



## Permanente Abstracts

### The Progressive Cost of Complications in Type 2 Diabetes Mellitus

*Brown JB, Pedula KL, Bakst AW; Arch Intern Med 1999 Sep 13;159(16):1873-80.*

**BACKGROUND:** A substantial proportion of the costs of diabetes treatment arises from treating long-term complications, particularly cardiovascular and renal disease. However, little is known about the progressive cost of these complications. Firmer knowledge would improve diabetes modeling and might increase the financial and organizational support for the prevention of diabetic complications.

**METHODS:** We analyzed nine years of clinical data on 11,768 members of a large group-model health maintenance organization who had probable type 2 diabetes mellitus. We ascertained the presence of cardiovascular and renal complications, staged the members' progression, and estimated their incremental costs by stage.

**RESULTS:** We found no significant differences between men and women in the prevalence or staging of complications. Per-person costs increased over baseline (\$2033) by more than 50% (\$1087) after initiation of cardiovascular drug therapy and/or use of a cardiologist, and by 360% (\$7352) after a major cardiovascular event. Abnormal renal function increased diabetes treatment costs by 65% (\$1337); advanced renal disease by 195% (\$3979); and end-stage renal disease by 771% (\$15,675). Both cardiovascular and renal diseases were more common among older subjects, but age did not affect the additional costs of these complications. Women had substantially higher medical care costs after controlling for age and presence of complications. Incremental cost estimates based solely on "labeled" events significantly underestimate true incremental cost.

**CONCLUSIONS:** In an aggregate population, the greatest cost savings would be achieved by preventing major cardiovascular events. For individuals, the greatest savings would be achieved by preventing progression to stage 3 renal disease.

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### Type 2 Diabetes: Incremental Medical Care Costs During the First Eight Years After Diagnosis

*Brown JB, Nichols GA, Glauber HS, Bakst AW; Diabetes Care 1999 Jul;22(7):1116-24.*

**OBJECTIVE:** To describe and analyze the time course of medical care costs caused by type 2 diabetes from the time of diagnosis through the first eight postdiagnostic years.

**RESEARCH DESIGN AND METHODS:** From electronic health maintenance organization (HMO) records, we ascertained the ongoing medical care costs for all members with type 2 diabetes who were newly diagnosed between 1988 and 1995. To isolate incremental costs (costs caused by the diagnosis of diabetes), we subtracted the costs of individually matched HMO members without diabetes from costs of members with diabetes.

**RESULTS:** The economic burden of diabetes is immediately apparent from the time of diagnosis. In year one, total medical costs were 2.1 times higher for patients with diabetes compared with those without diabetes. Diabetes-associated incremental costs (type 2 diabetic costs minus matched costs for people without diabetes) averaged \$2257 per type 2 diabetic patient per year during the first eight postdiagnostic years. Annual incremental costs varied relatively little over the period but were higher during years one, seven, and eight because of higher-cost hospitalizations for causes other than diabetes or its complications.

**CONCLUSIONS:** For the first eight years after diabetes diagnosis, patients with type 2 diabetes incurred substantially higher costs than matched nondiabetic patients, but those high costs remained largely flat. Once the growth in costs due to general aging is controlled for, it appears that diabetic complications do not increase incremental costs as early as is commonly believed. Additional research is needed to better understand how diabetes and its diagnosis affect medical care costs over longer periods of time.

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### Reduction of Vertebral Fracture Risk in Postmenopausal Women with Osteoporosis Treated with Raloxifene: Results from a Three-Year Randomized Clinical Trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators [See Comments]

*Eitinger B, Black DM, Mitlak BH, Knickerbocker RK, Nickelsen T, Genant HK, et al; JAMA 1999 Aug 18; 282(7):637-45. Correction in: JAMA 1999 Dec 8; 282(22):2124.*

**CONTEXT:** Raloxifene hydrochloride, a selective estrogen receptor modulator, prevents bone loss in postmenopausal women, but whether it reduces fracture risk in these women is not known.

**OBJECTIVE:** To determine the effect of raloxifene therapy on risk of vertebral and nonvertebral fractures.



**DESIGN:** The Multiple Outcomes of Raloxifene Evaluation (MORE) study, a multicenter, randomized, blinded, placebo-controlled trial.

**SETTING AND PARTICIPANTS:** A total of 7705 women aged 31 to 80 years in 25 countries who had been postmenopausal for at least two years and who met World Health Organization criteria for having osteoporosis. The study began in 1994 and had up to 36 months of follow-up for primary efficacy measurements and nonserious adverse events and up to 40 months of follow-up for serious adverse events.

**INTERVENTIONS:** Participants were randomized to 60 mg/d or 120 mg/d of raloxifene or to identically appearing placebo pills; in addition, all women received supplemental calcium and cholecalciferol.

**MAIN OUTCOME MEASURES:** Incident vertebral fracture was determined radiographically at baseline and at scheduled 24- and 36-month visits. Nonvertebral fracture was ascertained by interview at six-month-interim visits. Bone mineral density was determined annually by dual-energy x-ray absorptiometry.

**RESULTS:** At 36 months of the evaluable radiographs in 6828 women, 503 (7.4%) had at least one new vertebral fracture, including 10.1% of women receiving placebo, 6.6% of those receiving 60 mg/d of raloxifene, and 5.4% of those receiving 120 mg/d of raloxifene. Risk of vertebral fracture was reduced in both study groups receiving raloxifene (for 60-mg/d group: relative risk [RR], 0.7; 95% confidence interval [CI], 0.5-0.8; for 120-mg/d group: RR, 0.5; 95% CI, 0.4-0.7). Frequency of vertebral fracture was reduced both in women who did and did not have prevalent fracture. Risk of nonvertebral fracture for raloxifene vs placebo did not differ significantly (RR, 0.9; 95% CI, 0.8-1.1 for both raloxifene groups combined). Compared with placebo, raloxifene increased bone mineral density in the femoral neck by 2.1% (60 mg) and 2.4% (120 mg) and in the spine by 2.6% (60 mg) and 2.7% (120 mg)  $P < 0.001$  for all comparisons). Women receiving raloxifene had increased risk of venous thromboembolus vs placebo (RR, 3.1; 95% CI, 1.5-6.2). Raloxifene did not cause vaginal bleeding or breast pain and was associated with a lower incidence of breast cancer.

**CONCLUSIONS:** In postmenopausal women with osteoporosis, raloxifene increases bone mineral density in the spine and femoral neck and reduces risk of vertebral fracture.

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### Pre-Enrollment Diets of Dietary Approaches to Stop Hypertension Trial Participants. DASH Collaborative Research Group

*Karanja NM, McCullough ML, Kumanyika SK, Pedula KL, Windhauser MM, Obarzanek E, et al; J Am Diet Assoc 1999 Aug;99(8 Suppl):S28-34.*

A large body of evidence suggests that several nutrients are related to blood pressure. Less is known about the eating patterns of special populations, such as those at risk for hypertension, or how demographic factors affect the diets of these populations. This article characterizes the usual diets of participants before they enrolled in the Dietary Approaches to Stop Hypertension (DASH) trial. During screening for DASH, 380 participants completed the National Cancer Institute food frequency questionnaire. Nutrient and food group intake, the Keys score (a measure of a diet's atherogenicity), and the Diet Quality Index were estimated from the food frequency questionnaire. The effects of age, sex, race, baseline weight, and education on these dietary factors were assessed among DASH participants and compared with similar data from the Third National Health and Nutrition Examination Survey and other published reports. Among DASH participants, African-Americans reported lower intakes of dairy products ( $P < .001$ ), calcium ( $P < .001$ ), and magnesium ( $P < .05$ ) than did whites. Older women reported greater intakes of calcium, magnesium, and potassium (all  $P < .05$ ) and less fat ( $P < .05$ ) than did younger women. Older men consumed fewer servings of fruits ( $P < .03$ ), less vitamin C ( $P < .05$ ), and had a higher Keys score ( $P < .05$ ) than did younger men. Heavier (body mass index  $\geq 25$ ) participants reported lower intakes of protein and potassium, but higher fat and energy intakes (all  $P < .05$ ). Taken together, these data show that younger, overweight African-American women have the least healthful diets, because they consume more atherogenic foods and fewer of the nutrients related to decreased blood pressure. Overall Diet Quality Index scores did not differ between African-American and white participants. Despite differences in dietary assessment methods between the population samples of DASH and the Third National Health and Nutrition Examination Survey, within each population sample, patterns of micronutrient intake were similar between African-American and white participants.

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### Women's Provider Preferences for Basic Gynecology Care in a Large Health Maintenance Organization

*Schmittiel J; Selby JV; Grumbach K; Quesenberry CP Jr; J Womens Health Gend Based Med 1999 Jul-Aug;8(6):825-33.*

To examine women's preferences for the type and sex of the provider of basic gynecological services and the correlates of these preferences, we mailed a cross-sectional survey to 8406 women in a large group model health maintenance organization (HMO) in northern California, with a response rate of 73.6%. Four questions asked women the type (obstetrician/gynecologist, nurse practitioner, or primary care physician) and sex of provider who performed their last pelvic examination and their preferences in type and sex of provider for these examinations. This was a random sample of female HMO members 35-85 years of age who were empaneled with a primary care physician from one of three categories: family practitioner, general internist, or subspecialist. Of the 5164 respondents who received their last pelvic examination at Kaiser Permanente, 56% had seen a gynecologist, 26% a nurse practitioner, and only 18% their own primary care physician for the examination. Of these women, 60.3% reported preferring a gynecologist for basic gynecology care, 12.6% preferred a nurse practitioner, 13.3% preferred their own primary care physician, and 13.8% had no preference. Patients of family practitioners were more likely to prefer their own primary care practitioner than patients of other types of doctors. The strongest independent predictor of preferring a gynecologist over the primary care physician was having seen a gynecologist for the last pelvic examination (OR = 28.3,  $p < 0.0001$ ). Other independent predictors of preferring a gynecologist were younger age, higher education and income, and having a male primary care physician. Of respondents, 52.2% preferred a female provider for basic gynecological care, and 42.0% had no preference for the sex of the provider. Preferring a female provider was strongly and independently associated with lower income, higher education, nonwhite race, having a male primary care physician, having an older primary care physician, and having seen a female provider at the last pelvic examination. In this HMO, a majority of women reported a preference for seeing an obstetrician/gynecologist for their routine gynecological care, despite having a primary care physician. This most likely reflects the strong influence of previous patient experience and that familiarity with a particular type of provider leads to preferences for

that type. This medical group's structure probably also affects preferences, as in this HMO, primary care physicians can be discouraged from performing pelvic examinations. Many women do prefer female providers for pelvic examinations, but a large percentage have no preference. These women often see male providers for basic gynecological care. As managed care places increasing emphasis on providing integrated, comprehensive primary care, this apparent preference for specialty gynecological care will require further study.

### The Diagnosis and Classification of Gestational Diabetes Mellitus: Is It Time to Change Our Tune?

*Schwartz ML; Ray WN; Lubarsky SL; Am J Obstet Gynecol 1999 Jun;180(6 Pt 1):1560-71.*

**OBJECTIVE:** This study was designed to determine the impact on our population of adopting the Carpenter and Coustan criteria for gestational diabetes mellitus in place of the currently used National Diabetes Data Group criteria, to review the evidence supporting replacement of the National Diabetes Data Group criteria with the Carpenter and Coustan criteria, and to propose analogous diagnostic criteria for diabetes in pregnant and nonpregnant women.

**STUDY DESIGN:** The National Diabetes Data Group criteria and the proposed Carpenter and Coustan criteria were both used to retrospectively review medical records of patients screened for gestational diabetes mellitus during 1995 and 1996, in the Kaiser Permanente Northwest Division. Computerized search was performed on automated data systems, and software was used for statistical analyses. A MEDLINE review of relevant literature was conducted.

**RESULTS:** Of 8857 pregnant women screened for gestational diabetes in 1995 and 1996, 284 (3.21%) met the National Diabetes Data Group criteria, whereas 438 (4.95%) met the Carpenter and Coustan criteria. We estimate that in our population, use of the Carpenter and Coustan criteria, in 1996, could at best have reduced the prevalence of infants weighing  $\geq 4000$  g from 17.1% to 16.9% and the prevalence of infants weighing  $\geq 4500$  g from 2.95% to 2.91%.

**CONCLUSIONS:** Replacing the National Diabetes Data Group criteria with the Carpenter and Coustan criteria would increase by 54% the number of pregnant women with a diagnosis of gestational diabetes mellitus and would also increase costs, while only minimally affecting prevalence of infant macrosomia. The



medical literature does not provide compelling evidence for adopting the Carpenter and Coustan criteria. Standardization of both measurement of venous plasma glucose level and diagnostic criteria for gestational diabetes mellitus is an important goal. Parallel criteria for diagnosis and classification of diabetes mellitus in pregnant and nonpregnant women should be developed.

### Safety and Immunogenicity of Heptavalent Pneumococcal CRM197 Conjugate Vaccine in Infants and Toddlers

*Shinefield HR; Black S; Ray P; Chang I; Lewis N; Fireman B; et al; Pediatr Infect Dis J 1999 Sep;18(9):757-63.*

**OBJECTIVES:** The objectives of this study were (1) to determine the safety and immunogenicity of heptavalent pneumococcal CRM197 conjugate (PNCRM7) vaccine in infants and (2) to determine the effect of concurrent hepatitis B immunization during the primary series and the effect of concurrent diphtheria and tetanus toxoid and acellular pertussis [DTaP (ACEL-IMUNE)] and conjugate CRM197 Haemophilus influenzae type b [HbOC (HibTITER)] immunization at time of the booster dose on the safety and immunogenicity of PNCRM7 and these other concurrently administered vaccines.

**METHODS:** This was a randomized double-blinded study in 302 healthy infants in the Northern California Kaiser Permanente (NCKP) Health Plan. Infants received either PNCRM7 vaccine or meningococcal group C conjugate vaccine as a control at two, four, and six months of age and a booster at 12 to 15 months of age. Study design permitted the evaluation of immunology and safety of concurrent administration of routine vaccines. Antibody titers were determined on blood samples drawn before and one month after the primary series and the booster dose.

**RESULTS:** After the third dose of PNCRM7, geometric mean concentrations (GMCs) ranged from 1.01 for serotype 9V to 3.72 microg/ml for serotype 14. More than 90% of all subjects had a post-third dose titer of  $>$  or  $=$  0.15 microg/mL for all serotypes, and the percentage of infants with a post-third dose titer of  $>$  or  $=$  1.0 microg/mL ranged from 51% for type 9V to 89% for type 14. After the PNCRM7 booster dose, the GMCs of all seven serotypes increased significantly over both post-Dose 3 and pre-Dose 4 antibody levels. In the primary series, there were no significant differences in GMCs of pneu-

mococcal antibodies between the subjects given PNCRM7 alone or concurrently with hepatitis B vaccine. At the toddler dose, concurrent administration of PNCRM7 and DTaP and HbOC resulted in a near conventional threshold for statistical significance of a post-Dose 4 GMC for serotype 23F [alone 6.75 microg/mL vs. concurrent 4.11 microg/mL ( $P = 0.057$ )] as well as significantly lower antibody GMCs for H. influenza polyribosylribitol phosphate, diphtheria toxoid, pertussis toxin, and filamentous hemagglutinin. For all antigens, there were no differences between study groups in defined antibody titers that are considered protective.

**CONCLUSION:** We conclude that PNCRM7 vaccine was safe and immunogenic. When this vaccine was administered concurrently at the booster dose with DTaP and HbOC vaccines, lower antibody titers were noted for some of the antigens when compared with the antibody response when PNCRM7 was given separately. Because the GMCs of the booster responses were all generally high and all subjects achieved similar percentages above predefined antibody titers, these differences are probably not clinically significant.

### Experience Using Radio Frequency Laptops to Access the Electronic Medical Record in Exam Rooms

*Dworkin LA; Krall M; Chin H; Robertson N; Harris J; Hughes J; Proc AMIA Symp 1999 Nov 6;741-4.*

Kaiser Permanente Northwest evaluated the use of laptop computers to access our existing comprehensive Electronic Medical Record in exam rooms via a wireless radiofrequency (RF) network. Eleven of 22 clinicians who were offered the laptops successfully adopted their use in the exam room. These clinicians were able to increase their exam room time with the patient by almost four minutes (25%), apparently without lengthening their overall work day. Patient response to exam room computing was overwhelmingly positive. The RF network response time was similar to the hardwired network. Problems cited by some laptop users and many of the eleven non-adopters included battery issues, different equipment layout and function, and inadequate training. IT support needs for the RF laptops were two to four times greater than for hardwired desktops. Addressing the reliability and training issues should increase clinician acceptance, making a successful general roll-out for exam room computing more likely.

## Rehospitalization in the First Two Weeks After Discharge from the Neonatal Intensive Care Unit

*Escobar GJ; Joffe S; Gardner MN; Armstrong MA; Folck BF; Carpenter DM; Pediatrics 1999 Jul;104(1):e2.*

**BACKGROUND:** High-risk newborns are known to have higher than average utilization of services after discharge from the neonatal intensive care unit (NICU). Most studies on this subject report aggregate data over periods ranging from one to three years postdischarge. Little is known about events that are temporally close to NICU discharge.

**OBJECTIVES:** To characterize rehospitalizations within the first two weeks after discharge from six community NICUs.

**METHODS:** We scanned electronic databases and reviewed the charts of rehospitalized infants from six NICUs in the Kaiser Permanente Medical Care Program. We subdivided infants into five groups based on gestational age (GA) and birth hospitalization length of stay (LOS): 1)  $\geq 37$  weeks' GA with  $< 4$  days' LOS (n = 2593); 2)  $\geq 37$  weeks' GA with  $\geq 4$  days' LOS (n = 1133); 3) from 33 to 36 weeks' GA with  $< 4$  days' LOS (n = 545); 4) from 33 to 36 weeks' GA with  $\geq 4$  days' LOS (n = 1196); and 5)  $< 33$  weeks' GA (n = 587). We performed bivariate and multivariate analyses to identify predictors that might be useful for practitioners.

**RESULTS:** There were 6054 newborns discharged alive from the six study NICUs between August 1, 1992 and December 31, 1995, and 99.5% of these infants remained in the health plan during the two weeks after NICU discharge. The overall rehospitalization rate was 2.72%, which is 20% higher than the rate among healthy term newborns in the Kaiser Permanente Medical Care Program (2.26%). The two most common reasons for rehospitalization were jaundice (62/165, 37.6%) and feeding difficulties (25/165, 15.2%). Infants with 33 to 36 weeks' GA and  $< 4$  days' LOS were rehospitalized at a significantly higher rate than were all other infants (5.69%); 71% of infants in this group were rehospitalized for jaundice. The following variables predicted rehospitalization in multivariate models:  $< 33$  weeks' GA (adjusted OR [AOR]: 1.88; 95% CI: 1.10-3.21), from 33 to 36 weeks' GA with  $< 96$  hours' LOS (AOR: 2.94; 95% CI: 1.87-4.62), and birth at facility B, which had the highest rehospitalization rate of the six facilities (AOR: 1.92; 95% CI: 1.39-2.65).

**CONCLUSIONS:** The rate of rehospitalization among NICU graduates is higher than among healthy term infants. Most of the rehospitalizations among infants with from 33 to 36 weeks' GA and  $< 4$  days' LOS are

for illnesses that are not life-threatening. Collaborative studies and new process and outcomes measures are needed to assess the effectiveness of follow-up strategies in high-risk newborns.

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## Continuation of Postmenopausal Hormone Replacement Therapy in a Large Health Maintenance Organization: Transdermal Matrix Patch Versus Oral Estrogen Therapy

*Ettinger B; Pressman A; Am J Manag Care 1999 Jun;5(6):779-85.*

**OBJECTIVE:** To determine possible differences in continuation of postmenopausal estrogen replacement therapy among women initiating treatment with transdermal estradiol versus those initiating treatment with oral estrogen.

**STUDY DESIGN:** A retrospective database search.

**PATIENTS AND METHODS:** We analyzed estrogen use among 45- to 74-year-old women who filled index prescriptions for estrogen during 1996 for either once-a-week transdermal estradiol or daily oral estrogen. Prescription use was analyzed separately for each of two groups: 276 hysterectomized women who filled prescriptions for estrogen alone (ERT) and 4182 women who filled prescriptions for medroxyprogesterone acetate (MPA) with estrogen (HRT) on the same day.

**RESULTS:** Risk of discontinuing therapy after 12 months ranged from 59% to 76% among the four subgroups: ERT with unopposed transdermal estradiol; ERT with unopposed oral estrogen; HRT with MPA-opposed transdermal estradiol; and HRT with MPA-opposed oral estrogen. The relative risk (RR) of discontinuation was significantly greater among women starting HRT with transdermal estradiol than among women starting oral estrogen (RR = 1.5; 95% confidence interval [CI] = 1.3 to 1.8). RR of discontinuation among women starting ERT with transdermal estradiol compared with women starting oral estrogen therapy was 1.3 (95% CI = 1.0 to 1.8).

**CONCLUSIONS:** Approximately two of three women who start either ERT or HRT discontinue therapy within a year, regardless of hysterectomy status. Furthermore, women who start ERT or HRT with a transdermal estradiol system are more likely to discontinue therapy.

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### Personal Perspective on Low-Dosage Estrogen Therapy for Postmenopausal Women

*Ettinger B; Menopause 1999 Fall;6(3):273-6*

**OBJECTIVE:** As evidenced by results from recent clinical trials and epidemiological studies that have examined the physiological and clinical effects of low levels of estradiol, it is now time to replace the widely held belief that less than the standard dosage of estrogen is without benefit.

**DESIGN:** Review of literature and personal experience.

**RESULTS:** Studies indicate that low-dosage estrogen can relieve vasomotor symptoms, can prevent bone loss, and may reduce the risk of coronary heart disease. However, to achieve these health benefits, long-term estrogen use is required. Women who use low dosages of estrogens are less likely to have unacceptable side effects, such as irregular bleeding, heavy bleeding, or breast tenderness. Thus, long-term continuation of hormone replacement therapy (HRT) may be improved if lower dosages are given, particularly if the HRT regimen is tailored to the needs of the patient.

**CONCLUSIONS:** Although standard-dosage estrogen remains the "gold standard" for HRT, having a low dosage as an alternative regimen can be useful. Attention of clinical researchers should focus on the effects of low-dosage estrogen on osteoporotic fractures and other health outcomes.

### Occupational Exposure to Antineoplastic Agents: Self-Reported Miscarriages and Stillbirths among Nurses and Pharmacists

*Valanis B; Vollmer WM; Steele P; J Occup Environ Med 1999;41(8):632-8.*

Insult to the germ cells of an ovum or sperm prior to pregnancy as well as exposures to a fetus during pregnancy can affect the outcome of a pregnancy. Antineoplastic agents are mutagenic and teratogenic, so the potential effects of exposure on reproduction are of concern to the workers who handle them. This study investigates pregnancy loss associated with occupational exposures to antineoplastic drugs by comparing rates of spontaneous abortion and stillbirths for pregnancies without antineoplastic exposure and exposed pregnancies in which the pregnant woman or the father handled antineoplastic agents either before or during the pregnancy. A total of 7094 pregnancies of 2976 pharmacy and nursing staff were examined. After age during pregnancy, prior gravidity, maternal smoking during the pregnancy, and occurrence of a

spontaneous abortion or stillbirth in a prior pregnancy were controlled for, exposure of the mother to or the handling of antineoplastic agents during the pregnancy was associated with a significantly increased risk of spontaneous abortion (odds ratio = 1.5; 95% confidence interval, 1.2 to 1.8) and combined risk of spontaneous abortion and stillbirth (odds ratio = 1.4; 95% confidence interval, 1.2 to 1.7) but not stillbirth alone. Among the wives of exposed men, too few stillbirths occurred to allow analysis. However, for spontaneous abortion and any loss, the patterns of increased risk were similar to those seen for women, although the odds ratios were not statistically significant.

### Barbiturates and Lung Cancer: a Re-Evaluation

*Friedman GD; Habel LA; Int J Epidemiol 1999 Jun;28(3):375-9.*

**BACKGROUND:** Barbiturates, particularly phenobarbital, have been shown to be a tumour promoter in animal experiments and were found to be associated with increased risk of lung cancer in our cohort follow-up study to screen pharmaceuticals for possible carcinogenic effects. Sixteen more years of follow-up have accumulated permitting a more detailed evaluation of this association.

**METHODS:** In all, 10,213 subscribers of the Kaiser Permanente Medical Care Program who received barbiturates between 1969 and 1973 from its San Francisco pharmacy were followed up through 1992 and their incidence of lung cancer at biennial intervals was compared with what was expected based on the experience of the entire pharmacy cohort (143,594). Smoking-habit data were available on about half of the barbiturate users and were used to adjust for cigarette smoking in both the observed/expected analysis and in Cox proportional hazards analysis.

**RESULTS:** The initially elevated standard morbidity ratio of 1.55 (95% CI: 1.25-1.91) with three to seven years of follow-up gradually decreased and stabilized at about 1.3 after 11-15 years of follow-up. This trend for diminishing relative risk over time was more pronounced among the never smokers but their initial excess risk was not statistically significant due to small numbers. A dose-response trend was observed, based on the number of prescriptions dispensed. Analytical control for cigarette smoking reduced but did not eliminate either the association or the dose-response trend. Most of the barbiturate-associated cases in never smokers were women and the predominant histological type was adenocarcinoma.



**CONCLUSIONS:** These findings from up to 23 years of follow-up are not conclusive because of the continuing small number of never smokers who developed lung cancer. However, they strengthen and refine previous observations of a barbiturate-lung cancer association, which is probably not fully explained by confounding by cigarette smoking. The diminution of excess risk over time is consistent with a tumour promoter effect. Findings among the never smokers suggest that this possible effect may be greatest on adenocarcinomas in women.

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### **Descriptive Characteristics of the Dietary Patterns Used in the Dietary Approaches to Stop Hypertension Trial. DASH Collaborative Research Group**

*Karanja NM; Obarzanek E; Lin PH; McCullough ML; Phillips KM; Swain JF; et al; J Am Diet Assoc 1999 Aug;99(8 Suppl):S19-27.*

The Dietary Approaches to Stop Hypertension trial was a randomized, multicenter, controlled feeding study to compare the effect on blood pressure of three dietary patterns: control, fruits and vegetables, and combination diets. The patterns differed in selected nutrients hypothesized to alter blood pressure. This article examines the food-group structure and nutrient composition of the study diets and reports participant nutrient consumption during intervention. Participants consumed the control dietary pattern during a three-week run-in period. They were then randomized either to continue on the control diet or to change to the fruits and vegetables or the combination diet for eight weeks. Sodium intake and body weight were constant during the entire feeding period. Analysis of variance models compared the nutrient content of the three diets. Targeting a few nutrients thought to influence blood pressure resulted in diets that were profoundly different in their food-group and nutrient composition. The control and fruits and vegetables diets contained more oils, table fats, salad dressings, and red meats and were higher in saturated fat, total fat, and cholesterol than was the combination diet. The fruits and vegetables and combination diets contained relatively more servings of fruits, juices, vegetables, and nuts/seeds, and were higher in magnesium, potassium, and fiber than was the control diet. Both the fruits

and vegetables and combination diets were low in sweets and sugar-containing drinks. The combination diet contained a greater variety of fruits, and its high calcium content was obtained by increasing low-fat dairy products. In addition, the distinct food grouping pattern across the three diets resulted in substantial differences in the levels of vitamins A, C, E, folate, B-6, and zinc.

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### **Excess Maternal Transmission of Type 2 Diabetes. The Northern California Kaiser Permanente Diabetes Registry**

*Karter AJ; Rowell SE; Ackerson LM; Mitchell BD; Ferrara A; Selby JV; et al; Diabetes Care 1999 Jun;22(6):938-43.*

**OBJECTIVE:** To assess excess maternal transmission of type 2 diabetes in a multiethnic cohort. Previous studies have reported higher prevalence of diabetes among mothers of probands with type 2 diabetes than among fathers. This analysis is vulnerable to biases, and this pattern has not been observed in all populations or races.

**RESEARCH DESIGN AND METHODS:** We assessed evidence for excess maternal transmission among 42,533 survey respondents with type 2 diabetes (probands) by calculating the prevalence of diabetes in their siblings and offspring. To assess data quality, we evaluated completeness of family history data provided. Accuracy of family information reported by probands was also evaluated by comparing survey responses in a subsample of 206 probands with family histories modified after further interviews with relatives.

**RESULTS:** Siblings ( $n = 60,532$ ) of probands with affected mothers had a greater prevalence of diabetes (20%) than those with affected fathers (17%) ( $P < 0.001$  for adjusted odds ratios). Prevalence of diabetes was higher among the offspring ( $n = 72,087$ ) of female (3.4%) versus male (2.2%) probands ( $P < 0.001$  for adjusted odds ratios). These patterns were evident in all races and both sexes; however, the effect size was clinically insignificant in African-Americans and male offspring. In general, probands provided more complete data about diabetes status for the maternal arm of the pedigree than the paternal arm. Completeness of knowledge was not related to proband sex, but was related to education



and race, and inversely to age. Accuracy of proband-reported family history was consistently good (kappa statistics generally > 0.70).

**CONCLUSIONS:** Excess maternal transmission was observed in all races and both sexes, although the size of the excess was negligible in African-Americans and male offspring. Potential reporting and censoring biases are discussed.

### The Sensitivity and Specificity of Forecasting High-Cost Users of Medical Care

*Meenan RT; O'Keeffe-Rosetti C; Hornbrook MC; Bachman DJ; Goodman MJ; Fishman PA; et al; Med Care 1999 Aug;37(8):815-23.*

**OBJECTIVES:** This study compares the ability of three risk-assessment models to distinguish high and low expense-risk status within a managed care population. Models are the Global Risk-Assessment Model (GRAM) developed at the Kaiser Permanente Center for Health Research; a logistic version of GRAM; and a prior-expense model. GRAM was originally developed for use in adjusting Medicare payments to health plans.

**METHODS:** Our sample of 98,985 cases was drawn from random samples of memberships of three staff/group health plans. Risk factor data were from 1992, and expenses were measured for 1993. Models produced distributions of individual-level annual expense forecasts (or predicted probabilities of high expense-risk status for logistic) for comparison to actual values. Prespecified "high-cost" thresholds were set within each distribution to analyze the models' ability to distinguish high and low expense-risk status. Forecast stability was analyzed through bootstrapping.

**RESULTS:** GRAM discriminates better overall than its comparators (although the models are similar for policy-relevant thresholds). All models forecast the highest-cost cases relatively well. GRAM forecasts high expense-risk status better than its comparators within chronic and serious disease categories that are amenable to early intervention but also generates relatively more false positives within these categories.

**CONCLUSIONS:** This study demonstrates the potential of risk-assessment models to inform care management decisions by efficiently screening managed care populations for high expense-risk. Such models can act as preliminary screens for plans that can refine model forecasts with detailed surveys. Future research should involve multiple-year data sets to explore the temporal stability of forecasts.

### Uterine Rupture Associated with the Use of Misoprostol in the Gravid Patient with a Previous Cesarean Section

*Plaut MM; Schwartz ML; Lubarsky SL; Am J Obstet Gynecol 1999 Jun;180(6 Pt 1):1535-42.*

**OBJECTIVE:** Our purpose is to report our experience with uterine rupture in patients undergoing a trial of labor after previous cesarean delivery in which labor was induced with misoprostol. The literature on the use of misoprostol in the setting of previous cesarean section is reviewed.

**STUDY DESIGN:** This report was based on case reports, a computerized search of medical records, and literature review.

**RESULTS:** Uterine rupture occurred in five of 89 patients with previous cesarean delivery who had labor induced with misoprostol. The uterine rupture rate for patients attempting vaginal birth after cesarean section was significantly higher in those who received misoprostol, 5.6%, than in those who did not, 0.2% (1/423,  $P = .0001$ ). Review of the literature reveals insufficient data to support the use of misoprostol in the patient with a previous cesarean delivery.

**CONCLUSION:** Misoprostol may increase the risk of uterine rupture in the patient with a scarred uterus. Carefully controlled studies of the risks and benefits of misoprostol are necessary before its widespread use in this setting.

### A Low-Cost Approach to Prospective Identification of Impending High Cost Outcomes

*Roblin DW; Juhn PI; Preston BJ; Della Penna R; Feitelberg SP; Khoury A; et al; Med Care 1999 Nov;37(11):1155-63.*

**OBJECTIVES:** The overall objective of this study was to define and evaluate patterns of use of medical services in the care of patients with chronic illness that represent circumstances which, if modified, might lead to reduction in risk of acute-level care.

**METHODS:** This was a retrospective observational study. The study population consisted of Kaiser Permanente enrollees at four sites during January 1993 through June 1995, who were 20 to 64 years of age and had two of three chronic diseases (diabetes, circulatory disorders, obstructive pulmonary disorders). Using logistic regression, the effect of primary care visit patterns and therapeutically risky drug combinations on likelihood of hospital admission in a subsequent 3-month period is adjusted



for age, gender, and disease state in the prior 12-month period.

**RESULTS:** Enrollees with visits to three or more different primary care physicians were 46% more likely to be admitted than expected ( $P < 0.01$ ) according to their age, gender, and disease state, and those with therapeutically risky drug combinations were 34% more likely to be admitted ( $P < 0.01$ ).

**CONCLUSIONS:** The risk adjustment models evaluated in this study defined care processes associated with increased risk of subsequent acute-level services. Those processes may represent nascent acute disease states or suboptimal organization of care delivery. The results of these models can be used to inform changes in organization and delivery of outpatient care that might improve patient outcomes.

### When Is Fasting Really Fasting? The Influence of Time of Day, Interval After a Meal, and Maternal Body Mass on Maternal Glycemia in Gestational Diabetes

*Sacks DA; Chen W; Wolde-Tsadik G; Buchanan TA; Am J Obstet Gynecol 1999 Oct;181(4):904-11.*

**OBJECTIVE:** The object of the study was to determine whether time of day, interval after a standard meal, and maternal body mass influence plasma glucose concentrations in women with gestational diabetes mellitus.

**STUDY DESIGN:** Identical mixed meals were administered on two separate occasions one week apart to 30 women with dietarily treated gestational diabetes and pregnancies between 28 and 38 weeks' gestation. One meal was administered at 7 AM (morning meal) and the other was administered at 9 PM (evening meal), each after a fast of  $\geq 5$  hours. The order of the meals (morning first versus evening first) was assigned randomly. Sixteen of the women had a body mass index  $\geq 27$  kg/m<sup>2</sup> (overweight) and 14 women had a body mass index  $< 27$  kg/m<sup>2</sup> (lean). Venous plasma concentrations of glucose, insulin, free fatty acids, beta-hydroxybutyrate, and bound and free cortisol were measured hourly for nine hours after each of the test meals.

**RESULTS:** When all women were considered together glucose concentrations after the morning meal were significantly greater at one hour, were not different at two hours, and were significantly lower from three through nine hours postprandially than those at corresponding times after the evening meal. Plasma beta-hydroxybutyrate and free fatty acid concentrations were higher between five and nine hours after the morning meal than at the same times after the evening

meal. Total and free cortisol levels were higher for the first seven hours after the morning feeding, reflecting known diurnal variation in cortisol concentrations. Overweight patients' glucose values were significantly greater than those of lean subjects during the last four hours of the overnight fast.

**CONCLUSIONS:** Among women with dietarily treated gestational diabetes the glucose concentrations were significantly higher from three to nine hours after an evening meal, whereas suppression of free fatty acids and beta-hydroxybutyrate was less sustained after a morning feeding. The mechanisms underlying these differences remain to be determined but may involve diurnal influences of counterregulatory hormones. The relationships between measurements of maternal glycemia and maternal and perinatal outcomes in pregnancies complicated by gestational diabetes may be clarified by establishing a uniform duration of a fast and by developing meal-specific preprandial and postprandial maternal glucose targets for these patients.

### Dietary Approaches to Stop Hypertension: Rationale, Design, and Methods. DASH Collaborative Research Group

*Vogt TM; Appel LJ; Obarzanek E; Moore TJ; Vollmer WM; Svetkey LP; et al; J Am Diet Assoc 1999 Aug;99(8 Suppl):S12-18.*

Epidemiologic studies across societies have shown consistent differences in blood pressure that appear to be related to diet. Vegetarian diets are consistently associated with reduced blood pressure in observational and interventional studies, but clinical trials of individual nutrient supplements have had an inconsistent pattern of results. Dietary Approaches to Stop Hypertension (DASH) was a multicenter, randomized feeding study, designed to compare the impact on blood pressure of three dietary patterns. DASH was designed as a test of eating patterns rather than of individual nutrients in an effort to identify practical, palatable dietary approaches that might have a meaningful impact on reducing morbidity and mortality related to blood pressure in the general population. The objectives of this article are to present the scientific rationale for this trial, review the methods used, and discuss important design considerations and implications.

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## Association of Asthma Control with Health Care Utilization and Quality of Life

Vollmer WM; Markson LE; O'Connor E; Sanocki LL; Fitterman L; Berger M; et al; *Am J Respir Crit Care Med* 1999 Nov;160(5 Pt 1):1647-52.

Asthma severity and level of asthma control are two related, but conceptually distinct, concepts that are often confused in the literature. We report on an index of asthma control developed for use in population-based disease management. This index was measured on 5181 adult members of a large health maintenance organization (HMO), as were various self-reported measures of health care utilization (HCU) and quality of life (QOL). A simple index of number of control problems, ranging from

none through four, exhibited marked and highly significant cross-sectional associations with self-reported HCU and with both generic and disease-specific QOL instruments, suggesting that each of the four dimensions of asthma control represented by these problems correlates with clinically significant impairment. Qualitatively similar results were found for control problems assessed relative to the past month and relative to the past year. Asthma control is an important "vital sign" that may be useful both for population-based disease management as well as for the management of individual patients. ❖

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## The Lighter Side of Medicine



Indicative-Informative Abstracts. IV. Abstracts of Monographs and Chapters. V. Less Common Types of Abstracts. VI. Varying the Order of Elements. VII. Position of the Bibliographic Citation for Abstracts in Access Services. ANSI/NISO Z39.14-1997 (R2009). ISSN: 1041-5653. Guidelines for Abstracts. Abstract: Guidance is presented for authors and editors preparing abstracts that represent the content of texts reporting on the results of experimental work or descriptive or discursive studies. Book of abstracts contains theses of plenary, oral and poster presentations which were presented on Mendeleev 2019, the XI International Conference on Chemistry for Young Scientists. The Mendeleev 2019 Conference held in Saint Petersburg (September 9-13, 2019), as a satellite event during the XXI Mendeleev Congress on General and Applied Chemistry, dedicated to the 150. Abstract. 1. During the last 10 years, use of the World-Wide-Web for educational purposes has increased dramatically. 2. However, very little empirical research has been carried out to determine the effectiveness of this use. 3. The aim of this study was therefore to investigate the effectiveness of using the World-Wide-Web on an EAP writing course. An abstract must be fully self-contained and make sense by itself, without further reference to outside sources or to the actual paper. It highlights key content areas, your research purpose, the relevance or importance of your work, and the main outcomes. It is a well-developed single paragraph of approximately 250 words in length, which is indented and single spaced. The function of the abstract is to outline briefly all parts of the paper.