

PROGRAM
AND
ABSTRACTS

15th Annual Meeting of the
American Society of Preventive Oncology
April 9 - 12, 1991

Holiday Inn Crowne Plaza
Seattle, Washington

Program Chairpersons: David Thomas
Barbara Rimer
Margaret Spitz

Sponsored by: American Society of Preventive Oncology, a
conference grant from National Institute of
Health/National Cancer Institute, Coca-Cola
Company, Hoffmann-LaRoche, Inc., Kraft General
Foods, and Kellogg Company

ASPO

The **American Society of Preventive Oncology** is an active and growing organization that is striving to:

- promote the exchange and dissemination of information and ideas relating to cancer prevention and control;
- identify and stimulate research areas in cancer prevention and control;
- foster the implementation of programs in cancer prevention and control.

The Executive Committee and Council members listed below are interested in hearing from prospective and current members.

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M.D.
Daniel G. Miller, M.D.
David Schottenfeld, M.D.

ANNOUNCEMENTS

MESSAGES

Contact Judy Bowser at the ASPO registration desk if you expect or wish to leave a message.

BANQUET

If you plan to attend the banquet and have not pre-registered, contact Judy Bowser at the ASPO registration desk as soon as possible.

SPECIAL ACKNOWLEDGEMENT

The ASPO Executive Committee offers special thanks to Drs. Thomas, Rimer, and Spitz, program chairpersons, for their tireless efforts in arranging this meeting.

CONTINUING MEDICAL EDUCATION CREDIT

The University of Washington School of Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to sponsor continuing medical education for physicians.

This program meets the criteria for 21 hours in Category 1 of the Physician's Recognition Award of the AMA.

Sponsored by: University of Washington School of Medicine

The evaluation form at the back of this program must be completed in order to receive CME credits. Please turn it in to Judy Bowser before leaving.

AGENDA

Tuesday, April 9

6:00 pm - 8:00 pm
Evergreen Ballroom
1st Floor

BUFFET DINNER - Study Group on Women's Cancers (Lewis Kuller, Chair)

- I.M. report on OCPs and breast cancer
- Breast cancer prevention trials proposals
- New screening technologies
- HRT and breast cancer
- Medicare changes and clinical trials of mammography
- Standardization of sex hormone measurements

8:00 pm - 9:30 pm

ASPO Executive Committee Meeting Executive Board Room - 5th Floor

Wednesday, April 10

7:30 am - 5:00 pm
Evergreen Ballroom entrance

REGISTRATION

8:30 am
Evergreen Ballroom

WELCOME

Robert Day, MD, PhD
Fred Hutchinson Cancer Center

8:45 am

"A TRIBUTE TO JOE CULLEN"

Ellen Gritz, PhD
Jonsson Comprehensive Cancer Center, Los Angeles

Presentation:

"Joseph W. Cullen Memorial Lectureship" Award
Dale Robinson, Marion Merrell Dow, Inc.

9:00 am

PRESIDENT'S ADDRESS:

The Prevention of Primary Liver Cancer
W. Thomas London, MD
Institute for Cancer Research, Philadelphia, PA

9:25 am - 9:40 am

REFRESHMENT BREAK

NOTES

AGENDA

9:40 am - 10:40 am

When is Cancer Prevention Cost Effective?

*Jonathan Fielding, MD, MPH, MBA
UCLA School of Public Health*

10:40 am - 12:30 pm

**SYMPOSIUM: Poverty and Cultural Diversity:
Cancer Control in Underserved Populations**

Moderator: Jon Kerner, PhD, Memorial Sloan-Kettering Cancer Center

Overview of the Problem - Poverty and Cultural Diversity. Who is at Risk?

Jon Kerner, PhD, Memorial Sloan-Kettering Cancer Center

Poverty's Barriers for Cancer Prevention and Control

Harold Freeman, MD, Harlem Hospital

Cultural Diversity Among Asian Populations: The Challenges for Cancer Control

Moon Chen, PhD, Ohio State University

Discussant: *Manuel Modiano, MD, University of Arizona*

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AGENDA

12:30 pm - 2:30 pm
Yosemite/McKinley Rooms
3rd Floor

LUNCHEON MEETINGS

CHEMOPREVENTION STUDY GROUP

(Chair, Rodger Winn)

Compliance Issues in Chemoprevention Trials

Reported Rates

Run-Ins

- Design • Length • Cut-off
- Problems of Management

Methodology of Compliance Measurement

- Self-Report • Pill Counts • Chemical Monitoring

Strategies to Enhance Compliance

- Organizational and Structural • Educational
- Attitudinal • Management of the Non-Complier

DIET STUDY GROUP (Chair, Walter Willett)

Priority Research Questions

Leader, Sue McPherson

Formal presentations followed by 1/2 hour
for questions and discussion

Advantages and Limitations of Various Research Strategies

Leader, Bruce Trock

Formal presentations followed by 1/2 hour
for questions and discussion

2:30 pm - 3:30 pm
Evergreen Ballroom

PRESENTED PAPERS

Chair, Margaret Spitz

NOTES

AGENDA

2:30 pm

The Isotretinoin-Basal Cell Carcinoma Prevention Trial (The ISO-BCC Study): Results of the Three Year Intervention Phase

Joseph A. Tangrea, RPh, MPH, National Cancer Institute

2:45 pm

Cardiovascular Risk Factor Effects of Tamoxifen in Postmenopausal Women

Richard R. Love, MD, MS, University of Wisconsin

3:00 pm

Dietary Fat and Breast Cancer: Eight-Year Follow-Up

Walter C. Willett, MD, PhD, Harvard University

3:15 pm

Dietary Fat and Breast Cancer: Preliminary Results from the Iowa Women's Health Study

Lawrence H. Kushi, ScD, University of Minnesota

3:30 pm

REFRESHMENT BREAK

3:45 pm - 6:00 pm

SYMPOSIUM: Reducing Colon Cancer Risk: Current Prevention Trials

Moderator: Rodger Winn, MD,
M.D. Anderson Cancer Center

Calcium and Dietary Trials: The Minnesota Studies

John Potter, MD, PhD, University of Minnesota

Nutritional Supplement Trials in Polyp Patients: The Dartmouth Studies

E. Robert Greenberg, MD, Dartmouth Medical School

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Dietary Intervention Trial in Polyp Patients: The NCI Trial

Arthur Schatzkin, MD, DrPH, National Cancer Institute

Calcium, Fiber and Piroxicam Trial in Polyp Patients: The Arizona Trials

David Alberts, MD, University of Arizona

6:30 pm
Evergreen Ballroom

REFRESHMENT HOUR

7:30 pm
Evergreen Ballroom

EVENING BANQUET

Medicine and the Media

*Nancy Snyderman, MD, Science Correspondent
KPIX-TV San Francisco, University of California-San
Francisco School of Medicine*

Thursday, April 11

7:30 am - 5:00 pm
Evergreen Ballroom Entrance

REGISTRATION

7:30 am
Evergreen Ballroom

**(AD HOC) MEETING TO CONSIDER
FORMATION OF A CANCER PREVENTION
TRIALS GROUP**

Maureen Henderson, MD, and Richard R. Love, MD

8:30 am

**DISTINGUISHED ACHIEVEMENT AWARDEE
ADDRESS: "Biological Markers: Issues for
Epidemiologists"**

*Barbara S. Hulka, MD, MPH, University of North
Carolina, Chair, Department of Epidemiology*

9:00 am - 9:15 am

REFRESHMENT BREAK

NOTES

AGENDA

9:15 am - 11:30 am

SYMPOSIUM: Can Genetic Epidemiology Be Applied to Cancer Prevention?

Moderator: Alfred Knudson, Jr., MD, PhD
Fox Chase Cancer Center

Identifying Populations at High Risk of Cancer
Fred Li, MD, Dana Farber Cancer Institute

Molecular Genetics of Cancer: Is Intervention Possible?
Louise Strong, MD, M.D. Anderson Cancer Center

Communicating Risk Information to Patients and the Public
John Beckwith, PhD, Harvard University

Discussant
Alfred Knudson, Jr., MD, PhD, Fox Chase Cancer Center

11:30 am - 12:30 pm

PRESENTED PAPERS
Chair, David Thomas

11:30 am

Ethnic Differences in the Lung Cancer Risk Associated with Smoking
Loic LeMarchand, MD, PhD, University of Hawaii

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11:45 am

Screening for Prostatic Cancer by Digital Rectal Examination: A Case-Control Study

Gary Friedman, MD, Kaiser Permanente

12:00 noon

Dipstick Urinalysis Screening, Microhematuria and Subsequent Malignancy in a Population-Based Sample of Asymptomatic Adults

Robert A. Hiatt, MD, PhD, Kaiser Permanente

12:15 pm

Social Acceptability of Smoking and African-Americans: The Community Intervention Trial for Smoking Cessation (COMMIT)

Jacqueline Royce, PhD, American Health Foundation

12:30 pm - 1:45 pm
Yellowstone Room
1st Floor

LUNCHEON

"The Ethics of Cancer Prevention Research"

Gilbert Omenn, MD, PhD, University of Washington

1:45 pm - 2:45 pm

SET UP POSTERS AT METRO II

2:45 pm - 6:15 pm
Evergreen Ballroom

SYMPOSIUM: Improving the Quality of Prevention Research

Moderator: Maureen Henderson, MD
Fred Hutchinson Cancer Center

Theory and Implementation of Rigorous Prevention Trials

Steven Self, PhD, Fred Hutchinson Cancer Center

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AGENDA

symposium continued

**Theory and Methods for Rigorous Community
Intervention Trials**

*Thomas Koepsell, MD, MPH, Fred Hutchinson
Cancer Center*

**Cost Considerations in the Design of the Cancer
Prevention Research Program**

Nicole Urban, ScD, Fred Hutchinson Cancer Center

**Quality Control of NCI-Initiated Cancer Prevention
Research Protocols**

*Maureen Henderson, MD, Fred Hutchinson Cancer
Center*

Discussant

Douglas Weed, MA, PhD, National Cancer Institute

**CARET: Primary Prevention Trials -- A Case In
Point**

*Gilbert Omenn, MD, PhD, University of Washington
James Grizzle, PhD, Fred Hutchinson Cancer Center
Mark Thornquist, PhD, Fred Hutchinson Cancer
Center*

6:30 pm - 8:30 pm
Fred Hutchinson Cancer Center
(Transportation will be provided
beginning at 6:15 pm)

POSTER SESSION/RECEPTION

8:30 pm

BEST POSTER AWARD

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AGENDA

Friday, April 12

7:30 am - 12:00 noon
Yellowstone Room entrance

REGISTRATION

8:00 am
Yellowstone Room

BUSINESS MEETING

9:00 am

REFRESHMENT BREAK

9:15 am - 11:30 am
Yellowstone Room

SYMPOSIUM: Tobacco Cessation for the 1990's

Moderator: C. Tracy Orleans, PhD, Fox Chase
Cancer Center

**Clinical Interventions in Tobacco Control: The
Critical Role of Health Care Providers**

*Marc Manley, MD, MPH, Division of Cancer
Prevention and Control, National Cancer Institute*

**Recent Advances in the Pharmacological Treatment
of Nicotine Dependence**

John Hughes, MD, University of Vermont

**The National Cancer Institute's COMMunity
Intervention Trial (COMMIT): Experiences from
the Community**

*Beti Thompson, PhD, Fred Hutchinson Cancer Center
Juliet Thompson, BA, Bellingham, WA, COMMIT*

Discussant

*John Slade, MD, University of Medicine and Dentistry
of New Jersey*

NOTES

AGENDA

12:00 noon - 1:30 pm
Parkside Restaurant
2nd Floor

LUNCHEON - Tobacco Study Group Meeting

Domestic Tobacco Marketing: Implications for Intervention

John Slade, MD, University of Medicine and Dentistry of New Jersey

1:30 pm - 4:00 pm
Room to be announced

WORKSHOP: Using the Media for Advocacy

(sponsored by Tobacco Group)

Michael Pertschuk, JD, Advocacy Institute, Washington, DC

Phillip Wilbur, MA, Advocacy Institute, Washington, DC

Media advocacy training for tobacco control advocates is an interactive program designed to build confidence. The skills training focuses on gaining access to the media and framing tobacco issues, including debating the tobacco industry and developing effective "media bites." The program uses small group exercises, based on real life situations.

The program has been used with the National Cancer Institute's COMMIT project. The workshop will be taught by Michael Pertschuk, co-director of the Advocacy Institute and former chairman of the Federal Trade Commission, and Phillip Wilbur, director of the Advocacy Institute's Smoking Control Advocacy Resource Center.

NOTES

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ABSTRACTS

INVITED SPEAKERS

Cost-Effectiveness for Cancer Prevention: Practical Concept or Chimera? Jonathan E. Fielding, M.D., M.P.H.

Cost-effectiveness is the amount of degree of output (such as a health outcome) per unit of monetary cost (1). It is commonly misused to suggest a conclusion that paying for an intervention is justified by analysis of inputs and outcomes.

Cost-effectiveness analysis requires reliable and valid data on efficacy, effectiveness, costs, and benefits in nonmonetary terms. No consensus decision rules exist for what health outcomes justify a particular level of expenditure, although QALYs help in comparing relative cost-effectiveness of different interventions. Without professional or social consensus, payers, health professionals, other providers, and patients often come to different investment conclusions.

The U.S. Preventive Services Task Force used explicit criteria, graded levels of evidence, and made related recommendations for 169 preventive interventions (2). Assessment of cost-effectiveness is easier for cancer screening than for primary prevention strategies, which usually impact several major classes of disease. Many primary prevention strategies require action outside the health services sphere.

Explicit criteria for priority setting, an improved research data base, new technologies and better targeting of subpopulations could increase consensus on cancer prevention priorities, but implementation decisions will be increasingly intertwined with debates on ethical issues.

1. Warner KE, Luce BL, Cost-Benefit and Cost-Effectiveness in Health Care: Principles, Practice, and Potential. Ann Arbor, MI, Health Administration Press, 1982.
2. Preventive Services Task Force. Guide to Clinical Preventive Services. An Assessment of the Effectiveness of 169 Interventions. Baltimore: Williams & Wilkins, 1980.

SHARE HARLEM HEALTH PROJECT:

MINORITY CANCER CONTROL

Jon F. Kerner, Ph.D., Rae Ann McMahan, MPH
In October 1987, Memorial Sloan-Kettering Cancer Center (MSKCC) and the Self-Help and Resource Exchange of New York (SHARE-NY), in collaboration with Harlem Hospital Center (HHC), the Breast Examination Center of Harlem (BECH), and the Harlem Unit of the American Cancer Society, was awarded a two-year grant from the U.S. DHHS Office of Minority Health to implement and evaluate the SHARE Harlem Health Project (SHHP). The SHHP was designed to link a health promotion and cancer prevention program onto the basic food and community service program of SHARE-NY. The implementation and evaluation of the SHHP was carried out in several phases. The first phase involved carrying out a series of three focus groups with current SHARE-NY participants from Harlem and community leaders from Harlem not involved with SHARE-NY. In the second phase of the project, the actual health promotion and cancer prevention program components were implemented. The third and final phase of the SHHP was to evaluate the process and outcome indicators of project successes and failures. In reviewing the three major intervention components of the SHHP, the overall assessment of the process and outcome information suggests that information was the most effective intervention, contributing to a major shift in cancer screening patterns, above and beyond the limited impact of the food package incentives.

Cultural Diversity among Asian populations: The challenges for cancer control. Moon S. Chen, Jr., Ph.D., M.P.H.

Cancer control targeted at Asian Americans is a challenge. For example, between 56% of Vietnamese men smoke (1). Second, Southeast Asians' awareness of chronic disease risk factors is low (2). Third, few ethnically specific cancer control strategies focus on Asians. Fourth, inadequate data exist to document the prevalence and incidence of cancer among Asians. While progress must be made to develop more adequate data collection and control strategies, the prerequisite to effective cancer control targeted at Asian Americans is attention to cultural diversity. Among factors that must be considered are the diversity of Asians in terms of national origin (from over 20 countries), nativity (94% among Cambodians versus 2% for native Hawaiians), languages spoken, educational levels (27% high school graduation rate among Laotians to 79% among Japanese), a bimodal distribution of income (6% among Japanese below the poverty level contrasted with a national high of 66% among Laotians) and varying degrees of English and native Asian literacy (3). Just as marketing attempts to incorporate values and perceptions in selling products, so must effective cancer control strategies aimed at Asian Americans incorporate ethnically specific characteristics and values.

¹ Jenkins C et al., Cancer risks and prevention practices among Vietnamese refugees. West J Med 1990 Jul; 153: 34-39.

² Chen MS Jr. et al. Promoting heart health for Southeast Asians: A database for planning interventions. Public Health Reports 1991, in press.

³ Asian American Health Forum Inc. Asian and Pacific Islander Population Statistics. Monograph Series 1, April, 1989.

Hispanic Cancer and Demographics: How Much Do We Know?,
Manuel R. Modiano, M.D., University of Arizona Cancer
Center, Tucson, Arizona 85724

Hispanics are the fastest growing minority population in the United States.

"Hispanics", "Latinos", "Chicanos", Mexican-Americans, Puerto Ricans, Cubans, etc, are, as can be implied by the wide variety of designations by which they are known, a very heterogeneous population, with different cultural, ethnic, geographic, and social backgrounds. The data available regarding the incidence, morbidity, and mortality from cancer in Hispanics is scarce, scattered, incomplete, and often outdated. (1) Furthermore, there is no clear definition of the term "Hispanic". Several studies have looked at access to medical care and barriers encountered by Hispanics. Few have examined in detail the variations within the Hispanic population. The aggregation of culturally distinct subgroups into a more inclusive "Hispanic" category assumes that persons of Mexican, Cuban and Puerto Rican extraction have similar needs, and experience similar barriers in using health services. There is, however, no clear evidence for this assumption.

Overall, Hispanics have 2 times the incidence of cervical cancer as do nonHispanic Whites, and are 7 times less likely to know the cancer warning signs. (2) New-Mexican Hispanics, and Mexican-Americans living in the West and Southwest also have a higher incidence of gastric, pancreas, and gall bladder cancer than Whites. Despite the fact that they have lower incidence of certain cancers, Hispanic mortality is strikingly similar to that of the general population. Protective factors which may account for the lower incidence of some of the cancers need to be explored. Demographic and epidemiologic data need to be improved.

(1) Cancer Statistics Review, 1973-1986, NIH Publication 89-2789. (2) Hispanic Cancer Control Program of the NCI. DCPC SPSB. Monograph.

The Etiology and Prevention of Colorectal Polyps: The Minnesota CPRU. John Potter, M.D., Ph.D., Roberd Bostick, M.D., M.P.H., Patricia Elmer, Ph.D., Patricia Grambsch, Ph.D., J. Michael Sprafka, M.P.H., Ph.D., James Wood, M.D.

An extensive body of evidence points to a lower risk of colon cancer in association with specific dietary patterns, especially a higher intake of vegetables. The route from these observations to a public health strategy is, however, neither simple nor direct. What needs to be established is that this association is biologically informative, that the relevant changes in diet are feasible, that those changes can be monitored in a reliable fashion and that study designs, mechanisms, and facilities are in place to test in humans likely causal pathways including the use of short-term outcomes. If this capacity to monitor process and intermediate steps is absent, failure of an intervention with cancer or polyps as an endpoint will be difficult to interpret. The steps in the sequence at which failure occurred - failure to change diet, inappropriate intervention, inappropriate at-risk population, no biologic response and/or inappropriate endpoint - will not be known.

Accordingly, the recently established Minnesota CPRU is designed to explore etiology, to develop and test intervention strategies, to develop and test methods of monitoring dietary change, to develop and test early outcome markers, and to test specific causal pathways. The initial program includes a case-control study of colorectal polyps, a study to test the feasibility of major dietary change, a double-blind study of the effect of calcium on epithelial proliferative index, studies to develop biochemical markers of dietary intake, and studies of self-report dietary methodology.

Nutritional Intervention Study of Polyp Patients: The Polyp Prevention Trial. Arthur Schatzkin, M.D., Dr.P.H., Elaine Lanza, Ph.D.

Laboratory, ecologic, and analytic epidemiologic evidence support a causal role for dietary factors--especially high fat, low fiber, and low vegetable and fruit intake--in the genesis of large bowel cancer. An intervention study would provide a strong test of the diet-large bowel cancer hypothesis. Adenomatous polyps of the large bowel provide a particularly useful endpoint for such a study because of the high prevalence rate, the high recurrence rate in those who have undergone polypectomy, and the link between polyps and cancer. Given the strong evidence for the adenoma-carcinoma sequence (extended by recent molecular genetics and biochemical findings), an intervention that reduces the recurrence of large bowel polyps would be highly likely to reduce the incidence of large bowel cancer. The NCI-sponsored Polyp Prevention Trial is a randomized controlled trial conducted among 2000 men and women at ten U.S. institutions to determine whether a low fat (20% calories from fat), high fiber (18 g/1000 kcal), and high vegetable and fruit (5-8 servings daily) dietary pattern, compared to the customary U.S. diet, will decrease the recurrence rate of large bowel adenomas. Each intervention group participant will be provided an individual education and counselling program aimed at providing the nutritional and behavioral skills necessary to make a lifestyle change to a low fat, high fiber, high vegetable and fruit eating plan. An attractive feature of this study is its capacity to examine the extent to which potential intermediate endpoints of large bowel carcinogenesis (such as epithelial cell hyperproliferation) truly mediate the relation between diet and subsequent neoplastic change.

Calcium and Trials in Polyp Patients. David S. Alberts, M.D.

Epidemiologic, animal and biochemical studies have suggested that diets high in total calories and animal fat and low in various dietary fibers, vegetables and micronutrients are generally associated with an increased incidence of colorectal cancer. Of these factors, calcium and wheat bran fiber dietary supplements have been used most intensively in recent clinical trials. Recently, Decosse et al. (1) have shown that chronic wheat bran fiber supplementation decreases rectal polyp recurrence in patients with familial adenomatous polyposis. Additionally, we have reported that a wheat bran fiber supplement of 13.5 g/day significantly decreased rectal mucosal cell DNA synthesis rates in colorectal cancer patients (2). Furthermore, in 1987, our group initiated a randomized, double blinded intermediate tumor marker trial in Sun City, Arizona in 100 resected colorectal adenoma patients comparing supplements of wheat bran fiber, calcium and their combination to placebo (2.0 grams wheat bran fiber and 250 mg elemental calcium/d). This phase II randomized trial achieved full patient accrual in August, 1989 and the preliminary results will be reported at this meeting. A phase III trial of wheat bran fiber vs. placebo in 1400 polyp patients with polyp recurrence rates as the primary endpoint has been initiated recently in the Phoenix Metropolitan area. The results of these ongoing studies will help to determine the potential importance of such dietary interventions in the reduction of colorectal cancer risk.

1. DeCosse J, Miller H, Lesser M. JNCI 1989;81:1290.
2. Alberts D, Einspahr J, Rees-McGee S, et al. JNCI 1990;82:1280.

Genetic Predisposition to Cancer. Alfred G. Knudson, Jr.,
M.D., Ph.D.

Mutations in the germline can impart to their hosts relative risks for particular cancers (compared to normal persons) of as much as five orders of magnitude. Some persons appear to be resistant to carcinogenesis. Others have genotypes that impart relative risks that seem to be in the range of 3-100; if heterozygotes have an advantage over both homozygotes, the frequency of the cancer-predisposing variant(s) can be high, producing a high attributable risk. Polymorphisms in the genes whose product proteins (e.g., P-450 enzymes and glutathione-S-transferase) are responsible for detoxification of many environmental chemicals are in this category. Other mutations produce very high relative risks to homozygotes (e.g., xeroderma pigmentosum and Bloom's syndrome) or heterozygotes (e.g., hereditary retinoblastoma and Li-Fraumeni syndrome), and the attributable risks are low. Identification of both classes of predisposed individuals is becoming possible by biochemical genetic means. In the second group genotypic diagnosis could lead to precise counselling of families. In the first group environmental risk avoidance could lead to a significant reduction in cancer incidence.

Identifying Populations at High Risk of Cancer.
Frederick P. Li, M.D.

Members of cancer families are at exceptionally high risk and can be studied as human models of cancer susceptibility. The rationale for investigating rare family cancers rests in Knudson's hypothesis which indicates that the germ line of familial cases can reveal the first mutation, and subsequent mutations are identified by comparing tumor DNA with the corresponding germ line DNA. To identify genes involved in familial cancers, we use clinical observations to identify the high risk patient, epidemiological studies to quantitate the excess risk, and laboratory investigations to examine the biological basis of susceptibility. In the syndrome of breast cancer and diverse childhood tumors (Li-Fraumeni syndrome), clinical and epidemiological studies have provided evidence for familial transmission in an autosomal dominant pattern. Carriers are prone to develop breast cancer and at least 6 other cancers in childhood and adolescence: acute leukemia, brain tumors, osteosarcoma, soft tissue sarcoma, adrenocortical carcinoma and gonadal germ cell tumors. Recent studies indicate that inherited mutations in the tumor suppressor gene, p53, is the molecular defect in these families. The finding provides a molecular test of exceptional susceptibility to cancer in select individuals. In other studies, clinical observations have identified populations at high cancer risk due to intense exposures to environmental carcinogens. This multidisciplinary research approach should be used with caution to avoid false-positive results.

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Communicating Information about Genetic Risks to the Public. Jonathan Beckwith, PhD.

New genetic techniques have increased the pace with which researchers are discovering genes for many conditions. This pace will be intensified as the Human Genome Initiative becomes fully operative. However, the readiness of social institutions and public understanding of genetics raise enormous problems in the application of new genetic tests. In the past, screening programs for sickle-cell trait, XYY males, β -thalassemia and other conditions have resulted in discrimination in insurance and employment, stigmatization, reduction in self-esteem and other forms of psychological damage (1). A survey has revealed cases of discrimination in employment, insurance, adoption or even obtaining a driver's license (2). The interests of the insurance industry, employers and biotechnology companies are forces accelerating the widespread use of genetic tests. The problems are exacerbated by the inadequate number of genetic counselors and the lack of basic understanding of genetic principles by both the public and many members of the medical community. The public often takes genetics to mean fated, considers carrier status for a genetic condition the same as the condition itself, and misunderstands concepts of risk. Misconceptions are aggravated by scientists' overblown statements about genetics. These problems may worsen as widespread genes for susceptibility to many cancers are found.

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ETHICAL ISSUES IN CONDUCTING CANCER PREVENTION

TRIALS. Gilbert S. Omenn, Univ of Washington School of Public Health and Fred Hutchinson Cancer Research Center, Seattle, WA

The Year 2000 goals of the National Cancer Program give high priority to prevention, seeking a significant counterpart to dominant investments in early diagnosis and better treatments. The NCI meanwhile has sought to provide a much stronger scientific base for its cancer control/cancer prevention mission, involving many investigators around the country and many NCI staff who have come to prevention trials from careers in cancer treatment research.

Prevention trials are very different from treatment trials. Most importantly, the subjects are not patients; they are voluntary participants, really partners, in the research. In therapy, considerable toxicity is commonly tolerated to maximize the chances for efficacy; in prevention, avoidance of toxicity is paramount. Investigators must fastidiously inform potential participants about all potential risks; describing the potential benefits is more difficult. Participants must be "hooked" into long-term participation, which is awkward when initial funding and consent may cover only pilot studies. Personal physicians are prone to blame study medications for non-specific common symptoms. People's diets may change or companies may aggressively promote the active agents; advising participants to avoid such preparations, which some people feel "cannot hurt", is a dilemma. Finally, in many prevention trials risk factors for the endpoint may decline; in CARET¹, we remain committed to helping participants stop smoking even if that would diminish our yield of lung cancer endpoints. Despite the complexity and difficulties, this research is feasible and sorely needed.

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Theory and Implementation of Rigorous Prevention Trials. Steven G. Self, Ph.D.

A prevention trial is "rigorous" if the trial results, whether positive or negative, can be convincingly attributed to the effect (or lack of effect) of the intervention. Such interpretation of a negative trial results requires a design that maintains adequate statistical power. We describe a framework within which the statistical power of a prevention trial can be estimated at the design stage and updated throughout the duration of the trial. The updated estimates of power incorporate the observed patterns over time of compliance to the intervention, drift in the control group and other aspects of the study cohort that affect power which might differ from those patterns assumed in the initial estimation of power. This monitoring will allow important departures from the initial design assumptions to be identified so that some remedial action can be initiated. A key element in this framework is the identification of a primary index of intervention effectiveness which 1) can be observed or estimated for trial participants as a measure of compliance to the intervention, and 2) has been quantitatively related to disease incidence in previous epidemiologic studies. Interpretation of a positive trial result depends not only on use of standard design principles such as randomization and blinded ascertainment of endpoints, it also depends on secondary analyses that use detailed individual-level data to characterize the pattern of the observed intervention effect. Thus, a mechanism for obtaining specific and detailed biological measurements from cohort members over time should be considered to be an integral part of the design of any large "rigorous" prevention trial.

Cost Considerations in the Design of Prevention Trials
Nicole Urban, Sc.D.

Prevention trials are inherently different from treatment trials because they involve tests of interventions conducted in healthy populations. If a prevention trial is designed as if it were a treatment trial, it is likely to be prohibitively expensive. Measurement of costs is important in a prevention trial, to ensure that the research is conducted efficiently, and to provide information needed to assess the cost-effectiveness of the intervention. Care must be taken in research design to realize efficiencies in recruitment, intervention, and follow up (1). Use of a case-cohort design (2) and attention to trial logistics (3) can reduce the costs of a prevention trial significantly. In judging the costs of a prevention trial, its investment value should be taken into consideration; its per-subject costs relative to those of the typical treatment trial are less relevant than the definitiveness and potential benefit to society of its results (4). In judging the community-wide value of a prevention intervention, its costs as well as its effectiveness should be taken into account. However, a prevention intervention should not be expected to yield a net monetary savings; the appropriate criterion for cost-effectiveness is that the prevention intervention yields a benefit worth its cost (5).

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Quality Control of NCI Initiated Cancer Prevention Research Protocols.
M. Henderson, M.D.

The nature of cancer prevention research is dictated by its biology, its multiple causes, and its concentration on environmental exposures.

The original NCI paradigm for five phases of cancer prevention research was developed from an excellent managerial plan for the development and testing of chemotherapeutic drugs. Although it served its immediate purposes, it should now be revised to provide more clarity and better support for the overall cancer prevention program as well as NCI Initiated projects.

The disadvantages that should be redressed include: the failure to understand that prevention intervention trials are conceptually different from randomized therapeutic trials. Failure to make this distinction has forced protocols for prevention trials to meet inappropriate requirements and their costs to be assessed out of context; the need for the specific nurturing and support of relevant laboratory based research has not been recognized; and research resources are being used to support demonstration and dissemination programs which could be more appropriately conducted by CDC or other federal agencies.

Administrative changes are also badly needed. Because NIH is short of Intramural positions and competitive salaries, the cancer prevention program cannot recruit and maintain teams of interdisciplinary scientists dedicated to the conceptualization, design, and implementation of cancer prevention research studies. It has to rely on ad hoc consultations and interim collaborations as substitutes. This leads to disjointed and unsatisfactory development of research concepts, questions, and designs.

The operating cancer prevention peer review system also has serious limitations. It is subjecting intervention trial protocols to excessive and inconsistent review. The use of ad hoc reviewers and members of a rotating Board of Scientific Counselors to review short and long-term studies is less than satisfactory. Project specific policy advisory groups have been used in a way that has led to excessive as well as inconsistent review.

There should now be enough experience in hand to make administrative changes and to redefine the paradigm to improve the quality of the research program and the quality control of the research projects.

Diagnosing and Treatment of Nicotine Dependent Smokers. John R. Hughes, M.D.

Dependence on nicotine is evidenced by the inability to stop smoking despite several attempts, continued use of tobacco despite a known tobacco-related illness, and a characteristic withdrawal syndrome (3). How much of nicotine's dependence potential is due to positive reinforcing effects (e.g., mood-regulation, improved performance, anorectic effects, decreased aggression) vs negative reinforcing effects (i.e., relief of withdrawal) is debatable. The dependence potential of nicotine via cigarettes is enhanced by its route of administration (inhalation) easy availability and social sanction. Nicotine dependence is similar to other drug dependences in terms of ability to recruit new users, craving and rate of relapse. As social pressure eliminates non-dependent smokers, future smokers will be those highly dependent on nicotine. At present, combined nicotine gum and behavior therapy are the best treatment for dependent smokers. These treatments produce 1 yr abstinence rates of 40% compared to 20% in control groups (2). A nicotine patch will be marketed this year and should supersede nicotine gum due to improved compliance and nicotine replacement. Clonidine is a promising non-nicotine therapy. Other therapies such as nicotine aerosols, vapors, inhalers and nasal sprays plus antidepressants are being tested. Whether pharmacotherapy is effective without a concomitant behavioral therapy (e.g., with M.D. advice alone) is debatable (1).

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The National Cancer Institute's COMMunity Intervention Trial (COMMIT): Experiences from the Community. Beti Thompson, Ph.D., Juliet Thompson, B.A.

COMMIT is a multisite collaborative trial in which a set of standardized interventions designed to encourage heavy smokers to stop smoking are implemented through community channels. Within eleven pairs of communities, ten in the United States and one in Canada, one community was randomized to an intervention condition and the other to comparison. Using community organization strategies and the standardized COMMIT protocol, local community groups and individuals undertook a number of smoking control activities. In this session, the experiences of one of the COMMIT intervention communities, Bellingham, WA, is presented. Currently, a 20 member Community Board and five Task Forces of local volunteers guide, plan, and implement project activities. Substantial community hours and financial resources have been contributed to the project, and project activities are well-received in the community. The Bellingham experience suggests that a structured approach to community mobilization around tobacco control is possible, that a standardized protocol can be followed in achieving such mobilization, that the unique nature of different communities can be accommodated in such a trial, and finally, that it is possible to develop a protocol for community organization that balances the research requirements of a trial with the needs of a community.

A Disease Model of Nicotine Dependence.
John Slade, M.D.

The conventional conceptualization of smoking, the cigarette/smoker dyad, limits understanding of nicotine dependence and limits options for the management and the prevention of this condition. A disease model which relates the agent (the tobacco industry) with both the host (people who smoke) and accidental hosts (people affected by tobacco smoke pollution) acting in the same overall environment shared by all three will be developed and discussed. The phenomenology of tobacco is more fully contained in the proposed model than in the conventional one, and a remarkably wide variety of useful control strategies emerge from it.

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Using the Media for Advocacy;
Michael Pertschuk, J.D., Phillip Wilbur, M.A.

The Using the Media for Advocacy training workshop is an interactive program designed to build confidence and a feeling of empowerment. The skills training focuses on gaining access to the media and framing tobacco issues, including debating the tobacco industry and developing effective "media bites." The program uses small group exercises, based on real-life situations, to maximize the utility of what is learned.

ABSTRACTS

ORAL PRESENTATIONS

The Isotretinoin-Basal Cell Carcinoma Prevention Trial (The ISO-BCC Study): Results of the Three Year Intervention Phase. Joseph A. Tangrea, R.Ph., M.P.H. for the ISO-BCC Study Group, Division of Cancer Prevention & Control, National Cancer Institute, Bethesda, Maryland 20892

The Isotretinoin - Basal Cell Carcinoma Prevention Trial (ISO-BCC Study) is a double-masked, randomized, placebo-controlled, multicenter clinical trial designed to evaluate the effectiveness of chronic administration of low dosage levels (10 mg) of a synthetic retinoid, isotretinoin, in reducing the incidence of basal cell carcinoma in a high risk population and determine the incidence and severity of side effects associated with this long-term treatment (1). Between 1984 and 1987, eight clinical centers enrolled 981 participants between the ages of 40 and 75, who had two or more biopsy proven basal cell carcinomas in the five years before trial entry. In order to monitor for skin cancer, potential treatment toxicity(2), and compliance, randomized participants were scheduled to report for follow-up clinic visits at two weeks, three months, six months and every six months for the duration of the trial. The three year intervention phase of the study ended in June, 1990. Trial participants continue to be followed off-intervention until June, 1991, the common close-out date for all clinical centers. Efficacy and toxicity results from the three year intervention phase will be presented. Implications for future retinoid chemoprevention trials will also be discussed.

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Cardiovascular risk factor effects of tamoxifen in postmenopausal women

Richard R. Love, Donald A. Wiebe, Polly A. Newcomb, V. Craig Jordan, Paul P. Carbone, Jan Feyzi, David L. DeMets.

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The possibility of a Tamoxifen Health Trial (THT) using this synthetic estrogen-antiestrogen in postmenopausal women to suppress preclinical breast cancer is under careful review. After age 60 myocardial infarction is the major cause of death in American women. We conducted a two year randomized, placebo-controlled toxicity trial of tamoxifen in 140 postmenopausal women previously diagnosed with axillary node-negative breast cancer as part of which at baseline, 3, 6, 12, 18 and 24 months evaluations for cardiovascular risk factors were made. Through 24 months, mean 12% total cholesterol and 20% LDL cholesterol decreases ($p=0.0001$) with tamoxifen treatment persisted. When tamoxifen treated women were divided into quintiles, the absolute and percentage decreases were greater for each successively greater baseline level: e.g., at 6 months the top quintile of women with a mean of 259 mg/dl cholesterol at baseline had a drop of 44 mg/dl (17%). HDL cholesterol fell with tamoxifen with the difference being statistically significant only at 12 months, (placebo -0.4 mg/dl, tamoxifen -4 mg/dl, $p=0.01$) but not for example at 24 months (placebo -5 mg/dl; tamoxifen -4 mg/dl, NS). At two measured timepoints, 3 and 12 months, Apolipoprotein A1 increased significantly (placebo 0,3; tamoxifen 8,11; $p=0.02$) and apolipoprotein B fell significantly at these times (placebo, -1, -2; tamoxifen -8, -7; $p=0.005$). Plasma glucose levels did not change between baseline and 12 month measurements with tamoxifen treatment, and weight, systolic and diastolic blood pressure did not change with treatment over 18 months.

These generally favorable cardiovascular risk factor changes are consistent with reports of decreased coronary heart disease (CHD) mortality or events with adjuvant tamoxifen treatment and support the inclusion of CHD endpoints in a THT in healthy postmenopausal women.

DIETARY FAT AND BREAST CANCER: EIGHT-YEAR FOLLOW-UP.

W. Willett, D. Hunter, M.J. Stampfer, G. Colditz, B. Rosner, F.E. Speizer. Harvard, Boston, MA.

To address the hypothesis that higher levels of dietary fat increase the risk of breast cancer, particularly among postmenopausal women, we extended the follow-up of 89,538 women to eight years. As in our four-year report (1), dietary data were primarily based on a 61-item food frequency questionnaire completed in 1980. Through May 31, 1988, 1,476 incident cases of breast cancer were diagnosed, including 794 among postmenopausal women.

After adjustment for age and total energy intake, weak and nonsignificant inverse associations were seen for total fat both overall (RR's for increasing quintiles = 1.0, 0.84, 0.97, 0.91, 0.90; 95% CI for top quintile = 0.76-1.05) and among postmenopausal women (RR's = 1.0, 0.87, 0.98, 0.93, 0.88. Similar inverse trends were observed without adjustment for energy intake; for tumors <2 cm and 2+ cm in diameter; for saturated, monounsaturated, and polyunsaturated fat and when using a more detailed and accurate dietary questionnaire completed in 1984 (685 subsequent cases). Although it has been suggested that an influence of dietary fat on breast cancer risk is primarily due to saturated fat intake among postmenopausal women (2), we observed no such effect (RR's = 1.0, 0.92, 0.96, 0.94, 0.88). Minimal associations were seen between level of fat intake calculated from the 1980 questionnaire and history of mammography obtained on our 1988 questionnaire. These data do not support the hypotheses that total or saturated fat intake among middle aged women has a major adverse influence on breast cancer incidence.

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Dietary Fat and Breast Cancer: Preliminary Results from the Iowa Women's Health Study. Lawrence Kushi, Thomas Sellers, John Potter, Susan Kaye, Christine Nelson, and Aaron Folsom.

The association of fat intake assessed in 1986 and subsequent risk of breast cancer was examined in a cohort of 41,837 Iowa women aged 55 to 69 years at baseline. Breast cancer incidence over three years was ascertained through the Iowa SEER Program, resulting in 345 cases who were free of cancer, postmenopausal and had completed dietary questionnaires at baseline. For a nested case-control analysis, 1607 controls were selected randomly. Mean fat intake did not differ between cases (69.7 ± 28.8 g) compared to controls (68.8 ± 29.7 g); mean energy intake was also similar (1810 kcal for cases, 1799 kcal for controls). The age- and energy-adjusted estimate of the relative risk for breast cancer comparing the highest quintile of fat intake to the lowest was 1.42 (95% C.I. 0.82 - 2.58). After adjusting for other breast cancer risk factors, including body mass index, age at menarche, family history of breast cancer, and educational attainment, this risk was reduced to 1.32 (95% C.I. 0.73 - 2.41). Relative risks in the intermediate quintiles were 1.00, 1.11 and 1.16; the test for trend was not significant ($p=0.32$). While these results are consistent with a weak positive association of fat intake with breast cancer in post-menopausal women (1), they are equally consistent with the results of other prospective studies showing no association (2), and thus provide little indication that this association is meaningful. Subsequent follow-up should provide additional power to determine more conclusively the nature of this association.

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Ethnic Differences in the Lung Cancer Risk Associated with Smoking. Loïc Le Marchand, Lynne R. Wilkens, Laurence N. Kolonel.

Mortality trends and ecologic data strongly suggest that the lung cancer risk associated with smoking is greater among Hawaiians than among the other ethnic groups in Hawaii. The authors combined data from two population-based case-control studies (1,2) to formally test this hypothesis among 830 cases and 1647 controls. A multiple logistic regression analysis adjusting for pack-years, occupation, education and age revealed that Hawaiian, Filipino and Caucasian male smokers were at 121%, 53%, and 46% greater risk for lung cancer than Japanese male smokers. These risk differences were statistically significant and were not explained by the type of cigarettes, the level of inhalation, or by an index of β -carotene intake. Similar results were obtained in females. The possibility that other dietary antioxidants and/or genetic risk factors are responsible for these ethnic differences needs to be investigated.

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Screening for Prostatic Cancer by Digital Rectal Examination: A Case-Control Study. Gary D. Friedman, M.D., Robert A. Hiatt, M.D., Charles P. Quesenberry, Jr., Ph.D., Joseph V. Selby, M.D.

Although commonly thought to be an effective method of screening for prostatic cancer (1), digital rectal examinations have yet to be shown by controlled study to help prevent progression of this disease. One hundred thirty-nine men with metastatic (stage D) prostatic cancer (cases) were compared with an equal number of matched men free of this condition (controls), with respect to rectal examinations recorded in their medical records up to, on average, 23 years before the cases' initial diagnosis of prostatic cancer. Although the cases had more examinations for prostate-related complaints, the numbers of examinations for routine screening were similar (10-year mean: cases, 2.45; controls, 2.52). After adjustment for racial differences, the relative risk of developing metastatic prostatic cancer for men with one or more screening rectal examinations compared with men with none in the ten years prior to initial diagnosis (excluding the last three months) was 0.9 with 95% confidence interval 0.5-1.7. The association was not strengthened by looking at shorter intervals before diagnosis. This study suggests that digital rectal examinations have little if any effect in preventing the development of metastatic prostatic cancer. If there is a small benefit, it will be difficult to demonstrate by conventional epidemiological study.

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Dipstick urinalysis screening, microhematuria and subsequent malignancy in a population based sample of asymptomatic adults. Robert A. Hiatt, MD, PhD, Juan D. Ordonez, MD, MPH.

The value of dipstick urinalysis screening for hemoglobin in asymptomatic older adults remains controversial(1). Questions remain as to whether the rate of detection of malignancy and other serious urinary tract disease justify screening and the risk and expense of subsequent workups(2). We studied the outcome of a positive dipstick for hemoglobin in a population-based sample of over 27,000 prepaid health plan members taking a multiphasic health checkup in 1980 and 1981 and followed for a mean of 6.8 years. Persons with known causes of hematuria, proteinuria, renal disease, or urinary tract symptoms were excluded. Of 374 women ≥ 55 years and 229 men ≥ 35 years with positive tests, 7(1.2%) malignancies and 177(29.4%) cases of moderately serious urinary tract disease were diagnosed subsequent to the index urinalysis. There was a direct relation between the degree of hematuria and the likelihood of subsequent cancer, but none of the malignancies were diagnosed within 5 years of the index urinalysis. The predictive value of microhematuria in this unselected population was lower than reported in other series and suggests that the yield from screening for hematuria may not justify the risk to patients generated by the subsequent workup.

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Social Acceptability of Smoking and African-Americans: The Community Intervention Trial for Smoking Cessation (COMMIT). Jacqueline Royce, Ph.D., Mario Orlandi, Ph.D., Norman Hymowitz, Ph.D., Kitty Corbett, Ph.D., Tyler Hartwell, Ph.D.

The excess smoking-related health burden for African-Americans is well known (1). Lower quit rates among African-Americans compared to whites regardless of SES explain their higher smoking prevalence rates (2). This report discusses baseline data from COMMIT, NCI's effort to influence the social acceptability of smoking at the community level. Data from telephone survey (early 1989) of a random sample of 11,968 adult smokers in eight urban communities in NY, NJ, CA, and NC are presented. Results suggest that compared to non-Hispanic white smokers, African-Americans start smoking at later ages, smoke fewer cigarettes per day, prefer menthol cigarettes, and report increased "nicotine dependence" (smoke within 10 minutes of awakening). African-American smokers are more likely to make quit attempts and reported a stronger desire to quit compared to white smokers regardless of background. In a stratified subsample of smokers and nonsmokers (N=2,436), African-Americans, compared to whites felt more strongly that smoking should be restricted. The study suggests that African-Americans find smoking socially unacceptable and are receptive to culturally appropriate smoking control efforts.

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ABSTRACTS

POSTER PRESENTATIONS

1

Breast Screening for Underserved Women. G. Harper, MD, P. Victor, BS, RN, B. Englisbe, BSN, MPA, E. Czajka, MD, E. Williams, MSW, R. DeConti, MD, J. Crucetti, MD, MPH.

Low socioeconomic status correlates with poor outcome in black women with breast cancer (1). The American Cancer Society (ACS) emphasizes economic status as the primary predictor for poor outcome in underserved populations (2). An outreach project of Albany Medical Center, Whitney Young Health Center (WYHC), Albany County Unit of ACS, and the Albany County Department of Health is a phase IV-V cancer control program funded by the NYS Health Dept. to increase access to and utilization of breast screening services among underserved women (3). Since Dec 1988, 529 asymptomatic women were screened; 61 were followups (11.5%). Mammograms were obtained in 501 (94.7%), cytologic or histologic specimens in 11 (2%), and breast cancers found in 7. Albany County is 7% minorities; target urban neighborhoods are up to 73% black--23.6% of women screened were minority. Nearly 50% of screened women had total household incomes <\$15000. Referrals to screening from physicians or provider staff (WYHC, Planned Parenthood) accounted for 181 women (38.6%), targeted promotions for 25%, "word of mouth" for 21.8%; the rest from media and education programs. Programs targeted to underserved patients can improve access to screening services; followup compliance is low. Although targeted promotions and word of mouth are important contributing factors, referrals from physicians or provider staff is the primary determinant for participation in screening.

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2

VALIDITY OF SELF-REPORTED MAMMOGRAPHY HISTORY

P. A. Newcomb, N. S. Weiss, D. Scholes, B. E. Young

Self-reports of mammography history are widely used to evaluate mammography utilization and effectiveness. To evaluate the sensitivity and specificity of self-reported mammography history, we compared interview responses with medical record information on a sample of women without breast cancer, aged 20-79, who were members of a large health maintenance organization. During the interview (for a case-control study of breast cancer), subjects were asked for a complete mammography history, including date of examination and facility. Information on mammography utilization was available from the medical records of all selected women (n=133), however, 10 women who reported having a mammogram at another facility were excluded as confirmatory medical record data was not available. The overall rate of agreement between self-reported mammography history during the HMO membership period and medical record documentation of this procedure was 93%. While the sensitivity (94%) and specificity (92%) of the self-report were high, the predictive value of the self-report was 70%. This relatively low rate likely reflects subjects' difficulty in recalling examinations that were truly during their HMO membership. Since few of the women had more than one mammogram, it was not possible to examine concordance with the total number of tests. These data suggest that self-reported mammography use is generally valid, although a woman's ability to recall dates of examinations may be limited.

Educational Benefits from a Community Skin Cancer Screening.
Marianne Berwick, Ph.D., M.P.H., Jean Bolognia, M.D. and Judith
 A. Fine.

While the most often evaluated benefit from public skin cancer screening programs is the detection of malignant or pre-malignant lesions, this study addresses the hypothesis that education regarding excessive sun exposure is a major benefit derived from these programs. Eighty-five percent of the 251 participants in a community skin cancer screening held in New Haven, CT, (1) in 1988 completed questionnaires prior to and six months to one year, by telephone, after the screening. Behavioral changes, such as decreased sun exposure and increased use of protection while in the sun, were associated with attending a community skin cancer screening program and were not accounted for by measured temporal trends in sun exposure. Screening category (negative screen=123, positive screen=128, true positive [confirmed on follow-up]=83, false positive=45, histologically confirmed=57, and recalcitrant=16) was not associated with changed behavior. Nor were other positive screening behaviors (such as regular BSE) (2), or a personal or family history of skin cancer. Older age and lower perception of risk for melanoma were associated with negative behavior changes (3) as found by Robinson. Knowledge and attitudes were positively associated with changed behavior. The authors conclude that community screening activities appear to promote behavior change.

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Strategies for the Reduction of Avoidable Cancer Mortality from Malignant Melanoma/Skin Cancer, Howard K. Koh, MD, FACP, Boston University Schools of Medicine and Public Health, Boston, MA 02118. The rapidly rising incidence and mortality rates of malignant melanoma have stimulated strategies for early detection and prevention. Our research, using Massachusetts and national data, has documented: 1) systematic underreporting of melanoma incidence, 2) disproportionately higher mortality rates in men compared to women, 3) increased melanoma mortality in the socioeconomically disadvantaged in Massachusetts, and 4) increased years of potential life lost from melanoma. In 1985, the American Academy of Dermatology launched free melanoma/skin cancer screening which has presently reached over 350,000 Americans. Our evaluation of this program, in Massachusetts and nationwide, shows: 1) a documented yield of melanoma of about 1 in 300 persons screened, 2) the appropriateness of the visual examination by a dermatologist as a cancer screening tool, and 3) 86% of the first 80 confirmed melanomas found in screening are less than 1.50 mm thick, with an associated expected survival rate of 95%. Future screening and prevention efforts, perhaps targeted to men and those of lower SES, are needed to decrease melanoma mortality rates. Refs: 1. Koh H, Caruso A, Gage I, et al: Evaluation of melanoma/skin cancer screening in Massachusetts. Preliminary results. *Cancer* 65:375-379, 1990. 2. Koh H, Adame N, Geller A, et al: Cancer-registry data on melanomas. *New Engl J Med* 323:922, 1990.

BREAST SELF EXAM (BSE): EFFECTS OF TRAINING MODALITY AMONG HIGH-RISK WOMEN. M. Stefanek, P. Wilcox. Johns Hopkins Oncology Center, Baltimore, Maryland, 21205.

The U.S. Preventive Services Task Force (1) concluded that BSE research should 1) focus upon women at high risk and 2) determine what constitutes and how best to teach a competent BSE.

Women (n=101) with a first degree relative with breast cancer were stratified by BSE frequency and randomized to a concentric circle pattern (CC) of training or a vertical strip pattern (VS), with assessment visits at 3, 6, 9 and 12 months following baseline assessment. Proficiency was assessed by audiotaped verbal description (2), 2 breast models and a projected grid (PG) allowing for determination of amount of tissue palpated during BSE (3). Baseline proficiency was poor and correlations across assessment modalities nonsignificant. Results at the 3 month follow-up demonstrated increased proficiency on lump detection performance and verbal description on both models in both groups. The VS was significantly superior to the CC ($t=3.0, p<.01$) on 1 of the 2 breast models. Significant improvement was maintained at the 6, 9 and 12 month follow-up. Projected grid measures also showed significant improvement in performance across both groups from baseline. Thus, women at increased risk may not be performing BSE proficiently. Increased emphasis on BSE proficiency is needed. BSE training (CC, VS) can enhance proficiency as measured by all three modalities. (Supported by NIH RFA 87-CA-37).

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Doctor-Patient Communication Improves Adherence to Colorectal Cancer Screening. Mary Daly, M.D., Ph.D., Colleen Burke-Sands, B.S., Joan James, P.A. C., Doris Gillespie, Paul Engstrom, M.D.

Despite growing evidence that screening for colorectal cancer can reduce mortality through early detection,⁽¹⁾ the currently recommended screening tests are vastly underutilized in this country. Older individuals, and those of low socioeconomic status are particularly underrepresented in screening programs. In an effort to improve cancer screening practices among older, inner city adults in Philadelphia, we have initiated a dual-focused education program which surveys both community residents and their physicians concerning cancer screening practices. Following the baseline surveys, we attend community group meetings and deliver an educational program which strongly encourages community residents over age 50 to ask their doctor about cancer screening tests. A total of 1205 individuals have completed a baseline health questionnaire. Ages range from 50 to 100, with a median age of 72. The sample is predominantly female (86%), the majority of whom are widowed and live alone. Less than 50% have completed a high school education. Despite their advanced age and generally limited education, 89% of the sample believed in the ability of stool blood testing and sigmoidoscopy to detect colorectal cancer early, and 93% believed in the curability of early stage colorectal cancer. Yet only 42% have had a recent stool blood test, and only 24% have undergone sigmoidoscopy within 5 years. Age was not a strong predictor of screening practices in this elderly population. However, individuals whose doctor expressed strong belief in regular cancer tests, and who had actually recommended cancer screening tests were more than twice as likely to have had a recent stool blood test ($p<0.001$), and sigmoidoscopy within the past 5 years ($p<0.001$). Those who were up to date with colorectal screening tests were also more likely to report having asked their doctor about getting cancer tests (40% vs. 15%, $p<0.001$). These data suggest that attempts to foster more communication between physicians and their patients regarding cancer screening may result in improved adherence to recommended cancer screening guidelines.

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Prospective Adherence to Fecal Occult Blood Testing. Ronald E. Myers, PhD, DSW, Christopher Jepson, PhD, Eric Ross, ScM, Thomas Wolf, MA, Caryn Lerman, PhD, Andrew Balshem, BA and Lois Millner, MSW.

A telephone survey was conducted with a random sample ($n=501$) of older adult members of an IPA/HMO to explain adherence to fecal occult blood (FOB) testing (1). Data were collected on sociodemographic background, knowledge, attitudes and beliefs about FOB testing (2). Subjects then were randomly assigned either to a "usual care" Control Group (advance letter + screening kit + reminder letter), or a Treatment Group (usual care + an educational booklet and instruction telephone call + a reminder telephone call) (3).

Stratified stepwise logistic regression analysis showed that for men ($n=163$), salience and coherence of testing ($OR=1.8$ for a 5-point increment on a 40-point scale), self-efficacy ($OR=1.4$) and treatment ($OR=6.0$) were significant independent predictors of adherence. For women ($n=197$), age ($OR=2.2$) and salience and coherence of testing ($OR=2.0$ for a 5-point increment on a 40-point scale) were significant independent predictors. The findings indicate that older women are more likely to do FOB tests than younger women; adherence can be increased by raising awareness that screening is easy, effective and important; and treatment increased adherence among men more than women.

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PROFILE OF A HEALTHY WORKING GROUP RECEIVING DIGITAL RECTAL EXAMS OR SIGMOIDOSCOPY. Susan Fontana PhD, RNC

The purpose of this study was to explore selected sociodemographic and lifestyle factors that might assist in developing a marketing strategy for a colorectal screening campaign. Also of interest, was whether the presence of general risk factors (i.e. smoking) or specific risk factors or warning signs for colorectal cancer (i.e. rectal bleeding, history of rectal growths) might influence persons to obtain a digital rectal exam or sigmoidoscopy.

A random sample of 50 employees was selected from a group of nearly 400 employees who participated in a Management Wellness Program. Secondary analysis was performed on data collected using a health risk appraisal questionnaire. The questionnaire included questions on sociodemographic factors, personal and family health history, emotional status and screening procedures obtained in the past year. Odds ratios with 95% confidence intervals were calculated for factors that might influence persons to obtain a digital rectal exam or sigmoidoscopy. Logistic regression was used to explore which risk factors and sociodemographic data might be useful in predicting whether individuals obtain a rectal exam or sigmoidoscopy.

Odds ratios for persons with a specific risk factor or warning symptom (i.e. history of rectal growths or rectal bleeding) for colorectal cancer were 1.13 (0.26, 4.76) for digital exams and 1.55 (0.21, 8.96) for sigmoidoscopy. Odds ratios for smokers were 1.35 (0.28, 6.63) and 1.18 (0.14, 8.36) relative to receiving a digital rectal exam or sigmoidoscopy in the past year. For the logistic regression models, present age and history of rectal growths or tumors were only marginally significant in predicting whether individuals obtain sigmoidoscopy. These findings suggest that beliefs about risk increasing factors might be useful in interventions aimed at increasing participation in colorectal screening campaigns.

Preliminary Results of a New Screening Protocol for Bladder Cancer in an Exposed Industrial Population. Thomas J. Mason, Ph.D., William P. Walsh, M.A., William J. Vogler, P.A., Kathleen Lee, R.N.

It is estimated that 21-25% of bladder cancer among U.S. white males is attributable to occupational exposures (1). The DuPont Chambers Works was a major producer of two chemicals that are now known to be human bladder carcinogens, as well as two other compounds that are suspected human bladder carcinogens. From 1954 to 1982, DuPont screened 1723 exposed employees annually using the Papanicolaou test for urinary cytology and microscopic urinalysis. A prior review of this screening program revealed that the 142 employees who later developed bladder cancer were approximately twice as likely to have had hematuria (2). Building on this finding, a 3-year screening study has been designed to evaluate a home self-testing protocol for microscopic hematuria as a method for early detection of treatable urologic conditions among exposed workers at this chemical plant (3). Every six months, subjects test their urine at home for the presence of blood for 14 consecutive days using the Ames Hemastix^R. Microscopic examination of the urinary sediment for erythrocytes is performed quarterly. Semiannual urine cytology testing is done on quarters alternating with the urinary dipstick. Over 875 employees have enrolled in this study. Compliance with screening has been very high: 95% completed the dipstick self-testing. Consistent with our prediction, 113 persons (15.5%) were found to have hematuria after one quarter of screening, and have been referred for diagnostic evaluation. A final diagnosis has been established for 39 patients, including one case of transitional cell carcinoma of the bladder. These preliminary results indicate that this self-testing screening protocol is acceptable to an industrial population and appears to be effective in the early detection of serious urologic diseases.

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Breast Cancer, Tissue Fatty Acids and Body Size, Stark, A., Garcia, F., Moon, T., Cartmel, B., McNamara, D., Villar, H., and Girdano, G., The University of Arizona. An unmatched case-control study was carried out to assess the association of breast cancer with subcutaneous adipocytes composition and with abdominal adiposity. Cases consisted of 48 white women of hispanic or non-hispanic origin with confirmed diagnosis of metastatic breast cancer. Controls included 135 hispanic and non-hispanic white women with no history of internal cancer. Adipose biopsies were collected from the right upper buttock of each subject and analyzed for 13 fatty acids using gas-liquid chromatography. Food consumption data were collected using Arizona Food Frequency Questionnaire. Analysis of data using non-parametric methods indicated lower concentrations of fatty acids 18:0, 18:2 and 18:3 ($P < 0.05$) and higher concentrations of fatty acids 20:0 and 20:1 ($P < 0.01$) among cases. Very low correlations with subcutaneous fatty acids and dietary fats were obtained. Abdominal obesity has been reported to be a risk factor for breast cancer. Subjects measured and reported their current height, weight, waist, and hip values using the Arizona Women Health Risk Appraisal Questionnaire. During a face-to-face interview, subjects recalled their height, and weight at the time of menarche. Abdominal obesity was assessed by calculating waist to hip ratio (W/H). The odd ratios for current weight, height, body mass index and W/H ratio were 1.4 (95% CI 0.68-2.0), 1.2 (95% CI 0.84-1.4), 1.79 (95% CI 0.76-4.2) and 1.4 (95% CI 0.68-2.0) respectively. The odd ratios for weight, height, and body mass index at the time of menarche were 1.4 (95% CI 0.68-2.0), 2.3 (95% CI 1.1-4.7) and 2.1 (95% CI 1.4-3.2) respectively. Although a low correlation between dietary fat and body fat composition was noted, body fat composition and body mass index at the time of menarche may be used as markers to assess the risk of breast cancer.

Endogenous serum hormones and risk of subsequent premenopausal breast cancer. K. Helzlsouer, G. Longcope, G. Gordon, T. Bush, G. Comstock.

Endogenous sex hormones have been implicated in the etiology of breast cancer. To examine this association, a nested case-control study was conducted using serum collected in 1974. Prediagnostic serum levels of androstenedione, dehydroepiandrosterone (DHEA), estrone, estradiol, progesterone, and prolactin were compared among 28 cases with premenopausal breast cancer and 56 controls matched on age and timing of blood collection during the day and the menstrual cycle. Seven cases reporting use of oral contraceptives were excluded from analysis. Breast cancer risk for women in the upper two thirds of serum progesterone relative to the lowest third was 0.59 (95% confidence interval (CI) 0.1-2.5). The risks of breast cancer in the highest third of DHEA and androstenedione levels relative to those in the lowest third were 0.27 (CI 0.03-2.9) and 2.77 (CI 0.5-16.2) respectively. No associations were observed for estrone, estradiol, or prolactin. These results, while not statistically significant, suggest a protective effect of serum progesterone against premenopausal breast cancer and are consistent with an observed increased incidence of premenopausal breast cancer in progesterone deficient infertile women (1). DHEA appears to have different effects for pre- and post-menopausal breast cancer (2). Consideration of prevention strategies based on altering the hormonal milieu is suggested.

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Plasma Selenium Status Predicts Colorectal Neoplasia

Larry C. Clark Ph.D., Gerald Combs Jr. Ph.D., Davey R. Deal M.D., Mary Reid RN MS, Beverly Sanders Jr., M.D., Bruce Turnbull Ph.D.

This study examines the association between baseline plasma selenium status and the prevalence of colorectal neoplasms in a defined population of patients. The study patients are participating in one of two chemoprevention trials of non-melanoma skin cancer using nutritional supplements of selenium. All patients currently participating in the trials (n=600) at our Macon Georgia clinic are being invited to be screened according to the ACS-NCI screening guidelines for colorectal cancer. This report includes the first 94 patients to complete their flexible sigmoidoscopy screening and diagnostic follow up colonoscopy. The plasma selenium status of all patients were determined prior to their screening invitation and all screening procedures are performed by a board certified gastroenterologist. There is a statistically significant association between a high baseline plasma selenium status before randomization (above the median value of 115 mcg/ml) and the diagnosis of colorectal neoplasms. The exact age adjusted odds ratio for this association is 0.16 with 95% confidence intervals of (.02, .90) with an exact $P=0.033$. A total of 11 patients have been diagnosed with adenomatous polyps, including one patient who was also diagnosed with a rectal adenocarcinoma. The exclusion of this patient slightly decreases the strength and the significance of the association $OR=0.19$ (.02, 1.10) $p=0.068$. A unique strength of this project is that it is screening a defined population of patients who were not selected for screening because of GI symptoms or a family history of colorectal cancer.

The causal significance of this observed association is strengthened because it is consistent with our earlier crosssectional study of selenium status in patients undergoing their initial colonoscopy $OR=3.6$ 95% CI (1.1, 13.2) (Clark, 1990) and an ecologic study of county forage selenium levels and county colon and rectal cancer mortality rates (Clark, 1991).

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INTESTINAL METAPLASIA OF THE STOMACH: IDENTIFICATION BY SELECTED STAINING, PREVALENCE & EPIDEMIOLOGY IN HISPANICS.
 Fennerty M, Sampliner R, Garewal H, McGee D, Modiano M.
 University of Arizona Health Sciences Center.

Intestinal metaplasia (IM) is felt to be a precursor lesion of gastric carcinoma (1). Ethnic sub-groups (i.e. Hispanics) at increased risk of gastric cancer have not been evaluated to determine the role of IM. We have studied prevalence & epidemiology among Hispanics and have developed a method to enhance recognition of IM by selective mucosal staining. **Methods:** Patients were systematically biopsied to determine the prevalence of IM. Selective mucosal staining with mucomyst (MM) & methylene blue (MB) was used. **Results:** Prevalence of IM in 250 Caucasians was 13%. Among 39 Hispanic patients, prevalence was 46% ($p < .0001$). Staining patterns with MM & MB were variable; subtle focal staining (SF), prominent focal staining (PF), & prominent diffuse staining (PD). Histologically, biopsies of these areas correlated with the amount of intestinal metaplasia $PD > PF > SF$. PD areas were fully "intestinalized" on biopsy. 16 of the 17 "stained" biopsies demonstrated IM versus 0 of 9 "non-stained" biopsies ($p < .0001$). **Conclusions:** 1) Hispanics have a 3.5 X higher prevalence than caucasians, similar to their increased risk of gastric cancer (2), 2) MM & MB is a clinically useful & accurate method to demonstrate IM endoscopically. This technique allows directed sampling of IM, as well as provides an objective method to quantitate IM prospectively, 3) IM is a preneoplastic lesion that lends itself to study in populations at increased risk of gastric carcinoma. (1) Correa P. A Human Model of Gastric Carcinogenesis. *Cancer Res* 1988; 48: 3554-3560. (2) Menck, et al. Cancer Incidence in the Mexican American. *JNCI* 1975: 53.

Clinical Studies of Indole-3-Carbinol as a Modulator of Estradiol Metabolism. J.J. Michnovicz and H.L. Bradlow, The Institute for Hormone Research, 145 E. 32nd St., New York, N.Y.

Research studies have demonstrated a strong association between estrogen metabolism and the incidence of breast cancer (1), and we have sought pharmacological means of altering both metabolism and subsequent risk (2). Indole-3-carbinol (I3C), obtained from cruciferous (e.g., cabbage) vegetables, is a known inducer of oxidative P-450 metabolism (3), and we therefore investigated the effects in humans of short-term oral exposure to this compound (6-7 mg/kg/d over 7 days). We used an *in vivo* radiometric test, which provides a highly specific measure of estradiol 2-hydroxylation before and after exposure to I3C. In a group of 12 healthy volunteers, the average extent of reaction increased by approximately 50% during this short exposure, affecting men and women equally. We also measured the urinary excretion of two key estrogen metabolites, 2-hydroxyestrone (2OHE1) and estriol (E3). We found that the relative excretion of 2OHE1 was significantly increased by I3C, further confirming the ongoing induction of this pathway. These results indicate that I3C favorably alters endogenous estrogen metabolism, and may therefore provide a novel "dietary" means for reducing cancer risk.

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Colonic Proliferation Biomarkers in a Seven Year Follow-up Study of Native Americans with Hereditary Non-Polyposis Colon Cancer (HNPCC). MJ Wargovich, PhD, PM Lynch, MD, HT Lynch, MD, J Lynch, RN, S. Lanspa, MD, T. Drouhard, MD, EE Deschner, PhD, MD Anderson Cancer Center, Houston, TX, Creighton University, Omaha, NB, Memorial Sloan Kettering Cancer Center, New York, NY.

A 7 year colonoscopic follow-up study with proliferation biomarkers was conducted on members of a Navajo family with HNPCC. Rectal biopsies of normal mucosa were examined by thymidine autoradiography (TA) in 1983 and again in 1989 thus providing cytokinetic information in this cohort over a period of biologic relevance. Paired analysis of labeling indices (LI) at baseline and at follow-up showed essentially no change i.e., normal labeling patterns ($p > .20$) with one exception, a subject presenting with an new adenoma in 1989 and a TA LI of 13.0%. Bromodeoxyuridine (BUDR) LI and TA LI were compared at follow-up and a good correlation of 0.84 was obtained ($p > .30$). Additionally at follow-up a standard polyethylene-glycol bowel preparation produced no effect on LI from TA or BuDR before and after preparation. These results suggest that colonic proliferation biomarkers in this HNPCC population were essentially stable over a 7 year period. Secondly, BUDR can effectively substitute for TA as a biomarker. The observed LI, putatively "normal" when compared to published data may reflect epigenetic factors (i.e. American Indian) that may reduce colonic proliferation in an otherwise genetically predisposed population for colon cancer.

FAMILY HISTORY OF CANCER AND ADENOSINE DIPHOSPHATE RIBOSYL TRANSFERASE (ADPRT). George C. Roush, MD, Margaretha Lund-Pero,^{1,2} MD, PhD, Julie Powell, BA, and Ronald W. Pero,^{1,2} PhD.

Enzymatic activity of adenosine diphosphate ribosyl transferase (ADPRT) is related to DNA repair and pro-oxidant status. Its activity can be measured in peripheral mononuclear leukocytes after challenge with agents such as hydrogen peroxide (activated ADPRT) or without such challenge (constitutive ADPRT). In the present study, activated ADPRT was more reproducible on retesting of 40 individuals (intraclass correlation coefficient +0.40, $P = 0.005$) than the constitutive ADPRT (intraclass correlation coefficient = -0.40, $P = 0.995$). Therefore, activated ADPRT was used in the analysis of family history of cancer. In 95 individuals, a history of one or more first degree relatives with cancer was related to lower levels of activated ADPRT with parameter estimate = -729.4, $P = 0.051$ (parameter estimate = -742.1, $P = 0.034$ for best fitting model). It was not possible to explain this inverse association on the basis of several potentially confounding variables including age, gender, body weight, or other factors. The association was particularly strong in men (parameter estimate = -1,482, $P = 0.017$). In previous studies, ADPRT has been found to be lower in persons with prior cancer or with pre-cancerous lesions. The present results are consistent with the concept of ADPRT as a measure of cancer susceptibility.

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Identification of High-Risk Environments: A Geographical Analysis of U.S. County Cancer Mortality Rates.
Karen Kafadar, Ph.D.

The Atlas of Cancer Mortality (1) stimulated much epidemiological research to study possible associations between environmental variables and certain cancers; e.g., shipyards and lung cancer (2), dietary factors and gastric cancer (3), lifestyle and pancreatic cancer (4). Geographic patterns may become clearer and may be revealed even more strongly when the rates have been adjusted for known risk factors such as a smoking surrogate for lung cancer. I will show that, using a statistical adjustment followed by a two-dimensional smoothing algorithm, the adjusted cancer mortality rates, when displayed on a map, show some interesting geographical patterns not previously identified. The etiologic implications of these patterns as well as their impact for stimulating prevention research will be presented.

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Reproducibility of mammographic pattern classification. Paolo Toniolo, MD; Karen L. Koenig, PhD; Alan R. Bleich, MD; Clifford Beinart, MD.

The imperfect reproducibility of Wolfe's classification of mammographic parenchymal patterns (MPP) may explain its limited clinical use, as well as inconsistencies that have been observed in epidemiological studies of breast cancer (1,2). In this paper, results are presented of a study to determine whether consensus to resolve inconsistencies between readers would improve the level of concordance in MPP categorization and could thus help reduce misclassification. One hundred consecutive mammograms from a large screening clinic were classified independently by two mammographers on two separate occasions, eight days apart. Coding was repeated in two consensus conferences several weeks later. The average intra-observer intraclass correlation coefficient (r_1) of the four patterns was 0.68, and the inter-observer r_1 was 0.65. After consensus, reproducibility improved markedly to 0.88. Estimates of the reduction in the amount of misclassification that would be obtained by consensus rating were produced using available data from previous studies. It is concluded that the added complication of consensus rating would be more than offset by a substantial increase in precision.

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How Food Sources of Total Fat Change as a Result of Dietary Intervention. R. Sue McPherson, Ph.D., Rebecca S. Reeves, M.S., R.D., L.D.

Dietary guidelines suggest that Americans lower their dietary intake of total fat to <30% of KCAL (1). The specific changes in food intake that people make when reducing their total fat in the diet are unknown (2). Thirty-eight women participated in a 12 week nutrition intervention to reduce total fat intake to <30% of KCAL, keeping 7-day food records before and after the intervention. Women lowered their % of KCAL from total fat from 36.5% to 30.2%. Foods consumed before and after intervention were assigned to 8 food groups and classified as high or lowfat. Subjects reduced the quantity of consumption of high fat dairy products (HFD), high fat meat, fish and poultry foods (HFMFP), high fat meat combination foods (HFMCOM), high fat grains and starchy vegetables (HFGV) and fats and oils (FO). Reduction in the quantity of consumption of high fat foods resulted in a lowering of the total grams of fat/person/day (gf/p/d) from 9.0 to 4.7 for HFD, 9.0 to 4.7 for HFMFP, 12.6 to 6.8 for HFMCOM, 16.0 to 8.5 for HFGV and 13.8 to 8.4 for FO. Increases were only evident for lowfat meat, fish and poultry foods. Individuals attempting to lower their total fat intake may benefit from these data suggesting that a variety of changes in the total diet are necessary to achieve the recommended reductions in fat intake.

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Cigarette Smoking in California in 1990. John P. Pierce, Ph.D., David M. Burns, M.D.

California voters initiated a 25 cent excise tax increase on cigarettes which came into effect in January 1989 (1). Part of the revenue from this tax has been used for interventions to reduce smoking prevalence in California. One of the activities funded by the Tobacco Tax Initiative was the 1990 California Tobacco Telephone Survey. This representative population survey of approximately 30,000 Californian households is divided into two representative samples: with the first sample comprising 9,249 households (response rate 73%). Prevalence data includes proxy information from other adults in the household and shows a decline in prevalence from an expected 24% to 20.8%. Half of Californian adult smokers have made an attempt to quit in the past year with four-fifths of those making such an attempt being unsuccessful. Thus, compared to national data (2) more people are trying to quit in California but they are not more successful. One-third of current smokers are in the action phase of change. However, over half the current smokers do not have health beliefs sufficient to motivate successful change.

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A Culture-Specific Approach to Smoking Prevention Among Minority Children. D.S. Tulskey, Ph.D., D.F. Cella, Ph.D., C.R. Thomas Jr., M.D., B. Sarafian, B.A. & C.R. Thomas Sr., Ph.D.

Successful smoking prevention with minority children may require innovative culture-specific approaches.^{1,2,3} An anti-smoking rap contest methodology was tested with 268 junior high school children from a predominantly minority school district (57% Black; 17% Hispanic). Pretest smoking attitudes and behaviors were collected at an introductory assembly, and posttest ratings were collected after the rap contest assembly (which was held within three weeks of the initial assembly). Most students entered the study with strong negative attitudes against smoking ($X=49.6$ out of a possible score of 60). One-fifth of the sample had tried smoking at least once in the past, but few (3%) reported smoking presently. Preference ratings were very high for the contest idea and execution. High ratings were the modal response for several components of the intervention -- video rap example (84%), audio rap example (78%), the oncologist's dialogue (80%), the idea of the contest (84%), and the assembly itself (82%). High posttest ratings were also obtained on the quality of the raps in the contests (80%), organization of the contests (70%), and the contest itself (79%). There was no significant change in attitudes towards smoking. However, there was a ceiling effect in which children started with highly negative attitudes against smoking. These data suggest that rap contests for smoking prevention may be effective because they are highly acceptable and culturally-relevant.

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Smoker Characteristics and the Efficacy of Nicotine Gum
M.C. Fiore, P.A. Newcomb, L. Ritter, P.M. Marcus

Nicotine gum, available in the U.S. since 1984, is used to assist smokers in their cessation efforts by relieving the physiological symptoms of nicotine withdrawal. To identify those characteristics of smokers most likely to successfully quit using nicotine gum as a cessation aid, we compared successful and unsuccessful nicotine gum users ($n=457$) utilizing weighted data from the 1987 Health Interview Survey (HIS). Among smokers surveyed during the 1987 HIS that made a quit attempt in the previous three years, 10.1% of current smokers and 7.5% of former smokers had ever tried nicotine gum. After controlling for demographic factors in a multivariate logistic regression model, we found that smoking cessation with nicotine gum was likely to be most successful in older smokers and those with shorter total duration of smoking (fewer quit attempts). Smokers not requiring a cigarette within one-half hour of rising were also more likely to succeed with nicotine gum. The number of cigarettes smoked was highly correlated with cessation success using nicotine gum. Individuals smoking 25 or more cigarettes per day were significantly more likely to succeed using nicotine gum when compared with those smoking less than 25 cigarettes per day ($p < .01$). Sex, education, having a primary care physician, body mass, and other characteristics of smoking were not associated with success with nicotine gum. These findings suggest that some characteristics of physiologic nicotine addiction are highly correlated with success with nicotine gum while others are not. One explanation for these observations is that heavily addicted smokers currently are prescribed an insufficient dose of nicotine replacement.

Patterns of Smokeless Tobacco Use Among Adolescent Females. Kenneth J. Simon, EdD, R. Craig Stotts, RN, DrPH: Cecil Pollard, PhD

The patterns of smokeless tobacco (ST) use among boys have been amply described in many studies. However, to date no study has had a large enough sample to describe this pattern among girls (1). A few studies have looked at older women who use snuff, but these data are largely nongeneralizable to adolescent females (2).

We conducted a survey of 4,230 West Virginia students in grades 5-12, yielding 66 females who were current or ex-users, and 920 male current or ex-users. Among males, 54% had tried smokeless tobacco by grades 5-6, 73% by grades 7-9, and 82% by grades 10-12. Among females, the figures were 17, 20, and 21%, respectively. Females were more likely to have started using ST regularly at ages 10-11, while boys typically began about 2 years later. Many other indicators of ST usage were very different for female users, suggesting that different approaches for boys and girls must be considered in designing programs aimed at preventing regular ST use or in working with current users.

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Sex differences in lung cancer risk associated with cigarette smoking. K. Osann, H. Anton-Culver, T. Kurosaki, T. Taylor, B.D. Culver.

The importance of cigarette smoking as a risk factor for specific histologic types of lung cancer has been examined in a case-control analysis of data from the Cancer Surveillance Program of Orange County, a population-based registry. Smoking habits were abstracted from medical records for 1168 men and 834 women diagnosed with primary lung cancer in 1984-1986 and 1851 men and 1656 women aged 30 or older with cancers not associated with smoking. Ninety-six percent of men and 89% of women with lung cancer were cigarette smokers compared to 55% of men and 34% of women with other cancers. The age-adjusted odds ratios (OR) associated with ever-smoking were 19.7 (95% confidence interval (CI) 14.4-26.9) for men and 15.2 (95% CI 12.0-19.3) for women. Although OR's are higher than reported in other studies (1,2) due to the low reported frequency of smoking among other cancers, the validity of comparisons between cell types is not affected. Comparison of cell types showed that male smokers experienced equal OR's for small cell and squamous cell carcinomas whereas women who smoked had higher OR's for small cell than squamous cell carcinoma. Although women experienced lower OR's than men for other cell types, women smokers were at higher risk than men for small cell carcinoma. These results confirm other reports (1,2) and suggest the existence of co-factors which increase risk for small cell carcinoma among female smokers.

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LUNG CANCER IN ALBERTA

Hans Berkel, M.D., Ph.D., Herta Gaedke

Trends in incidence, mortality and survival for lung cancer were examined using data from the (population-based) Alberta Cancer Registry for the 25-year period 1964-1988. In this period a total of 12,762 patients (3190 females and 9572 males) were diagnosed with lung cancer.

Incidence rates in males increased steadily until the early 1980's after which a plateau was reached, while in recent years a tendency to decline can be seen. Incidence rates in females keep rising dramatically, resulting in a decline in M/F-ratio from 16.4 in 1964 to 2.4 in 1988. When this trend continues it is expected that female-rates will surpass male-rates early in the next century.

A total of 205,674 person years of life were calculated to be lost, an average of more than 16 years per patient. The median survival time was always less than one year. The 5-year actuarial survival did not change significantly over the study period, however both in males and females the short term (1-year) survival increased. Survival is poorer with increasing age at diagnosis.

It has been described that cigarette smoking is more strongly associated with squamous and small cell lung cancer than with adenocarcinoma's in the lung. In males the "smoking-related" histologic types of lung cancer decreased while the "non-smoking-related" histologic types increased (test for trend: $p < 0.01$). In females the reverse pattern was present (test for trend $p < 0.05$). These changes in the relative distribution of histologic types of lung cancer are consistent with known changes in smoking habits. It illustrates the need for smoking-intervention in targeted groups.

How to Help Your Patients Stop Smoking: A National Program to Train Physicians in Smoking Cessation Techniques. Corinne Husten, MD; Marc Manley, MD, MPH.

The National Cancer Institute is conducting a national program to teach physicians smoking cessation techniques using a train-the-trainers model. Clinical trials have shown that physicians can have a significant impact on the smoking rates of their patients using a brief clinical intervention and simple organizational procedures^{1,2}. NCI is conducting seminars (in collaboration with professional and voluntary organizations) to show "trainers" how to teach these techniques to community physicians, and has developed a training guide containing all materials needed to conduct courses. The trainers are assisted in conducting classes by the collaborating organizations, and NCI provides a physician manual for every person trained. NCI's goal is to train 2000 trainers, and each trainer is being asked to teach 50 physicians, which will result in 100,000 physicians nationwide being trained in these techniques. Evaluation of this program will include a survey of trained physicians and physician trainers using a pre-test/post-test design to assess the extent to which the techniques have been incorporated into practice, and a survey of trainers to determine how the program was implemented. A more complete description of the analysis plan, and data on program dissemination will be presented.

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SMOKING BEHAVIOR FOLLOWING DIAGNOSIS IN PATIENTS WITH STAGE I NON-SMALL CELL LUNG CANCER

Ellen R. Gritz, Ph.D., Rosane Nisenbaum, M.S., Ph.D., Robert E. Elashoff, Ph.D., E. Carmack Holmes, M.D. (For the Lung Cancer Study Group), UCLA.

Few studies have attempted to document the smoking behavior of lung cancer patients post diagnosis (1). The Lung Cancer Study Group (LCSG) collected self-reported smoking status from all patients enrolled in clinical trials at entry (baseline) and prospectively at every followup visit. Smoking behavior of 840 patients with resected stage I non-small cell lung cancer who were current or former smokers at baseline was analyzed for up to four years following diagnosis. Current smokers were predominantly male (69.2%), white (90.4%), had a mean age of 60.6 years, and were heavy smokers (mean=28.8 cigarettes/day, 40.0 years smoked, 61.9% smoked 25 or more cigarettes/day). At one year followup, only 16.8% of the 317 current smokers who were followed for two years or longer continued to smoke, while 83.2% of patients either quit permanently (53.0%) or for some time period (30.2%). By two years, permanent cessation stabilized at over 40%; however, the prevalence of continued smoking decreased through all periods of followup. Subjects who attempted cessation or quit permanently were more likely to be female and healthier than continuous smokers.

These high cessation rates in a lung cancer patient population may result from several factors: disease severity combined with potential survival benefit; a "teachable moment" combined with a bonded provider-patient relationship; and ongoing physician and nursing support for cessation (2,3).

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Quantifying Breast Cancer Risk in a Consultation Clinic. Victor G. Vogel, M.D., M.H.S., Nancy Ainslie, R.N., Melissa L. Bondy, Ph.D., Rodger J. Winn, M.D.

We provide consultation and screening services in a comprehensive cancer center to women who are at increased risk for breast cancer (1). Using a conditional logistic regression model derived from a cohort of 285,000 screened women (2), we assigned risk scores to the index cases from 39 pedigrees we have evaluated since 1988. Five risk factors are considered: subject age, age at menarche, number of first degree relatives (FDR) with breast cancer, parity, and history of breast biopsy. A relative risk and a lifetime probability of developing breast cancer are calculated and communicated to the subject and her family members. The mean age of these women is 41 ± 9.9 years, and their mean age at menarche was 13 ± 1 years. Their mean age at first live birth was 25 ± 6 years; 28% were nulliparous. Among 39 index subjects, 21 had one FDR with breast cancer; 13 had two; and four had three FDRs. One pedigree showed paternal transmission. Twenty-three percent reported prior breast biopsy. Calculated relative risks of developing breast cancer ranged from 1.70 to 21.5 (mean 6.18 ± 5). Each woman is given a risk-specific screening recommendation. Genetic studies in this population are ongoing (3). These clinics can serve as a source of subjects for prevention trials and epidemiologic studies. The validity of the risk assessment methodology must be evaluated prospectively, and each woman's risk reassessed annually.

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Women At High Genetic Risk Of Breast Cancer: Surveillance Behavior And Psychological Distress. K.M. Kash, Ph.D. & J.C. Holland, M.D., Memorial Sloan-Kettering Cancer Center, and M. Halper, M.P.H. & D.G. Miller, M. D., Strang Cancer Prevention Center, NY 10021.

This study reports surveillance behavior and psychological distress of 120 women in a breast protection program who had two or more first degree relatives with breast cancer. The Health Belief Model (1) and standard measures of social desirability, social support, psychological distress (Brief Symptom Inventory-[BSI-GSI]), and cancer anxiety were used to assess women within two years of entry to the program. 94% came for scheduled mammograms; 69%, for regular clinical examinations; but only 40% performed breast self-examination (BSE) monthly at home. Using a discriminant function analysis, women who did not keep regular appointments for clinical examination were highest on cancer anxiety ($p < .005$). Poor monthly BSE was predicted (using multiple regression analysis) by poor prior performance of BSE ($p < .0001$) and higher generalized anxiety ($p < .02$). High psychological distress was predicted by greater perceived barriers to surveillance ($p < .007$); low social desirability ($p < .002$); and an interaction of low social support and high perceived barriers ($p < .03$). High anxiety resulted in poor surveillance behavior. These data support need for psychological interventions in high risk women to reduce distress, improve surveillance behavior, and assure early detection of curable breast cancer.

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National Registry for Women with Family Histories of Breast Cancer: A Tool for Cancer Control and Genetic Research. Gladys Rosenthal, M.S., Marilyn Halper, M.P.H., Matthew B. Lubin, M.D.

A national high risk breast cancer registry is comprised of 1500 women from clinical breast programs at Strang Cancer Prevention Center and Memorial Hospital, and a national cohort of women who supply family history, risk factor information and prior screening actions. The mean age of participants is 44 years. Forty percent of the women over age 40 had never had a mammogram suggesting a lack of prior screening (1). High risk women may need a baseline mammogram at earlier ages and more frequent breast examinations. Women are provided risk assessment, surveillance guidelines, mammography reminders and newsletters. Health status and family history are updated yearly. Pedigrees are reviewed to determine suitability for genetic research. A high risk registry can promote improvement in screening health behaviors which could influence breast cancer mortality, as well as supply rare families for genetic studies.

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**A COMPARISON OF BREAST CANCER RISK FACTORS IN
PREMENOPAUSAL BLACK AND WHITE WOMEN**
TH Maltzman, PM Marcus, PA Newcomb

While the overall age adjusted breast cancer incidence rate in the US is higher in white women than black women, breast cancer incidence for women younger than 45 years is higher in the black population. To investigate this differential, we examined determinants of breast cancer risk in black (n=1277) and white women (n=5656) less than 45 years of age using weighted data from the 1987 National Health Interview Survey (Cancer Epidemiology Study). Young black women were less likely to be nulliparous than young white women (26.4% black vs 35.2% white) and also tended to be younger than 20 years at first birth (67.4% vs 39.6%). Fewer black women tended to be lean (≤ 23 kg/m²) (37.9 black vs 58.1% white). A similar distribution was observed in both groups of women for early age at menarche (age ≤ 12 years). There were no differences in prevalence for family history of breast cancer (3.5% of both black and white women had at least one primary relative with breast cancer). There were, however, differences in lactation history between young black and white women. Young black women were less likely to breast feed than young white women (27.5 vs 51.8%). Based on this data, lactation was the only risk factor identified in this study that could explain the higher incidence of breast cancer in young black women.

Risk factors in familial and sporadic breast cancer: The Iowa Women's Health Study. Sellers TA, Kushi LH, Potter JD, Kaye S, Nelson C, Folsom AR.

A positive family history (FH) of breast cancer (BC) reflects shared cultural factors and/or genetic predisposition. To determine if reproductive and anthropomorphic risk factors are modified by FH, we performed nested case-control analyses on data from a cohort study of 41,837 Iowa women aged 55-69. During 3 years of follow-up, 367 first-primary BC cases occurred; 1713 controls were randomly selected for analysis. Family history of BC reported at baseline was used to further stratify cases and controls into 4 groups: FH-pos cases (n=60), FH-neg cases (n=307), FH-pos controls (n=198) and FH-neg controls (n=1515). Irrespective of family history, cases had significantly lower parity, earlier age at first pregnancy, longer time between menarche and first pregnancy and greater weight change since age 18. Since FH-pos controls were remarkably similar to FH-pos cases, we applied analysis-of-variance techniques, adjusted for multiple tests, using FH-neg controls as the reference group. Factors associated with FH-neg BC only include 1.1 kgs lower weight at age 18, 2.9 kgs higher current weight, 1 kg/m² greater BMI and 4 mos. earlier age at menarche (all p < 0.01). These results suggest etiologic differences between familial and sporadic occurrences of breast cancer that may direct research into the underlying biologic mechanisms.

Role of Family History in Breast Cancer Risk. Brenda Breuer, Ph.D., M.P.H., Gladys Rosenthal, M.S., Daniel G. Miller, M.D.

The purposes of this study were: 1) To determine whether family history contributes to the risk of developing breast cancer independently of the other risk factors included in a multivariate model, published by Gail et al. (1), and 2) To determine whether the Gail model is appropriate for medical counselling of women with an extensive family history of breast cancer. Regarding the first aim, 361 women who had a history of first degree relatives with breast cancer were compared to 549 women who had no such history. The two groups were statistically similar with respect to biopsy experience, age at menarche, and age at first livebirth, strongly suggesting that the pathways associating breast cancer to these biological factors differ from those relating family history to breast cancer. Regarding the second aim of this study, in an analysis limited to women with affected first degree relatives, laterality in those relatives was significantly associated with the risk of developing breast cancer, even after adjusting for other parameters in the Gail model. We therefore conclude that the Gail model may be inappropriate for counselling women with an extensive family history of breast cancer.

Gail, MH, et al., Projecting Individualized Probabilities of Developing Breast Cancer for White Females who Are Being Examined Annually. JNCI 1989;81:1879-1886

AWARENESS OF RISK AND SCREENING AMONG WOMEN WITH A FAMILY HISTORY OF BREAST CANCER.

C. Lerman PhD, M. Daly MD, C. Sands, E. Ross, MS, K. Buetow PhD, B. Rimer DrPH, and P. Engstrom, MD.

Women with one or more first-degree relatives with breast cancer (FDRs) have a 2 to 13-fold increased risk of developing breast cancer.¹ This study compared the risk perceptions and screening practices of women with 1 FDR (n=132) and 2 FDRs (n=63) to an age-matched control sample of women with no family history (n=145). Subjects were women aged 50 and older who were participants in a breast screening program offered by the HMO PA/NJ and responded to a telephone interview. Although significant between-group differences in risk perceptions were observed (p<.001), a substantial proportion of women with 1 FDR (53%) and 2 FDRs (28%) were unaware of their increased breast cancer risk. Mammography rates were high, perhaps due to unique aspects of the HMO such as free mammograms. However, women with 1 FDR (71%) were no more likely than controls (73%) to have had their annual mammograms. Overall, women with 2 FDRs (86%) were more likely than controls to have had their annual mammograms (p=.02). However, logistic analyses indicated that this relationship between familial risk and screening was modified by age (p<.01). Among women over age 65, there were no differences in mammography rates between those with 2 FDRs and controls (70% for each). Rates of clinical breast exam, breast self-exam and physician recommendations for mammography all were independent of familial risk. These findings highlight the need for health education targeted to women at high risk due to family history and to their physicians.

¹ Sattin RW, Rubin GL, Webster IA et al: Family history and the risk of breast cancer. JAMA 253: 1908, 1985.

PSYCHOLOGICAL SIDE-EFFECTS OF CERVICAL CANCER SCREENING AMONG MINORITY WOMEN. C. Lerman Ph.D., Fox Chase Cancer Center and S. Miller Ph.D., Temple University

Concerns about possible adverse effects of cervical cancer screening have been raised (1). This study evaluated the psychological consequences of positive cervical screening (Pap) tests in a lower-income minority population. Subjects were 224 women aged 15-40; 106 subjects had negative results and 118 had positive results which required follow-up by colposcopy. Telephone interviews, conducted three months following receipt of results, evaluated the impact of test result on psychological responses. Of the women with positive results, 65% had complied with follow-up; none had cervical cancer. The results showed that 30% of women with positive tests worried often about cervical cancer, 25% had impairments in daily functioning, 50% had decreased sexual interest and 40% had sleep disturbance. These rates of impairment were significantly elevated compared to those reported by women with negative tests. These effects were most pronounced among women who did not comply with colposcopy. Regression analyses showed that the psychological impact of a positive test was independent of demographic and sexual behavior confounder variables. Health education targeted to psychologically vulnerable screeners may reduce distress and enhance compliance. (2,3)

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- (2) Paskett ED: Compliance behavior in women with abnormal pap smears. *Med Care* 1990;28(7):643.
- (3) Wilkinson C: Anxiety caused by abnormal result of a cervical smear test. *Br Med J* 1990;300:440.

Hislop TG, Band PR, Clarke H, Smith J, Deschamps M. Utilization patterns for Pap smear screening in Native women in British Columbia

Cervical cancer mortality in Native women in B.C. is four times that of non-Native women (1). Pap smear utilization patterns were examined in 4 school districts which had the highest provincial cervical cancer mortality rates (2), and which represented both coastal and interior bands. Utilization rates were determined by linkage of the Native Band membership listing with the provincial cervical cytology screening registry. The age adjusted rate for Pap smear ever users was 49.0% ranging by Band from 36.5% to 69.6%; the rate for current users (i.e. Pap smear within the last three years) was 34.9% ranging from 25.1% to 59.0%, and for ex-users (i.e. last Pap smear prior to 3 years ago) was 14.1% ranging from 7.4% to 25.5%. This compares to the provincial average of 85% for ever users (3). Pap smear utilization rates in Native women differed by age group: younger women were more likely to have Pap smears than older women. Native women and their health care providers are being interviewed to identify factors which influence participation in the provincial cervical cytology screening program.

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2. Band PR et al. Atlas of Cancer Mortality in British Columbia 1956-1983. *Stat Can Catalogue* 85-565, 1989.
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Funded by the Community/Hospital Partnership Programme, British Columbia Ministry of Health

Cervical Cytology Quality Assurance in Washington State. Victoria Taylor, B.M. B.S., M.P.H. and Floyd Frost, Ph.D.

Failures in cervical cancer prevention have been partially attributed to laboratory errors, and it is believed that significant differences in performance and reliability exist between cytology laboratories.¹⁻⁴ The objectives of this study were to establish a profile of cervical cytology laboratories in Washington State and identify quality assurance problems amenable to correction through education or legislation. All 43 Washington laboratories that perform cervical cytology were surveyed by mail during 1989. Completed surveys were returned by 86% of the laboratories. Nearly half (43%) of the respondents reported processing less than 10,000 Pap smear cases annually. Only one-third (35%) of the respondents reported participating in relevant proficiency programs. Smaller cytology laboratories were compensating their cytotechnologists on the basis of the number of slides read and allowing Pap smears to be read outside the confines of the laboratory. The results of this study suggest that cytotechnologists in larger Washington laboratories have been exceeding work load limits recommended by professional associations. Recent legislation includes regulations that address cervical cytology quality assurance.⁴ However, continued efforts will need to be made to encourage voluntary adoption of cost-effective quality control measures.

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Cervical Cancer Screening Practices by Hispanic Women: Lester S. Gorelic, Ph.D., Connie Dresser, RDPH, LN, Douglas Weed, M.D., Ph.D., Barry Graubard, M.A., Elva Ruiz, B.A.

Data from the Hispanic Health and Nutrition Examination Survey (HHANES) were analyzed for age-specific patterns of cervical cancer screening practice patterns in Mexican American, Cuban American and Puerto Rican women. Unadjusted analyses showed 75% of Hispanic women ages 19-74 had Pap smears within two years prior to interview. The age-specific patterns showed that 72% of women 19-24 years, 89% of women 25-34 years, 77% of women 35-44 years, 66% of women 45-54 years, 62% of women 55-64 years and 46% of women 65-74 years obtained Pap smears during this time period. There were significant ethnic differences in the age-specific patterns among Hispanic subgroups for ages 35-44 (88% Puerto Rican; 75% Mexican American; 75% Cuban American); 45-54 (78.6% Puerto Ricans; 65% Mexican Americans; 62% Cuban Americans); and ages 65-74 years (74%, Puerto Ricans; 42% Mexican Americans; 49% Cuban Americans).

Hispanic women never screened for cervical cancer comprised 20-25% of the Hispanic sample. Most of these women were in age categories 19-24 and 55 years and older. The data also show significant demographic and acculturation differences between the unscreened and screened women. A larger proportion of unscreened women were not born in the United States (excluding Puerto Rico), had a lower income, and did not have private health insurance as compared with the screened women. Additionally, a larger proportion could not read English and had a lower level of education.

This analysis of the HHANES data shows diminished use of Pap smears with increasing age by Hispanic women, and identifies two subpopulations of Hispanic women who never had Pap smears. Future interventions to improve cervical cancer screening rates for Hispanic women will have to incorporate these findings into their design.

Family Physicians' Cervical Cancer Screening Practices. Mack T. Ruffin IV, M.D., M.P.H.

Over 15 million Pap smears are done annually (1), but very limited data has been collected to evaluate the practices of physicians collecting these smears. A national study of family physicians was performed to answer the following questions: 1) what percentage of outpatient visits are for Pap smears? 2) What tools are routinely used in collecting smears? 3) What risk factors do physicians know for cervical cancer? 4) What percentage of their population do they feel are at risk? 5) Do physicians know important features about their cytology service? 6) Are physicians aware of the possible significance of endocervical elements in a Pap smear? 7) Do physician characteristics predict level of expertise with cervical cancer screening?

A mailed self-administered questionnaire was sent to 5400 family physicians chosen at random from the active membership of AAFP.

The response to the survey was 80% of the sample. The mean percentage of outpatient visits for Pap smear was 10.5% (95% confidence interval 8.2-12.8%). The most commonly used tools were a combination of a spatula and cytobrush, 23.5% with many other combinations of tools used. Adherence to ideal collection protocol (2) was generally good. The knowledge about risk factors was limited. The knowledge about their cytology service was poor. Awareness about potential significance of endocervical elements was limited. Certain characteristics such as age, training, type of practice, and location of practice were predictive of ideal cervical cancer screening practices.

A variety of cervical cancer screening practices were found among family physicians. Certain groups of physicians can be identified as targets for interventions to change practice and improve effectiveness of screening.

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- 2) American College of Obstetrics and Gynecology. Cervical cytology: Evaluation and management of abnormalities. *ACOG Technical Bulletin* November 8, 1984.

Trends in the Surgical Treatment of Breast Intraductal Carcinoma *in situ*. A. Coleman, L-M Wun, L. Kessler. National Cancer Institute, Bethesda, MD 20892.

This study examined trends in the surgical treatment of breast intraductal carcinoma *in situ* in the USA. The questions investigated were: (1) Is breast conserving surgery or mastectomy more often done? (2) Does the type of treatment vary by age, race, marital status, geographical area, or tumor size? Data on 2375 cases, of *in situ* breast carcinoma, from the standard 9 registries in the SEER database (1983-87) were used. In summary, 1) mastectomy is done more frequently than breast conserving treatment although the latter is increasing in use; 2) there is variability in the treatment by age ($p = 0.009$), geographical area ($p < 0.001$), year of diagnosis ($p < 0.001$), and tumor size ($p < 0.001$). These findings are consistent with the current lack of consensus in the literature (1) and point to the need for clinical trials on treatment of breast carcinoma *in situ*. As the incidence of breast cancer *in situ* increases due to early detection by mammography (2), recommendations for specific treatment which will provide local tumor control and better cosmetic results are needed.

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A Mathematical Model to Predict the Effect of Tamoxifen Chemoprevention. Bruce Trock, Ph.D., Eric Ross Sc.M.

There is currently no basis for making quantitative predictions about the impact of tamoxifen in healthy women that is grounded in epidemiologic data and mechanistic assumptions. We have modified the two-stage carcinogenesis model of Moolgavkar (1) and used it to simulate the impact of tamoxifen on age-specific breast cancer incidence for women with various risk profiles. The model incorporates parameters that represent the effects of reproductive and menstrual events on cell number and proliferation rates. The chemo-suppressive effect of tamoxifen may involve growth suppression of occult malignant cells, as well as inhibition of the promotion stage of carcinogenesis. Therefore, we explored extensions of the model to permit effects on clonal growth of malignant cells. A number of simulations were performed to explore changes in incidence associated with different assumptions about the biological effects of tamoxifen. We used the model to explore a number of currently unresolved issues relative to a chemoprevention trial that were recently discussed by Love (2), including (a) expected size of risk reduction, (b) length of time before an effect is observed, (c) effects in pre- vs. post-menopausal women, and (d) effects in "high" vs. "normal" risk women. We also examined the effects of age at the start of tamoxifen administration, and stopping tamoxifen after varying treatment durations. The model may also be useful as a more realistic basis for sample size estimation, as suggested by Byar (3).

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Genetic Epidemiology of Childhood Brain Tumors. Melissa L. Bondy, Ph.D., Edward Lustbader, Ph.D., Louise C. Strong, M.D.

A rare familial cancer syndrome involving childhood brain tumors (CBT), breast cancers, sarcomas and an array of other tumors has been described (Li and Fraumeni, 1969, 1988). This study describes the extent to which cancer occurs among relatives of CBT patients and estimates the contribution of heredity to CBT etiology. The study includes 243 confirmed CBT patients referred to the University of Texas M.D. Anderson Cancer Center between the years 1944 and 1983, diagnosed under the age of 15 years and resident in the U.S. or Canada. Family histories were obtained from the proband's first degree relatives (parents, siblings and offspring) and second degree relatives; by sequential sampling rules. To determine if excess cancer occurs in relatives, we compared the cancer experience in the study population to that expected in the general population using Connecticut Tumor Registry age-, race-, sex-, and calendar year-specific rates. The standardized incidence ratio (SIR) for cancer among 1099 first and second degree relatives was 0.88 (39 observed (O) and 44.18 expected (E); 95% confidence interval (CI)=0.63-1.21). A significant excess of colon cancer was observed among the proband's first degree relatives (O/E=5/1.61; 95% CI=1.00-7.24). Segregation analysis supported multifactorial inheritance in a small percentage of the families. There was no evidence for a major gene. Heredity played a role in the etiology of the CBT in 4% of the study families: including 4 (1.7%) due to known hereditary syndromes (nevroid basal cell carcinoma syndrome and von Recklinghausen neurofibromatosis), 4 (1.7%) with multifactorial inheritance and possibly 2 (1%) to the Li-Fraumeni cancer family syndrome.

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Cigarettes, Alcohol, Coffee and Caffeine as Risk Factors for Colorectal Adenomas. W.C. Lee, A.I. Neugut, G. Garbowski, K.A. Forde, J. Waye, M. Treat, C. Fenoglio-Preiser. Columbia University College of Physicians and Surgeons, New York, N.Y., 10032.

Adenomatous polyps (AP) are known to be precursor lesions for most cases of colorectal carcinoma, but risk factors are largely unknown. Between 4/86 and 3/88, structured interviews by telephone (71%) or self-administered (29%) were conducted on 2001 patients from three colonoscopy practices in New York City. Of these, 271 pathologically confirmed incident AP cases and 457 controls (without present or prior colorectal neoplasia) were compared by multiple logistic regression over quartiles, adjusting for age and sex. Significant odds ratios (highest:lowest quartile) were found for cigarette smoking (1.78, 95% C.I. 1.20-2.66), for coffee consumption (1.58, 1.02-2.44) and for caffeine consumption (1.54, 1.00-2.38). Significant linear trend P-values were also found for these variables. No significant association was observed for alcohol consumption (0.88, 0.58-1.35). After adjusting for coffee or caffeine consumption, cigarette smoking remained a significant factor while adjustment for cigarette smoking eliminated the coffee and caffeine associations with APs. Thus among the lifestyle factors tested, cigarette smoking appears to be a significant risk factor for APs.

Comparisons of Strategies to Prevent Breast Cancer Mortality. Deborah J. Bowen, Ph.D., Nicole Urban, Sc.D., David Carrell, Ph.D., Susan Kinne, Ph.D.

A health system is intended to meet the health needs of the population. In the face of continuing demands for choice among ways to invest in breast cancer control, a particular decision-making system, cost-effectiveness analysis, is used to compare primary versus secondary (1) versus tertiary (2) prevention of breast cancer mortality.

Results show that the cost-effectiveness of screening for breast cancer using mammography as compared with treating clinically present disease still remains debateable. The cost-effectiveness of screening can be improved by screening biennially rather than annually, because 75% of the effectiveness can be achieved at half the cost, yielding a cost per year of life saved of \$25,728. However, the dietary intervention program saves approximately the same number of life years (99%) as screening at less than 18% of the cost per year of life saved. Although biennial screening is an improvement over annual screening, it does not compare favorably with the dietary intervention because the dietary intervention saves more years of life at a lower cost per year of life saved. These results will be discussed in terms of allocating resources for prevention strategies.

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Staging Communities' Readiness to Change. Deborah J. Bowen, Ph.D., Susan Kinne, Ph.D., Nicole Urban, Sc.D.

Community interventions to change health related behavior are currently the focus of much research and practice. Understanding the readiness of a given community to make or support such changes is an essential first step in the process. There is currently no standardized instrument or model available to assess readiness to change at the community level. This paper will present such an instrument and describe the process of assessing a community's readiness to change. The readiness to change model from smoking cessation (1) was combined with the literature on community change (2) to form the basis for this instrument. Four communities were staged using this instrument. Results showed that communities which were more ready to change had more resources available to the health planners, more networking among community organizations, and more expressed enthusiasm for new and innovative projects. The use of this instrument helped in the planning of interventions to increase mammography use among women in a target population. The use of this technique will be valuable to any health professional planning community programs and interventions.

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Increasing the Effectiveness of Worksite Smoking Policies as a Strategy to Reduce Employee Smoking Behavior. Susan E. Sullivan, PhD, MPH, Victor J. Strecher, PhD, MPH and Donald R. Shopland.

In addition to reducing exposure to environmental tobacco smoke, restrictive smoking policies in the workplace hold great promise for reducing cigarette consumption and the prevalence of smoking among adults in the workforce (1). Although several studies found reductions in smoking at work and/or overall consumption (2,3,4), none of these found substantial quit rates among employees exposed to a worksite policy. The effect of worksite smoking policies on behavior change has yet to live up to the expectations of many, including smokers themselves (4). Drawing on three worksite surveys conducted by the authors, this presentation identifies and discusses several factors that may account for a relatively weak association between policy and reductions in smoking, and offers specific recommendations to increase the impact of worksite smoking restrictions on behavior change. The data suggest that many employees do not know what their worksite's smoking policy is, enforcement is inadequate, and employees have reported that compliance is much lower than employers estimate. Under these circumstances, any positive effect the policy might have on reducing smoking are likely to be diminished. These findings suggest that simply having a smoking policy on paper may not be enough to facilitate behavior change, but that greater attention must be given to implementation aspects of worksite smoking policies if this strategy is to be an effective means of reducing smoking among working adults.

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"The Relationship Between Nutrition & the Development of Cancer in Men at High Risk for AIDS", Duncan, Debra, Ph.D. (candidate), Rosenbaum, Ernest, M.D.

The study utilized data from the San Francisco Mens Health Study (SFMHS) to explore the relationship between dietary intake and subsequent development of Kaposi's Sarcoma (KS) and other cancers in a cohort of men at high risk for AIDS.

The SFMHS is a prospective study observing the natural history of AIDS conducted on a probability sample of 1034 single men aged 25 to 54 years who resided in San Francisco with the highest cumulative AIDS incidence through December 1983. As of 1988, 900 men were still in the study, and their immune function and other variables continue to be monitored every 6 months.

In 1984, dietary information was collected during the first wave of SFMHS data collection, using the Health Habits and History Questionnaire (HHHQ), a food frequency questionnaire developed at the National Cancer Institute (NCI).

The study took place as an adjunct to the original study of the natural history of AIDS, and as an adjunct to a study that is exploring the relationship between dietary intake and nutritional status determined at study baseline, and subsequent development of impaired immune function or development of AIDS.

Cancer Control in a Community Hospital - A Five Year Experience

Applied Cancer Control - The transfer of Cancer Control to Medical Practice has been a stated goal of the National Cancer Institute. (1) Consistent with this goal, a Cancer Control Program of Education, Prevention, and Detection was established in June 1985 in a Community Hospital; the Audrain Medical Center, Mexico, Missouri. Asymptomatic participants were screened with a life-time medical history obtained, cancer risk factors assessed and site-specific physical examination carried out. Emphasis was on the five major cancer sites of skin, breast, colorectal, prostate, and cervix. This direction was provided by the experiences of others involved in large scale cancer screenings. (2) (3) (4) (5). Attention was also given any other site or symptom that was a concern to the participant. Mammograms and Papsmeears were performed. All participants had Hemoccult II fecal occult blood studies. One-on-one counselling was encouraged and appropriate preventive strategies were discussed. A report of the visit was promptly mailed to the physician and a copy to the participant.

Results: One proven cancer has been diagnosed in every 35 participants.

Conclusion: There is a strong professional and public support for a community hospital based cancer control program. The program must be geographically accessible, reasonably priced, and conducted with a demonstrated level of competence.

**Cancer Prevention Education
in U.S. Medical Schools**

Robert M. Chamberlain, Ph.D., Richard F. Bakemeier, M.D., Richard E. Gallagher, Ph.D., Joseph F. O'Donnell, M.D., Charles E. Kupchella, Ph.D., Janet A. Parker, M.D., George J. Hill, M.D., C. Michael Brooks, Ed.D.

The Cancer Education Survey collected data from 125 of 128 U.S. Medical Schools on the current status of cancer-related educational activities for undergraduate medical students. The study was conducted by a Steering Committee of the American Association for Cancer Education, with funding from the American Cancer Society. The survey obtained data concerning institutional characteristics in support of undergraduate medical student cancer education, i.e. administrative structures, current cancer-related curricula, sources of financial support, and anticipated changes in these characteristics.

Institutions were also queried on specific topics of cancer prevention, detection, and diagnosis that might be taught as identifiable areas of instruction for medical students. Three-fourths of the 125 institutions had a lecture on the principles of cancer screening and among those, nearly three-fourths classified it as a part of a required course or rotation. Detection of common cancers is taught in virtually all institutions. The least likely cancer prevention lecture topics are related to smoking prevention and cessation, a well verified cancer risk. Also, no consistent pattern emerges which might indicate that association with a cancer center imparts to a medical school a greater emphasis on delivery of cancer prevention topics.

Experience with a Cancer Prevention Clinic. Bassford T, Hauck L, Santa Cruz V, Rosenberg R, Modiano M, Alberts D.

The National Cancer Institute objectives for the year 2000 emphasize primary prevention, early detection and attention to high risk groups (1). The Cancer Prevention Clinic (CPC) at the Arizona Cancer Center provides assessment of patients at increased risk of cancer due to family history, lifestyle and occupation. Risk assessment is based on use of a focused cancer health risk appraisal tool (2), family genograms, personal health history and physical examination. Patients and referring physicians receive a prevention plan with recommendations for lifestyle changes and early detection regimens, developed by a team including medical oncologists, family practitioners, genetic counselors, social workers, residents and students. Risk profiles are also provided for family members of patients when appropriate. Patients have ranged in age from 26 to 81 years. Fifty-Six percent were self referred, 22% physician referred, and 22% referred by another source. Fourteen percent of patients seen were at increased risk for colon cancer by virtue of having an affected first degree relative, an additional 3% were diagnosed as belonging to families with HNPCC, 6% had a family history suggestive of HNPCC (3). Sixteen percent of patients had a single first degree relative with breast cancer. An additional 5% were members of a family with a familial breast cancer syndrome while 15% had a suggestive family history (4). One percent were found to have an ovarian cancer family syndrome. Importantly, previous unrecognized risk factors for cancer were identified in 63% of patients. It is too early in the CPC experience to quantify endpoints such as mortality reduction. Patient satisfaction has been high (means of 4.14-4.67 in a five point Likert scale in a six item questionnaire). CPC patients have proven to be a motivated group for participation in cancer prevention and control research activities.

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Linda K. Birenbaum, RN, PhD, Perry Watts, BS, MSS
Identifying Bereaved Children's Problems and Educating Parents

Purpose

This paper provides a conceptual and empirical description of the most frequently reported sibling problems prior to and after the death of a child from cancer and examines the psychometric properties of scales measuring the psychosocial and physiological reactions to loss.

Methods

Secondary analysis of a prospective longitudinal study of siblings response to dying and death of a child from cancer was conducted. The Child Behavior Checklist (CBCL) was used as a source of extracting 42 items that represented the children's bereavement literature. The CBCL has been used in other children's cancer studies and has demonstrated reliability and validity. Cronbach's alpha was run on two scales: psychosocial and physical symptoms. These findings were compared to normative data that included children who were referred for mental health services and a control group of nonreferred children.

Results

Bereaved children's symptomatology is midway between normal children and children referred for mental health problems. Children's bereavement conforms to the adult literature in that the anniversary date heightens bereavement symptomatology. Parents assessment of children are moderately correlated with teacher's assessment.

Conclusions

Children's bereavement responses can be measured by 42 items that can be quickly administered to parents. Bereaved parents can accurately describe their children's symptoms. These items could be used as criteria for selecting children who need special intervention. Intervention with these children should prevent bereavement problems in adulthood.

The Importance of Qualitative Demographic Variables in the Application of Cancer Prevention Community Interventions: The Case of Religious Organizations.
 Barbara L. Wells, Ph.D., Thomas M. Lasater, Ph.D.,
 Richard A. Carleton, M.D., and John W. Horn, M.Sc.

Increasingly, religious organizations (ROs) are being used as channels for cancer control and prevention. Although studies of disease prevention activities in religious organizations have thus far demonstrated many successes(1-3), rarely are cultural profiles of these institutions compiled prior to or during the delivery of health programming. Such profiles can be integral to planning and implementing intervention strategies for cancer prevention in the substantial and diverse populations served by ROs. This presentation reports on a study conducted in 20 ROs prior to a multifactorial health intervention delivered in them. An extensive cultural profile was developed of each RO. Collectively, 28 qualitative variables were found to adequately describe the nature of the activities within the ROs, and can affect the nature of the disease prevention efforts in each institution. Each of these variables and its components will be presented in terms of the social and demographic patterns of the membership, leadership, and activity characteristics of the ROs.

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RECRUITMENT OF MINORITIES TO CLINICAL TRIALS: PHYSICIANS AS A REFERRAL SOURCE. Paola Villar-Werstler, B.S., Lois J. Loescher, M.S., R.N., Manuel R. Modiano, M.D., David S. Alberts, M.D.

Recruitment of minorities to clinical trials is low. Preliminary figures from the National Cancer Institute show that 7% of minorities are enrolled in clinical trials compared with 22% of the general population (personal communication, C. Baquet). Physicians' hesitations to enroll patients into clinical trials contribute to this problem.(1) The objective of our study was to educate physicians with minority patients about clinical trials. Sixty-six physicians in Tucson were given educational materials: the NCI's pamphlet on clinical trials, a brochure designed for this study, and the Arizona Cancer Center(ACC) clinical trials newsletter. A questionnaire was mailed to 35 physicians who personally met with the investigator to determine their minority patient population, referring practices regarding clinical trials, and reactions to the educational intervention. Twenty-nine (83%) responded and the majority (55%) felt that the educational approach was beneficial although its cost-effectiveness should be evaluated. Following the intervention, three (10%) of the physicians referred minorities to clinical trials as compared to a national average of 3%.(2) Enrollment of minorities to clinical trials at the Arizona Cancer Center has increased from 13.4% in 1987 to 22.0% and 41.5% in 1988 and 1989, respectively.

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2. Merz B. NCI Seeks to Boost Study Participation. *JAMA* 260 (10):1337, 1988.

Effect of Setting of Physician Practice on Cancer Screening Rates of Patients. C. Burke Sands, M. Daly, M.D., Ph.D., S. Workman, M.P.H., J. James, PA-C, D. Gillespie, and P. Engstrom, M.D.

Although at increased risk for cancer, older adults are screened less often than guidelines recommend (1). Many barriers prevent the delivery of early detection and disease prevention activities in the primary care setting (2). A multi-staged educational program was developed to improve cancer screening rates in older adults by addressing the barrier of poor patient/physician communication. Community residents and their primary care physicians were targeted. During an educational program in group settings, information was collected on the individual's screening history, cancer knowledge and attitudes, level of communication with their physicians, and physician's name. Individuals were encouraged to communicate with their physicians about cancer screening. We then conducted interviews with their primary care physicians.

Results indicated that patient reported screening rates were related to the type of setting of their primary care physicians. Patients of solo and group private practitioners reported lower rates of adherence to screening recommendations than those seeing physicians in clinic settings. Fifty-seven percent of the women receiving primary care from physicians in solo or group private practice reported a recent mammogram while seventy-nine percent of those receiving care in a private, public, or hospital outpatient clinic reported a recent mammogram ($p < .001$). Fifty-three percent of patients of solo/group practitioners reported recent stool blood testing versus seventy-six percent of those seen in a clinic setting ($p < .001$). These differences are not explained by age or educational level and suggest that barriers unique to private solo or group practices may result in underutilization of cancer screening.

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- 2 Becker, MH and Janz, NK. Practicing Health Promotion: The Doctor's Dilemma. *Annals of Internal Medicine* 113(6), 1990.

Strategies for Adherence Enhancement in Cancer Prevention Trials. Lisa Giordano, M.A., J. Atwood, Ph.D., F.A.A.N., L. Sennott-Miller, Ph.D., D. Alberts, M.D., and D. Earnest, M.D.

As part of an interdisciplinary approach to studying the effectiveness of various chemopreventive agents in Phase II and III clinical prevention trials, an Adherence Core of scientists from various behavioral science disciplines has been actively guiding strategies for assessing and enhancing adherence and compliance in four community-based studies. These strategies have been developed based on a theoretically guided model of Health Behavior in Cancer Prevention (1). The adherence interventions are both individualized to target adherence failures and generalized to promote good adherence in all study participants. All interventions are based on specific model variables which are hypothesized to impact adherence either concomitantly or uniquely. These variables include: demographics, social support, health status, knowledge about colon cancer, satisfaction with the client/provider relationship, health threat (severity and susceptibility), threat reduction (benefits/barriers ratio), self-efficacy, health locus of control, and health value orientation. Health Behavior Questionnaires are administered at baseline and upon adherence failure so that profiles may be generated which indicate those variables which need to be targeted for an individualized intervention when adherence is less than 75%. Newsletters are distributed throughout the trial which are also based on the model variables above and target specific variables at times when they are predicted to have the most impact on adherence as part of the generalized intervention. This presentation will outline both the generalized and individualized adherence enhancement strategies which can be adapted for similar studies, and for Phase IV and Phase V trials.

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Innovative Roles of Nurse Practitioners in Doing Cancer Prevention Work with the Poor. Nancy Lim, R.N., M.S.N., F.N.P., Masa Rambo, R.N., M.S., F.N.P., Mark Renneker, M.D.

A nurse practitioner managed clinic for cancer prevention and early detection with the poor has been developed as part of an American Cancer Society national demonstration project in a predominantly African American inner city community (West Oakland, CA) (1). Nurse practitioners are the primary clinicians in this project. Their work includes assessing cancer risks, providing education about cancer, teaching self examination techniques, referring for specialty screening procedures, and providing overall case management. A presentation on this pilot project will include a description of the ways nurse practitioners can be effectively utilized in doing cancer prevention with the poor (2). Data from a study in progress on patients' perceptions of nurse practitioners working in these expanded capacities will also be presented.

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ATBC LUNG CANCER PREVENTION STUDY. Olli P. Heinonen,¹ Demetrius Albanes,² Jarmo Virtamo,¹ Philip R. Taylor,² Jaason Haapakoski,¹ Brenda K. Edwards,² Matti Rautalahti,¹ Anne Hartman,² Juni Palmgren,¹ and Jussi K. Huttunen.² ¹National Public Health Institute, Helsinki 00140, Finland and ²National Cancer Institute, Bethesda, MD 20892.

The Alpha-Tocopherol, Beta-Carotene Lung Cancer Prevention Trial, or ATBC Study, is investigating the efficacy of alpha-tocopherol (50 mg) and beta-carotene (20 mg) in a double-blind, randomized 2x2 factorial design trial aimed at preventing lung cancer among 50-69 year old male smokers. After the completion of a feasibility study (1), recruitment for the full-scale trial took place between 1985 and 1988, and the trial ends in 1993 after an average follow-up of over six years. A postal survey screening for potential trial participants was sent to 291,000 men living in southern Finland, and 76% responded. Of these, 25% were current smokers (≥ 5 cigarettes daily), of whom 80% wished to participate. We invited the smokers willing to participate (43,000) to one of the 14 study clinics, and 29,200 were randomized after eliminating men who had stopped smoking (2800), who had cancer, severe coronary heart disease, or took carotene or tocopherol supplements regularly (4200), who no longer wanted to participate (3900), or with whom we had no further contact (2700). The number entered represents 10% of age-eligible men in the areas surveyed. Of the 29,200 men randomized, 22,600 (77%) remain on study, and men completing four years of follow-up showed a 23% cumulative dropout rate (excluding deaths, 19%). Compliance with the daily capsule regimen is high, with 94% of participants taking over 90% of their allotted capsules. In a sample of participants, serum levels of beta-carotene and alpha-tocopherol increased significantly in the respective active treatment groups. Smoking cessation has occurred at an annual rate of 4%. To date, there has been no significant agent-related toxicity. The successful start of the ATBC Study demonstrates the feasibility of such a large-scale trial for the prevention of a common, hard-to-treat cancer.

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ABSTRACTS

CARET PARTICIPANTS

THE CAROTENE AND RETINOL EFFICACY TRIAL (CARET): A CASE STUDY FOR THE SYMPOSIUM ON STRATEGIES FOR CANCER PREVENTION TRIALS. Gilbert S. Omenn, CARET co-investigators and staff, Seattle, WA

CARET is a randomized, placebo-controlled, double-blind trial of the combination of beta-carotene 30 mg/day and vitamin A (25,000 IU retinyl palmitate/day) in populations at high risk for lung cancer: smokers and former smokers, and asbestos-exposed workers who smoked. The trials was proposed in 1982 as part of our Cancer Prevention Research Unit and funded in 1983. The medicines became available in mid-1985. Pilot studies demonstrated achievement of recruitment goals, negligible toxicity, and high compliance. The smokers cohort consisted of 1029 women and men, age 50-69, recruited from health insurance rolls. The asbestos workers cohort of 816 men, age 45-74, was recruited from workers compensation systems, unions, physicians, and lawyers. In 1988 these participants became the Vanguard population for CARET, which aims to randomize a total of 13,700 smokers and 4300 asbestos-exposed workers in study centers in Seattle, Portland, San Francisco, Baltimore, Connecticut, and Irvine, CA. As of 12/31/90, 6245 participants have been randomized.

We will introduce multiple practical aspects of developing and managing this scale of cancer prevention trial. Thornquist will present our strategy and methods for monitoring risk factors during the accrual period, to adjust sample size requirements and cost projections. Subsequently, our group will present posters on training and certification, recruitment, data management, quality assurance, symptom management, endpoints, and cost projections.

USING THE ACCRUAL PERIOD TO UPDATE SAMPLE SIZE ESTIMATES IN CARET. Mark D. Thornquist and CARET co-investigators and staff, Seattle, WA

The Carotene and Retinol Efficacy Trial (CARET) is a ten-year chemoprevention study of lung cancer that plans to randomize approximately 18,000 asbestos-exposed workers and heavy smokers. CARET is built upon a three-year pilot study that randomized 1,845 participants. The sample size for CARET depends on nine factors: accrual timing, adherence to the study protocol, lung cancer incidence in the study population, loss of participants to competing risks, maximal potential chemopreventive effect, time lag to full effectiveness of the study vitamins, loss of participants to follow-up, p-value, and power. Since the accrual period for CARET will last several years, we are using that time to monitor the first four of these factors and to update the estimated sample size as needed. Accrual timing is monitored through actual accrual numbers and projections of future accrual; protocol adherence is monitored through mean medication rate; and lung cancer incidence and loss to competing risks are projected based on the distribution of time-dependent risk factors (such as age and smoking history) for lung cancer and death in the accrued population. Carrying forward the pilot study participants into the full-scale trial is particularly valuable for this monitoring, since they provide the best information on long-range adherence to the protocol and rate of appearance of study endpoints. This evolving sample size estimate will account for secular trends in the distribution of risk factors. By including cost estimates, we can compare alternative accrual options.

As examples of the types of analyses that can be done, we can determine the effect on sample size if:

- half of all current smokers randomized in CARET quit smoking in the first year after randomization.
- we decrease the number of participants to be randomized while increasing follow-up time.
- we can re-activate half of those who drop out from the study.
- accrual at some study centers is delayed.

TRAINING STAFF FOR MULTI-CENTER CHEMO-PREVENTION TRIALS. Bernedine M. Lund, Karen Anderson and Ann LaRose-Christianson, CARET staff, Seattle, WA

CARET (Carotene and Retinol Efficacy Trial) is a multi-center double-blind randomized chemo-prevention trial to determine whether retinol and beta-carotene can reduce the incidence of lung cancer high-risk populations: heavy smokers and asbestos-exposed workers. Six Study Centers (SC) have been organized to recruit and follow the projected 18,000 participants (not patients). The CARET Coordinating Center (CC) is responsible for the training of all SC staff, including interviewers who apply eligibility criteria and monitor participants for adverse effects. The CC developed extensive training procedures to assess staff knowledge and ability to perform all aspects of SC functions.

Training techniques include:

- workshops for SC managers, interviewers, and data coordinators
- video tape of limited physical exam
- review by interviewers and key-entry by data coordinators of five sample participant records constructed to highlight problems and errors
- CARET Pursuit exercise, a game based on CARET protocol (designed in the format of Trivial Pursuit) which has proved very popular with SC staff
- written exercises organized by job function. The SCs send the exercises to the CC for grading and feedback.
- observation on-site by CC staff using task-specific checklists. SCs use the same checklists to evaluate staff performance throughout the year and for training new staff.
- annual quality assurance site visits by the CC and on-site training sessions.

RECRUITMENT TO CHEMOPREVENTION TRIALS: THE CARET EXPERIENCE. Gary E. Goodman, CARET co-investigators and staff, Seattle, WA

The methods of recruitment to chemoprevention trials vary between specific target populations. For example, recruitment of former cancer patients who have an increased incidence of second primary or patients with premalignant conditions such as familial polyposis is relatively straightforward. These patients are integrated into the medical community and are frequently seen by medical oncologists.

Recruitment of populations with increased cancer risk factors but who are healthy presents a more difficult challenge. These populations are not in regular contact with the medical community and frequently do not appreciate their own risk factors. In the CARET Seattle Study Center, we have recruited smokers and recent ex-smokers via a mailing to age-selected (50-69 years old) subscribers of the Blue Cross/Blue Shield Insurance plans in the Puget Sound region. This mailing consisted of an informational letter and a five-item questionnaire to evaluate eligibility and interest. The return rate for this questionnaire, eligibility, and willingness to join the trial varied by county, age group, and sex. For example, among 40,622 Blue Shield subscribers residing in King County (Seattle and environs), 10.9% were interested in joining the trial and 2.0% were ultimately randomized. Among 49,568 Blue Cross subscribers, only 3% were interested and 0.9% were ultimately randomized. Our results suggest that recruitment from even relatively homogeneous populations (age-selected health insurance subscribers) will vary. The low rate of return of the initial questionnaire (14.4% and 4.1% respectively) suggests that efforts to increase public awareness and interest in cancer prevention may improve recruitment.

**DATA MANAGEMENT FOR A LARGE-SCALE, LONG-TERM
CHEMOPREVENTION TRIAL: EXPERIENCES OF CARET.**

Mark Schmidt, Jo Ann Hartline, CARET staff, Seattle, WA

The Carotene and Retinol Efficacy Trial (CARET) Coordinating Center has responsibility for managing and analyzing data collected by six CARET Study Centers. CARET presents challenging data management problems due to the combination of:

- the large number of participants (18,000)
- the large number of data items collected per average contact (over 400) to monitor symptoms, risk factors, adherence, endpoints and other study events
- the large number of participant contacts over the duration of the trial (10 years)

We developed systems to:

- monitor and project recruitment and accrual
- monitor data, track vitamins and serum samples
- track the occurrence and evaluation of endpoints
- provide feedback reports to the Study Centers

We present our experience with a distributed data management system, and reasons for our increasing tendency to centralize this system, to promote consistency, efficiency and cost-effectiveness.

**DESIGN OF QUALITY ASSURANCE PROGRAMS IN
CHEMOPREVENTION TRIALS.**

Garnet L. Anderson, CARET co-investigators and staff, Seattle, WA

The Carotene and Retinol Efficacy Trial (CARET) is designed to recruit 18,000 high-risk individuals and follow them for an average of 7 years. During this period, CARET will collect 400,000 vials of serum, dispense 54 million capsules, document 1700 cancer endpoints and 2700 deaths, conduct 185,000 in-person interviews and 150,000 telephone interviews, perform 20,000 spirometries and review 4300 chest X-rays. We focus our quality assurance monitoring on the data on which the analyses and results rely most heavily.

For CARET serum collection and analyses we adopted the case-cohort design¹. We randomly sample a 10% cohort of participants whose serum will be analyzed prospectively for carotenoids, retinol and retinyl palmitate. These results track secular trends, lag-time effects of supplementation, and adherence to placebo and active treatment. An independent 10% sample of participants is selected for collection of blind duplicate samples to measure intra-run variability. Other quality assurance procedures adopted in our laboratory are: blinding laboratory personnel to treatment assignment, forming large high and low serum pools to measure intra- and inter-run reliability, and participating in the National Institute of Standards and Technology Round Robin Analyses to assure external validity.

Quality assurance measures for vitamins include maintaining separate storage rooms for the supplements prior to labelling with participant identification, visual and laboratory checks on all incoming shipments to assure uniformity and proper preparation, and laboratory checks on a sample of capsules returned by participants to compare to their assigned treatment.

1. Prentice R. A case-cohort design for epidemiologic cohort studies and disease prevention trials. *Biometrika* 1986;73:1-11.

**ENDPOINT REVIEW PROCESS IN A MULTICENTER LUNG
CANCER CHEMOPREVENTION TRIAL.** Karen Anderson, Bill Wilson,
Gilbert S. Omenn, and CARET co-investigators and staff, Seattle, WA

One of the major roles of the Coordinating Center for the Carotene and Retinol Efficacy Trial (CARET) is to track, evaluate and confirm the endpoints of 18,000 participants to be followed at six Study Centers. The primary endpoint is lung cancer or malignant mesothelioma (pleural or peritoneal). The secondary endpoints are diagnoses of other malignancies and mortality from all causes. We project 670 lung cancer cases. Endpoint data collection begins when a Study Center (SC) is notified that a randomized participant has been diagnosed or suspected of having cancer or the participant has died. Since this is not a treatment trial, data collection requires active follow-up. The SCs request information from various sources and submit medical records and death certificates to the Coordinating Center's Endpoint Specialist, who prepares case reports on each endpoint and codes following SEER and ICD-9-CM guidelines. The study's pathology consultant reviews pathology and cytology reports and examines specimens for every case of lung cancer, mesothelioma, and unknown primary with tumor in the lung. An oncologist and an internist review all available evidence supporting the occurrence and classification of an endpoint. Endpoints are classified according to the extent and the reliability of supporting evidence. The Endpoints Committee Chairman evaluates discrepancies between the reviewers. The case is reviewed by the Endpoints Committee if the Chairman is unable to agree with either of the reviewers. All endpoints data are reviewed semi-annually by an external (international) Safety and Endpoints Committee for CARET.

SIDE EFFECT MANAGEMENT ON CHEMOPREVENTION TRIALS.
Gary E. Goodman, CARET co-investigators and staff, Seattle, WA

Chemoprevention agents have a potential for use in a healthy cancer-free population and must have a low incidence of both short- and long-term side effects. Even though they are administered to high-risk groups, the absolute risk of cancer is low in these individuals. Any agents causing morbidity, mortality, or side effects requiring medical intervention may be more of a detriment than a health benefit.

Chemoprevention agents must undergo careful evaluation for common and rare, as well as major and minor side effects. In CARET, we have designed a symptom assessment, monitoring, and management program for participants receiving beta-carotene 30 mg/day and retinol 25,000 units/day. Two pilot studies testing these agents initiated recruitment in January 1985. Participants in these trials were later combined to form the Vanguard Population for CARET. Vanguard participants are evaluated at three-month intervals by either standardized telephone health questionnaire or a clinical visit with physical examination. Twelve symptoms and physical signs are graded on a standardized grading scale. Participants who have an increase in their symptom grade above a standardized "threshold" level are placed on symptom management. The study vitamins are discontinued and held until threshold grade symptoms resolve. The participant then receives a series of challenges with the study vitamins. Those symptoms persisting for two months after discontinuing the study vitamins are assumed to be unrelated. Those symptoms which recur with each challenge are considered to be associated with the study vitamins. This symptom management program is designed to maintain participants on full dose vitamins unless treatment-related symptoms are clearly established.

**BENEFITS AND APPLICATION OF ONGOING COST ANALYSIS
FOR MULTI-CENTER CHEMO-PREVENTION TRIALS. Cim
Edelstein, Addy Tseng, CARET co-investigators and staff, Seattle, WA**

Budget analysis and cost controls are as essential to the success of a multi-center chemo-prevention trial as the design and execution of the scientific plan. In addition to justifying the study for funding, well-planned and comprehensive cost analysis provides principal investigators, managers, and funding sources with answers which are crucial to development and successful completion of a prevention trial.

The CARET cost analysis model considers sample size parameters and financial estimates to optimize both trial design and cost effectiveness. Sample size calculations determine the number of study centers and their accrual schedules, mix of asbestos-exposed workers and heavy smokers, and duration of the study. These data, design implementations, and cost factors drive the cost analysis model. The key cost factors are variable unit costs that are associated with each task and fixed costs which are not task oriented, for example, rent.

The CARET cost analysis model, which can be modified for other programs, generates specific financial and planning benefits:

- generating savings through protocol changes that do not interfere with scientific validity
- illustrating trade-offs between increasing recruitment size and reducing the duration of the trial
- accommodating manpower constraints by shifting work from regional Study Centers to the Seattle based Coordinating Center
- highlighting the consequences of accrual shortfalls
- justifying expansion of recruitment at an existing study center versus addition of a new study center

