLUSIONS: Heterozygous rare variants in TREM2 are associated with a significant increase in the risk of Alzheimer's disease. (Fundied by Alzheimer's Research UK and others.)


BACKGROUND: Sequence variants, including the epsilon4 allele of apolipoprotein E, have been associated with the risk of the common late-onset form of Alzheimer's disease. Few rare variants affecting the risk of late-onset Alzheimer's disease have been found. METHODS: We obtained the genome sequences of 2261 Icelanders and identified sequence variants that were likely to affect protein function. We imputed these variants into the genomes of patients with Alzheimer's disease and control participants and then tested for an association with Alzheimer's disease. We performed replication tests using case-control series from the United States, Norway, The Netherlands, and Germany. We also tested for a genetic association with cognitive function in a population of unaffected elderly persons. RESULTS: A rare missense mutation (rs75932628-T) in the gene encoding the triggering receptor expressed on myeloid cells 2 (TREM2), which was predicted to result in an R47H substitution, was found to confer a significant risk of Alzheimer's disease in Iceland (odds ratio, 2.92; 95% confidence interval [CI], 2.09 to 4.09; P=3.42x10(-10)). The mutation had a frequency of 0.46% in controls 85 years of age or older. We observed the association in additional sample sets (odds ratio, 2.90; 95% CI, 2.16 to 3.91; P=2.1x10(-12) in combined discovery and replication samples). We also found that carriers of rs75932628-T between the ages of 80 and 100 years without Alzheimer's disease had poorer cognitive function than noncarriers (P=0.003). CONCLUSIONS: Our findings strongly implicate variant TREM2 in the pathogenesis of Alzheimer's disease. Given the reported anti-inflammatory role of TREM2 in the brain, the R47H substitution may lead to an increased predisposition to Alzheimer's disease through impaired containment of inflammatory processes. ( Funded by the National Institute on Aging and others.)


BACKGROUND: Cognitive impairment and Alzheimer's disease (AD) are increasingly considered a major public health problem. The MemoVie cohort study aims to investigate the living conditions or risk factors under which the normal cognitive capacities of the senior population in Luxembourg (>/>= 65 year-old) evolve (1) to mild cognitive impairment (MCI) - transitory non-clinical stage - and (2) to AD. Identifying MCI and AD predictors undeniably constitutes a challenge in public health in that it would allow interventions which could protect or delay the occurrence of cognitive disorders in elderly people. In addition, the MemoVie study sets out to generate hitherto unavailable data, and a comprehensive view of the elderly population in the country. METHODS/DESIGN: The
study has been designed with a view to highlighting the prevalence in Luxembourg of MCI and AD in the first step of the survey, conducted among participants selected from a random sample of the general population. A prospective cohort is consequently set up in the second step, and appropriate follow-up of the non-demented participants allows improving the knowledge of the preclinical stage of MCI. Case-control designs are used for cross-sectional or retrospective comparisons between outcomes and biological or clinical factors. To ensure maximal reliability of the information collected, we decided to opt for structured face to face interviews. Besides health status, medical and family history, demographic and socio-cultural information are explored, as well as education, habitat network, social behavior, leisure and physical activities. As multilingualism is expected to challenge the cognitive alterations associated with pathological ageing, it is additionally investigated. Data relative to motor function, including balance, walk, limits of stability, history of falls and accidents are further detailed. Finally, biological examinations, including ApoE genetic polymorphism are carried out. In addition to standard blood parameters, the lipid status of the participants is subsequently determined from the fatty acid profiles in their red blood cells. The study obtained the legal and ethical authorizations. DISCUSSION: By means of the multidisciplinary MemoVie study, new insights into the onset of cognitive impairment during aging should be put forward, much to the benefit of intervention strategies as a whole.


Maladies cardio-vasculaires


CONTEXT: Clopidogrel pretreatment is recommended for patients with acute coronary syndromes (ACS) and stable coronary artery disease who are scheduled for percutaneous coronary intervention (PCI), but whether using clopidogrel as a pretreatment for PCI is associated with positive clinical outcomes has not been established. OBJECTIVE: To evaluate the association of clopidogrel pretreatment vs no treatment with mortality and major bleeding after PCI. DATA SOURCES: MEDLINE, EMBASE, Cochrane Controlled Trials Register databases, and reference lists of qualifying articles. STUDY SELECTION Studies reporting clinical data on mortality and major bleeding were included. Of the 392 titles identified, 15 articles published between August 2001 and September 2012 met the inclusion criteria: 6 randomized controlled trials (RCTs), 2 observational analyses of RCTs, and 7 observational studies. DATA EXTRACTION: Quality of studies was assessed with the Ottawa Scale and the Jadad Score as appropriate. Results were independently extracted by 2 reviewers. A random-effect model was applied. Pretreatment was defined as the administration of clopidogrel before PCI or catheterization. The main analysis was performed on RCTs and confirmed by observational analyses and observational studies. Prespecified subgroups--clinical presentation and clopidogrel loading dose--were analyzed. The primary efficacy and safety end points were all-cause mortality and major bleeding. Secondary end points included major cardiac events. RESULTS: Of the 37,814 patients included in the meta-analysis, 8,608 patients had participated in RCTs; 10,945, in observational analyses of RCTs; and 18,261, in observational studies. Analysis of RCTs showed that clopidogrel pretreatment was not
associated with a reduction of death (absolute risk, 1.54% vs 1.97%; OR, 0.80; 95% CI, 0.57-1.11; P = .17) but was associated with a lower risk of major cardiac events (9.83% vs 12.35%; OR, 0.77; 95% CI, 0.66-0.89; P < .001). There was no significant association between pretreatment and major bleeding overall (3.57% vs 3.08%; OR, 1.18; 95% CI, 0.93-1.50; P = .18). Analyses from observational analyses of RCTs and observational studies were consistent for all results.

CONCLUSIONS: Among patients scheduled for PCI, clopidogrel pretreatment was not associated with a lower risk of mortality but was associated with a lower risk of major coronary events


OBJECTIVES: We compared the incidence of recurrent or fatal cardiovascular disease in patients using Brazil's government-run Family Health Program (FHP) with those using non-FHP models of care. METHODS: From 2005 to 2010, we followed outpatients discharged from city public hospitals after a first ever stroke for stroke recurrence and myocardial infarction, using data from all city hospitals, death certificates, and outpatient monitoring in state-run and private units. RESULTS: In the follow-up period, 103 patients in the FHP units and 138 in the non-FHP units had exclusively state-run care. Stroke or myocardial infarction occurred in 30.1% of patients in the FHP group and 36.2% of patients in non-FHP care (rate ratio [RR] = 0.85; 95% confidence interval [CI] = 0.61, 1.18; P = .39); 37.9% of patients in FHP care and 54.3% in non-FHP care (RR = 0.68; 95% CI = 0.50, 0.92; P = .01) died. FHP use was associated with lower hazard of death from all causes (hazard ratio [HR] = 0.58; P = .005) after adjusting for age and stroke severity. The absolute risk reduction for death by all causes was 16.4%. CONCLUSIONS: FHP care is more effective than is non-FHP care at preventing death from secondary stroke and myocardial infarction


OBJECTIVE: To clarify associations of fish consumption and long chain omega 3 fatty acids with risk of cerebrovascular disease for primary and secondary prevention. DESIGN: Systematic review and meta-analysis. DATA SOURCES: Studies published before September 2012 identified through electronic searches using Medline, Embase, BIOSIS, and Science Citation Index databases. ELIGIBILITY CRITERIA: Prospective cohort studies and randomised controlled trials reporting on associations of fish consumption and long chain omega 3 fatty acids (based on dietary self report), omega 3 fatty acids biomarkers, or supplementations with cerebrovascular disease (defined as any fatal or non-fatal ischaemic stroke, haemorrhagic stroke, cerebrovascular accident, or transient ischaemic attack). Both primary and secondary prevention studies (comprising participants with or without cardiovascular disease at baseline) were eligible. RESULTS: 26 prospective cohort studies and 12 randomised controlled trials with aggregate data on 794,000 non-overlapping people and 34,817 cerebrovascular outcomes were included. In cohort studies comparing categories of fish intake the pooled relative risk for cerebrovascular disease for 2-4 servings a week versus <1 servings a week was 0.94 (95% confidence intervals 0.90 to 0.98) and for >/= 5 servings a week versus 1 serving a week was 0.88 (0.81 to 0.96). The relative risk for cerebrovascular disease comparing the top thirds of baseline long chain omega 3 fatty acids with the bottom thirds for circulating biomarkers was 1.04 (0.90 to 1.20) and for dietary
Exposures was 0.90 (0.80 to 1.01). In the randomised controlled trials the relative risk for cerebrovascular disease in the long chain omega 3 supplement compared with the control group in primary prevention trials was 0.98 (0.89 to 1.08) and in secondary prevention trials was 1.17 (0.99 to 1.38). For fish or omega 3 fatty acids the estimates for ischaemic and haemorrhagic cerebrovascular events were broadly similar. Evidence was lacking of heterogeneity and publication bias across studies or within subgroups. CONCLUSIONS: Available observational data indicate moderate, inverse associations of fish consumption and long chain omega 3 fatty acids with cerebrovascular risk. Long chain omega 3 fatty acids measured as circulating biomarkers in observational studies or supplements in primary and secondary prevention trials were not associated with cerebrovascular disease. The beneficial effect of fish intake on cerebrovascular risk is likely to be mediated through the interplay of a wide range of nutrients abundant in fish.


BACKGROUND: In some randomized trials comparing revascularization strategies for patients with diabetes, coronary-artery bypass grafting (CABG) has had a better outcome than percutaneous coronary intervention (PCI). We sought to discover whether aggressive medical therapy and the use of drug-eluting stents could alter the revascularization approach for patients with diabetes and multivessel coronary artery disease. METHODS: In this randomized trial, we assigned patients with diabetes and multivessel coronary artery disease to undergo either PCI with drug-eluting stents or CABG. The patients were followed for a minimum of 2 years (median among survivors, 3.8 years). All patients were prescribed currently recommended medical therapies for the control of low-density lipoprotein cholesterol, systolic blood pressure, and glycated hemoglobin. The primary outcome measure was a composite of death from any cause, nonfatal myocardial infarction, or nonfatal stroke. RESULTS: From 2005 through 2010, we enrolled 1900 patients at 140 international centers. The patients' mean age was 63.1 +/- 9.1 years, 29% were women, and 83% had three-vessel disease. The primary outcome occurred more frequently in the PCI group (P=0.005), with 5-year rates of 26.6% in the PCI group and 18.7% in the CABG group. The benefit of CABG was driven by differences in rates of both myocardial infarction (P<0.001) and death from any cause (P=0.049). Stroke was more frequent in the CABG group, with 5-year rates of 2.4% in the PCI group and 5.2% in the CABG group (P=0.03). CONCLUSIONS: For patients with diabetes and advanced coronary artery disease, CABG was superior to PCI in that it significantly reduced rates of death and myocardial infarction, with a higher rate of stroke. (Funded by the National Heart, Lung, and Blood Institute and others; FREEDOM ClinicalTrials.gov number, NCT00086450.)


(12) JEFFREY RR. *A multidisciplinary meeting on revascularisation in patients with diabetes and angina would be helpful*. BMJ. 2012, vol. 345, p.e6739


Not all obese adults have cardiometabolic abnormalities. It is unknown whether this is true in children and, if true, whether children who have metabolically healthy overweight/obesity (MHO) will also have favorable cardiometabolic profiles in adulthood. These aspects were examined in 1,098 individuals who participated as both children (aged 5-17 years) and adults (aged 24-43 years) in the Bogalusa Heart Study between 1997 and 2002 in Bogalusa, Louisiana. MHO was defined as being in the top body mass index quartile, while low density lipoprotein cholesterol, triglycerides, mean arterial pressure, and glucose were in the bottom 3 quartiles, and high density lipoprotein cholesterol was in the top 3 quartiles. Forty-six children (4.2%) had MHO, and they were more likely to retain MHO status in adulthood compared with children in other categories (P < 0.0001). Despite markedly increased obesity in childhood and in adulthood, these same MHO
children and adults showed a cardiometabolic profile generally comparable to that of nonoverweight/obese children ($P > 0.05$ in most cases). Moreover, there was no difference in carotid intima-media thickness in adulthood between MHO children and nonoverweight/obese children. Further, carotid intima-media thickness in adulthood was lower in MHO children than in metabolically abnormal, overweight/obese children ($P = 0.003$). In conclusion, the MHO phenotype starts in childhood and continues into adulthood.


BACKGROUND: Previous studies have demonstrated links between cardiovascular disease and physical inactivity and poor air quality, which are both associated with neighborhood greenness. However, no studies have directly investigated neighborhood greenness in relation to coronary heart disease risk. We investigated the effect of neighborhood greenness on both self-reported and hospital admissions of coronary heart disease or stroke, accounting for ambient air quality, socio-demographic, behavioral and biological factors. METHOD: Cross-sectional study of 11,404 adults obtained from a population representative sample for the period 2003-2009 in Perth, Western Australia. Neighborhood greenness was ascertained for a 1600 m service area surrounding the residential address using the mean and standard deviation of the Normalized Difference Vegetation Index (NDVI) obtained from remote sensing. Logistic regression was used to assess associations with medically diagnosed and hospitalization for coronary heart disease or stroke. RESULTS: The odds of hospitalization for heart disease or stroke was 37% (95% CI: 8%, 57%) lower among adults in neighborhoods with highly variable greenness (highest tertile) compared to those in predominantly green, or predominantly non-green neighborhoods (lowest tertile). This effect was independent of the absolute levels of neighborhood greenness. There was weaker evidence for associations with the mean level of neighborhood greenness.

CONCLUSION: Variability in neighborhood greenness is a single metric that encapsulates two potential promoters of physical activity - an aesthetically pleasing natural environment and access to urban destinations. Variability in greenness within a neighborhood was negatively associated with coronary heart disease and stroke.


The type A behavior pattern (TABP) was described in the 1950s by cardiologists Meyer Friedman and Ray Rosenman, who argued that TABP was an important risk factor for coronary heart disease. This theory was supported by positive findings from the Western Collaborative Group Study and the Framingham Study. We analyzed tobacco industry documents to show that the tobacco industry was a major funder of TABP research, with selected results used to counter concerns regarding tobacco and health. Our findings also help explain inconsistencies in the findings of epidemiological studies of TABP, in particular the phenomenon of initially promising
results followed by negative findings. Our analysis suggests that these "decline effects" are partly explained by tobacco industry involvement in TABP research


OBJECTIVE: To do an indirect comparison analysis of apixaban against dabigatran etexilate (2 doses) and rivaroxaban (1 dose), as well as of rivaroxaban against dabigatranetexilate (2 doses), for their relative efficacy and safety against each other, with particular focus on the secondary prevention population for stroke prevention in atrial fibrillation. A secondary objective was to do the same analysis in the primary prevention cohort. DESIGN: Indirect treatment comparisons of phase III clinical trials of stroke prevention in atrial fibrillation, with a focus on the secondary prevention cohorts. A secondary analysis was done on the primary prevention cohort. DATA SOURCES: Medline and Central (up to June 2012), clinical trials registers, conference proceedings, and websites of regulatory agencies. STUDY SELECTION: Randomised controlled trials of rivaroxaban, dabigatran, or apixaban compared with warfarin for stroke prevention in atrial fibrillation. RESULTS: In the secondary prevention (previous stroke) subgroup, when apixaban was compared with dabigatran (110 mg and 150 mg twice daily) for efficacy and safety endpoints, the only significant difference seen was less myocardial infarction (hazard ratio 0.39, 95% confidence interval 0.16 to 0.95) with apixaban compared with dabigatran 150 mg twice daily. No significant differences were seen in efficacy and most safety endpoints between apixaban or dabigatran 150 mg twice daily versus rivaroxaban. Less haemorrhagic stroke (hazard ratio 0.15, 0.03 to 0.66), vascular death (0.64, 0.42 to 0.99), major bleeding (0.68, 0.47 to 0.99), and intracranial bleeding (0.27, 0.10 to 0.73) were seen with dabigatran 110 mg twice daily versus rivaroxaban. In the primary prevention (no previous stroke) subgroup, apixaban was superior to dabigatran 110 mg twice daily for disabling or fatal stroke (hazard ratio 0.59, 0.36 to 0.97). Compared with dabigatran 150 mg twice daily, apixaban was associated with more stroke (hazard ratio 1.45, 1.01 to 2.08) and with less major bleeding (0.75, 0.60 to 0.94), gastrointestinal bleeding (0.61, 0.42 to 0.89), and other location bleeding (0.74, 0.58 to 0.94). Compared with rivaroxaban, dabigatran 110 mg twice daily was associated with more myocardial infarction events. No significant differences were seen for the main efficacy and safety endpoints between dabigatran 150 mg twice daily and rivaroxaban, or in efficacy endpoints between apixaban and rivaroxaban. Apixaban was associated with less major bleeding (hazard ratio 0.61, 0.48 to 0.78) than rivaroxaban. CONCLUSIONS: For secondary prevention, apixaban, rivaroxaban, and dabigatran had broadly similar efficacy for the main endpoints, although the endpoints of haemorrhagic stroke, vascular death, major bleeding, and intracranial bleeding were less common with dabigatran 110 mg twice daily than with rivaroxaban. For primary prevention, the three drugs showed some differences in relation to efficacy and bleeding. These results are hypothesis generating and should be confirmed in a head to head randomised trial


IMPORTANCE: In threatened preterm labor, maintenance tocolysis with nifedipine, after an initial course of tocolysis and corticosteroids for 48 hours, may improve perinatal outcome. OBJECTIVE: To determine whether maintenance tocolysis with nifedipine will reduce adverse perinatal outcomes due to premature birth. DESIGN, SETTING, AND PARTICIPANTS: APOSTEL-II (Assessment of Perinatal Outcome with Sustained Tocolysis in Early Labor) is a double-blind, placebo-controlled trial performed in 11 perinatal units including all tertiary centers in The Netherlands. From June 2008 to February 2010, women with threatened preterm labor between 26 weeks (plus 0 days) and 32 weeks (plus 2 days) gestation, who had not delivered after 48
hours of tocolysis and a completed course of corticosteroids, were enrolled. Surviving infants were followed up until 6 months after birth (ended August 2010). INTERVENTION: Randomization assigned 406 women to maintenance tocolysis with nifedipine orally (80 mg/d; n = 201) or placebo (n = 205) for 12 days. Assigned treatment was masked from investigators, participants, clinicians, and research nurses. MAIN OUTCOME MEASURES: Primary outcome was a composite of adverse perinatal outcomes (perinatal death, chronic lung disease, neonatal sepsis, intraventricular hemorrhage >grade 2, periventricular leukomalacia >grade 1, or necrotizing enterocolitis). Analyses were completed on an intention-to-treat basis. RESULTS: Mean (SD) gestational age at randomization was 29.2 (1.7) weeks for both groups. Adverse perinatal outcome was not significantly different between groups: 11.9% (24/201; 95% CI, 7.5%-16.4%) for nifedipine vs 13.7% (28/205; 95% CI, 9.0%-18.4%) for placebo (relative risk, 0.87; 95% CI, 0.53-1.45). CONCLUSIONS AND RELEVANCE: In patients with threatened preterm labor, nifedipine-maintained tocolysis did not result in a statistically significant reduction in adverse perinatal outcomes when compared with placebo. Although the lower than anticipated rate of adverse perinatal outcomes in the control group indicates that a benefit of nifedipine cannot completely be excluded, its use for maintenance tocolysis does not appear beneficial at this time. TRIAL REGISTRATION: trialregister.nl Identifier: NTR1336


OBJECTIVE: To investigate the long term effect of hormone replacement therapy on cardiovascular outcomes in recently postmenopausal women. DESIGN: Open label, randomised controlled trial. SETTING: Denmark, 1990-93. PARTICIPANTS: 1006 healthy women aged 45-58 who were recently postmenopausal or had perimenopausal symptoms in combination with recorded postmenopausal serum follicle stimulating hormone values. 502 women were randomly allocated to receive hormone replacement therapy and 504 to receive no treatment (control). Women who had undergone hysterectomy were included if they were aged 45-52 and had recorded values for postmenopausal serum follicle stimulating hormone. INTERVENTIONS: In the treatment group, women with an intact uterus were treated with triphasic estradiol and norethisterone acetate and women who had undergone hysterectomy received 2 mg estradiol a day. Intervention was stopped after about 11 years owing to adverse reports from other trials, but participants were followed for death, cardiovascular disease, and cancer for up to 16 years. Sensitivity analyses were carried out on women who took more than 80% of the prescribed treatment for five years. MAIN OUTCOME MEASURE: The primary endpoint was a composite of death, admission to hospital for heart failure, and myocardial infarction. RESULTS: At inclusion the women on average were aged 50 and had been postmenopausal for seven months. After 10 years of intervention, 16 women in the treatment group experienced the primary composite endpoint compared with 33 in the control group (hazard ratio 0.48, 95% confidence interval 0.26 to 0.87; P=0.015) and 15 died compared with 26 (0.57, 0.30 to 1.08; P=0.084). The reduction in cardiovascular events was not associated with an increase in any cancer (36 in treated group v 39 in control group, 0.92, 0.58 to 1.45; P=0.71) or in breast cancer (10 in treated group v 17 in control group, 0.58, 0.27 to 1.27; P=0.17). The hazard ratio for deep vein thrombosis (2 in treated group v 1 in control group) was 2.01 (0.18 to 22.16) and for stroke (11 in treated group v 14 in control group) was 0.77 (0.35 to 1.70). After 16 years the reduction in the primary composite outcome was still present and not associated with an increase in any cancer. CONCLUSIONS: After 10 years of randomised treatment, women receiving hormone replacement therapy early after menopause had a significantly reduced risk of mortality, heart failure, or myocardial infarction,
without any apparent increase in risk of cancer, venous thromboembolism, or stroke. TRIAL REGISTRATION: ClinicalTrials.gov NCT00252408


OBJECTIVE: To determine whether a 3 x 2 table, using an intention to diagnose approach, is better than the "classic" 2 x 2 table at handling transparent reporting and non-evaluable results, when assessing the accuracy of a diagnostic test. DESIGN: Based on a systematic search for diagnostic accuracy studies of coronary computed tomography (CT) angiography, full texts of relevant studies were evaluated to determine whether they could calculate an alternative 3 x 2 table. To quantify an overall effect, we pooled diagnostic accuracy values according to a meta-analytical approach. DATA SOURCES: Medline (via PubMed), Embase (via Ovid), and ISI Web of Science electronic databases. ELIGIBILITY CRITERIA: Prospective English or German language studies comparing coronary CT with conventional coronary angiography in all patients and providing sufficient data for a patient level analysis. RESULTS: 120 studies (10,287 patients) were eligible. Studies varied greatly in their approaches to handling non-evaluable findings. We found 26 studies (including 2298 patients) that allowed us to calculate both 2 x 2 tables and 3 x 2 tables. Using a bivariate random effects model, we compared the 2 x 2 table with the 3 x 2 table, and found significant differences for pooled sensitivity (98.2 (95% confidence interval 96.7 to 99.1) v 92.7 (88.5 to 95.3)), area under the curve (0.99 (0.98 to 1.00) v 0.93 (0.91 to 0.95)), positive likelihood ratio (9.1 (6.2 to 13.3) v 4.4 (3.3 to 6.0)), and negative likelihood ratio (0.02 (0.01 to 0.04) v 0.09 (0.06 to 0.15); (P<0.05)). CONCLUSION: Parameters for diagnostic performance significantly decrease if non-evaluable results are included by a 3 x 2 table for analysis (intention to diagnose approach). This approach provides a more realistic picture of the clinical potential of diagnostic tests.


BACKGROUND: Patients who are hospitalized with a first or recurrent stroke often are discharged with new medications or adjustment to the doses of pre-admission medications, which can be confusing and pose safety issues if misunderstood. The purpose of this pilot study was to assess the feasibility of medication coaching via telephone after discharge in patients with stroke. METHODS: Two-arm pilot study of a medication coaching program with 30 patients (20 intervention, 10 control). Consecutive patients admitted with stroke or TIA with at least 2 medications changed between admission and discharge were included. The medication coach contacted intervention arm patients post-discharge via phone call to discuss risk factors, review medications and triage patients' questions to a stroke nurse and/or pharmacist. Intervention and control participants were contacted at 3 months for outcomes. The main outcomes were feasibility (appropriateness of script, ability to reach participants, and provide requested information) and participant evaluation of medication coaching. RESULTS: The median lengths of the coaching and follow-up calls with requested answers to these questions were 27 minutes and 12 minutes, respectively, and participant evaluations of the coaching were positive. The intervention participants were more likely to have seen their primary care provider than were control participants by 3 months post discharge. CONCLUSIONS: This medication coaching study executed early after discharge demonstrated feasibility of coaching and educating stroke patients
with a trained coach. Results from our small pilot showed a possible trend towards improved appointment-keeping with primary care providers in those who received coaching.


CONTEXT: An estimated 10% to 20% of patients cannot tolerate statins or adequate doses to achieve treatment goals. Plasma proprotein convertase subtilisin/kexin type 9 (PCSK9) binds to low-density lipoprotein (LDL) receptors, promoting their degradation and increasing LDL cholesterol levels. In phase 1 studies, a human monoclonal antibody to PCSK9, AMG145, was well tolerated and reduced LDL cholesterol levels. Phase 1 studies, a human monoclonal antibody to PCSK9, AMG145, was well tolerated and reduced LDL cholesterol levels. DESIGN, SETTING, AND PATIENTS: A 12-week, randomized, double-blind, placebo- and ezetimibe-controlled, dose-ranging study conducted between July 2011 and May 2012 in statin-intolerant adult patients at 33 international sites. INTERVENTION: Patients were randomized equally to 1 of 5 groups: AMG145 alone at doses of 280 mg, 350 mg, or 420 mg; AMG145 at 420 mg plus 10 mg of ezetimibe; or 10 mg of ezetimibe plus placebo. AMG145 or placebo was administered subcutaneously every 4 weeks. MAIN OUTCOME MEASURES: The primary end point was percentage change from baseline to week 12 in ultracentrifugation-measured LDL cholesterol. Other end points included measures of safety and tolerability of different doses of AMG145 and AMG145 plus ezetimibe. RESULTS: Of 236 patients screened, 160 were randomized (mean age, 62 years; 64% female; mean baseline LDL cholesterol, 193 mg/dL); all patients had intolerance to 1 or more statins because of muscle-related events. At week 12, mean changes in LDL cholesterol levels were -67 mg/dL (-41%; 95% CI, -49% to -33%) for the AMG145, 280-mg, group; -70 mg/dL (-43%; 95% CI, -51% to -35%) for the 350-mg group; -91 mg/dL (-51%; 95% CI, -59% to -43%) for the 420-mg group; and -110 mg/dL (-63%; 95% CI, -71% to -55%) for the 420-mg/ezetimibe group compared with -14 mg/dL (-15%; 95% CI, -23% to -7.0%) for the placebo/ezetimibe group (P < .001). Four serious adverse events were reported with AMG145 (coronary artery disease, acute pancreatitis, hip fracture, syncope). Myalgia was the most common treatment-emergent adverse event during the study, occurring in 5 patients (15.6%) in the 280-mg group (n = 32); 1 patient (3.2%) in the 350-mg group (n = 31), 1 patient (3.1%) in the 420-mg group (n = 32), 6 patients (20.0%) receiving 420-mg AMG145/ezetimibe, and 1 patient (3.1%) receiving placebo/ezetimibe. CONCLUSION: In this phase 2 study in statin-intolerant patients, subcutaneous administration of a monoclonal antibody to PCSK9 significantly reduced LDL cholesterol levels and was associated with short-term tolerability. TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01375764


OBJECTIVE: To investigate whether varenicline is associated with an increased risk of serious cardiovascular events compared with another drug used for smoking cessation, bupropion.


CONTEXT: Autopsies of US service members killed in the Korean and Vietnam wars demonstrated that atherosclerotic changes in the coronary arteries can appear early in the second and third decades of life, long before ischemic heart disease becomes clinically apparent.

OBJECTIVE: To estimate the current prevalence of coronary and aortic atherosclerosis in the US armed forces.

DESIGN, SETTING, AND PARTICIPANTS: Cross-sectional study of all US service members who died of combat or unintentional injuries in support of Operations Enduring Freedom and Iraqi Freedom/New Dawn between October 2001 and August 2011 and whose cardiovascular autopsy reports were available at the time of data collection in January 2012. Prevalence of atherosclerosis was analyzed by various demographic characteristics and medical history.

Classifications of coronary atherosclerosis severity were determined prior to data analysis and designed to provide consistency with previous military studies: minimal (fatty streaking only), moderate (10%-49% luminal narrowing of >/=1 vessel), and severe (>/=50% narrowing of >/=1 vessel). MAIN OUTCOME MEASURES: Prevalence of coronary and aortic atherosclerosis in the US armed forces and by age, sex, self-reported race/ethnicity, education, occupation, service branch and component, military rank, body mass index at military entrance, and International Classification of Diseases, Ninth Revision, Clinical Modification, diagnoses of cardiovascular risk factors.

RESULTS: Of the 3832 service members included in the analysis, the mean age was 25.9 years (range, 18-59 years) and 98.3% were male. The prevalence of any coronary atherosclerosis was 8.5% (95% CI, 7.6%-9.4%); severe coronary atherosclerosis was present in 2.3% (95% CI, 1.8%-2.7%), moderate in 4.7% (95% CI, 4.0%-5.3%), and minimal in 1.5% (95% CI, 1.1%-1.9%). Service members with atherosclerosis were significantly older (mean [SD] age, 30.5 [8.1] years) than those without (mean [SD] age, 25.3 [5.6] years; P < .001). Comparing atherosclerosis prevalence among those with and without cardiovascular risk factor diagnoses (11.1% [95% CI, 10.1%-12.1%]), there was a greater prevalence among those with a diagnosis of dyslipidemia (50.0% [95% CI, 30.3%-69.7%]; age-adjusted prevalence ratio [PR], 2.09 [95% CI, 1.43-3.06]), hypertension (43.6% [95% CI, 27.3%-59.9%]; age-adjusted PR, 1.88 [95% CI, 1.34-2.65]), or obesity (22.3% [95% CI, 15.9%-28.7%]; age-adjusted PR, 1.47 [95% CI, 1.10-1.96]), but smoking (14.1% [95% CI, 8.0%-20.2%]) was not significantly associated with a higher prevalence of atherosclerosis (age-adjusted PR, 1.12 [95% CI, 0.73-1.74]). CONCLUSION: Among deployed
US service members who died of combat or unintentional injuries and received autopsies, the prevalence of atherosclerosis varied by age and cardiovascular risk factors


Insulin resistance, which plays a key role in the development of diabetes mellitus, is a putative modifiable risk factor for stroke. The aim of this study was to investigate if markers of insulin resistance were associated with risk of stroke in the general elderly population. This study was part of the large population-based Rotterdam Study and included 5,234 participants who were aged 55 years or older and stroke free and diabetes free at baseline (1997-2001). Fasting insulin levels and homeostasis model assessment for insulin resistance were used as markers for insulin resistance. Cox regression was used to determine associations between insulin resistance markers and stroke risk, adjusted for age, sex, and potential confounders. During 42,806 person-years of follow-up (median: 8.6 years), 366 first-ever strokes occurred, of which 225 were cerebral infarctions, 42 were intracerebral hemorrhages, and 99 were unspecified strokes. Fasting insulin levels were not associated with risk of any stroke, cerebral infarction, or intracerebral hemorrhage. Homeostasis model assessment for insulin resistance, which almost perfectly correlated with fasting insulin levels, was also not associated with risk of stroke or stroke subtypes. In conclusion, in this population-based cohort study among nondiabetic elderly, insulin resistance markers were not associated with risk of stroke or any of its subtypes.

http://www.ncbi.nlm.nih.gov/pubmed/22440092

BACKGROUND: Coronary heart disease and stroke are leading causes of mortality and ill health in Scotland, and clear associations have been found in previous studies between air pollution and cardiovascular disease. This study aimed to use routinely available data to examine whether there is any evidence of an association between short-term exposure to particulate matter (measured as PM(1)(0), particles less than 10 micrograms per cubic metre) and hospital admissions due to cardiovascular disease, in the two largest cities in Scotland during the years 2000 to 2006.

METHODS: The study utilised an ecological time series design, and the analysis was based on overdispersed Poisson log-linear models. RESULTS: No consistent associations were found between PM(1)(0) concentrations and cardiovascular hospital admissions in either of the cities studied, as all of the estimated relative risks were close to one, and all but one of the associated 95% confidence intervals contained the null risk of one. CONCLUSIONS: This study suggests that in small cities, where air quality is relatively good, then either PM(1)(0) concentrations have no effect on cardiovascular ill health, or that the routinely available data and the corresponding study design are not sufficient to detect an association.


OBJECTIVES: We examined the relationship between everyday and major discrimination and alcohol and drug use disorders in a nationally representative sample of African Americans and Black Caribbeans. METHODS: With data from the National Survey of American Life Study, we employed multivariable logistic regression analyses--while controlling for potential confounders--to examine the relationship between everyday and major discrimination and substance use disorders on the basis of Diagnostic and Statistical Manual of Mental Disorders criteria. RESULTS: Every 1 unit increase in the everyday discrimination scale positively predicted alcohol (odds ratio [OR] = 1.02; P < .01) and drug use (OR = 1.02; P < .05) disorders. Similarly, each additional major discrimination event positively predicted alcohol (OR = 1.10; P < .05) and drug use (OR = 1.15; P < .01) disorders. CONCLUSIONS: To our knowledge, this study is the first to examine problematic usage patterns rather than infrequent use of alcohol and drugs in a national sample of African American and Black Caribbean adults and the first to examine this particular relationship in a national sample of Black Caribbeans


BACKGROUND: The degree to which parental alcohol abuse is a risk factor for offspring mental distress is unclear, due to conflicting results of previous research. The inconsistencies in previous findings may be related to sample characteristics and lack of control of confounding or moderating factors. One such factor may be the gender of the abusing parent. Also, other factors, such as parental mental health, divorce, adolescent social network, school functioning or self-esteem, may impact the outcome. This study examines the impact of maternal and paternal alcohol abuse on adolescent mental distress, including potentially confounding, mediating or moderating effects of various variables. METHODS: Data from the Nord-Trondelag Health Study (HUNT), a Norwegian population based health survey, from 4012 offspring and their parents were analyzed. Parental alcohol abuse was measured by numerical consumption indicators and CAGE, whereas offspring mental distress was measured by SCL-5, an abbreviated instrument tapping symptoms of anxiety and depression. Statistical method was analysis of variance. RESULTS: Maternal alcohol abuse was related to offspring mental distress, whereas no effect could be shown of paternal alcohol abuse. Effects of maternal alcohol abuse was partly mediated by parental mental distress, offspring social network and school functioning. However, all effects were relatively small. CONCLUSIONS: The results indicate graver consequences for offspring of alcohol abusing mothers compared to offspring of alcohol abusing fathers. However, small effect sizes suggest that adolescent offspring of alcohol abusing parents in general manage quite well
Paludisme

(1) **Too much to ask.** Nature. 2012 Nov. 22, vol. 491, n° 7425, pp.495-496  


BACKGROUND: The candidate malaria vaccine RTS,S/AS01 reduced episodes of both clinical and severe malaria in children 5 to 17 months of age by approximately 50% in an ongoing phase 3 trial. We studied infants 6 to 12 weeks of age recruited for the same trial. METHODS: We administered RTS,S/AS01 or a comparator vaccine to 6537 infants who were 6 to 12 weeks of age at the time of the first vaccination in conjunction with Expanded Program on Immunization (EPI) vaccines in a three-dose monthly schedule. Vaccine efficacy against the first or only episode of clinical malaria during the 12 months after vaccination, a coprimary end point, was analyzed with the use of Cox regression. Vaccine efficacy against all malaria episodes, vaccine efficacy against severe malaria, safety, and immunogenicity were also assessed. RESULTS: The incidence of the first or only episode of clinical malaria in the intention-to-treat population during the 14 months after the first dose of vaccine was 0.31 per person-year in the RTS,S/AS01 group and 0.40 per person-year in the control group, for a vaccine efficacy of 30.1% (95% confidence interval [CI], 23.6 to 36.1). Vaccine efficacy in the per-protocol population was 31.3% (97.5% CI, 23.6 to 38.3). Vaccine efficacy against severe malaria was 26.0% (95% CI, -7.4 to 48.6) in the intention-to-treat population and 36.6% (95% CI, 4.6 to 57.7) in the per-protocol population. Serious adverse events occurred with a similar frequency in the two study groups. One month after administration of the third dose of RTS,S/AS01, 99.7% of children were positive for anti-circumsporozoite antibodies, with a geometric mean titer of 209 EU per milliliter (95% CI, 197 to 222). CONCLUSIONS: The RTS,S/AS01 vaccine coadministered with EPI vaccines provided modest protection against both clinical and severe malaria in young infants. (Funded by GlaxoSmithKline Biologicals and the PATH Malaria Vaccine Initiative; RTS,S ClinicalTrials.gov number, NCT00866619.)

(3) **ARROW KJ, DANZON PM, GELBAND H, JAMISON D, et al.** The Affordable Medicines Facility- -malaria: killing it slowly.  

(4) **BEER N, ALI AS, ESKILSSON H, JANSSON A, et al.** A qualitative study on caretakers’ perceived need of bed-nets after reduced malaria transmission in Zanzibar, Tanzania.  

BACKGROUND: The elimination of malaria in Zanzibar is highly dependent on sustained effective coverage of bed-nets to avoid malaria resurgence. The Health Belief Model (HBM) framework was used to explore the perceptions of malaria and bed-net use after a noticeable reduction in malaria incidence. METHODS: Nineteen in-depth interviews were conducted with female and male caretakers of children under five in North A district, Zanzibar. Deductive content analysis was used to identify meaning units that were condensed, coded and assigned to pre-determined elements of the HBM. RESULTS: Awareness of malaria among caretakers was high but the illness was now seen as easily curable and uncommon. In addition to the perceived advantage of providing protection against malaria, bed-nets were also thought to be useful for avoiding mosquito nuisance, especially during the rainy season when the malaria and mosquito burden is
The discomfort of sleeping under a net during the hot season was the main barrier that interrupted consistent bed-net usage. The main cue to using a bed-net was high mosquito density, and children were prioritized when it came to bed-net usage. Caretakers had high perceived self-efficacy and did not find it difficult to use bed-nets. Indoor Residual Spraying (IRS), which was recognized as an additional means of mosquito prevention, was not identified as an alternative for bed-nets. A barrier to net ownership was the increasingly high cost of bed-nets. CONCLUSIONS: Despite the reduction in malaria incidence and the resulting low malaria risk perceptions among caretakers, the benefit of bed-nets as the most proficient protection against mosquito bites upholds their use. This, in combination with the perceived high self-efficacy of caretakers, supports bed-net usage, while seasonality interrupts consistent use. High effective coverage of bed-nets could be further improved by reinforcing the benefits of bed-nets, addressing the seasonal heat barrier by using nets with larger mesh sizes and ensuring high bed-net ownership rates through sustainable and affordable delivery mechanisms.


Although sickle cell trait protects against severe disease due to Plasmodium falciparum, it has not been clear whether sickle trait also protects against asymptomatic infection (parasitemia). To address this question, the authors identified 171 persistently smear-negative children and 450 asymptomatic persistently smear-positive children in Bancoumana, Mali (June 1996 to June 1998). They then followed both groups for 2 years using a cohort-based strategy. Among the 171 children with persistently negative smears, the median time for conversion to smear-positive was longer for children with sickle trait than for children without (274 vs. 108 days, P < 0.001; Cox hazard ratio = 0.56, 95% confidence interval: 0.33, 0.96; P = 0.036). Similar differences were found in the median times to reinfection after spontaneous clearance without treatment (365 days vs. 184 days; P = 0.01). Alternatively, among the 450 asymptomatic children with persistently positive smears, the median time for conversion to smear-negative (spontaneous clearance) was shorter for children with sickle trait than for children without (190 vs. 365 days; P = 0.02). These protective effects of sickle trait against asymptomatic P. falciparum infection under conditions of natural transmission were demonstrable using a cohort-based approach but not when the same data were examined using a cross-sectional approach.


BACKGROUND: It is unclear how long it takes for health interventions to transition from research and development (R&D) to being used against diseases prevalent in resource-poor countries. We undertook an analysis of the time required to begin implementation of four vaccines and three malaria interventions. We evaluated five milestones for each intervention, and assessed if the milestones were associated with beginning implementation. METHODS: The authors screened World Health Organization (WHO) databases to determine the number of years between first regulatory approval of interventions, and countries beginning implementation. Descriptive analyses of temporal patterns and statistical analyses using logistic regression and Cox proportional hazard models were used to evaluate associations between five milestones and the beginning of implementation for each intervention. The milestones were: (A) presence of a coordinating group focused on the intervention; (B) availability of an intervention tailored to developing country health systems; (C) international financing commitment, and; (D) initial and (E) comprehensive WHO recommendations. Countries were categorized by World Bank income criteria. RESULTS: Five years after regulatory approval, no low-income countries (LICs) had begun implementing any of the vaccines, increasing to an average of only 4% of LICs after 10
years. Each malaria intervention was used by an average of 7% of LICs after five years and 37% after 10 years. Four of the interventions had similar implementation rates to hepatitis B vaccine (HepB), while one was slower and one was faster than HepB. A financing commitment and initial WHO recommendation appeared to be temporally associated with the beginning of implementation. The initial recommendation from WHO was the only milestone associated in all statistical analyses with countries beginning implementation (relative rate = 1.97, P < 0.001).

CONCLUSIONS: Although possible that four milestones were not associated with countries beginning implementation, we propose an alternative interpretation; that the milestones were not realized early enough in each intervention's development to shorten the time to beginning implementation. We discuss a framework built upon existing literature for consideration during the development of future interventions. Identifying critical milestones and their timing relative to R&D, promises to help new interventions realize their intended public health impact more rapidly


BACKGROUND: Appropriate home management of illness is vital to efforts to control malaria. The strategy of home management relies on caregivers to recognize malaria symptoms, assess severity and promptly seek appropriate care at a health facility if necessary. This paper examines the management of severe febrile illness (presumed malaria) among children under the age of five in rural Koulikoro Region, Mali. METHODS: This research examines in-depth case studies of twenty-five households in which a child recently experienced a severe febrile illness, as well as key informant interviews and focus group discussions with community members. These techniques were used to explore the sequence of treatment steps taken during a severe illness episode and the context in which decisions were made pertaining to pursuing treatments and sources of care, while incorporating the perspective and input of the mother as well as the larger household. RESULTS: Eighty-one participants were recruited in 25 households meeting inclusion criteria. Children's illness episodes involved multiple treatment steps, with an average of 4.4 treatment steps per episode (range: 2-10). For 76% of children, treatment began in the home, but 80% were treated outside the home as a second recourse. Most families used both traditional and modern treatments, administered either inside the home by family members, or by traditional or modern healers. Participants' stated preference was for modern care, despite high rates of reported treatment failure (52%, n=12), however, traditional treatments were also often deemed appropriate and effective. The most commonly cited barrier to seeking care at health facilities was cost, especially during the rainy season. Financial constraints often led families to use traditional treatments. CONCLUSIONS: Households have few options available to them in moments of overlapping health and economic crises. Public health research and policy should focus on the reducing barriers that inhibit poor households from promptly seeking appropriate health care. Enhancing the quality of care provided at community health facilities and supporting mechanisms
by which treatment failures are quickly identified and addressed can contribute to reducing subsequent treatment delays and avoid inappropriate recourse to traditional treatments.


(12) GULLAND A. *Project to increase availability of malaria drug has worked, study finds.* BMJ. 2012, vol. 345, p.e7451

(13) GULLAND A. *Cheap malaria drug is going to wrong people, says charity.* BMJ. 2012, vol. 345, p.e7157


Platelets restrict the growth of intraerythrocytic malaria parasites by binding to parasitized cells and killing the parasite within. Here, we show that the platelet molecule platelet factor 4 (PF4 or CXCL4) and the erythrocyte Duffy-antigen receptor (Fy) are necessary for platelet-mediated killing of Plasmodium falciparum parasites. PF4 is released by platelets on contact with parasitized red cells, and the protein directly kills intraerythrocytic parasites. This function for PF4 is critically dependent on Fy, which binds PF4. Genetic disruption of Fy expression inhibits binding of PF4 to parasitized cells and concomitantly prevents parasite killing by both human platelets and recombinant human PF4. The protective function afforded by platelets during a malarial infection may therefore be compromised in Duffy-negative individuals, who do not express Fy.


BACKGROUND: Malaria is one of the greatest causes of mortality worldwide. Use of the most effective treatments for malaria remains inadequate for those in need, and there is concern over the emergence of resistance to these treatments. In 2010, the Global Fund launched the Affordable Medicines Facility--malaria (AMFm), a series of national-scale pilot programmes designed to increase the access and use of quality-assured artemisinin based combination therapies (QAACTs) and reduce that of artemisinin monotherapies for treatment of malaria. AMFm involves manufacturer price negotiations, subsidies on the manufacturer price of each treatment purchased, and supporting interventions such as communications campaigns. We present findings on the effect of AMFm on QAACT price, availability, and market share, 6-15 months after the delivery of subsidised ACTs in Ghana, Kenya, Madagascar, Niger, Nigeria, Uganda, and Tanzania (including Zanzibar). METHODS: We did nationally representative baseline and endpoint surveys of public and private sector outlets that stock antimalarial
treatments. QAACTs were identified on the basis of the Global Fund's quality assurance policy. Changes in availability, price, and market share were assessed against specified success benchmarks for 1 year of AMFm implementation. Key informant interviews and document reviews recorded contextual factors and the implementation process. FINDINGS: In all pilots except Niger and Madagascar, there were large increases in QAACT availability (25.8-51.9 percentage points), and market share (15.9-40.3 percentage points), driven mainly by changes in the private for-profit sector. Large falls in median price for QAACTs per adult equivalent dose were seen in the private for-profit sector in six pilots, ranging from US$1.28 to $4.82. The market share of oral artemisinin monotherapies decreased in Nigeria and Zanzibar, the two pilots where it was more than 5% at baseline. INTERPRETATION: Subsidies combined with supporting interventions can be effective in rapidly improving availability, price, and market share of QAACTs, particularly in the private for-profit sector. Decisions about the future of AMFm should also consider the effect on use in vulnerable populations, access to malaria diagnostics, and cost-effectiveness. FUNDING: The Global Fund to Fight AIDS, Tuberculosis and Malaria, and the Bill & Melinda Gates Foundation.

(1) Chocolate at the checkout is a risk to public health. BMJ. 2012, vol. 345, p.e6921

(2) Randomised trials link sugary drinks to weight gain in children. BMJ. 2012, vol. 345, p.e6442


BACKGROUND: Obesity is a major global epidemic and a burden to society and health systems. It is well known risk factor for a number of chronic medical conditions with high morbidity and mortality. This study aimed to provide an estimate of the direct costs associated to outpatient and inpatient care of overweight and obesity related diseases in the perspective of the Brazilian Health System (SUS). METHODS: Population attributable risk (PAR) was calculated for selected diseases related to overweight and obesity and with the following parameters: Relative risk (RR) \( \geq 1.20 \) or \( \geq 1.10 \) and < 1.20, but important problem of public health due its high prevalence. After a broad search in the literature, two meta-analysis were selected to provide RR for PAR calculation. The prevalence rates of overweight and obesity in Brazilians with \( \geq 18 \) years were obtained from large national survey. The national health database (DATASUS) was used to estimate the annual cost of the Brazilian Unified Health System (SUS) with the diseases included in the analysis. The extracted values were stratified by sex, type of service (inpatient or outpatient care) and year. Data were collected from 2008 to 2010 and the results reflect the average of 3 years. Brazilian costs were converted into US dollars during the analysis using a
purchasing power parity basis (2010). RESULTS: The estimated total costs in one year with all
diseases related to overweight and obesity are US$ 2,1 billion; US$ 1,4 billion (68.4% of total
costs) due to hospitalizations and US$ 679 million due to ambulatory procedures. Approximately
10% of these cost is attributable to overweight and obesity. CONCLUSION: The results confirm
that overweight and obesity carry a great economic burden for Brazilian health system and for the
society. The knowledge of these costs will be useful for future economic analysis of preventive
and treatment interventions

309, n° 2, p.134

(6) COLBERT JA, ADLER JN. Clinical decisions. Sugar-sweetened beverages--polling results. N

(7) DAVIS CL, WALLER JL, POLLOCK NK. Exercise for overweight children and diabetes risk--
reply. JAMA. 2013 Jan. 9, vol. 309, n° 2, pp.133-134


(9) EYLER AA, NGUYEN L, KONG J, YAN Y, et al. Patterns and predictors of enactment of state
vol. 102, n° 12, pp.2294-2302

OBJECTIVES: We developed a content review for state policies related to childhood obesity, and
we have quantitatively described the predictors of enactment. METHODS: We collected an
inventory of 2006 through 2009 state legislation on 27 childhood obesity topics from legislative
databases. We coded each bill for general information, topic content, and other appropriate
components. We conducted a general descriptive analysis and 3 multilevel analyses using bill-
and state-level characteristics to predict bill enactment. RESULTS: Common topics in the 27% of
the bills that were enacted were community physical activity access, physical education, and
school food policy. Committee and bipartisan sponsorship and having term limits significantly
predicted enactment in at least 1 model. Bills with safe routes to school or health and nutrition
content were twice as likely to be enacted. Bills containing product and menu labeling or soda and
snack taxes were significantly less likely to be enacted. CONCLUSIONS: Bipartisan and
committee support and term limits are important in bill enactment. Advocacy efforts can be
tailored to increase awareness and sense of priority among policymakers

(10) FLEGAL KM, KIT BK, ORPANA H, GRAUBARD BI. *Association of all-cause mortality with
overweight and obesity using standard body mass index categories: a systematic review

IMPORTANCE: Estimates of the relative mortality risks associated with normal weight,
overweight, and obesity may help to inform decision making in the clinical setting. OBJECTIVE:
To perform a systematic review of reported hazard ratios (HRs) of all-cause mortality for
overweight and obesity relative to normal weight in the general population. DATA SOURCES: PubMed and EMBASE electronic databases were searched through September 30, 2012, without language restrictions. STUDY SELECTION: Articles that reported HRs for all-cause mortality using standard body mass index (BMI) categories from prospective studies of general populations of adults were selected by consensus among multiple reviewers. Studies were excluded that used nonstandard categories or that were limited to adolescents or to those with specific medical conditions or to those undergoing specific procedures. PubMed searches yielded 7034 articles, of which 141 (2.0%) were eligible. An EMBASE search yielded 2 additional articles. After eliminating overlap, 97 studies were retained for analysis, providing a combined sample size of more than 2.88 million individuals and more than 270,000 deaths. DATA EXTRACTION: Data were extracted by 1 reviewer and then reviewed by 3 independent reviewers. We selected the most complex model available for the full sample and used a variety of sensitivity analyses to address issues of possible overadjustment (adjusted for factors in causal pathway) or underadjustment (not adjusted for at least age, sex, and smoking). RESULTS: Random-effects summary all-cause mortality HRs for overweight (BMI of 25-<30), obesity (BMI of >/=30), grade 1 obesity (BMI of 30-<35), and grades 2 and 3 obesity (BMI of >/=35) were calculated relative to normal weight (BMI of 18.5-<25). The summary HRs were 0.94 (95% CI, 0.91-0.96) for overweight, 1.18 (95% CI, 1.12-1.25) for obesity (all grades combined), 0.95 (95% CI, 0.88-1.01) for grade 1 obesity, and 1.29 (95% CI, 1.18-1.41) for grades 2 and 3 obesity. These findings persisted when limited to studies with measured weight and height that were considered to be adequately adjusted. The HRs tended to be higher when weight and height were self-reported rather than measured. CONCLUSIONS AND RELEVANCE: Relative to normal weight, both obesity (all grades) and grades 2 and 3 obesity were associated with significantly higher all-cause mortality. Grade 1 obesity overall was not associated with higher mortality, and overweight was associated with significantly lower all-cause mortality. The use of predefined standard BMI groupings can facilitate between-study comparisons


OBJECTIVES: To describe the association and its magnitude between body mass index category, sex, and cardiovascular disease risk parameters in school aged children in highly developed countries. DESIGN: Systematic review and meta-analysis. Quality of included studies assessed by an adapted version of the Cochrane Collaboration’s risk of bias assessment tool. Results of included studies in meta-analysis were pooled and analysed by Review Manager version 5.1. DATA SOURCES: Embase, PubMed, EBSCOHost's cumulative index to nursing and allied health literature, and the Web of Science databases for papers published between January 2000 and December 2011. REVIEW METHODS: Healthy children aged 5 to 15 in highly developed countries enrolled in studies done after 1990 and using prospective or retrospective cohort, cross sectional, case-control, or randomised clinical trial designs in school, outpatient, or community settings. Included studies had to report an objective measure of weight and at least one prespecified risk parameter for cardiovascular disease. RESULTS: We included 63 studies of 49 220 children. Studies reported a worsening of risk parameters for cardiovascular disease in overweight and obese participants. Compared with normal weight children, systolic blood pressure was higher by 4.54 mm Hg (99% confidence interval 2.44 to 6.64; n=12 169, eight studies) in overweight children, and by 7.49 mm Hg (3.36 to 11.62; n=8074, 15 studies) in obese children. We found similar associations between groups in diastolic and 24 h ambulatory systolic blood pressure. Obesity adversely affected concentrations of all blood lipids; total cholesterol and triglycerides were 0.15 mmol/L (0.04 to 0.25, n=5072) and 0.26 mmol/L (0.13 to 0.39, n=5138) higher in obese children, respectively. Fasting insulin and insulin resistance were significantly higher in obese participants but not in overweight participants. Obese children had a significant increase in left ventricular mass of 19.12 g (12.66 to 25.59, n=223), compared with normal weight children. CONCLUSION: Having a body mass index outside the normal range significantly
worsens risk parameters for cardiovascular disease in school aged children. This effect, already substantial in overweight children, increases in obesity and could be larger than previously thought. There is a need to establish whether acceptable parameter cut-off levels not considering weight are a valid measure of risk in modern children and whether methods used in their study and reporting should be standardised.


BACKGROUND: Error in self-reported measures of obesity has been frequently described, but the effect of self-reported error on recruitment into diabetes prevention programs is not well established. The aim of this study was to examine the effect of using self-reported obesity data from the Finnish diabetes risk score (FINDRISC) on recruitment into the Greater Green Triangle Diabetes Prevention Project (GGT DPP). METHODS: The GGT DPP was a structured group-based lifestyle modification program delivered in primary health care settings in South-Eastern Australia. Between 2004-05, 850 FINDRISC forms were collected during recruitment for the GGT DPP. Eligible individuals, at moderate to high risk of developing diabetes, were invited to undertake baseline tests, including anthropometric measurements performed by specially trained nurses. In addition to errors in calculating total risk scores, accuracy of self-reported data (height, weight, waist circumference (WC) and Body Mass Index (BMI)) from FINDRISCs was compared with baseline data, with impact on participation eligibility presented. RESULTS: Overall, calculation errors impacted on eligibility in 18 cases (2.1%). Of n = 279 GGT DPP participants with measured data, errors (total score calculation, BMI or WC) in self-report were found in n = 90 (32.3%). These errors were equally likely to result in under- or over-reported risk. Under-reporting was more common in those reporting lower risk scores (Spearman-rho = -0.226, p-value < 0.001). However, underestimation resulted in only 6% of individuals at high risk of diabetes being incorrectly categorised as moderate or low risk of diabetes. CONCLUSIONS: Overall FINDRISC was found to be an effective tool to screen and recruit participants at moderate to high risk of diabetes, accurately categorising levels of overweight and obesity using self-report data. The results could be generalisable to other diabetes prevention programs using screening tools which include self-reported levels of obesity.


BACKGROUND: We describe the design and present the results of the first year of a population-based study of screening for type 2 diabetes in individuals at high risk of developing the disease. High risk is defined as having abdominal obesity. METHODS: Between 2006 and 2007, 79,142 inhabitants of two Dutch municipalities aged 40-74 years were approached to participate in screening. Eligible participants had a self-reported waist circumference of \( \geq 80 \text{ cm} \) for women and \( \geq 94 \text{ cm} \) for men, and no known pre-existing diabetes. Of the respondents (\( n = 20,578 \); response rate 26%), 16,135 were abdominally obese. In total, 10,609 individuals gave written informed consent for participation and were randomized into either the screening (\( n = 5305 \)) or the control arm (\( n = 5304 \)). Participants in the screening arm were invited to have their fasting plasma glucose (FPG) measured and were referred to their general practitioner (GP) if it was \( \geq 6.1 \text{ mmol/L} \). In addition, blood lipids were determined in the screening arm, because abdominal obesity is often associated with cardiovascular risk factors. Participants in both arms received written healthy lifestyle information. Between-group differences were analyzed with Chi-square tests and logistic regression (categorical variables) and unpaired t-tests (continuous variables).

RESULTS: The screening attendance rate was 84.1%. Attending screening was associated with age at randomization (OR = 1.03, 95% CI 1.02-1.04), being married (OR = 1.57, 95% CI 1.33-1.83) and not smoking currently (OR = 0.52, 95% CI 0.44-0.62). Of the individuals screened, 5.6% had hyperglycemia, and a further 11.6% had an estimated absolute cardiovascular disease risk of 5% or higher, according to the Systematic Coronary Risk Evaluation risk model. These participants were referred to their GP. CONCLUSIONS: Self-reported home-assessed waist circumference could feasibly detect persons at high risk of hyperglycemia or cardiovascular disease. Continuation of the large-scale RCT is warranted to test the hypothesis that targeted population-based screening for type 2 diabetes leads to a significant reduction in cardiovascular morbidity and mortality. TRIAL REGISTRATION: ISRCTN75983009

KMIETOWICZ Z. Obese patients get inadequate care before and after bariatric surgery, finds review. BMJ. 2012, vol. 345, p.e6890


The proportion of children suffering from chronic illnesses—such as asthma and obesity, which have significant environmental components—is increasing. Chronic disease states previously seen only in adulthood are emerging during childhood, and health inequalities by social class are increasing. Advocacy to ensure environmental health and to protect from the biological embedding of toxic stress has become a fundamental part of pediatrics. We have presented the rationale for addressing environmental and social determinants of children’s health, the epidemiology of issues facing children’s health, recent innovations in pediatric medical education that have incorporated public health principles, and policy opportunities that have arisen with the passage of the 2010 Patient Protection and Affordable Care Act


Not all obese adults have cardiometabolic abnormalities. It is unknown whether this is true in children and, if true, whether children who have metabolically healthy overweight/obesity (MHO) will also have favorable cardiometabolic profiles in adulthood. These aspects were examined in 1,098 individuals who participated as both children (aged 5-17 years) and adults (aged 24-43 years) in the Bogalusa Heart Study between 1997 and 2002 in Bogalusa, Louisiana. MHO was defined as being in the top body mass index quartile, while low density lipoprotein cholesterol, triglycerides, mean arterial pressure, and glucose were in the bottom 3 quartiles, and high density lipoprotein cholesterol was in the top 3 quartiles. Forty-six children (4.2%) had MHO, and they were more likely to retain MHO status in adulthood compared with children in other categories (P < 0.0001). Despite markedly increased obesity in childhood and in adulthood, these same MHO children and adults showed a cardiometabolic profile generally comparable to that of nonoverweight/obese children (P > 0.05 in most cases). Moreover, there was no difference in carotid intima-media thickness in adulthood between MHO children and nonoverweight/obese children. Further, carotid intima-media thickness in adulthood was lower in MHO children than in metabolically abnormal, overweight/obese children (P = 0.003). In conclusion, the MHO phenotype starts in childhood and continues into adulthood.


LUDWIG DS, BLUMENTHAL SJ, WILLETT WC. Opportunities to reduce childhood hunger and obesity: restructuring the Supplemental Nutrition Assistance Program (the Food Stamp Program). JAMA. 2012 Dec, vol. 308, n° 24, pp.2567-2568


OBJECTIVES: We analyzed the Japan's walking-to-school practice implemented in 1953 for lessons useful to other cities and countries. METHODS: We reviewed background documents (gray literature, online government information, local policy documents, and regulations) for existing regulations in several urban settings. We also contacted boards of education. RESULTS: Each municipality has a board of education in charge of public schools, which considers the geography, climate, and the transport situation to determine the method of commuting. Because there is high availability of schools in urban areas and most are located within walking range of the children's homes, walking is the most common method. There are different safety initiatives depending on the district's characteristics. Parents, school staff, and local volunteers are involved in supervision. CONCLUSIONS: The walk-to-school practice has helped combat childhood obesity by providing regular physical activity. Recommendations to cities promoting walking to school are (1) base interventions on the existing network of schools and adapt the provision to other local organizations, (2) establish safety measures, and (3) respond specifically to local characteristics. Besides the well-established safety interventions, the policy's success may also be associated with Japan's low crime rate.
BACKGROUND: Recreational facilities are an important community resource for health promotion because they provide access to affordable physical activities. However, despite their health mandate, many have unhealthy food environments that may paradoxically increase the risk of childhood obesity. The Alberta Nutrition Guidelines for Children and Youth (ANGCY) are government-initiated, voluntary guidelines intended to facilitate children’s access to healthy food and beverage choices in schools, childcare and recreational facilities, however few recreational facilities are using them. METHODS: We used mixed methods within an exploratory multiple case study to examine factors that influenced adoption and implementation of the ANGCY and the nature of the food environment within three cases: an adopter, a semi-adopter and a non-adopter of the ANGCY. Diffusion of Innovations theory provided the theoretical platform for the study. Qualitative data were generated through interviews, observations, and document reviews, and were analysed using directed content analysis. Set theoric logic was used to identify factors that differentiated adopters from the non-adopter. Quantitative sales data were also collected, and the quality of the food environment was scored using four complementary tools. RESULTS: The keys to adoption and implementation of nutrition guidelines in recreational facilities related to the managers’ nutrition-related knowledge, beliefs and perceptions, as these shaped his decisions and actions. The manager, however, could not accomplish adoption and implementation alone. Intersectoral linkages with schools and formal, health promoting partnerships with industry were also important for adoption and implementation to occur. The food environment in facilities that had adopted the ANGCY did not appear to be superior to the food environment in facilities that had not adopted the ANGCY. CONCLUSIONS: ANGCY uptake may continue to falter under the current voluntary approach, as the environmental supports for voluntary action are poor. Where ANGCY uptake does occur, changes to the food environment may be relatively minor. Stronger government measures may be needed to require recreational facilities to improve their food environments and to limit availability of unhealthy foods.


Prioritization of obesity prevention and management policy is based on one's understanding of the health risks associated with increasing body weight. However, there is evidence that the magnitude of these health risks may be changing over time. Here, the authors analyze the theoretical drivers of these changes and then examine whether there is empirical evidence to support the theory. They conclude that, although the mortality risks associated with increasing body weight may be decreasing over time, the overall health burden appears likely to increase


Florida resident birth certificates for 2004-2006 were linked to the Centers for Disease Control and Prevention's National ART Surveillance System and were used to investigate 1) whether the association of assisted reproductive technology (ART) with preterm birth varies by prepregnancy body mass index and 2) whether the association varies by plurality. Preterm birth was defined as early preterm birth (gestation <34 weeks) and late preterm birth (gestation 34-36 weeks). Descriptive statistics and multinomial logistic regression were used to explore maternal and infant differences by ART status and plurality. Of 581,403 women included in the study, 24.0% were overweight, 18.6% were obese, 7.3% had late preterm birth, 2.6% had early preterm birth, and 0.67% conceived through ART. Among singleton births, ART was associated with increased early preterm birth risk among underweight (odds ratio (OR) = 2.94, 95% confidence interval (CI): 1.27, 6.81), overweight (OR = 1.75, 95% CI: 1.12, 2.72), and obese (OR = 2.37, 95% CI: 1.51, 3.71) women. Among twins, ART was significantly associated with increased risk among overweight (OR = 1.61, 95% CI: 1.12, 2.32) and obese (OR = 1.85, 95% CI: 1.18, 2.90) women. Differences in the associations between ART and early preterm birth by body mass index and plurality warrant further investigation.


BACKGROUND: To review studies undertaken in South Africa (SA) which included sugar intake associated with dental caries, non-communicable diseases, diabetes, obesity and/or micronutrient dilution, since the food-based dietary guideline: "Use foods and drinks that contain sugar sparingly and not between meals" was promulgated by the Department of Health (DOH) in 2002. METHODS: Three databases (PubMed, Cochrane Library, and ScienceDirect), and SA Journal of Clinical Nutrition (SAJCN), DOH and SA Medical Research Council (SAMRC) websites were searched for SA studies on sugar intake published between 2000 and January 2012. Studies were included in the review if they evaluated the following: sugar intake and dental caries; sugar intake and non-communicable diseases; sugar and diabetes; sugar and obesity and/or sugar and micronutrient dilution. RESULTS: The initial search led to 12 articles in PubMed, 0 in Cochrane, 35 in ScienceDirect, 5 in the SAJCN and 3 reports from DOH/SAMRC. However, after reading the abstracts only 7 articles from PubMed, 4 from SAJCN and 3 reports were retained for use as being relevant to the current review. Hand searching of reference lists of SAJCN articles produced two more articles. Intake of sugar appears to be increasing steadily across the South African (SA) population. Children typically consume about 50 g per day, rising to as much as 100 g per day in adolescents. This represents about 10% of dietary energy, possibly as much as 20%. It has been firmly established that sugar plays a major role in development of dental caries. Furthermore, a few studies have shown that sugar has a diluting effect on the micronutrient content of the diet which lowers the intake of micronutrients. Data from numerous systematic reviews have shown that dietary sugar increases the risk for development of both obesity and type 2 diabetes. Risk for...
development of these conditions appears to be especially strong when sugar is consumed as sugar-sweetened beverages. CONCLUSION: Based on the evidence provided the current DOH food-based dietary guideline on sugar intake should remain as is


http://www.ncbi.nlm.nih.gov/pubmed/23299595


OBJECTIVES: We investigated early childhood disparities in high body mass index (BMI) between Black and White US children. METHODS: We compared differences in Black and White children's prevalence of sociodemographic, prenatal, perinatal, and early life risk and protective factors; fit logistic regression models predicting high BMI ( >/= 95th percentile) at age 4 to 5 years to 2 nationally representative samples followed from birth; and performed separate and pooled-survey estimations of these models. RESULTS: After adjustment for sample design-related variables, models predicting high BMI in the 2 samples were statistically indistinguishable. In the pooled-survey models, Black children's odds of high BMI were 59% higher than White children's (odds ratio [OR] = 1.59; 95% confidence interval [CI] = 1.32, 1.92). Sociodemographic predictors reduced the racial disparity to 46% (OR = 1.46; 95% CI = 1.17, 1.81). Prenatal, perinatal, and early life predictors reduced the disparity to nonsignificance (OR = 1.18; 95% CI = 0.93, 1.49). Maternal prepregnancy obesity and short-duration or no breastfeeding were among predictors for which racial differences in children's exposures most disadvantaged Black children.
CONCLUSIONS: Racial disparities in early childhood high BMI were largely explained by potentially modifiable risk and protective factors


BACKGROUND: Speed of eating, an important aspect of eating behaviour, has recently been related to loss of control of food intake and obesity. Very little time is allocated for lunch at school and thus children may consume food more quickly and food intake may therefore be affected. Study 1 measured the time spent eating lunch in a large group of students eating together for school meals. Study 2 measured the speed of eating and the amount of food eaten in individual school children during normal school lunches and then examined the effect of experimentally increasing or decreasing the speed of eating on total food intake. METHODS: The time spent eating lunch was measured with a stop watch in 100 children in secondary school. A more detailed study of eating behaviour was then undertaken in 30 secondary school children (18 girls). The amount of food eaten at lunch was recorded by a hidden scale when the children ate amongst their peers and by a scale connected to a computer when they ate individually. When eating individually, feedback on how quickly to eat was visible on the computer screen. The speed of eating could therefore be increased or decreased experimentally using this visual feedback and the total amount of food eaten measured. RESULTS: In general, the children spent very little time eating their lunch. The 100 children in Study 1 spent on average (SD) just 7 (0.8) minutes eating
lunch. The girls in Study 2 consumed their lunch in 5.6 (1.2) minutes and the boys ate theirs in only 6.8 (1.3) minutes. Eating with peers markedly distorted the amount of food eaten for lunch; only two girls and one boy maintained their food intake at the level observed when the children ate individually without external influences (258 (38) g in girls and 289 (73) g in boys). Nine girls ate on average 33% less food and seven girls ate 23% more food whilst the remaining boys ate 26% more food. The average speed of eating during school lunches amongst groups increased to 183 (53)% in the girls and to 166 (47)% in the boys compared to the speed of eating in the unrestricted condition. These apparent changes in food intake during school lunches could be replicated by experimentally increasing the speed of eating when the children were eating individually.

CONCLUSIONS: If insufficient time is allocated for consuming school lunches, compensatory increased speed of eating puts children at risk of losing control over food intake and in many cases over-eating. Public health initiatives to increase the time available for school meals might prove a relatively easy way to reduce excess food intake at school and enable children to eat more healthily.

SIDA


The visualization of RNA conformational changes has provided fundamental insights into how regulatory RNAs carry out their biological functions. The RNA structural transitions that have been characterized so far involve long-lived species that can be captured by structure characterization techniques. Here we report the nuclear magnetic resonance visualization of RNA transitions towards ‘invisible’ excited states (ESs), which exist in too little abundance (2-13%) and for too short a duration (45-250 mus) to allow structural characterization by conventional techniques. Transitions towards ESs result in localized rearrangements in base-pairing that alter building block elements of RNA architecture, including helix-junction-helix motifs and apical loops. The ES can inhibit function by sequestering residues involved in recognition and signalling or promote ATP-independent strand exchange. Thus, RNAs do not adopt a single conformation, but rather exist in
rapid equilibrium with alternative ESs, which can be stabilized by cellular cues to affect functional outcomes


BACKGROUND: Short-course antiretroviral therapy (ART) in primary human immunodeficiency virus (HIV) infection may delay disease progression but has not been adequately evaluated.

METHODS: We randomly assigned adults with primary HIV infection to ART for 48 weeks, ART for 12 weeks, or no ART (standard of care), with treatment initiated within 6 months after seroconversion. The primary end point was a CD4+ count of less than 350 cells per cubic millimeter or long-term ART initiation. RESULTS: A total of 366 participants (60% men) underwent randomization to 48-week ART (123 participants), 12-week ART (120), or standard care (123), with an average follow-up of 4.2 years. The primary end point was reached in 50% of the 48-week ART group, as compared with 61% in each of the 12-week ART and standard-care groups. The average hazard ratio was 0.63 (95% confidence interval [CI], 0.45 to 0.90; P=0.01) for 48-week ART as compared with standard care and was 0.93 (95% CI, 0.67 to 1.29; P=0.67) for 12-week ART as compared with standard care. The proportion of participants who had a CD4+ count of less than 350 cells per cubic millimeter was 28% in the 48-week ART group, 40% in the 12-week group, and 40% in the standard-care group. Corresponding values for long-term ART initiation were 22%, 21%, and 22%. The median time to the primary end point was 65 weeks (95% CI, 17 to 114) longer with 48-week ART than with standard care. Post hoc analysis identified a trend toward a greater interval between ART initiation and the primary end point the closer that ART was initiated to estimated seroconversion (P=0.09), and 48-week ART conferred a reduction in the HIV RNA level of 0.44 log(10) copies per milliliter (95% CI, 0.25 to 0.64) 36 weeks after the completion of short-course therapy. There were no significant between-group differences in the incidence of the acquired immunodeficiency syndrome, death, or serious adverse events.

CONCLUSIONS: A 48-week course of ART in patients with primary HIV infection delayed disease progression, although not significantly longer than the duration of the treatment. There was no evidence of adverse effects of ART interruption on the clinical outcome. (Funded by the Wellcome Trust; SPARTAC Controlled-Trials.com number, ISRCTN76742797, and EudraCT number, 2004-000446-20.)


BACKGROUND: The relationship between the timing of the initiation of antiretroviral therapy (ART) after infection with human immunodeficiency virus type 1 (HIV-1) and the recovery of CD4+ T-cell counts is unknown. METHODS: In a prospective, observational cohort of persons with acute or early HIV-1 infection, we determined the trajectory of CD4+ counts over a 48-month period in partially overlapping study sets: study set 1 included 384 participants during the time window in which they were not receiving ART and study set 2 included 213 participants who received ART soon after study entry or sometime thereafter and had a suppressed plasma HIV viral load. We investigated the likelihood and rate of CD4+ T-cell recovery to 900 or more cells per cubic millimeter within 48 months while the participants were receiving viral-load-suppressive ART. RESULTS: Among the participants who were not receiving ART, CD4+ counts increased spontaneously, soon after HIV-1 infection, from the level at study entry (median, 495 cells per cubic millimeter; interquartile range, 383 to 622), reached a peak value (median, 763 cells per
cubic millimeter; interquartile range, 573 to 987) within approximately 4 months after the estimated date of infection, and declined progressively thereafter. Recovery of CD4+ counts to 900 or more cells per cubic millimeter was seen in approximately 64% of the participants who initiated ART earlier (<4 months after the estimated date of HIV infection) as compared with approximately 34% of participants who initiated ART later (>4 months) (P<0.001). After adjustment for whether ART was initiated when the CD4+ count was 500 or more cells per cubic millimeter or less than 500 cells per cubic millimeter, the likelihood that the count would increase to 900 or more cells per cubic millimeter was lower by 65% (odds ratio, 0.35), and the rate of recovery was slower by 56% (rate ratio, 0.44), if ART was initiated later rather than earlier. There was no association between the plasma HIV RNA level at the time of initiation of ART and CD4+ T-cell recovery.

CONCLUSIONS: A transient, spontaneous restoration of CD4+ T-cell counts occurs in the 4-month time window after HIV-1 infection. Initiation of ART during this period is associated with an enhanced likelihood of recovery of CD4+ counts. (Funded by the National Institute of Allergy and Infectious Diseases and others.)


In mammals, one of the most pronounced consequences of viral infection is the induction of type I interferons, cytokines with potent antiviral activity. Schlafen (Slfn) genes are a subset of interferon-stimulated early response genes (ISGs) that are also induced directly by pathogens via the interferon regulatory factor 3 (IRF3) pathway. However, many ISGs are of unknown or incompletely understood function. Here we show that human SLFN11 potently and specifically abrogates the production of retroviruses such as human immunodeficiency virus 1 (HIV-1). Our study revealed that SLFN11 has no effect on the early steps of the retroviral infection cycle, including reverse transcription, integration and transcription. Rather, SLFN11 acts at the late stage of virus production by selectively inhibiting the expression of viral proteins in a codon-usage-dependent manner. We further find that SLFN11 binds transfer RNA, and counteracts changes in the tRNA pool elicited by the presence of HIV. Our studies identified a novel antiviral mechanism within the innate immune response, in which SLFN11 selectively inhibits viral protein synthesis in HIV-infected cells by means of codon-bias discrimination.


Developing a vaccine for human immunodeficiency virus (HIV) may be aided by a complete understanding of those rare cases in which some HIV-infected individuals control replication of the virus. Most of these elite controllers express the histocompatibility alleles HLA-B*57 or HLA-B*27 (ref. 3). These alleles remain by far the most robust associations with low concentrations of plasma virus, yet the mechanism of control in these individuals is not entirely clear. Here we vaccinate Indian rhesus macaques that express Mamu-B*08, an animal model for HLA-B*27-mediated elite control, with three Mamu-B*08-restricted CD8(+) T-cell epitopes, and demonstrate that these vaccinated animals control replication of the highly pathogenic clonal simian immunodeficiency virus (SIV) mac239 virus. High frequencies of CD8(+) T cells against these Vif and Nef epitopes in the blood, lymph nodes and colon were associated with viral control. Moreover, the frequency of the CD8(+) T-cell response against the Nef RL10 epitope (Nef amino acids 137-146) correlated significantly with reduced acute phase viraemia. Finally, two of the eight vaccinees lost control of viral replication in the chronic phase, concomitant with escape in all three targeted epitopes, further implicating these three CD8(+) T-cell responses in the control of viral replication. Our findings indicate that narrowly targeted vaccine-induced virus-specific CD8(+) T-cell responses can control replication of the AIDS virus.


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**Tuberculose**


BACKGROUND: In Ethiopia where there is no strong surveillance system and diagnostic facilities are limited, the real burden of tuberculosis (TB) lymphadenitis is not well known. Therefore, we conducted a study to estimate the prevalence of TB lymphadenitis in Southwest Ethiopia.

METHODS: A community based cross-sectional study was conducted from February to March 2009 in the Gilgel Gibe field research area. A total of 30,040 individuals 15 years or older in 10,882 households were screened for TB lymphadenitis. Any individual 15 years or older with lumps in the neck, armpits or groin up on interview were considered TB lymphadenitis suspect. The diagnosis of TB lymphadenitis was established when acid fast bacilli (AFB) smear microscopy of fine needle aspiration (FNA) sample, culture or cytology suggested TB. HIV counseling and testing was offered to all TB lymphadenitis suspects. Descriptive and bivariate analysis was done using SPSS version 15. RESULTS: Complete data were available for 27,597 individuals. A total of 87 TB lymphadenitis suspects were identified. Most of the TB lymphadenitis suspects were females (72.4%). Sixteen cases of TB lymphadenitis were confirmed. The prevalence of TB lymphadenitis was thus 58.0 per 100,000 people (16/27,597) (95% CI 35.7-94.2). Individuals who had a contact history with chronic coughers (OR 5.58, 95% CI 1.23-25.43) were more likely to have TB lymphadenitis. Lymph nodes with caseous FNA were more likely to be positive for TB lymphadenitis (OR 5.46, 95% CI 1.69-17.61). CONCLUSION: The prevalence of TB lymphadenitis in Gilgel Gibe is similar with the WHO estimates for Ethiopia. Screening of TB lymphadenitis particularly for family members who have contact with chronic coughers is recommended. Health extension workers could be trained to screen and refer TB lymphadenitis suspects using simple methods.


BACKGROUND: Monitoring the outcome of tuberculosis treatment and understanding the specific reasons for unsuccessful treatment outcome are important in evaluating the effectiveness of tuberculosis control program. This study investigated tuberculosis treatment outcomes and predictors for unsuccessful treatment outcome in the Tigray region of Ethiopia. METHODS: Medical records of smear-positive pulmonary tuberculosis (PTB) patients registered from September 2009 to June 2011 in 15 districts of Tigray region, Northern Ethiopia, were reviewed. Additional data were collected using a structured questionnaire administered through house-to-house visits by trained nurses. Tuberculosis treatment outcomes were assessed according to WHO guidelines. The association of unsuccessful treatment outcome with socio-demographic and clinical factors was analyzed using logistic regression model. RESULTS: Out of the 407 PTB patients (221 males and 186 females) aged 15 years and above, 89.2% had successful and 10.8% had unsuccessful treatment outcome. In the final multivariate logistic model, the odds of unsuccessful treatment outcome was higher among patients older than 40 years of age (adj. OR=2.50, 95% CI: 1.12-5.59), family size greater than 5 persons (adj. OR=3.26, 95% CI: 1.43-7.44), unemployed (adj. OR=3.10, 95% CI: 1.33-7.24) and among retreatment cases (adj. OR=2.00, 95% CI: 1.37-2.92) as compared to their respective comparison groups. CONCLUSIONS: Treatment outcome among smear-positive PTB patients was satisfactory in the Tigray region of Ethiopia. Nonetheless, those patients at high risk of an unfavorable treatment outcome should be identified early and given additional follow-up and social support


BACKGROUND: Treatment of latent tuberculosis infection (LTBI) is a key component in U.S.
tuberculosis control, assisted by recent improvements in LTBI diagnostics and therapeutic regimens. Effectiveness of LTBI therapy, however, is limited by patients' willingness to both initiate and complete treatment. We aimed to evaluate the demographic, medical, behavioral, attitude-based, and geographic factors associated with LTBI treatment initiation and completion of persons presenting with LTBI to a public health tuberculosis clinic. METHODS: Data for this prospective cohort study were collected from structured patient interviews, self-administered questionnaires, clinic intake forms, and U.S. census data. All adults (>17 years) who met CDC guidelines for LTBI treatment between January 11, 2008 and May 6, 2009 at Wake County Health and Human Services Tuberculosis Clinic in Raleigh, North Carolina were included in the study. In addition to traditional social and behavioral factors, a three-level medical risk variable (low, moderate, high), based on risk factors for both progression to and transmission of active tuberculosis, was included for analysis. Clinic distance and neighborhood poverty level, based on percent residents living below poverty level in a person’s zip code, were also analyzed. Variables with a significance level <0.10 by univariate analysis were included in log binomial models with backward elimination. Models were used to estimate risk ratios for two primary outcomes: (1) LTBI therapy initiation (picking up one month’s medication) and (2) therapy completion (picking up nine months INH therapy or four months rifampin monthly). RESULTS: 496 persons completed medical interviews and questionnaires addressing social factors and attitudes toward LTBI treatment. 26% persons initiated LTBI therapy and 53% of those initiating completed therapy. Treatment initiation predictors included: a non-employment reason for screening (RR 1.6, 95% CI 1.0-2.5), close contact to an infectious TB case (RR 2.5, 95% CI 1.8-3.6), regular primary care(RR 1.4, 95% CI 1.0-2.0), and history of incarceration (RR 1.7, 95% CI 1.0-2.8). Persons in the "high" risk category for progression/transmission of TB disease had higher likelihood of treatment initiation (p < 0.01), but not completion, than those with lower risk. CONCLUSIONS: Investment in social support and access to regular primary care may lead to increased LTBI therapy adherence in high-risk populations


The purpose of this study was to examine tuberculosis (TB) population dynamics and to assess potential infection risk in Taiwan. A well-established mathematical model of TB transmission built on previous models was adopted to study the potential impact of TB transmission. A probabilistic risk model was also developed to estimate site-specific risks of developing disease soon after recent primary infection, exogenous reinfection, or through endogenous reactivation (latently infected TB) among Taiwan regions. Here, we showed that the proportion of endogenous reactivation (53-67%) was larger than that of exogenous reinfection (32-47%). Our simulations showed that as epidemic reaches a steady state, age distribution of cases would finally shift toward older age groups dominated by latently infected TB cases as a result of endogenous reactivation. A comparison of age-weighted TB incidence data with our model simulation output with 95% credible intervals revealed that the predictions were in an apparent agreement with observed data. The median value of overall basic reproduction number (R(0)) in eastern Taiwan ranged from 1.65 to 1.72, whereas northern Taiwan had the lowest R(0) estimate of 1.50. We
found that total TB incidences in eastern Taiwan had 25-27% probabilities of total proportion of infected population exceeding 90%, whereas there were 36-66% probabilities having exceeded 20% of total proportion of infected population attributed to latently infected TB. We suggested that our Taiwan-based analysis can be extended to the context of developing countries, where TB remains a substantial cause of elderly morbidity and mortality.


Since the 2009 Lancet Health in South Africa Series, important changes have occurred in the country, resulting in an increase in life expectancy to 60 years. Historical injustices together with the disastrous health policies of the previous administration are being transformed. The change in leadership of the Ministry of Health has been key, but new momentum is inhibited by stasis within the health management bureaucracy. Specific policy and programme changes are evident for all four of the so-called colliding epidemics: HIV and tuberculosis; chronic illness and mental health; injury and violence; and maternal, neonatal, and child health. South Africa now has the world's largest programme of antiretroviral therapy, and some advances have been made in implementation of new tuberculosis diagnostics and treatment scale-up and integration. HIV prevention has received increased attention. Child mortality has benefited from progress in addressing HIV. However, more attention to postnatal feeding support is needed. Many risk factors for non-communicable diseases have increased substantially during the past two decades, but an ambitious government policy to address lifestyle risks such as consumption of salt and alcohol provide real potential for change. Although mortality due to injuries seems to be decreasing, high levels of interpersonal violence and accidents persist. An integrated strategic framework for prevention of injury and violence is in progress but its successful implementation will need high-level commitment, support for evidence-led prevention interventions, investment in surveillance systems and research, and improved human-resources and management capacities. A radical system of national health insurance and re-engineering of primary health care will be phased in for 14 years to enable universal, equitable, and affordable health-care coverage. Finally, national consensus has been reached about seven priorities for health research with a commitment to increase the health research budget to 2.0% of national health spending. However, large racial differentials exist in social determinants of health, especially housing and sanitation for the poor and inequity between the sexes, although progress has been made in access to basic education, electricity, piped water, and social protection. Integration of the private and public sectors and of services for HIV, tuberculosis, and non-communicable diseases needs to improve, as do surveillance and information systems. Additionally, successful interventions need to be delivered widely. Transformation of the health system into a national institution that is based on equity and merit and is built on an effective human-resources system could still place South Africa on track to achieve Millennium Development Goals 4, 5, and 6 and would enhance the lives of its citizens.


BACKGROUND: Tuberculosis (TB) surveillance systems have some pitfalls outside of a National Tuberculosis Program and lack of efficient surveillance hampers accurate epidemiological quantification of TB burden. In the present study we assessed the quality of surveillance at the
University Hospital in Pisa (UHP), Italy, and TB incidence rates over a ten year period (1999-2008). METHODS: Assessment of underreporting was done by record-linkage from two sources: databases of TB diagnoses performed in the UHP and the Italian Infectious Disease Surveillance (IIDS) system. Two different databases were examined: a) TB diagnoses reported in the Hospital Discharge Records (HDR) from three Units of UHP (Respiratory Pathophysiology, Pulmonology and Infectious Diseases Units) (TB database A); b) TB diagnoses reported in HDR of all Units of UHP plus TB positive cases obtained by the Laboratory Register (LR) of UHP (TB database B). For the TB database A, the accuracy of TB diagnosis in HDR was assessed by direct examination of the Clinical Record Forms of the cases. For the TB database B, clinical and population data were described, as well as the trend of incidence and underreporting over 10 yrs. RESULTS: In the first study 293 patients were found: 80 patients (27%) with a confirmed TB diagnosis were underreported, 39 of them were microbiologically confirmed. Underreporting was related to age (Reported vs Non Reported, mean age: 49.27 +/- 20 vs 55 +/- 19, p < 0.005 ), diagnosis (smear positive vs negative cases 18.7 vs 81.2%, p = 0.001), microbiological confirmation (49% vs 51%, p < 0.05), X-ray findings (cavitary vs non-cavitary cases: 12.5 vs 87.5%, p = 0.001) but not to nationality.In the second study, 666 patients were found. Mean underreporting rate was 69.4% and decreased over time (68% in 1999, 48% in 2008). Newly diagnosed TB cases were also found to decrease in number whereas immigration rate increased. Underreporting was related to nationality (Immigrants vs Italians: 18% vs 68%, p < 0.001), diagnosis (microbiological confirmation: 25% vs 75%, p < 0.01), kind of hospital regimen (hospitalized patients vs Day Hospital: 70% vs 16%, p < 0.001), and position of TB code in the HDR (TB code in first position vs in the following position: 39.5% vs 45% p < 0.001). CONCLUSIONS: TB is underreported in Pisa, particularly in older patients and those without microbiological confirmation. The TB code in first position of HDR seems fairly accurate in confirming TB diagnosis


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