#### ABSTRACT

# Abstracts from Nippon Eiseigaku Zasshi (Japanese Journal of Hygiene) vol. 67, no. 1

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A Comprehensive Review of Literature to Investigate Development of Global Knowledge and Consensus on Asbestos Carcinogenicity: Up to the Report and Recommendations by UICC Working Group in 1964

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This author comprehensively reviewed the literature on asbestos carcinogenicity up to the Report and Recommendations by Union Internationale Contra Cancrum (UICC) Working Group on asbestos and cancer in 1964. The first cases of mesothelioma and lung cancer in necropsied patients with asbestosis were reported in 1933 and 1934, respectively. After that, various studies examining the association between each of the diseases and asbestos exposure had been carried out until the meeting of the UICC Working Group: case report studies, case series studies, prevalence studies, historical cohort studies, and case-control studies. Newly reported studies including experimental studies in that meeting all supported the association. These findings on asbestos and cancer correspond well with Hill's criteria, which were just then advocated for evaluating causality epidemiologically. The Report and Recommendations by the Working Group concluded, "There is evidence of an association between exposure to asbestos and malignant neoplasia." and "The types of tumors... are... (1) carcinoma of the lungs, and (2) diffuse mesothelioma of the pleura and peritoneum." This author considers that the causal association between lung cancer or mesothelioma and asbestos was established at the meeting of UICC Working Group in 1964, not by the report on asbestos carcinogenicity in International Labour Organization (ILO) or International Agency for Research on Cancer (IARC) expert meetings in 1972, as the Japanese government announced. The amount of asbestos import in Japan doubled from 130,000 to 280,000 tons annually from 1964 to 1972. The government should have recognized the global knowledge on asbestos carcinogenicity in 1964; the amount of asbestos import could have been reduced greatly.

### Relationship of Maternal Malnutrition Caused by Di(2-ethylhexyl) Phthalate Exposure with Lifestyle Disease in Offspring

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The hypothesis that offspring growing up malnourished during their fetal period have a high risk of lifestyle diseases in later life has been attracting great attention. Although animal experiments and epidemiological studies have been reported, most of them focused on the deficiency of maternal malnutritional elements or starvation. We found that di(2-ethylhexyl) phthalate (DEHP) decreased maternal plasma triglyceride levels, which is a significant source of nutrients for fetuses, in mice. Therefore, we analyzed how offspring exposed to malnutritional status during their fetal period develop potential adverse effects in later life. Male and female wild-type (mPPARa), Ppara-null, and hPPARa mice were treated with diets containing 0 or 0.05 % DEHP. After 4 weeks, males and females in the same genotype and dose group were mated. After continued exposure until weaning, each group was divided into two groups, and one of them was dissected. The remaining was further divided into two subgroups; one was fed normal feed (control-diet group), while the other was fed a high-fat diet (HFD group). After 8-week feeding, all the mice were dissected. In the control-diet group, DEHP exposure at the fetal and pup stages increased food consumption in mPPARa and hPPARa mice, but not in Ppara-null mice. In contrast, DEHP exposure decreased plasma leptin levels in mPPAR $\alpha$  and hPPAR $\alpha$  mice at the weaning stage. In the HFD group, DEHP exposure at the fetal and pup stages influenced neither food consumption nor leptin levels. These findings suggest that maternal malnutrition may be caused by not only nutritional deficiency but also exposure to some chemicals such as DEHP, and the latter case may also influence feeding behavior in offspring. These effects may be related to hepatic PPAR $\alpha$  and diminished by HFD feeding. Further study is warranted as to whether such feeding behavior influences the risk of lifestyle diseases such as obesity.

#### Parent-Child Relationships and Mindfulness

Nippon Eiseigaku Zasshi, 67, 27–36 (2012) Kouichi Yoshimasu<sup>1</sup>, Hidefumi Oga<sup>2</sup>, Ryo Kagaya<sup>3</sup>, Makiko Kitabayashi<sup>4</sup>, Yuki Kanaya<sup>4</sup> <sup>1</sup>Department of Hygiene, School of Medicine, Wakayama Medical University <sup>2</sup>Japanese Society of Mindful Life <sup>3</sup>Social Welfare Corporation of Sumida Ward <sup>4</sup>Department of Health and Nutrition, Faculty of Health Science, Tsukuba International University

Psychological approaches such as mindfulness-based stress reduction or mindfulness-based cognitive therapy could be effective for relieving a wide range of psychosocial stresses or frictions between parents and children. Several interventional approaches based on mindfulness have been shown to be useful for improving parent-child relationships not only among healthy families but also among those with difficult psychopathologies. Particularly in the relationships of parents with their children with developmental disorders such as autism or attention-deficit/hyperactivity disorders, these approaches may play an important role in that the motivations of both parents and children could be enhanced because they can actually feel that their mental condition improves through meaningful parent-child interactions that they experience in their daily lives. These approaches are also expected to improve communications between mothers and children through the development of a finely honed sensitivity. One practical example is shown for the mental growth of children by the mindfulness-based dietary education and the secondary effects of this education on the parents. We can also apply these effective methods to the improvement of general interpersonal relationships.

## Effect of Cardiovascular Risk Factors on Individual and Population Medical Expenditures: A 10-Year Cohort Study of 4,535 National Health Insurance Beneficiaries in Shiga

Nippon Eiseigaku Zasshi, 67, 38-43 (2012)

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A 10-year follow-up cohort study of 4,535 National Health Insurance beneficiaries aged 40–69 years in Shiga was performed as part of a research project conducted by the Health Promotion Research Committee of the Shiga National Health Insurance Organizations in 2002. The relationship between cardiovascular risk factors and medical expenditures during the 10-year study period has been examined in this cohort. For example, there was a positively graded correlation

between blood pressure and individual total medical expenditures per month. The odds ratio for cumulative hospitalization and hazard ratio for all-cause mortality in severe hypertensives were also higher than those in normotensives. However, from the viewpoint of the entire population, the excess medical expenditures attributable to hypertension within the total medical expenditures were higher for mild-tomoderate hypertensives than for severe hypertensives. On the other hand, although individual medical expenditures per month were 1.7fold higher for participants with 2 or 3 risk factors and obesity, which was broadly equivalent to metabolic syndrome, than for those without these factors, the excess medical expenditures determined by risk clustering within the total medical expenditures were higher in normal-weight people than in obese people because of the higher prevalence of normal weight. These findings suggest that high-risk individuals are a good target of a high-risk approach, such as intensive health guidance, from the viewpoint of medical expenditures. However, another approach for the majority with a low-to-moderate cardiovascular risk should be considered, because they account for a greater proportion of the excess medical expenditures. Another way to solve this problem may be a population approach with an effective method of providing information to citizens.

#### **Evaluation of Health Promotion Programs Using Health Checkup Data and Medical Receipts**

Nippon Eiseigaku Zasshi, 67, 44-49 (2012)

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*Objectives*: In a research project on the evaluation of health promotion programs using a health dataset including health checkup data and medical receipts, which was supported by a research grant from the Ministry of Health, Labour and Welfare, the potential preventive factors that influence disease severity and medical expenditure were studied.

*Methods*: A dataset from a city with a population of 36,544 and a large elderly population (31.1 %) was studied using 12 elementary school geographical areas as the basis of classification. A dataset from a company of 4,780 employees was analyzed to determine changes in health checkup data related to metabolic syndrome over 3 years. A simulation model to identify factors that are important for reducing the incidence of complications such as ischemic heart disease and stroke was developed.

*Results*: Geographical analyses showed a negative association between the rate of participation in health checkup and the prevalence of noncommunicable diseases. The percentage of new patients who started pharmaceutical treatment was lower in the health-advice-intervention group (5.2 %) than in the nonintervention group (29.6 %). A simulation model to identify factors that are important for reducing the incidence of complications was developed using data on health checkup participation, percentage of those who undertook a lifestyle-modification program, and compliance with medical treatment among others.

*Conclusions*: Various health data including those on health checkup participation, percentage of those who undertook a lifestyle modification program, and compliance under medical treatment over 3 years were helpful in evaluating health promotion programs.

# Lifetime Medical Expenditures of Smokers and Nonsmokers

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*Objectives*: The aim of this study was to examine which of the two groups have higher lifetime medical expenditures; male smokers or male nonsmokers. We conducted this investigation using a Japanese single cohort database to calculate long-term medical expenditures and 95 % confidence intervals.

*Methods*: We first constructed life tables for male smokers and male nonsmokers from the age of 40 years after analyzing their mortality rates. Next, we calculated the average annual medical expenditures of each of the two groups, categorized into survivors and deceased. Finally, we calculated long-term medical expenditures and performed sensitivity analyses.

*Results*: The results showed that although smokers had generally higher annual medical expenditures than nonsmokers, the former's lifetime medical expenditure was slightly lower than the latter's because of a shorter life expectancy that resulted from a higher mortality rate. Sensitivity analyses did not reverse the order of the two lifetime medical expenditures.

*Conclusions*: In conclusion, although smoking may not result in an increase in lifetime medical expenditures, it is associated with diseases, decreased life expectancy, lower quality of life (QOL), and generally higher annual medical expenditures. It is crucial to promote further tobacco control strategically by maximizing the use of available data.

### Practical Use of E-Claim Data for Regional Healthcare Planning

Nippon Eiseigaku Zasshi, 67, 56–61 (2012) Kenji Fujimori Hokkaido University Hospital, Center for Regional Healthcare and Certified Educator Support

Japanese E-claim data contain comprehensive medical procedures and are adapted nationwide. Almost 94 % of hospitals and pharmacies claim medical records for payment electronically. Although the handling and analysis of E-claim data are not as easy as those of Diagnosis Procedure Combination (DPC) data, these data contain important and useful information for the next regional healthcare planning of local governments in Japan.

In this paper, we explain some examples of a healthcare delivery system in each region and patients' behavior in Hokkaido obtained from the Joint Program for E-claim database of Hokkaido University Hospital and the Hokkaido local government. Differences between the E-claim data format and the DPC data format are also described in terms of data analysis. Some suggestions are provided for the E-claim data format of the next generation.

# Readmission Rate for Health Care Delivery System Assessment

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*Objectives*: The health care system in Japan has undergone major changes, with increasing focus on specialization and continuity of care in its organization and delivery. Reducing the average length of stay is central to this plan. Readmission is often seen as an avoidable consequence of early discharges. And therefore, the readmission rate is used to assess the quality and efficiency of care. In this study, the main subjects in the implementation of readmission rate as an indicator are laid out and the framework for readmission in acute myocardial infarction (AMI) patients is applied.

*Methods*: Literature review concerning readmission in AMI patients was conducted to understand the key points of the framework of the readmission. We then used insurance claims data to implement readmission as an indicator. The study sample consisted of 2,332 patients hospitalized due to AMI in Kyoto Prefecture from April 2009 to March 2010.

*Results*: The 30-day readmission rate after AMI discharge was 3.7 % (87/2,332), with the majority of these admissions due to coronary disease (38 %). This rate was extremely low compared to the results reported in other countries, with readmission rates as high as 20 % observed in the US. However, we observed that countries with high readmission rates had correspondingly short lengths of stay (LOS), and countries such as Germany and Japan with low readmission rates had long LOS.

*Conclusions*: The readmission rate in Japan is low compared with those in other countries although mean LOS is long. The use of readmission rate may have applications in understanding trends in healthcare quality as Japan attempts to reduce LOS durations.

## Changes in Mental Health Index, Serum Biochemical Parameters and Neutrophil Function after Start of the Wheelchair Use at a Nursing Home in Korea

Nippon Eiseigaku Zasshi, 67, 67-75 (2012)

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*Objectives*: In Korea, long-term care insurance has been provided to the elderly since 2008. We conducted a health survey of the elderly in a nursing home in Korea from 2007 to 2010. Since the introduction of the insurance system, many of the elderly have started using wheelchairs. We aimed to determine the effect of using wheelchairs on mental health index, serum biochemical parameters, and neutrophil function.

*Methods*: The subjects were 32 elderly persons (mean age 74.44  $\pm$  5.79 years) who could walk unaided in 2007 and were not bedridden until 2010. We classified the subjects into the walking group (subjects could walk unaided or with a cane until 2010; 10 men, 9 women) and the wheelchair group (subjects required the use of a wheelchair from 2007 to 2010; 2 men, 11 women).

We determined stress score, stress tolerance, subjective well-being score in accordance with the Philadelphia Geriatric Center Morale Scale, and serum biochemical parameters. We also analyzed oxidant production and phagocytosis by neutrophils and estimated the balance between oxidant production and phagocytosis by correlation analysis. *Results*: Increases in the stress tolerance of the wheelchair group in 2008 and 2009 and the subjective well-being score in 2009 in the survey were observed. However, in 2010, the stress tolerance and the subjective well-being score decreased to the levels in 2007. In 2010, the levels of serum albumin and high-density lipoprotein cholesterol of the wheelchair group were significantly lower than those of the walking group, and the balance between phagocytosis and oxidant production in the wheelchair group improved.

### DNA Damage in Human Pleural Mesothelial Cells Induced by Exposure to Carbon Nanotubes

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*Objectives*: Nanomaterials are currently used in electronics, industrial materials, cosmetics, and medicine because they have useful physicochemical properties, such as strength, conductivity, durability, and chemical stability. As these materials have become widespread, many questions have arisen regarding their effects on health and the environment. In particular, recent studies have demonstrated that carbon nanotubes (CNTs) cause significant inflammation and mesothelioma in vivo. In this study, we investigated the potential risk posed by singlewalled carbon nanotube (SWCNT) and multiwalled carbon nanotube (MWCNT) exposure in human pleural mesothelial cells.

*Methods*: CNT cytotoxicity was determined by a trypan blue exclusion assay, and DNA damage was detected by an alkaline comet assay. The concentration of 8-oxodeoxyguanosine (8-OHdG) in DNA was measured by high performance liquid chromatography with electrochemical detection. The expression of base excision repair enzymes in the cell was estimated by immunoblot analysis.

*Results*: We observed inhibitory effects on cell proliferation and the induction of DNA damage following exposure of cells to purified CNTs that were suspended in dispersion medium. However, accumulation of 8-OHdG in DNA was not found. In addition, the expression levels of base excision enzymes that are involved in hOGG1, hMTH1, and MYH in MeT-5A cells remained unchanged for 24 h after carbon nanotube exposure.

*Conclusions*: CNTs significantly inhibit cell proliferation and decrease DNA damage in human pleural mesothelial cells. Our results

indicate that the mechanism of CNT-induced genotoxicity is different from that following exposure to reactive oxygen species, which causes oxidative DNA modifications and 8-OHdG production. Further investigation is required to characterize the specific DNA mutations that occur following CNT exposure.

# Recruitment Officers' Attitude toward Smoking Habits of Applicants

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*Objectives*: This study sought to determine the implications of smoking cessation/prevention policy in college students.

*Methods*: We conducted an internet survey to investigate the attitude of recruitment officers in a company concerning acceptance evaluation and smoking of applicants.

*Results*: Among 838 respondents, more than one-half had unfavorable impressions when they saw new employees or college students smoking. Among the respondents, 3.7 % answered that their companies had already introduced the policy of considering smoking status during acceptance evaluation to be acceptance policies, and 14.3 % answered that this introduction is under consideration. Among the remaining 687 respondents, 7.6 % answered that it can be included in the acceptance policies in the future and 45.7 % answered it will not be included in the policies but can be considered during acceptance evaluation itself. Regarding their personal impression, 30 % have experienced the case in which smoking status might have affected acceptance and 48.7 % answered that it might affect acceptance in the future.

*Conclusions:* Our study clarified that smoking status affected acceptance evaluation by recruitment officers in not a little cases although smoking status is not included in formal acceptance policies. Considering that there are only a few countermeasures for smoking among college students, job hunting activities can be a good opportunity for smoking cessation/prevention among them in collaboration with companies, colleges, and policy makers.