

Recent Publications

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RESEARCH UPDATE

A KAISER PERMANENTE
NORTHERN CALIFORNIA
QUARTERLY NEWSLETTER

PRODUCED BY
THE DIVISION OF RESEARCH
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Getting Involved in Pharmaceutical-Funded Research

Joe Selby, MD, MPH

Director, Division of Research

This year, The Permanente Medical Group (TPMG) clinician researchers conducted more than \$13 million worth of research funded by pharmaceutical companies. These studies often evaluate important new therapies (new vaccines, exciting treatments for cancer and HIV, depression, osteoporosis, and prevention of breast cancer). They build the evidence on which TPMG practices evidence-based medicine and, in some cases, provide our patients with early access to promising new therapies. Many could not be conducted without the financial support of industry sponsors. For all these reasons, TPMG, the Kaiser Foundation Research Institute (KFRI), and the Division of Research are highly supportive of involvement of TPMG clinicians in industry-sponsored studies.

However, research collaborations with for-profit sponsors bring risks, and Kaiser Permanente has much more to lose than most academic research centers. Conflicts of interest, and even the appearance of conflict, risk eroding the trust and confidence of Kaiser members in their health care providers. Recent media scrutiny of pharmaceutical-funded research has been intense and generally negative, focusing on biased reporting of findings and on adverse consequences for poorly informed patients. To the credit of KFRI, TPMG, and our researchers, these negative stories have not featured Kaiser patients or studies.

Some of the problems encountered by academic scientists can be traced back to poorly written contracts. KFRI's legal support team has developed a model agreement for clinical trials and carefully reviews all proposed contracts prior to organizational signature for features such as publication rights and data ownership. Staff are available for consultation and advice throughout the contract

development process (510-987-3431).

Northern California's Institutional Review Board, also administered through KFRI, must approve all proposed studies concentrating particularly on issues related to patient safety and informed consent. TPMG and our associated Medical Groups in all other regions have recently developed a standard guideline for avoiding conflict of interest when accepting funds from industry sponsors. These will be available shortly through the office of TPMG Associate Executive Director Dr. Sharon Levine.

A less obvious risk involves doing the "wrong study." Industry sponsors design studies that meet their needs (getting FDA approval, establishing the superiority of their product). Kaiser Permanente's needs may differ. For example, clinical trials pitting an expensive new product against placebos or obviously inadequate dosages of presently available drugs may prove that new products are better than nothing. However, they don't help Kaiser Permanente decide whether to switch from current practice to the new product. Moreover, they can increase pressures to add the new product to our formulary, either by altering community practice or by creating a group of Kaiser patients or providers who've become accustomed to using the medication. To check for such potential discrepancies of interest, the Pharmaceutical Review Committee of the Central Research Committee, chaired by Dr. Phillip Heller, Hayward, works closely with KFRI to review all proposals that would be funded by industry sponsors.

A third risk is that study budgets, often prepared hastily by investigators pressured by sponsors to meet company funding deadlines, can fail to capture all the costs of the study. In other situations,

(continued on page 8)

RECENT
PUBLICATIONS

Publications by researchers in the Northern California region during the months of September through November 2000 are presented below. Section I provides citations and brief descriptions of lead-authored publications; section II provides co-authored publications. If you have recently published

a paper and would like it to be included in an issue of *Research Update*, please send a Lotus Notes to Lyn Wender, or call 510-450-2205 (8-481-2205). If you would like a copy of one of the articles, contact your local library or call the DOR Library at 510-450-2182 (8-481-2182).

I. Lead-Authored Publications

Backer HD,* Mohle-Boetani JC, Werner SB, Abbott SL, Farrar J, Vugia DJ. HIGH INCIDENCE OF EXTRA-INTESTINAL INFECTIONS IN A SALMONELLA HAVANA OUTBREAK ASSOCIATED WITH ALFALFA SPROUTS. *Public Health Rep* 2000;115:339-45. **Funding Source:** None. (***Hayward:** 510-784-5423)

To determine a vehicle and point source for an outbreak of Salmonella Havana, the authors conducted a case-control study and traceback investigation of 14 residents of California and 4 from Arizona with onsets of illness from April 15, 1998, to June 15, 1998, and Salmonella Havana infections with identical PFGE patterns. Seventeen patients were women; 17 were adults; 9 (50%) had diarrheal illness; 6 (33%) had urinary tract infections; 2 (11%) had sepsis; and 1 had an infected surgical wound after appendectomy. Four patients were hospitalized and 1 died. Eating alfalfa sprouts was associated with S. Havana infection (OR=10.0; 95% confidence interval 1.2, 83.1; p=0.01). This outbreak resulted in a high incidence of extra-intestinal infections, especially urinary tract infections, and high morbidity. Raw alfalfa sprouts, often considered a safe "health food," can be a source of serious foodborne disease outbreaks.

Baer ET.* IATROGENIC MENINGITIS: THE CASE FOR FACE MASKS. *Clin Infect Dis* 2000;31:519-21. **Funding Source:** None. (***Richmond: retired; contact etbaer@pol.net**)

This paper presents support for the hypothesis that Viridans streptococci meningitis after lumbar puncture is likely caused by dispersal of the organism from the upper airway of medical personnel. Support for this hypothesis include the occurrence of this condition in clusters (more than one case belonging to a particular physician) and the finding that DNA fingerprinting and fatty acid analysis of the organism, in such a case, matched the isolate from a throat swab of the operating neurologist. Strict adherence to sterile technique, including wearing a face mask while performing lumbar puncture, is urged as a national standard. Resistance by medical personnel to this suggestion as reported in several references is puzzling.

Bakshi N,* Rauf S, Fenton GE, Maselli RA. DIAGNOSTIC DIFFICULTIES IN PATIENTS WITH ADULT BOTULISM TYPE A. *J Clin Neuromusc Dis* 2000;2:18-21. **Funding**

Source: None. (***Oakland:** 510-596-7534)

Although the electrodiagnostic abnormalities in botulism have been well characterized, the expected abnormalities, such as facilitation of compound muscle action potential amplitudes after sustained activation or with repetitive stimulation at fast rates, may not always be present, especially early in the disease. This may lead to electrodiagnostic difficulties and sometimes a delay in establishing a diagnosis. The authors describe four serologically proven cases of type A botulism in adults that illustrate the variability in electrodiagnostic findings in this disease.

Black S,* Shinefield H. VACCINES AND OTITIS MEDIA. *Pediatr Ann* 2000;29:648-51. **Funding Source:** None. (***Division of Research:** 510-450-2251)

The microbiologic causes of acute otitis media (AOM) have been documented by studies of middle ear aspirations sent for bacteriologic cultures, viral cultures, and polymerase chain reaction analysis. In the largest series, 38% of positive cultures were due to *Streptococcus pneumoniae*, 27% to *Haemophilus influenzae*, 10% to *Moraxella*, 3% to group A streptococcus, and 2% to *Staphylococcus aureus*, with the remaining infections due to other bacteria. In children, respiratory syncytial virus was the most common viral isolate. Increasing antibiotic resistance of pneumococci, *H. influenzae*, and *Moraxella* has made treatment of otitis media more difficult, prompting a renewed effort to prevent rather than treat AOM. Vaccines have recently been approved or are in development. This article reviews the rationale for and current status of vaccines directed against the primary pathogens of otitis media in childhood.

Caan BJ,* Flatt SW, Rock CL, Ritenbaugh C, Newman V, Pierce JP, for the Women's Healthy Eating and Living Group. LOW-ENERGY REPORTING IN WOMEN AT RISK FOR BREAST CANCER RECURRENCE. *Cancer Epidemiol Biomarkers Prev* 2000;9:1091-7. **Funding Source:** National Cancer Institute. (***Division of Research:** 510-450-2116)

This study examined the extent of low-energy reporting and its relationship with demographic and lifestyle factors in women previously treated for breast cancer. Examined were data from 1137 women, aged 18-70, diagnosed with stage I, II, or III primary, operable breast cancer, and

(Lead-Authored Publications continued)

enrolled in the Women's Healthy Eating and Living Study within 4 years after diagnosis. The criteria classified 25.6% as low-energy reporters (LERs) and 10.8% as very LERs. Women with body mass index >30 were twice as likely to be LERs and women with a history of weight gain or fluctuations were 1-1/2 times as likely. Age, ethnicity, alcohol intake, supplement use, and exercise level were also related to LER. Characteristics associated with low-energy reporting in this group are similar to those observed in other populations and might affect observed diet and breast cancer associations in epidemiological studies.

Chen GL,* Bagley DH. URETEROSCOPIC MANAGEMENT OF UPPER TRACT TRANSITIONAL CELL CARCINOMA IN PATIENTS WITH NORMAL CONTRALATERAL KIDNEYS. *J Urol* 2000;164:1173-6. **Funding Source:** None.

(*Hayward: 510-784-4499)

This study sought to determine whether ureteroscopic tumor resection with vigilant surveillance is a safe alternative to nephroureterectomy or segmental ureterectomy. Patients with isolated upper tract filling defects and a normal contralateral kidney were diagnosed ureteroscopically with papillary low intermediate grade appearing transitional cell carcinoma. Biopsies of the lesions were obtained. Patients with cytopathological results of high grade transitional cell carcinoma underwent nephroureterectomy. Surveillance consisted of ureteroscopy every 3 months until tumor-free, then ureteroscopy every 6 months. Twenty-three patients with normal creatinine underwent ureteroscopic tumor resection. After the primary tumor was treated, 8 patients remained tumor-free and 15 had multiple recurrences, which were treated ureteroscopically. All 23 patients are alive without evidence of disease progression. It was concluded that ureteroscopic treatment is a safe alternative to nephroureterectomy in select patients when vigilant ureteroscopic follow-up is used.

Chen GL,* El-Gabry EA, Bagley DH. SURVEILLANCE OF UPPER URINARY TRACT TRANSITIONAL CELL CARCINOMA: THE ROLE OF URETEROSCOPY, RETROGRADE PYELOGRAPHY, CYTOLOGY AND URINALYSIS. *J Urol* 2000;164:1901-4. **Funding Source:** None. (*Hayward: 510-784-4499)

Patients with upper tract transitional cell carcinoma were treated with ureteroscopic resection and followed with surveillance to determine the validity and accuracy of urinalysis, bladder cytology, upper tract biopsy/cytology, and retrograde pyelography in detecting recurrence compared to endoscopic findings. There were 23 patients with previously resected low grade upper tract transitional cell carcinoma who underwent a total of 88 surveillances; 56 recurrences were detected ureteroscopically, including 11 associated bladder recurrences. In patients without bladder recurrences, urinalysis had a sensitivity of 37.5%, specificity 85%; bladder cytology had a sensitivity of 50%, specificity 100%; retrograde pyelography had a sensitivity of 71.7%, specificity 84.7%; ureteroscopic biopsy/cytology had a sensitivity of 93.4%, specificity 65.2%. The findings indicated that--compared to

ureteroscopy--urinalysis, bladder cytology, retrograde pyelography, and ureteroscopic cytology/biopsy are less valid and accurate in detecting upper tract transitional cell carcinoma recurrences. Ureteroscopic evaluation was recommended.

Collen MF.* HISTORICAL EVOLUTION OF PREVENTIVE MEDICAL INFORMATICS IN THE USA. *Methods Inf Med* 2000;39:204-7. **Funding Source:** None. (*Division of Research: 510-450-2122)

A major reorganization of healthcare services is occurring in the United States. It has evolved from the solo- and group-practice models of the 1940s with fee-for-service and insurer-indemnification financing that used paper-based information systems to support preventive medical services. In the 1990s there emerged nation-wide, managed-care plans employing enhanced computer-based information systems with online preventive medical practice guidelines and Internet-supported home-care telemedicine. It is helpful to review how this major reengineering of medicine has come about.

Ettinger B.* MEETING THE EVOLVING THERAPEUTIC NEEDS OF POSTMENOPAUSAL WOMEN. *J Bone Miner Metab* 2000;18:299-304. **Funding Source:** Eli Lilly. (*Division of Research: 510-450-2131)

Whenever new therapies become available, physicians have a professional responsibility to learn as much as possible about their appropriate clinical use. The recent emergence of new agents has quickly expanded the options available to clinicians and their patients in the area of long-term therapy and osteoporosis prevention after menopause. With this expansion has come confusion about the appropriate utilization of each agent. Such confusion is compounded by the fact that current therapies have distinct clinical profiles and by the growing importance of customizing care to a woman's personal preferences and health profile. This article focuses on the emergence of raloxifene hydrochloride as a long-term therapeutic option for certain postmenopausal women. The role of raloxifene as it relates to other therapies is addressed in four case studies, and practical suggestions for clinical decision making are made.

Klatsky AL.* ALCOHOL AND CARDIOVASCULAR DISEASES: AN HISTORICAL OVERVIEW. In: R. Paoletti et al. (eds), *Moderate Alcohol Consumption and Cardiovascular Disease.* Kluwer Academic Publishers, The Netherlands:1-9. **Funding Source:** None. (*Division of Research: 510-450-2757)

Disparities in relationships of alcohol to cardiovascular conditions make it desirable to consider several disorders separately. (1) Alcoholic cardiomyopathy was perceived 150 years ago, but understanding was clouded by recognition of beriberi and synergistic toxicity from alcohol with arsenic or cobalt. (2) A link between heavy drinking and hypertension is established, but a mechanism remains elusive. (3) The "holiday heart syndrome" has been known for 25 years; data remain sparse about the total role of heavier drinking in cardiac rhythm disturbances. (4) Failure of studies to distinguish types of stroke impeded understanding; it now seems probable that alcohol

(Lead-Authored Publications continued)

increases risk of hemorrhagic stroke but lowers risk of ischemic stroke. (5) Angina relief by alcohol was reported in 1786. Recent studies support a protective effect of alcohol against coronary disease. Comparisons suggest beverage choice a factor, but the "French Paradox" remains unresolved.

Klatsky AL,* Armstrong MA. SEX-BASED DIFFERENCES IN CAUSES OF HOSPITALIZATION FOR CORONARY HEART DISEASE. *The Permanente Journal* 2000;4:16-21. **Funding Source: Kaiser Foundation Research Institute. (*Division of Research: 510-450-2757)**

Sex differences in clinical presentation of coronary heart disease (CHD) have been described. Sex and other CHD hospitalization predictors were prospectively studied in 56,926 men and 72,008 women who provided baseline data at prior examinations. Cox models with 10 covariates were used to study first CHD hospitalizations. Male/female relative risks (RR) were greater ($P < 0.001$) for acute myocardial infarction (AMI); ($n=1757$, multivariate $RR=2.7$) or chronic ischemic heart disease ($n=573$, $RR=3.3$) than for other acute syndromes ($n=848$, $RR=1.5$) or angina ($n=753$, $RR=1.6$). Most CHD predictors were strongly related to CHD risk in women, but this was similar for the CHD diagnostic subsets. The risk of later death was similar for the sexes. These data show major independent sex differences in CHD hospitalization diagnoses, with men at greater risk of AMI and women at greater risk of stable or unstable angina.

Lawry MA,* Haneke E, Strobeck K, Martin S, Zimmer B, Romano PS. METHODS FOR DIAGNOSING ONYCHOMYCOSIS: A COMPARATIVE STUDY AND REVIEW OF THE LITERATURE. *Arch Dermatol* 2000;136:1112-6. **Funding Source: Dept of Dermatology, University of California, Davis. (*South Sacramento: 916-688-2935)**

This cross-sectional study of 63 adult men and women sought to identify the sensitivity of several diagnostic tests for onychomycosis. Nail samples underwent 6 diagnostic tests. Histopathologic examination with periodic acid-Schiff stain (PAS) (PATHPAS) was 85% sensitive. Sensitivities for potassium hydroxide dissolution and centrifugation combined with PAS, fluorescent brightener, or chlorazol black E were 57%, 53%, and 53%. Culture on Sabouraud agar with chloramphenicol and cycloheximide was 32% sensitive; on Littman-oxgall agar, 23%. The most sensitive combination of tests, both culture methods plus PATHPAS, was 94% sensitive. The difference between sensitivity of PATHPAS alone and in combination with culture was not statistically significant. When onychomycosis is suspected clinically, it was concluded, PATHPAS of the nail is the most sensitive of the diagnostic tests evaluated. Because it is quickly performed and operator independent, PATHPAS is practical for clinical and research purposes.

Marelich GP,* Murin S, Battistella F, Inciardi J, Vierra T, Roby M. PROTOCOL WEANING OF MECHANICAL VENTILATION IN MEDICAL AND SURGICAL PATIENTS BY RESPIRATORY CARE PRACTITIONERS AND NURSES:

EFFECT ON WEANING TIME AND INCIDENCE OF VENTILATOR-ASSOCIATED PNEUMONIA. *Chest* 2000;118:459-67. **Funding Source: The Hibbard E. Williams, MD, Research Fund. (*South Sacramento: 916-688-4229)**

This randomized, controlled study sought to determine the effects of a single ventilator management protocol (VMP) used in medical and surgical ICUs on the duration of mechanical ventilation and the incidence of ventilator-associated pneumonia (VAP). Three hundred eighty-five patients were studied; age, sex, illness\injury severity, and duration of respiratory failure at time of randomization were comparable in intervention and control groups. The median duration of mechanical ventilation was reduced by 2.33 days (47%) without affecting mortality or ventilator discontinuation failure rates. The study found a difference ($p=0.061$) in the incidence of clinically defined VAP between VMP and control trauma patients. The impact of VMP on VAP incidence was less for medical patients. These results suggest that VMPs are highly effective means of improving care.

Meng MV,* St Lezin M. TRIMETHOPRIM-SULFAMETHOXAZOLE INDUCED RECURRENT ASEPTIC MENINGITIS. *J Urol* 2000;164:1664-5. **Funding Source: Not available. (*Oakland: 510-596-6796 [M St Lezin])**

Antibiotic use is widespread in daily urological practice. Complications of therapy are common and readily recognized. However, rare side effects may not be so easily identified. Reported in this article is a case of recurrent episodes of aseptic meningitis secondary to use of trimethoprim and sulfamethoxazole for urinary tract infection, and the importance of recognizing this condition is underscored.

Mertens JR,* Weisner CM. PREDICTORS OF SUBSTANCE ABUSE TREATMENT RETENTION AMONG WOMEN AND MEN IN AN HMO. *Alcohol Clin Exp Res* 2000;24: 1525-33. **Funding Sources: National Institute on Alcohol Abuse and Alcoholism R37 AA10359; National Institute on Drug Abuse R01 DA08728. (*Division of Research: 510-450-2167)**

This study sought to identify factors that influence alcohol and drug treatment retention in an insured outpatient population. Recruited were 317 women and 599 men from an outpatient, abstinence-based, alcohol and drug treatment program. One pattern of predictors of increased retention was shared by women and men: fewer and less severe drug problems. Most predictors were gender-specific. Predictors among women were: having higher incomes, belonging to ethnic categories other than African-American, being unemployed, being married, and having lower levels of psychiatric severity; among men: being older, receiving employer suggestions to enter treatment, and having abstinence goals. These findings highlight the importance of examining aspects of the course of treatment separately by gender. They differ from past studies conducted on public populations and suggest treatment factors that may enhance retention among insured populations, including employer referrals, psychiatric services, and drug-related services.

(Lead-Authored Publications continued)

Selby JV.* EXPLAINING RECENT DECLINES IN COLORECTAL CANCER INCIDENCE: WAS IT THE SIGMOIDOSCOPE? *Am J Med* 2000;109:332-4. **Funding Source:** None. (*Division of Research: 510-450-2106)

Colorectal cancer has declined substantially during the past 20 years throughout the U.S. This editorial explores a number of possible contributing factors for these declines, and concludes that sigmoidoscopic screening is a highly plausible contributing factor to the steep declines observed. Because a third of all important lesions will be missed by sigmoidoscopy alone, attention must be directed to identifying suitable methods for screening the right colon. In the meantime, this evidence for an important effect of sigmoidoscopy should spur continued promotion of this underused screening test.

Slaughter J.* KAISER PERMANENTE: INTEGRATING AROUND A CARE DELIVERY MODEL. *J Ambulatory Care Manage* 2000;23:39-47. **Funding Source:** None. (*San Rafael: 415-444-2316)

The risk-adjusted payment model mandated for Medicare + Choice organizations by the Balanced Budget Act of 1997 has significant implications for health care organizations that offer the Medicare + Choice program. The accurate capture of visit-based chronic medical conditions via ICD-9-CM diagnosis codes in the ambulatory care setting will become the focus of data capture, requiring significant retooling of ambulatory care operations. Kaiser Permanente (KP) will be challenged to develop the infrastructure at the ambulatory care level to capture this data with the bulk of the effort falling to the caregivers. The risk payment model requires the accurate and complete identification of the illness burden of the population and rewards health plans and medical groups for efficient management of patients' chronic problems. This model aligns well with KP's healthcare delivery model. The demands for data for the payment model should enhance KP's capacity to identify and manage its population's illnesses.

Sternfeld B,* Cauley J, Harlow S, Liu G, Lee M. ASSESSMENT OF PHYSICAL ACTIVITY WITH A SINGLE GLOBAL QUESTION IN A LARGE, MULTIETHNIC SAMPLE OF MIDLIFE WOMEN. *Am J Epidemiol* 2000;152:678-87. **Funding Sources:** National Institute on Aging; National Institute for Nursing Research. (*Division of Research: 510-450-2195)

This cross-sectional survey compared responses from a randomly selected community-based sample of 13,621 African-American, Chinese, Hispanic, Japanese, and white women to a single, global physical activity question. Respondents rated their activity level as much less, less, the same as, more, or much more than other women their age. Physical activity rating varied minimally by race/ethnicity. The proportions of women who rated themselves much less active and much more active ranged from 3.1% for whites to 4.8% for Japanese and from 13.6% for Japanese to 16.4% for African-Americans. A high level of activity was associated with excellent health, single marital status, higher education, lower body mass index, and older age.

These findings suggest that a comparative rating of physical activity may rank women by activity level within a specific racial/ethnic group but may not capture differences across racial/ethnic groups.

Thompson M,* Gee S, Larson P, Kotz K, Northrop L. HEALTH AND LOYALTY PROMOTION VISITS FOR NEW ENROLLEES: RESULTS OF A RANDOMIZED CONTROLLED TRIAL. *Patient Educ Couns* 2001;42:53-65. **Funding Source:** Not available. (*San Francisco: 415-202-2000)

Managed care needs effective ways to orient new members, enhance trust and loyalty, and offer prevention and self-care education and services. Adult enrollees were randomly assigned to one of three intervention conditions (individual physician visit, physician plus health educator visit, group visit of eight new members led by a physician and health educator) or a random control group (n=278). Outcomes were via pre- and post-visit questionnaires, 20-min telephone survey at baseline, and a 6-month follow-up. Compared to controls, attendees of the three interventions had higher satisfaction, self-rated prevention knowledge, acceptance of health plan guidelines, and were more likely to plan to remain in the health plan. Group visit attendees stood out as experiencing the greatest benefits and were likely to report saving a telephone call or visit to their doctor by using a self-care handbook.

Weisner C,* McLellan AT, Hunkeler EM. ADDICTION SEVERITY INDEX DATA FROM GENERAL MEMBERSHIP AND TREATMENT SAMPLES OF HMO MEMBERS. ONE CASE OF NORMING THE ASI. *J Subst Abuse Treat* 2000;19:103-9. **Funding Source:** National Institute on Alcohol Abuse and Alcoholism 09750. (*Division of Research: 510-450-2156)

The Addiction Severity Index (ASI) is a widely used interview among substance-dependent populations in treatment for clinical and research purposes. Its value has been diminished by the lack of normative data. This study included four scales from the ASI collected on samples of HMO subscribers. ASI data were collected on alcohol, drug, medical, and psychiatric composite scales and partial data on employment scale. A sample of 327 adult HMO members were admitted to treatment for alcohol and/or drug addiction and administered the same ASI items. The membership reported some problems in most of the ASI problem areas, although at levels of severity below those seen in the clinical sample. Membership and clinical samples were similar in medical status and employment. Alcohol, drug, and psychiatric status were more severe in the clinical sample. The authors discuss implications for treatment planning and outcome evaluation.

Weisner C,* Mertens J, Parthasarathy S, Moore C, Hunkeler EM, Hu T, Selby JV. THE OUTCOME AND COST OF ALCOHOL AND DRUG TREATMENT IN AN HMO: DAY HOSPITAL VERSUS TRADITIONAL OUTPATIENT REGIMENS. HEALTH MAINTENANCE ORGANIZATION. *Health Serv Res* 2000;35:791-812. **Funding Source:** National

(Lead-Authored Publications continued)

Institute on Drug Abuse R01DA08728; National Institute on Alcohol Abuse and Alcoholism R37AA10359. (*Division of Research: 510-450-2156)

This randomized controlled trial compared outcome and cost-effectiveness of two primary addiction treatment options, day hospitals (DH) and traditional outpatient programs (OP). Subjects were 668 adult patients entering the alcohol and drug treatment program. The study also included 405 nonrandomized, "treatment assignment as usual" patients. Follow-up interviews and urinalysis were conducted. Program costs were calculated. Both study arms showed significant improvement in all drug and alcohol measures. There were no overall differences in outcomes between DH and OP programs, but DH subjects with midlevel psychiatric severity had better outcomes in the DH program. In the "treatment assignment as usual" group, individuals in the DH program had better abstinence outcomes than those in the OP program.

II. Co-Authored Publications

Frazao JM, Elangovan L, Maung HM,* Chesney RW, Acchiardo SR, Bower JD, Kelley BJ, Rodriguez HJ, Norris KC, Robertson JA, Levine BS, Goodman WG, Gentile D, Mazess RB, Killo DM, Douglass LL, Bishop CW, Coburn JW. INTERMITTENT DOXERCALCIFEROL (1 α -HYDROXYVITAMIN D₂) THERAPY FOR SECONDARY HYPERPARATHYROIDISM. *Am J Kidney Dis* 2000;36:550-61. (*Hayward: 510-784-4936)

Humphreys K, Weisner C.* USE OF EXCLUSION CRITERIA IN SELECTING RESEARCH SUBJECTS AND ITS EFFECT ON THE GENERALIZABILITY OF ALCOHOL TREATMENT OUTCOME STUDIES. *Am J Psychiatry* 2000;57:588-94. (*Division of Research: 510-450-2156)

Newman TB, Xiong B,* Gonzales VM, Escobar GJ. PREDICTION AND PREVENTION OF EXTREME NEONATAL HYPERBILIRUBINEMIA IN A MATURE HEALTH MAINTENANCE ORGANIZATION. *Arch Pediatr Adolesc Med* 2000;154:1140-7. (*Division of Research: 510-450-2178)

Petitti DB, Sidney S,* Quesenberry CP Jr. HORMONE REPLACEMENT THERAPY AND THE RISK OF MYOCARDIAL INFARCTION IN WOMEN WITH CORONARY RISK FACTORS. *Epidemiology* 2000;11:603-6. (*Division of Research: 510-450-2108)

Saltz L, Cox J, Blanke C, Rosen LS, Fehrenbacher L,* Moore MJ, Maroun JA, Ackland SP, Locker PK, Pirodda N, Elfring GL, Miller LL, for the Irinotecan Study Group. IRINOTECAN PLUS FLUOROURACIL AND LEUCOVORIN FOR METASTATIC COLORECTAL CANCER. *N Engl J Med* 2000; 343:905-14. (*Vallejo: 707-651-2787)

Samowitz WS, Curtin K, Schaffer D,* Robertson M, Leppert M, Slattery ML. RELATIONSHIP OF KI-RAS MUTATIONS IN COLON CANCERS TO TUMOR LOCATION, STAGE, AND SURVIVAL: A POPULATION-BASED STUDY. *Cancer Epidemiol Biomarkers Prev* 2000;9:1193-7. (*Division of Research: 510-450-2225)

Schmidt L, Weisner C.* ESTIMATING ALCOHOL PROBLEMS IN SMALL AREAS: CONTRASTING DATA SOURCES, DEFINITIONS, AND MEASURES. In: Wilson RA, Dufour MC, eds. *The Epidemiology of Alcohol Problems in Small Geographic Areas*. NIAAA Research Monograph No. 36;2000. Bethesda, MD:National Institute on Alcohol Abuse and Alcoholism. (*Division of Research: 510-450-2156)

Shaw GM, Todoroff K, Schaffer DM,* Selvin S. MATERNAL HEIGHT AND PREPREGNANCY BODY MASS INDEX AS RISK FACTORS FOR SELECTED CONGENITAL ANOMALIES. *Paediatr Perinat Epidemiol* 2000;14:234-9. (*Division of Research: 510-450-2225)

Shlipak MG, Go AS,* Frederick PD, Malmgren J, Barron HV, Canto JG. TREATMENT AND OUTCOMES OF LEFT BUNDLE-BRANCH BLOCK PATIENTS WITH MYOCARDIAL INFARCTION WHO PRESENT WITHOUT CHEST PAIN. NATIONAL REGISTRY OF MYOCARDIAL INFARCTION 2 INVESTIGATORS. *J Am Coll Cardiol* 2000;36:706-12. (*Division of Research: 510-450-2382)

Slattery ML, Curtin K, Anderson K, Ma KN, Ballard L, Edwards S, Schaffer D,* Potter J, Leppert M, Samowitz WS. ASSOCIATIONS BETWEEN CIGARETTE SMOKING, LIFESTYLE FACTORS, AND MICROSATELLITE INSTABILITY IN COLON TUMORS. *J Natl Cancer Inst* 2000;92:1831-6. (*Division of Research: 510-450-2225)

Slattery ML, Kampman E, Samowitz W, Caan BJ,* Potter JD. INTERPLAY BETWEEN DIETARY INDUCERS OF GST AND THE GSTM-1 GENOTYPE IN COLON CANCER. *Int J Cancer* 2000;87:728-33. (*Division of Research: 510-450-2116)

Recently Funded Projects

COMPARISON OF THE SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF THREE CONSISTENCY LOTS OF FROZEN MEASLES, MUMPS, RUBELLA AND VARICELLA VACCINE (MMRV) IN HEALTHY CHILDREN

Principal Investigator: **Steve Black, MD**

Funding Agent: **Merck and Company, Inc.**

Title defines study.

A PROSPECTIVE, RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED TRIAL TO ASSESS THE SAFETY OF FROZEN FLUMIST IN HEALTHY CHILDREN AND ADOLESCENTS (AV019)

Principal Investigator: **Steve Black, MD**

Funding Agent: **Aviron**

Title defines study.

(Recently Funded Projects continued)

OPERATIONAL MEASURES OF ALCOHOL PROBLEMS IN AN HMO

Principal Investigator: **Carol Conell, PhD**

Funding Agent: **National Institute on Alcohol Abuse and Alcoholism**

Capture-recapture analysis is used to estimate the prevalence of alcohol abuse and dependence within Northern California Kaiser Permanente from 1995-1999, and to explore demographic and temporal variation in prevalence.

UNSTUDIED INFANTS: LOW RISK BABIES IN A HIGH RISK PLACE

Principal Investigator: **Gabriel Escobar, MD**

Funding Agent: **Agency for Healthcare Research and Quality**

This bi-coastal (California and Massachusetts) investigation will focus on moderately premature infants (30-34 weeks gestation), who are admitted to an intensive care or special nursery setting, to characterize the epidemiology, treatment and outcomes of babies considered to be at low risk for an adverse outcomes.

A PERINATAL HEALTH SERVICES RESEARCH LABORATORY PILOT

Principal Investigator: **Gabriel Escobar, MD**

Funding Agent: **Agency for Healthcare Research and Quality**

The goal of this pilot study is to 1) conduct exploratory analyses of the Neonatal Minimum Data Set so as to define a new perinatal research agenda, and 2) develop a framework for collaborations between universities and managed care organization research units.

A MULTICENTER, PHASE III, RANDOMIZED CONTROLLED STUDY OF THERATOPE® VACCINE FOR METASTATIC BREAST CANCER (BIOMIRA STN-BR-104)

Principal Investigator: **Louis Fehrenbacher, MD**

Funding Agent: **Biomira, Inc.**

Title defines study.

A RANDOMIZED, OPEN-LABEL, MULTICENTER PHASE III STUDY COMPARING THE EFFICACY AND SAFETY OF GEMCITABINE AND IRINOTECAN HCl (CPT-11) TO GEMCITABINE ALONE IN PATIENTS WITH LOCALLY ADVANCED OR METASTATIC PANCREATIC CANCER WHO HAVE NOT RECEIVED PRIOR SYSTEMIC THERAPY

Principal Investigator: **Louis Fehrenbacher, MD**

Funding Agent: **Pharmacia and Upjohn Company**

Title defines study.

A PILOT STUDY OF MRI AND BIOMARKERS IN OSTEOARTHRITIS

Principal Investigator: **Jeffrey Fessel, MD**

Funding Agent: **Glaxo Wellcome, Inc.**

This study is an attempt to find biomarkers that correlate with progression of osteoarthritis. Approximately 150 markers will be studied, including those present in plasma, synovial fluid, urine, and on the surface of peripheral blood leukocytes. These markers will be correlated with the presence or absence of progressive changes in cartilage as seen in repeated MRIs.

SOCIODEMOGRAPHIC DATABASE

Principal Investigator: **Nancy Gordon, ScD**

Funding Agent: **Garfield Memorial Foundation**

This project will pilot test collection of sociodemographic data from all adult members in the Kaiser Permanente Oakland and Vallejo medical facility service populations. Questionnaire data will ultimately be linked

with computerized utilization data about preventive services and chronic disease management to study whether and how member sociodemographic characteristics affect the likelihood that members get guideline-concordant primary and secondary preventive services in Kaiser Permanente.

HIV/AIDS MEASUREMENT FIELD TRIAL: PRENATAL TESTING FOR HIV

Principal Investigator: **Michael Ralston, MD**

Funding Agent: **Centers for Disease Control**

This study reviews the medical records of 250 randomly selected Kaiser Permanente women members who gave birth in 1998 to determine the proportion of these women who were offered HIV testing as part of their prenatal care, as is the standard of care.

BAT-26 MUTATIONS AND FLEXIBLE SIGMOIDOSCOPY COLORECTAL CANCER SCREENING

Principal Investigator: **T.R. Levin, MD**

Funding Agent: **EXACT Laboratories**

This study will examine the prevalence of microsatellite instability and other molecular markers in colorectal adenocarcinoma tumor tissue found in patients whose initial screening sigmoidoscopy was negative for adenomatous polyps or cancer.

EVALUATION OF RISK FACTORS FOR BARRETT'S ESOPHAGUS

Principal Investigator (Kaiser Permanente)*: **T.R. Levin, MD**

Funding Agent: **National Institute of Diabetes and Digestive and Kidney Diseases**

This case-control study will evaluate dietary, medication and other risk factor exposures among cases with Barrett's esophagus and age and gender matched controls.

IMPROVING QUALITY OF CARE THROUGH A MULTIDISCIPLINARY HEADACHE MANAGEMENT PROGRAM

Principal Investigator: **Marie Mulligan, MD**

Funding Agent: **Glaxo Wellcome, Inc.**

A headache program utilizing group visits and telephone follow-up, focusing on disability and quality of life related to headache.

KAISER SOCIAL AND MEDICAL MODEL ADDICTION RECOVERY TRIAL (SMART)

Principal Investigator (Kaiser Permanente)*: **Sujaya Parthasarathy, PhD**

Funding Agent: **National Institute on Drug Abuse**

This is a randomized clinical trial comparing two types of substance abuse treatment: an intensive, outpatient (day hospital) program and a residential recovery program. This study measures patient utilization of health, medical and social services, identifies patient characteristics associated with successful treatment outcomes in each setting, and analyzes the relative cost-effectiveness of the two programs.

ACCELERATING THE CYCLE OF RESEARCH THROUGH A NETWORK OF INTEGRATED DELIVERY SYSTEMS PROJECT: RESEARCHING THE IMPLEMENTATION OF PRACTICE GUIDELINES DEVELOPED ON THE BASIS OF AHRQ-SUPPORTED EVIDENCE REPORTS WITH PRIORITY POPULATIONS

Principal Investigator: **Joe Selby, MD, MPH**

Funding Agent: **Agency for Healthcare Research and Quality**

This project, directed by the Lovelace Clinic Foundation using the

(Recently Funded Projects continued)

Lovelace Health System population, will study the implementation of Otitis Media practice guidelines developed on the basis of AHRQ-supported evidence reports in a pediatric population.

A PHASE II TRIAL FOR THE TREATMENT OF PATIENTS WHO ARE UNABLE TO TOLERATE ALLOPURINOL

Principal Investigator: **Stephen Sidney, MD, MPH**

Funding Agent: **ILEX**

This is a study of allopurinol prescribing habits of Kaiser Permanente physicians to determine the potential feasibility of a clinical trial using oxypurinol in patients who are intolerant to allopurinol.

PREDICTORS OF SPONTANEOUS CEREBRAL AVM HEMORRHAGE

Principal Investigator (Kaiser Permanente)*: **Stephen Sidney, MD, MPH**

Funding Agent: **National Institute of Neurological Disorders and Stroke**

This is a study of the natural history of cerebral arteriovenous malformations (AVMs) including incidence, prevalence, treatment, and hemorrhage rates.

CRN PROJECT 2 (DETECT) SUPPLEMENT: DESIGN, IMPLEMENTATION AND ANALYSIS OF A CLINICIAN SURVEY

Principal Investigator: **Carol Somkin, PhD**

Funding Agent: **National Cancer Institute**

As part of a larger study on the determinants of invasive cervical and late stage breast cancer, this study will gather information from primary care providers and radiologists about whether the implementation of breast and cervical cancer policies and procedures described by leaders in the HMO is actually reflected in the clinicians' practices.

CRN STUDY SUPPLEMENT: PILOT STUDY TO IDENTIFY ORGANIZATIONAL BARRIERS TO HMO PARTICIPATION

Principal Investigator: **Carol Somkin, PhD**

Funding Agent: **National Cancer Institute**

This pilot study will survey managed care physicians and plan leaders to identify major organizational barriers that may deter managed care organizations from participating in cancer clinical trials, which can be used to develop approaches to overcoming these barriers that can later be empirically tested.

TELEPHONE TREATMENT OF UNCOMPLICATED CYSTITIS IN WOMEN

Principal Investigator: **David R. Vinson, MD**

Funding Agent: **Bayer Corporation**

This study will describe and analyze the outcomes of women treated for presumed uncomplicated cystitis over the telephone through the Call Center to demonstrate that a telephone treatment protocol that uses well-trained triage nurses, careful patient selection, and physician oversight can manage uncomplicated cystitis both effectively and safely.

FOLLOW-UP STUDY OF MEDICAID CHEMICAL DEPENDENCY PATIENTS IN A PRIVATE HMO: DO HIGH MEDICAL COSTS COME DOWN OVER TIME?

Principal Investigator: **Larry Walter, MA**

Funding Agent: **Robert Wood Johnson Foundation (RWJF)**

This study, a follow-up to a previous RWJF-funded study, follows a cohort of Medicaid Kaiser Permanente members who were patients in the Vallejo Chemical Dependency Recovery Program (CDRP) to compare their long-term medical costs to matched comparison groups of non-Medicaid CDRP patients and general Kaiser members.

AN OPEN-LABEL SAFETY STUDY OF CARVEDILOL IN PATIENTS WHO PARTICIPATED IN THE COPERNICUS STUDY (MF 4477/SB 287) THAT DETERMINED THE EFFECT OF CARVEDILOL ON MORTALITY IN PATIENTS WITH SEVERE CHRONIC HEART FAILURE

Principal Investigator: **Dana Weisshaar, MD**

Funding Agent: **SmithKline Beecham Pharmaceuticals**

Title defines study.

**(Kaiser Permanente) indicates a subcontract to the Division of Research and that the investigator is the principal investigator for the Kaiser Permanente portion of the study.*

(J. Selby, continued from page 1)

Getting Involved in Pharmaceutical-Funded Research

a company may tell investigators that there's a specified amount of money available, "take it or leave it." Whether reimbursement is negotiated using a detailed line-item budget or a per-patient fee, agreements must cover all costs incurred. These include all physician and staff time, additional protocol-driven diagnostic tests, and additional visits. There is no justification for covering any of these costs with member dues. Ideally, budgets should always be prepared by our organization and presented to the sponsor, not vice versa. Knowing what to charge for, and how much to charge, is not always clear-cut. KFRI has recently added Dr. Steve Stoller, an economist familiar with our cost accounting systems and with budget negotiations. Steve (510-987-2777) has developed a systematic approach to assessing and budgeting the costs of clinical trials. TPMG researchers are strongly encouraged to consult with Steve **early** in the negotiation process to insure that reasonable budgets are put together.

These supportive services are more complete and expert than those available to academic researchers. They should be. Kaiser Permanente is in a better position to benefit from engaging in well-designed, industry-sponsored research, and more likely to suffer from research misadventures. If you are considering getting involved in research, I urge you to take advantage of all these resources before signing on.

