Permanente Abstracts

Heritability of Longitudinal Changes in Coronary Heart Disease Risk Factors in Women Twins

Friedlander Y, Austin MA, Newman B, Edwards K, Mayer-Davis EI, King MC. Am J Hum Genet 1997 Jun;60(6):1502-12.

Numerous studies have demonstrated genetic influences on levels of coronary heart disease (CHD) risk factors, but there also may be genetic effects on the intraindividual variation in these risk factors over time. Changes in risk factors are likely to reflect genetic-environmental interactions and may have important implications for understanding CHD risk. The present study examines the heritability of changes in CHD risk factors, using data from the two examinations by the Kaiser Permanente Women Twins Study, performed a decade apart. The sample consisted of 348 pairs of women twins who participated in both examinations, including 203 MZ pairs and 145 DZ pairs. Average ages at the two examinations were 41 and 51 years, respectively. By means of three different statistical analytic approaches, moderate heritability estimates were demonstrated for changes in LDL cholesterol (h2 = .25-.36) and in HDL cholesterol (h2 = .23-.58), some of which were statistically significant. Although small to moderate heritability estimates were found for systolic blood pressure (.18-.37; $p < .05$ for some estimates), no genetic influence on changes in diastolic blood pressure was detected. Based on longitudinal twin data in women, this study demonstrates a genetic influence on changes in both lipoprotein risk factors and systolic blood pressure over a decade. In addition to environmental factors, which clearly are operating, the effect of various "variability genes" may be acting independently of the genetic influences on the absolute levels of these risk factors. Both mapping the gene(s) underlying intraindividual variations in these CHD risk factors and understanding their function(s) could lead to targeted intervention strategies to reduce CHD risk among genetically susceptible individuals.

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Epidemiology and Outcome of Patients Hospitalized with Acute Lower Gastrointestinal Hemorrhage: a Population-Based Study

Longstreth GF. Am J Gastroenterol 1997 Mar;92(3):419-24.

Objectives: Population-based data on the epidemiology and outcome of patients hospitalized with acute lower gastrointestinal hemorrhage (ALGIH) are lacking. This survey of the incidence, etiology, therapy, and long-term outcome of patients with ALGIH was conducted in a defined population.

Methods: In a large health maintenance organization, discharge data and colonoscopy records were used to identify adults hospitalized with ALGIH from 1990 to 1993. Data were collected by record review and telephone calls.

Results: Two hundred nineteen patients had 235 hospitalizations, yielding an estimated annual incidence rate of 20.5 patients/100,000 (24.2 in males versus 17.2 in females, $p < .001$). The rate increased >200-fold from the third to the ninth decades of life. Diagnoses were: colonic diverticulosis, 91 (41.6%); colorectoral malignancy, 20 (9.1%); ischemic colitis, 19 (8.7%); miscellaneous, 63 (28.8%); and unknown, 26 (11.9%). Eight (3.6%) patients died in the hospital (5 of 206 (2.4%) with hemorrhage before admission versus 3 of 13 (23.1%) with hemorrhage after admission, $p < .001$). Follow-up of 210 of 211 (99.5%) survivors was 34.0 +/- 1.1 months. In the 83 diverticulosis patients without definitive therapy, the hemorrhage recurrence rate (Kaplan-Meier method) was 9% at 1 year, 10% at 2 years, 19% at 3 years, and 25% at 4 years. In the 89 diverticulosis patients who survived hospitalization, all-cause mortality rates (none from hemorrhage) were 11% at 1 year, 15% at 2 years, 18% at 3 years, and 20% at 4 years.

Conclusions: Hospitalization with ALGIH is related to age and male gender. After hemorrhage from colonic diverticulosis, the leading cause, rates of ALGIH recurrence and unrelated death are similar during the next 4 years.

"Hospitalization with ALGIH is related to age and male gender."

Specialty Differences in the Management of Asthma. A Cross-Sectional Assessment of Allergists' Patients and Generalists Patients in a Large HMO.

Vollmer WM, O'Hollaren M, Ettinger KM, Stibolt T, Wilkins J, Buist AS, Linton KL, Osborne ML. Arch Intern Med 1997 Jun 9;157(11):1201-8.

Objective: To examine the differences in medical management and quality of life between patients with asthma who receive their primary asthma care from allergists and those who receive their care from generalists in a large health maintenance organization (HMO).

Methods: We conducted a cross-sectional study of patients with asthma in a large HMO (Kaiser Permanente, Northwest Region, Portland, Ore). Participants were 392 individuals aged 15 through 55 years with physician-diagnosed asthma, taking anti-asthma medications, reporting current asthma symptoms, and receiving asthma care from an allergist or from a generalist. Primary outcomes included characteristics of asthma, health care utilization, and quality of life.

Results: Patients cared for by allergists tended to have more severe asthma than those cared for by generalists ($p < .01$). The allergists' patients tended

to be older (38.6 +/- 9.6 years vs 35.7 +/- 12.6 years, $p < .01$), more atopic (91% vs 78%, $p < .01$), and more likely to report perennial (rather than seasonal) asthma (26% vs 36%, $p < .04$) than the generalists' patients. Patients receiving their primary asthma care from an allergist were considerably more likely than generalists' patients to report using inhaled anti-inflammatory agents ($p < .01$), oral steroids ($p < .01$), and regular (daily) breathing medications to control their asthma ($p < .01$). Allergists' patients were more likely to have asthma exacerbations treated in a clinic setting rather than an emergency department ($p < .01$). Furthermore, allergists' patients reported significantly improved quality of life as measured by several dimensions of the SF-36 scale (physical functioning, role emotional, bodily pain, and general health: $p < .05$).

Conclusions: These findings suggest that specialist care of asthma is of benefit for patients with asthma in a large HMO. Specifically, the allergists' patients conformed more closely to national asthma management guidelines and reported better quality of life than did the generalists' patients.

Extending Health Maintenance Organization Insurance to the Uninsured. A Controlled Measure of Health Care Utilization

Bograd H, Ritzwoller DP, Calonge N, Shields K, Hanrahan M. JAMA 1997;277:1067-72.

Objective: To investigate the utilization of health care services of previously uninsured low-income patients after becoming insured by a health maintenance organization (HMO).

Design: Retrospective study of utilization in a previously uninsured study group compared with an age- and sex-matched randomly selected control group of commercial HMO enrollees.

Setting: Group model HMO

Patients: A study group of 346 previously uninsured low-income patients and 382 controls.

Measures: Outpatient visits of primary and specialty care, outpatient pharmacy, laboratory, and radiology use, and inpatient admissions and hospital days over a 2-year period. Self-reported health status measures were obtained to control for differences in health status.

Principal Findings: There were no differences between the study and control groups in hospital admissions, hospital days, and measures of outpatient laboratory, pharmacy, and radiology use. The odds of having an outpatient visit per patient per month was 30% higher for the study group. Approximately half the increase in the odds ratio for outpatient visits were related to the worse self-perceived health status of the study group. While both groups utilized more services in the early phase of their enrollment, the intensity of this start-up was similar for both groups.

Conclusions: Compared with a commercial group of the same age and sex, the patterns of utilization were similar and the financial costs of care were only moderately more for a previously uninsured group provided with comprehensive HMO insurance. With the growth of managed care, these data should be beneficial in the development of health care programs for the growing number of uninsured Americans.

" ... allergists' patients conformed more closely to national asthma management guidelines and reported better quality of life than did the generalists' patients."

Efficacy and Cost-Effectiveness of Multihole Fine-Needle Aspiration of Head and Neck Masses

Mui S, Li T, Rasgon BM, Hilsinger RL Jr, Rumore G, Puligandla B, Sawicki J. Laryngoscope 1997;107:759-64.

To determine whether the specimen from fine-needle aspiration (FNA) biopsy of head and neck masses has greater diagnostic accuracy when using multihole needles than when using conventional, single-hole needles, we did a prospective, randomized, single-blinded study comparing diagnoses obtained using both types of needles in FNA biopsies of head and neck masses. Eighty-eight patients served as their own controls and had 91 FNA biopsies with both multihole and single-hole, 22-gauge needles. Order of biopsy was randomized and was unknown to the cytopathologist. No statistically significant differences were noted in quantity of specimen material obtained, quality of fixation, or diagnostic value between the multihole and conventional needle. We found no advantage in using the more costly multihole needle in FNA biopsy of head and neck masses.

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Heritability of Factors of the Insulin Resistance Syndrome in Women Twins

Edwards KL, Newman B, Mayer E, Selby JV, Krauss RM, Austin MA. Genet Epidemiol 1997;14(3):241-53.

The insulin resistance syndrome (IRS) is characterized by a combination of interrelated coronary heart disease (CHD) risk factors, including low high-density lipoprotein cholesterol (HDL-C) levels, obesity and increases in triglyceride (TG), blood pressure, small low-density lipoprotein particles (LDL), and both fasting and postload plasma insulin and glucose. Using factor analysis, we previously identified 3 uncorrelated factors that explained 66% of the variance among these variables, based on data from women participating in examination 2 of the Kaiser Permanente Women Twins Study in Oakland, CA during 1989-1990. The factors were interpreted as: 1) body mass/fat distribution, 2) insulin/glucose, and 3) lipids: TG,

HDL-C, LDL peak particle diameter. In this analysis, heritability of each of the factors was estimated based on data from 140 monozygotic and 96 dizygotic pairs of non-diabetic women twins. Heritability estimates were calculated using the classical approach, the analysis of variance (ANOVA) approach, and the maximum likelihood approach. For the body mass/fat distribution factor heritability estimates suggest moderate genetic influences; 0.61 ($p < 0.001$), 0.14 ($p > 0.05$), and 0.71 ($p < 0.001$), respectively. The insulin/glucose factor appeared to be highly heritable, with estimates of 0.87, 0.92, and 0.57 (all $p < 0.001$), respectively. The heritability estimates for the lipid factor were moderate and consistent across methods: 0.25 ($p < 0.10$), 0.32 ($p < 0.05$), and 0.30 ($p < 0.05$), respectively. These results are consistent with genetic influences on each of the 3 "factors," and suggest that both genetic and environmental effects are involved in the clustering of IRS risk factors.

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Stanford-Kaiser Permanente G1 study for Clinical Stage I to IIA Hodgkin's Disease: Subtotal Lymphoid Irradiation Versus Vinblastine, Methotrexate, and Bleomcycin Chemotherapy and Regional Irradiation

Horning SJ, Hoppe RT, Mason J, Brown BW, Hancock SL, Baer D, Rosenberg SA. J Clin Oncol 1997 May;15(5):1736-44.

Purpose: We have demonstrated that a relatively mild chemotherapy regimen, vinblastine, methotrexate, and bleomycin (VBM), and involved-field radiotherapy (IFRT) could substitute for extended-field radiotherapy in patients with favorable Hodgkin's disease (HD) who have been laparotomy-staged. The purpose of this study is to determine if VBM and regional radiotherapy can substitute for extended-field radiotherapy in favorable clinical stage (CS) I and II HD.

Patients and Methods: Seventy-eight patients with favorable CS I and II HD were randomly assigned to subtotal lymphoid irradiation (STLI) or VBM chemotherapy and regional radiotherapy. Randomization was stratified on the basis of age, sex, number of Ann Arbor sites, histology, and institution. Patients were evaluated for freedom from progressive HD, survival, and toxicity. Results were compared with the predecessor trial in pathologically staged patients.

Results: With a median follow-up period of 4 years, the rate of freedom from progressive HD was 92% (95% confidence interval [CI], 88% to 96%) for patients treated with STLI and 87% (95% CI, 81% to 93%) for patients treated with VBM and regional radiotherapy. Six of seven patients who relapsed are alive and in remission following successful second-line therapy.

Conclusion: Given the caveat of a small number of patients, the results of extended-field radiotherapy and VBM and regional radiotherapy are comparable with a median follow-up period of 4 years. VBM serves as a paradigm to reduce late effects in favorable early-stage HD. We do not advocate its routine use in clinical practice, but instead encourage participation in clinical trials with the objective of maintaining efficacy while reducing toxicity in CS I and II HD.

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Marijuana Use and Mortality

Sidney S, Beck JE, Tekawa IS, Quesenberry CP, Friedman GD. Am J Public Health, 1997 Apr;87(4):585-90.

Objectives: The purpose of this study was to examine the relationship of marijuana use to mortality.

Methods: The study population comprised 65171 Kaiser Permanente Medical Care Program enrollees, aged 15 through 49 years, who completed questionnaires about smoking habits, including marijuana use, between 1979 and 1985. Mortality follow-up was conducted through 1991.

Results: Compared with nonuse or experimentation (lifetime use six or fewer times), current marijuana use was not associated with a significantly increased risk of non-acquired immunodeficiency syndrome (AIDS) mortality in men (relative risk [RR] = 1.12, 95% confidence interval [CI] = 0.89, 1.39) or of total mortality in women (RR = 1.09, 95% CI = 0.80, 1.48). Current marijuana use was associated with increased risk of AIDS mortality in men (RR = 1.90, 95% CI = 1.33, 2.73), an association that probably was not casual but most likely represented uncontrolled confounding by male homosexual behavior. This interpretation was supported by the lack of association of marijuana use with AIDS mortality in men from a Kaiser Permanente AIDS database. Relative risks for ever use of marijuana were similar.

Conclusions: Marijuana use in a prepaid health care-based study cohort had little effect on non-AIDS mortality in men and on total mortality in women.