Cancer Study History

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Abstract: Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries. This paper collects some literatures for cancer study history.
[Smith MH. **Cancer Study History.** *Cancer Biology* 2011;1(3):13-76]. (ISSN: 2150-1041). http://www.cancerbio.net. 3

Keywords: cancer; biology; research; life; disease; history

1. Introduction

Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Literatures

Anaissie, E. J., T. H. Mahfouz, et al. (2004). "The natural history of respiratory syncytial virus infection in cancer and transplant patients: implications for management." Blood **103**(5): 1611-7.

Respiratory syncytial virus (RSV) has been reported to cause severe morbidity and mortality among cancer patients receiving chemotherapy with or without autologous peripheral blood stem cell transplantation (APBSCT). However, little is known about the natural history of this infection in these patients, and current standard practice, aerosolized ribavirin plus intravenous immunoglobulin (IVIG), is extremely expensive, difficult to use, and not supported by controlled clinical trials. The purpose of this observational study was to determine the frequency, seasonality, morbidity, and mortality of RSV infection in a group of cancer patients receiving cytotoxic chemotherapy with neither ribavirin nor IVIG treatment. During the period of October 3, 1997, through October 14, 1998, 190 cancer patients (median age, 58 years; 71 women) underwent viral nasopharyngeal washing prior to chemotherapy. Multiple myeloma (MM) accounted for most patients (147, 77%). RSV was recovered from cultures taken from 71 patients (37%) throughout the year, although more frequently during fall and winter seasons (P <.001) than spring and summer. Serious respiratory complications developed in 19 (27%) of 71 RSV-positive patients versus 24 (20%) of 119 patients whose RSV cultures were negative (P =.384). The presence of renal failure or increased lactate dehydrogenase (LDH) prior to chemotherapy and the development of mucositis were the only predictive factors for severe respiratory complications. Recovery of RSV from nasopharyngeal washings among cancer patients is common, occurs throughout the year, and does not appear to increase serious morbidity or mortality. RSV infection may not necessarily be a contraindication for APBSCT or an indication for therapy with aerosolized ribavirin and IVIG.

Andersen, M. R., D. Bowen, et al. (2003). "Awareness and concern about ovarian cancer among women at risk because of a family history of breast or ovarian cancer." Am J Obstet Gynecol **189**(4 Suppl): S42-7.

Research on women at risk for breast cancer because of family history suggests that a substantial proportion need education and counseling to assist them in their efforts to understand their risk of breast cancer and that some do not get appropriate breast cancer screening. Although women at high genetic risk for breast cancer are at elevated risk for ovarian cancer as well, few studies have examined these women's needs for education and counseling about ovarian cancer risk. This study examined awareness of ovarian cancer, perceived risk of breast and ovarian cancer, interest in genetic testing, and use of screening for breast and ovarian cancer in a population-based sample of women at high risk for breast and ovarian cancer because of a strong family history of cancer at one or both sites. We found that most high-risk women are not getting the information and care they

need with respect to their risk for ovarian cancer. Almost 75% have not heard much about their risk for ovarian cancer. More than 90% failed to use 1 or another of 2 possible tests used for ovarian cancer screening regularly.

Andriole, G., D. Bostwick, et al. (2005). "The effects of 5alpha-reductase inhibitors on the natural history, detection and grading of prostate cancer: current state of knowledge." J Urol **174**(6): 2098-104.

PURPOSE: The Prostate Cancer Prevention Trial (PCPT) showed that the 5alpha-reductase inhibitor (5ARI) finasteride significantly decreased the 7-year period prevalence of prostate cancer vs placebo. However, Gleason score 7-10 tumors were significantly more common in the finasteride vs the placebo group. We considered data on the effects of 5ARIs on prostate cancer natural history and detection. MATERIALS AND METHODS: A detailed review was performed of the literature identified from the MEDLINE database examining the effects of 5ARIs on prostate cancer prevalence and tumor histopathology. RESULTS: In PCPT there were fewer biopsies performed for cause in the finasteride vs the placebo group and the proportion of high grade tumors in the treatment groups did not diverge with time. Given that finasteride has an effect on prostate specific antigen and prostate volume, which are key factors in triggering prostate biopsies, they may be significant confounders of Gleason score results. Prostate shrinkage in the finasteride treated group may minimize biopsy sampling error. Furthermore, histological studies have shown that 5ARIs have a significant effect on prostate architecture, which can make the interpretation of prostate specimens in men treated with 5ARIs difficult. Further evaluation of PCPT findings will help determine the true nature of these observations. CONCLUSIONS: 5ARIs decrease the risk of prostate cancer but also alter the detection of disease through effects on prostate specific antigen, and prostate volume and histology. The weight of evidence suggests an artifactual effect of finasteride on Gleason grading in the PCPT. The role of 5ARIs for prostate cancer chemoprevention needs further examination before it can be considered for wide recommendation.

Aoki, K. (2006). "Early history of cancer epidemiology and prevention in Japan." Asian Pac J Cancer Prev **7**(2): 170-6.

Cancer epidemiological research has a long and distinguished history and as we continue our work in ever expanding new fields, molecular or otherwise, it is perhaps worthwhile to take time out occasionally to ponder what lessons we can learn from the past. Many of the paradigms which are presently accorded respect in fact were hinted at by very early work and it is fitting that we take a look at how previous developments knit with the present status of cancer research in different areas of the world. For this purpose the present review focuses on cancer epidemiology in Japan, in the hope of gleaning advantage from past experience in planning future programs.

Aucoin, M. W. and R. J. Wassersug (2006). "The sexuality and social performance of androgen-deprived (castrated) men throughout history: implications for modern day cancer patients." Soc Sci Med **63**(12): 3162-73.

Androgen-deprivation therapy (ADT) via either surgical or chemical castration is the standard treatment for advanced prostate cancer (PCa). In North America, it is estimated that more than 40,000 men start ADT each year. The side effects of this treatment are extensive and include gynecomastia, erectile dysfunction, and reduced libido. These changes strongly challenge patients' self-identity and sexuality. The historical term for a man who has been castrated is 'eunuch', now a pejorative term implying overall social and sexual impotence. In this paper, we review key historical features of eunuch social performance and sexuality from a variety of cultures in order to assess the validity of contemporary stereotypes of the androgen-deprived male. Data were taken from secondary sources on the history of Byzantium, Roman Antiquity, Early Islamic societies, the Ottoman Empire, Chinese Dynasties, and the Italian Castrati period. This cross-cultural survey shows that castrated men consistently held powerful social positions that yielded great political influence. Many eunuchs were recognized for their loyalty, managerial style, wisdom, and pedagogical skills. Furthermore, rather than being consistently asexual and celibate, they were often sexually active. In certain cultures, they were objects of sexual desire for males, or females, or both. Collectively, the historical accounts suggest that, given the right cultural setting and individual motivation, androgen deprivation may actually enhance rather than hinder both social and sexual performance. We conclude that eunuch history contradicts the presumption that androgen deprivation necessarily leads to social and sexual impotence. The capabilities and accomplishments of eunuchs in the past gives patients on ADT grounds for viewing themselves in a positive light, where they are neither socially impotent nor sexually chaste.

Bardia, A., P. Novotny, et al. (2009). "Efficacy of nonestrogenic hot flash therapies among women stratified by breast cancer history and tamoxifen use: a pooled analysis." Menopause **16**(3): 477-83.

OBJECTIVE: Various nonestrogenic therapies have been found to be effective in mitigating hot flashes, but it has been unclear whether the efficacy varies by whether women have had breast cancer and/or were taking tamoxifen. METHODS: This study used data from Mayo Clinic/North Central Cancer Treatment Group clinical trials that evaluated the efficacy of any nonestrogenic agent for hot flashes and had information on breast cancer history or tamoxifen use. Statistically significant changes from the fourth treatment week versus the baseline week, using individual patient data, were assessed using Student's t test. RESULTS: A total of 1,396 women from 20 hot flash studies were eligible for analysis. Overall, women without breast cancer had a similar percentage of baseline hot flash score at week 4, as did those with breast cancer (53% vs 50%, P = 0.92). Women who were not taking tamoxifen had a significantly lower percentage of hot flash score at week 4 as compared with those who used tamoxifen (54% vs 61%, P = 0.01). However, this was due to a higher reduction in hot flash scores in the placebo arms among women not receiving tamoxifen; the percentage reduction in hot flash scores at week 4 from baseline in the active therapy arms of the randomized placebo-controlled trials (ie, excluding placebo arms) was similar among the tamoxifen users and nonusers (difference in mean percentage reduction, 5.7; 95% CI, -1.76 to 13.16). CONCLUSIONS: Some nonestrogenic therapies seem to be useful for reducing hot flashes, irrespective of the etiology of hot flashes.

Baumgartner, K. B., W. C. Hunt, et al. (2004). "Association of body composition and weight history with breast cancer prognostic markers: divergent pattern for Hispanic and non-Hispanic White women." Am J Epidemiol **160**(11): 1087-97.

Body composition and weight gain are breast cancer risk factors that may influence prognosis. The Health, Eating, Activity, and Lifestyle Study was designed to evaluate the relations of body composition, weight history, hormones, and lifestyle factors to prognosis for women with breast cancer. In the cross-sectional analysis of this cohort study specific to 150 Hispanic and 466 non-Hispanic White women in New Mexico diagnosed between 1996 and 1999, the authors hypothesized that obesity measures are associated with baseline prognostic markers and that these associations are modified by ethnicity. Ethnic-stratified multiple logistic regression analyses showed divergent results for a tumor size of 1.0 cm or more and, to a lesser extent, positive lymph node status. Among Hispanics, the highest quartile for body mass index (29.5 vs. <22.5 kg/m2: odds ratio (OR) = 0.16, 95% confidence interval (CI): 0.03, 0.84) and for waist circumference (> or =95.0 vs. <78.5 cm: OR = 0.09, 95% CI: 0.01, 0.78) was significantly associated with a reduced tumor size. In contrast, for overweight and obese non-Hispanic White women, there was an increased association with obesity-related measures, particularly striking for the highest quartile of waist circumference (OR = 2.76, 95% CI: 1.45, 5.26). These findings suggest that Hispanics may have a different breast cancer phenotype than non-Hispanic Whites, which associates differently with body composition and weight history.

Beebe-Dimmer, J. L., D. P. Wood, Jr., et al. (2004). "Use of complementary and alternative medicine in men with family history of prostate cancer: a pilot study." Urology **63**(2): 282-7.

OBJECTIVES: To describe the use of complementary and alternative medicines (CAMs) among men with a family history of prostate cancer and to evaluate the relationship between selected sociodemographic and behavioral characteristics and the use of CAMs. METHODS: Unaffected brothers of men diagnosed with prostate cancer were asked to participate in a short computer-assisted telephone interview. The survey focused primarily on the use of different vitamins, herbal supplements, and medications, some of which are marketed for prostate health or prostate cancer prevention. RESULTS: A total of 111 men completed the survey, representing 66% of eligible study subjects. Of the 111 men, 61 (55%) reported currently taking some form of CAM, with 30% taking a vitamin or supplement purported to have prostate-specific benefits. The prevalence of CAM use generally increased with increasing age; however, men who were younger than their affected brother at the time of the diagnosis of prostate cancer were more likely to use CAMs than were older brothers. CONCLUSIONS: Most men with a family history of prostate cancer take vitamins and supplements, some of which are believed to prevent future cancer occurrence. The results of this study and others provide some insight into the determinants of potentially beneficial health behaviors in high-risk individuals.

Benjamin, C., M. Flynn, et al. (2008). "The use of the life course paradigm and life course charts to explore referral for family history of breast cancer." Int J Nurs Stud **45**(1): 95-109.

BACKGROUND: Life course research methodologies are used extensively in historical and social science research. In 1998 the life course paradigm was introduced to provide a way of tracing the interplay of person and setting. The method has had a very limited use in nursing research, but in this study it was utilized as a way of capturing dynamic

change by placing the individual within a context of four domains; location in time and place, linked lives, human agency and timing of lives. OBJECTIVE: To describe the paradigm, review its use in healthcare research and provide a specific example of its use in healthcare. DESIGN: This paper discusses a novel method of creating life course charts for a qualitative study exploring the differing experiences of women referred from primary care to specialist services due to a family history of breast cancer. SETTING: A nurse-led breast cancer family history clinic in the UK. PARTICIPANTS: Twenty-two women. METHODS: Life charts were used in conjunction with a grounded theory approach to analyse data collected from semi-structured interviews. FINDINGS: Twenty-two life charts were created and the ability to layer the charts of multiple women to visualise similarities and differences aided the analysis. The life charts were a useful tool in the development of theoretical understandings and the psychosocial process of realisation of risk emerged as central to the initiation of referral. This was often apparent when approaching the age of an affected relative (anticipated onset) or when current circumstances emulate past experience (generational transference). CONCLUSIONS: This approach to charting complex psychological, social and contextual factors throughout the life course was methodologically beneficial and could have a wider utility in nursing and healthcare research. As a research tool it enhanced a holistic approach to patient care issues and was helpful as an aid to understanding health behaviours linked to familial risk.

Blichert-Toft, M., P. Christiansen, et al. (2008). "Danish Breast Cancer Cooperative Group--DBCG: History, organization, and status of scientific achievements at 30-year anniversary." Acta Oncol **47**(4): 497-505.

DBCG (Danish Breast Cancer Cooperative Group) constitutes a multidisciplinary organization established in 1975 by the Danish Surgical Society. The purpose involves first and foremost a nation-wide standardization of breast cancer treatment based on novel therapeutic principles, collaboration between experts handling diagnostic work-up, surgery, radiotherapy, medical oncology, and basic research, and, further, complete registration of relevant clinical data in a national data base attached to DBCG. Data are processed by the Secretariat personnel composed of statisticians, data managers, and data secretaries making current analyses of outcome results feasible. DBCG is run by the Executive Committee consisting of expert members appointed by their respective society. From 1978 the DBCG project gained widely accession from participating units, and since then nearly all newly diagnosed breast cancer incident cases are reported and registered in the national data base. Today, the data base includes approximately 80 000 incidents of primary breast cancer. Annually, the Secretariat receives roughly 1.5 million parameters to be entered into the data base. Over time DBCG has generated seven treatment programmes including in situ lesions and primary invasive breast cancer. Probands are subdivided into risk groups based on a given risk pattern and allocated to various treatment programmes accordingly. The scientific initiatives are conducted in the form of register- and cohort analysis or randomized trials in national or international protocolized settings. Yearly, about 4 000 new incident cases of primary invasive breast cancer and about 200 in situ lesions enter the national programmes. Further, about 600 women with hereditary disposition of breast cancer are registered and evaluated on a risk scale. The main achievements resulted in a reduction of relative risk of death amounting up to 20% and increased 5-year overall survival ascending from 60% to roughly 80%. This article is partly based on a Danish paper to be published in the Centenary Jubilee book of the Danish Surgical Society, 2008.

Bowen, D. J., E. Ludman, et al. (2003). "Achieving utility with family history: colorectal cancer risk." Am J Prev Med **24**(2): 177-82.

Family history of chronic disease is rapidly becoming a research tool for targeting participants at increased risk. Its current usefulness in clinical practice remains unknown. This paper details the possible utility and complications in using family history in a primary care setting, using colorectal cancer risk as the health issue. Where available, we cite data to support the issues that could arise. Where there are no studies, we invite further research. The potential of family history as a health improvement tool is still under review.

Brewer, B. G., R. A. Mitchell, et al. (2009). "Embryonic vaccines against cancer: an early history." Exp Mol Pathol **86**(3): 192-7.

Almost 100 years have passed since the seminal observations of Schone showing that vaccination of animals with fetal tissue would prevent the growth of transplantable tumors. Many subsequent reports have affirmed the general idea that immunologic rejection of transplantable tumors, as well as prevention of carcinogenesis, may be affected by vaccination with embryonic/fetal material. Following a decade of intense research on this phenomenon during approximately 1964-1974, interest appears to have waned. This earlier experimental work may be particularly pertinent in view of the rising interest in so-called cancer stem

cells. We believe that further work - perhaps involving the use of embryonic stem cells as immunogens - is warranted and that the results reviewed herein support the concept that vaccination against the appearance of cancers of all kinds is a real possibility.

Brudnak, M. A. and S. G. Hoener (2003). "Plato, Sun Tsu, and the Art of War (on cancer). Can we learn from history?" Med Hypotheses **60**(4): 603-6.

Cancer, in all its guises is on the rise along with the population growth. While not the leading cause of death in the world, it may soon garner that unfortunate honor. In the US, it is second only to heart disease. The 'war on cancer' declared in the US by Richard Milhouse Nixon is not being won. At present, treatment modalities are limited to resection, immunotoxins, radiation, chemotherapy, genomeceuticals, and variations on those themes. It is anticipated that with the emerging human genome data, most of these areas will be expanded, with the possible exception of radiation. However, all these approaches have two things in common. First, they have met with limited success. Second, they all work around the similar idea of containment and eradication in situ of the disease. This paper presents an alternative and novel way of looking at the research and treatment options for cancer taking two lessons from history. First, is Plato's dialectic where 'truth' is uncovered by examining a situation from two opposite directions at once. Second, from Sun Tsu's treaty on the Art of War, where he recommends that when faced with a superior opponent, one method of dealing with the situation is to provoke them, anger them, cause them to move. The second tactic wears out the opponent and presents them in a more favorable situation for assault. It is suggested herein that perhaps cancer can be attacked by first assisting its growth, and causing metastasis to a location more favorable to attack with the common mechanisms cited above.

Burke, W., J. O. Culver, et al. (2000). "Genetic counseling for women with an intermediate family history of breast cancer." Am J Med Genet **90**(5): 361-8.

Women with a family history of breast cancer often over-estimate their personal risk for cancer and may view themselves as candidates for genetic testing even when the likelihood of an informative test result is low. We report here on genetic counseling of women with an intermediate family history of breast cancer, defined as women who have one or more biological relatives with breast cancer but whose pedigree suggests a low likelihood of autosomal dominant transmission. A genetic counseling protocol based on traditional genetic counseling strategies was developed with additional components added to address the needs of women with moderately increased breast cancer risk. These additional components included information about non-genetic risk factors, comparisons of high and moderate risk pedigrees, and evaluation of personal risk based on both genetic and nongenetic risk factors. Most participants liked the genetic counseling and found it useful. At baseline, participants over-estimated both their personal risk of breast cancer and that of the average woman. After counseling, estimates of personal and average risk of breast cancer were lower, although both remained higher than actual risk. Most participants reported that they felt less worried about breast cancer after receiving their personal-risk estimate. At baseline, most women judged themselves to be candidates for genetic testing and expressed interest in testing. The number who considered themselves candidates for testing was reduced after counseling (60% versus 82%) but still constituted a majority. Similarly, interest in testing was partially reduced by counseling (60% versus 91%). We conclude that genetic counseling can help women with an intermediate family history of breast cancer to develop more accurate views of their risk, reduce their breast cancer worry, and aid some of them in developing a more realistic view of genetic testing.

Castellsague, X. (2008). "Natural history and epidemiology of HPV infection and cervical cancer." Gynecol Oncol **110**(3 Suppl 2): S4-7.

Cervical cancer is the most common cancer affecting women in developing countries. It has been estimated to have been responsible for almost 260 000 deaths annually, of which about 80% occurred in developing countries. Persistent infection by certain oncogenic HPV types is firmly established as the necessary cause of most premalignant and malignant epithelial lesions of the cervix and of a variable fraction of neoplastic lesions of the vulva, vagina, anus, penis, and oropharynx. There are more than 100 known HPV genotypes, at least 15 of which can cause cancer of the cervix and other sites. HPV 16 and 18, the two most common oncogenic types, cause approximately 70% of all cervical cancers worldwide. HPV, especially genotypes 6 and 11, can also cause genital warts. HPV is highly transmissible and it is now considered the most common sexually transmitted infection in most populations. Although most women infected with the virus become negative within 2 years, women with persistent high-risk HPV infections are at greatest risk for developing cervical cancer. Since the identification of HPV as the necessary cause of cervical cancer, HPV-based technology has become the centre of novel primary and secondary cervical cancer prevention strategies by the introduction of HPV testing in screening and of

HPV vaccines in preadolescent girls and young women. If implemented widely and wisely the deployment of these protocols has the potential to complete Papanicolaou's goal of cervical cancer eradication by extending the benefits of prevention to the developing populations of the world.

Cerhan, J. R., D. M. Grabrick, et al. (2004). "Interaction of adolescent anthropometric characteristics and family history on breast cancer risk in a Historical Cohort Study of 426 families (USA)." Cancer Causes Control **15**(1): 1-9.

OBJECTIVE: To determine whether the association of adolescent anthropometric characteristics with breast cancer is modified by a family history of the disease. METHODS: These interactions were evaluated in a historical cohort of 426 families of breast cancer probands diagnosed between 1944 and 1952 at the University of Minnesota. The occurrence of breast cancer and the measurement of risk factors in sisters, daughters, granddaughters, nieces and marry-ins was determined through telephone interviews and mailed questionnaires conducted from 1991-1996. Cox proportional hazards regression, accounting for age, birth cohort, adult body mass index (BMI), and clustering within families, was used to estimate relative risks (RR) and 95% confidence intervals (CIs) of breast cancer. RESULTS: Among 4632 women from 426 families available for analysis, there were 175 breast cancers. There was a strong interaction between degree of relationship to proband and relative weight at age 12 on breast cancer risk ($p < 0.001$). Among sisters and daughters of the probands, risk of breast cancer was slightly increased in those with below average weight at age 12 (RR = 1.55; 95% CI = 0.66-3.64), and strongly increased in those with above average weight (RR = 4.25; 95% CI = 1.71-10.5), compared to those with average weight. In contrast, among marry-ins, there was a weak positive association for those with below average weight at age 12 (RR = 1.61; 95% CI = 0.91-2.83), while there was an inverse association for above average weight (RR = 0.75; 95% CI = 0.26-2.16), compared to those with average weight. There were no significant interactions between degree of relationship to proband and height ($p = 0.55$), weight at age 18 ($p = 0.22$) and BMI at age 18 ($p = 0.63$) on breast cancer risk. CONCLUSIONS: Family history appears to modify the effect of obesity in early adolescence on subsequent breast cancer risk, and may identify differing etiologic pathways.

Chan, J. A., J. A. Meyerhardt, et al. (2008). "Association of family history with cancer recurrence and survival among patients with stage III colon cancer." Jama **299**(21): 2515-23.

CONTEXT: A family history of colorectal cancer in a first-degree relative increases the risk of developing colorectal cancer. However, the influence of family history on cancer recurrence and survival among patients with established disease remains uncertain. OBJECTIVE: To examine the association of family history of colorectal cancer with cancer recurrence and survival of patients with colon cancer. DESIGN, SETTING, AND PARTICIPANTS: Prospective observational study of 1087 patients with stage III colon cancer enrolled in a randomized adjuvant chemotherapy trial (CALGB 89803) between April 1999 and May 2001. Patients provided data on family history at baseline and were followed up until March 2007 for disease recurrence and death (median follow-up, 5.6 years). In a subset of patients, we assessed microsatellite instability (MSI) and expression of the mismatch repair (MMR) proteins MLH1 and MSH2 in tumor specimens. MAIN OUTCOME MEASURES: Disease-free survival, recurrence-free survival, and overall survival according to the presence or absence of a family history of colorectal cancer. RESULTS: Among 1087 eligible patients, 195 (17.9%) reported a family history of colorectal cancer in a first-degree relative. Cancer recurrence or death occurred in 57 of 195 patients (29%; 95% confidence interval [CI], 23%-36%) with a family history of colorectal cancer and 343 of 892 patients (38%; 95% CI, 35%-42%) without a family history. Compared with patients without a family history, the adjusted hazard ratios (HRs) among those with 1 or more affected first-degree relatives were 0.72 (95% CI, 0.54-0.96) for disease-free survival, 0.74 (95% CI, 0.55-0.99) for recurrence-free survival, and 0.75 (95% CI, 0.54-1.05) for overall survival. This reduction in risk of cancer recurrence or death associated with a family history became stronger with an increasing number of affected first-degree relatives. Compared with participants without a family history of colorectal cancer, those with 1 affected relative had a multivariate HR of 0.77 (95% CI, 0.57-1.04) for disease-free survival. For participants with 2 or more affected relatives, we observed a greater reduction in risk (multivariate HR for disease-free survival, 0.49; 95% CI, 0.23-1.04; P for trend with increasing number of affected relatives = .01). The improved disease-free survival associated with a family history was independent of tumoral MSI or MMR status. CONCLUSION: Among patients with stage III colon cancer receiving adjuvant chemotherapy, a family history of colorectal cancer is associated with a significant reduction in cancer recurrence and death.

Chan, J. M., D. M. Latini, et al. (2005). "History of diabetes, clinical features of prostate cancer, and

prostate cancer recurrence-data from CaPSURE (United States)." Cancer Causes Control **16**(7): 789-97.

OBJECTIVES: There is a growing epidemiologic literature suggesting an inverse association between history of diabetes and risk of incident prostate cancer. To our knowledge, the relationship between diabetes and tumor features and risk of recurrence among men with prostate cancer has not been examined previously. We hypothesized that men with diabetes would present with more favorable prostate cancer and experience lower risk of recurrence. METHODS: We identified 691 men with diabetes at the time of prostate cancer diagnosis, among 6722 men diagnosed with prostate cancer in 1989 to 2002 within CaPSURE(TM), a community-based prostate cancer registry study. We compared clinical and socio-demographic variables by diabetes status, using chi2 tests, t-tests, and multinomial logistic regression. We examined recurrence rates for prostate cancer among patients with and without diabetes using Kaplan-Meier log-rank tests and Cox proportional hazard models. RESULTS: In multivariate analyses, history of diabetes was not associated with any diagnostic clinical parameter, and treatment-specific recurrence rates for prostate cancer generally did not differ by diabetes history. Among men with low-prognostic risk or who were younger at prostate cancer diagnosis, being diabetic (versus not) was associated with an elevated risk of recurrence after radiation therapy, in multivariate analyses. CONCLUSIONS: Contrary to data suggesting that diabetes may be modestly protective against risk of incident prostate cancer, we did not observe any evidence of an inverse association between history of diabetes and aggressiveness at diagnosis or risk of recurrence, in this population of men with prostate cancer.

Cigna, A. A., D. Nassisi, et al. (2004). "Dose due to scattered radiation in external radiotherapy: a prostate cancer case history." Radiat Prot Dosimetry **108**(1): 27-32.

One of the authors was subjected to external radiotherapy with 6 MeV photons to treat a prostate cancer. The dose due the radiation scattered by the target was measured by means of pen dosemeters distributed along the body. Subsequently, both the equivalent dose delivered to some organs and the effective dose delivered to the body, due to scattering only, were evaluated.

Clark, D. (2007). "From margins to centre: a review of the history of palliative care in cancer." Lancet Oncol **8**(5): 430-8.

Palliative care and hospices have developed rapidly since the late 1960s. The pioneering work of Cicely Saunders was instrumental in drawing attention to the end-of-life care needs of patients with advanced malignant disease. Palliative care began to be defined as a subject of activity in the 1970s and came to be synonymous with the physical, social, psychological, and spiritual support of patients with life-limiting illness, delivered by a multidisciplinary team. Palliative care services have developed in many settings and have often been closely related to oncology. The worldwide need for this type of care remains much greater than the available provision, but there are encouraging signs of recognition by policymakers and influential bodies, and interest in palliative care has never been greater. This paper charts the modern history of such care around the world and concludes on some current issues and future challenges.

Cohen, M. (2006). "Breast cancer early detection, health beliefs, and cancer worries in randomly selected women with and without a family history of breast cancer." Psychooncology **15**(10): 873-83.

BACKGROUND: Early detection practices (EDP) consist of clinical breast examination (CBE) and mammography. Breast self-examination (BSE) is no longer generally recommended, but many women still perform it. AIMS: To compare EDP, health beliefs, and cancer worries in women with and without a family history of breast cancer in a population-based sample. METHODS: 489 women aged 21-60 were randomly sampled from the entire Jewish female population of Israel; 61 (12.5%) had a family history of breast cancer. Participants answered questionnaires by phone, including demographic details, EDP performance, health beliefs, and cancer worries. RESULTS: Rates of CBE were similar in women with and without a family history ($p>0.05$). For women over 40, rates of undergoing mammography screening were similar ($p>0.05$), but regular attendance was reported more by women with a family history ($p<0.05$). More women under 40 with a family history of breast cancer attended mammography ($p<0.05$), but only about 14% had ever undertaken mammography screening and 27% had ever undertaken CBE. More than 50% of the women had performed BSE, while significantly more women with a family history reported its over-performance ($p<0.01$). Women with a family history reported higher perceived susceptibility ($p<0.01$), higher cancer worries ($p<0.05$), and fewer barriers to mammography ($p<0.05$). According to logistic regression analysis, higher odds of EDP were significantly related to perceiving fewer barriers and having higher cancer worries. A positive family history was related to

higher odds of women undergoing mammography. Perceived susceptibility was significantly related to higher odds of BSE only. Over-performance of BSE was significantly related to having a positive family history, higher susceptibility, and higher cancer worries. CONCLUSIONS: (1) A high rate of women did not undergo CBE or mammography screening. Women under 40 with a family history of breast cancer who have never undergone CBE or mammography merit special attention. (2) The change in guidelines on BSE necessitates further study of its over-performance in relation to cancer worries. (3) Interventions are needed to promote attendance for CBE and mammography in younger women with a positive family history.

Comis, R. L. (2003). "A brief history of the research and treatment of lung cancer from 1970 to 2003." Int J Clin Oncol **8**(4): 230-3.

Lung cancer accounts for one-third of all cancer deaths worldwide. Once considered untreatable, lung cancer patients now have several different treatment options, and the potential for more effective therapies is promising. Clinical trials conducted during the past 25 to 30 years in the United States Cooperative Group System and throughout the world have defined the standard of care and made several initial treatment therapies possible. This article includes a summary of major findings of significant trials for varying disease stages; reviews major drug developments; and includes and a discussion of unanswered questions and trials currently underway that may provide the answers. Depending on the stage of disease, various therapeutic combinations can be effective in improving the time to progression, response, safety, and survival of lung cancer patients. Much has been accomplished on behalf of lung cancer patients. However, 80% to 90% of patients who develop lung cancer will die of their disease. Many questions remain to be answered, especially in the area of targeted therapies.

Coogan, P. F., L. Rosenberg, et al. (2000). "NSAIDs and risk of colorectal cancer according to presence or absence of family history of the disease." Cancer Causes Control **11**(3): 249-55.

BACKGROUND: We undertook the present analyses to determine whether family history of colorectal cancer in a parent or sibling modifies the inverse association of nonsteroidal anti-inflammatory drug (NSAID) use with colorectal cancer risk. METHODS: We used data from two case-control studies of colorectal cancer. The hospital-based Case Control Surveillance Study included 1526 patients with primary colorectal cancer, 4192 cancer controls and 6036 noncancer controls. A population-based study conducted in Massachusetts enrolled 1201 incident cases of colorectal cancer and 1201 community controls. Data on NSAID use and risk factors for colorectal cancer were collected by interview. RESULTS: In both studies there was a reduction in the odds ratios among subjects who used NSAIDs regularly continuing into the previous year, regardless of family history. In the Case Control Surveillance data, the odds ratio was 0.4 (95% CI 0.2-0.9) among subjects with a family history and 0.5 (95% CI 0.4-0.7) among subjects without a family history. The comparable odds ratios in the Massachusetts data were 0.5 (95% CI 0.3-0.9) and 0.7 (95% CI 0.6-0.9). CONCLUSIONS: These data indicate that regular continuing NSAID use is associated with a reduced risk of colorectal cancer among persons with a family history of the disease, as well as those without such a history.

Cowan, R., B. Meiser, et al. (2008). "The beliefs, and reported and intended behaviors of unaffected men in response to their family history of prostate cancer." Genet Med **10**(6): 430-8.

PURPOSE: Genetic testing for hereditary cancer facilitates medical management and improves health outcomes. Genetic testing is not currently available for prostate cancer, but trials are underway to investigate if antiandrogens and selenium have a preventive role for at-risk individuals. To inform future genetic counseling, we sought to understand the pre-existing beliefs and behaviors of men with a family history of prostate cancer and explore their intention to adopt possible preventive behaviors in response to test results. METHODS: A survey was completed by 280 men (response: 59%). RESULTS: The belief that diet influenced prostate cancer risk was held by 73% of participants, whereas 37% believed in medication/natural therapies. Thirty-nine percent reported at least one change to their diet, alcohol consumption, smoking, exercise patterns, vitamin/mineral/supplement intake and/or medication/natural therapy in response to their family history. The men expressed interest in genetic testing with 92% "definitely" or "probably" interested. Definite interest was associated with number of affected relatives and prostate cancer-related anxiety. A positive genetic test would motivate 93% of men to make at least one behavioral change. CONCLUSIONS: Participants commonly believed behavioral factors influenced prostate cancer risk and reported that they would alter their behavior to reduce risk after (hypothetical) genetic testing.

Dalessandri, K. M., G. L. Firestone, et al. (2004). "Pilot study: effect of 3,3'-diindolylmethane supplements on urinary hormone metabolites in

postmenopausal women with a history of early-stage breast cancer." Nutr Cancer **50**(2): 161-7.

Dietary indoles, present in Brassica plants such as cabbage, broccoli, and Brussels sprouts, have been shown to provide potential protection against hormone-dependent cancers. 3,3'-Diindolylmethane (DIM) is under study as one of the main protective indole metabolites. Postmenopausal women aged 50-70 yr from Marin County, California, with a history of early-stage breast cancer, were screened for interest and eligibility in this pilot study on the effect of absorbable DIM (BioResponse-DIM) supplements on urinary hormone metabolites. The treatment group received daily DIM (108 mg DIM/day) supplements for 30 days, and the control group received a placebo capsule daily for 30 days. Urinary metabolite analysis included 2-hydroxyestrone (2-OHE1), 16-alpha hydroxyestrone (16alpha-OHE1), DIM, estrone (El), estradiol(E2), estriol (E3), 6beta-hydroxycortisol (6beta-OHC), and cortisol in the first morning urine sample before intervention and 31 days after intervention. Nineteen women completed the study,for a total of 10 in the treatment group and 9 in the placebo group. DIM-treated subjects, relative to placebo, showed a significant increase in levels of2-OHE1 (P=0. 020), DIM (P =0. 045), and cortisol (P = 0.039), and a nonsignificant increase of 47% in the 2-OHE1/16alpha-OHE1 ratio from 1.46 to 2.14 (P=0.059). In this pilot study, DIM increased the 2-hydroxylation of estrogen urinary metabolites.

de Jong-Tieben, L. M., R. J. Berkhout, et al. (2000). "The prevalence of human papillomavirus DNA in benign keratotic skin lesions of renal transplant recipients with and without a history of skin cancer is equally high: a clinical study to assess risk factors for keratotic skin lesions and skin cancer." Transplantation **69**(1): 44-9.

DNA of the epidermodysplasia-verruciformis associated subgroup of HPV (EV-HPV) is frequently detected in biopsies of premalignant lesions and nonmelanoma skin cancers of renal transplant recipients. The prevalence of EV-HPVs, however, has never been systematically studied in benign keratotic skin lesions of patients with or without a history of skin cancer. This study included 42 renal transplant recipients with and 36 without a history of skin cancer. A total of 176 skin biopsies were tested for the presence of EV-HPV DNA, using a nested polymerase chain reaction (PCR). METHOD: EV-HPV typing was done by comparison of the sequence of the amplified PCR products with the sequence of all known EV-HPVs. The natural history of the development of keratotic skin lesions was studied. The number of keratotic skin lesions rapidly increased after transplantation. This increase was most pronounced in patients who developed skin cancer. The prevalence of EV-HPV DNA in benign keratotic skin lesions was equally high in patients with and without a history of skin cancer, i.e., 55 and 53% in the two groups, respectively. A large variety of EV-HPV types was found, but of these none were predominantly present in either patient groups. A higher prevalence of EV-HPV DNA was found in benign skin lesions from sun-exposed sites, but only in patients with a history of skin cancer. The association between the number of keratotic skin lesions and the development of skin cancer strongly supports the hypothesis that EV-HPVs play a role in cutaneous oncogenesis. The equally high prevalence of EV-HPV infection in patients with and without a history of skin cancer, however, may indicate that besides EV-HPV infection, other factors, such as sun exposure may also be important.

Desai, M. M., M. L. Bruce, et al. (2001). "Validity of self-reported cancer history: a comparison of health interview data and cancer registry records." Am J Epidemiol **153**(3): 299-306.

Few studies have addressed the accuracy of self-reported cancer history, although epidemiologic studies routinely use self-reported information as the sole source of exposure or outcome data or as a criterion for exclusion from study participation. In this paper, false-negative reporting of cancer history is examined in a community-based sample by comparing interview data with tumor registry records. Subjects were participants in the 1980 New Haven Epidemiologic Catchment Area study; in 1995, cancer records (from 1935 onward) were obtained by linking the sample to the Connecticut Tumor Registry. Analyses focused on 263 individuals who had at least one tumor reported to the Connecticut Tumor Registry prior to participation in the Epidemiologic Catchment Area study. The overall rate of false-negative reporting was 39.2%. Logistic regression analysis revealed that false-negative reporting was significantly associated with non-White race, older age, increased time since cancer diagnosis, number of previous tumors, and type of cancer treatment received. In addition, false-negative reporting varied widely by cancer site, ranging from 0% for melanoma skin cancer to 83.3% for central nervous system cancers. The false-negative rate for breast cancer was 20.8%, that for colon and prostate cancers was 42.1%, and that for bladder cancer was 61.5%. Implications of these findings for prevalence estimation and future epidemiologic studies are discussed.

deVere White, R. W., R. M. Hackman, et al. (2004). "Effects of a genistein-rich extract on PSA levels in

men with a history of prostate cancer." Urology **63**(2): 259-63.

OBJECTIVES: To determine whether supplemental amounts of soy isoflavone (genistein-rich extract) would lower prostate-specific antigen (PSA) levels more than 50% in patients with prostate cancer (CaP). METHODS: A total of 62 men (mean age 73.6 years, range 61.4 to 89.3) with histologically proven CaP who had two consecutive elevated PSA readings were accrued during a 13-month period. An open-label pilot study was conducted for 6 months in which the patients took capsules containing the genistein-rich extract three times daily by mouth. The subjects were in one of five groups: after radical retropubic prostatectomy (n = 9), after radiotherapy (n = 17), after both radical retropubic prostatectomy and radiotherapy (n = 6), off-cycle during hormonal therapy (intermittent hormones; n = 14), or active surveillance (n = 16). The primary endpoint for the trial was a 50% reduction in the PSA level at 6 months compared with before treatment. RESULTS: Of the 62 men enrolled, 52 were available for evaluation at 6 months. Three patients discontinued because of adverse events (diarrhea) and seven because of personal choice. One of 52 patients had a more than 50% reduction in the PSA level (1.9% response, 95% confidence interval 0.1% to 10.3%). An additional 7 patients had PSA reductions that were less than 50%. All 8 patients with lower PSA levels at 6 months were in the active surveillance (watchful waiting) treatment subgroup. Repeated measure regression models allowing for correlation between initial levels and change also indicated a decline in PSA in this group compared with other groups: 0 of 52 had a complete response, 9 (17%) had a partial response, 8 (15%) had stable disease, and 35 (67%) had disease progression. In the 9 patients with a partial response, 6 had pathologic findings that were moderately differentiated, 2 had well-differentiated findings, and 1 had poorly differentiated findings. Therefore, the response in this group of patients did not appear to be driven by the Gleason score. The total testosterone level was lowered in one of the patients responding, but it was higher in five others. CONCLUSIONS: A genistein-rich extract as the sole treatment for CaP did not reduce PSA levels by 50% or more in 51 of 52 subjects. Thus, it does not appear to be an effective treatment for CaP when given alone. However, 8 of 13 evaluated patients in the active surveillance group had either no rise or a decline in PSA levels of less than 50%. More study is warranted for those choosing active surveillance.

Dove-Edwin, I., P. Sasieni, et al. (2005). "Prevention of colorectal cancer by colonoscopic surveillance in individuals with a family history of colorectal cancer: 16 year, prospective, follow-up study." Bmj **331**(7524): 1047.

OBJECTIVE: To determine to what extent individuals with various family histories of colorectal cancer (from one to three or more affected first degree relatives) benefit from colonoscopic surveillance. DESIGN: Prospective, observational study of high risk families, followed up over 16 years. SETTING: Tertiary referral family cancer clinic in London. PARTICIPANTS: 1678 individuals from families registered with the clinic. Individuals were classified according to the strength of their family history: hereditary non-polyposis colorectal cancer (if they fulfilled the Amsterdam criteria), and one, two, or three affected first degree relatives (moderate risk). INTERVENTIONS: Colonoscopy was initially offered at five year intervals or three year intervals if an adenoma was detected. MAIN OUTCOME MEASURES: The incidence of adenomas with high risk pathological features or cancer. This was analysed by age, the extent of the family history, and findings on previous colonoscopies. The cohort was flagged for cancer and death. Incidence of colorectal cancer and mortality during over 15,000 person years of follow-up were compared with those expected in the absence of surveillance. RESULTS: High risk adenomas and cancer were most common in families with hereditary non-polyposis colorectal cancer (on initial colonoscopy 5.7% and 0.9%, respectively). In the families with moderate risk, these findings were particularly uncommon under age 45 (1.1% and 0%) and on follow-up colonoscopy if advanced neoplasia was absent initially (1.7% and 0.1%). The incidence of colorectal cancer was substantially lower-80% in families with moderate risk (P = 0.00004), and 43% in families with hereditary non-polyposis colorectal cancer (P = 0.06)-than the expected incidence in the absence of surveillance when the family history was taken into account. CONCLUSIONS: Colonoscopic surveillance reduces the risk of colorectal cancer in people with a strong family history. This study confirms that members of families with hereditary non-polyposis colorectal cancer require surveillance with short intervals. Individuals with a lesser family history may not require surveillance under age 45, and if advanced neoplasia is absent on initial colonoscopy, surveillance intervals may be lengthened. This would reduce the demand for colonoscopic surveillance.

Du, Y., I. Cullum, et al. (2007). "Fusion of metabolic function and morphology: sequential [18F]fluorodeoxyglucose positron-emission tomography/computed tomography studies yield new insights into the natural history of bone metastases in breast cancer." J Clin Oncol **25**(23): 3440-7.

PURPOSE: By monitoring bone metastases with sequential [(18)F]fluorodeoxyglucose positron-emission tomography/computed tomography ([(18)F]FDG-PET/CT) imaging, this study investigates the clinical relevance of [(18)F]FDG uptake features of bone metastases with various radiographic appearances. PATIENTS AND METHODS: Bone metastases were found in 67 of 408 consecutive patients with known/suspected recurrent breast cancer on [(18)F]FDG-PET/CT, characterized by CT morphology changes and/or bony [(18)F]FDG uptake. Twenty-five of the patients had sequential [(18)F]FDG-PET/CT examinations (86 studies) over an average follow-up period of 23 months. The temporal changes in [(18)F]FDG uptake and corresponding CT morphology features of 146 bone lesions identified in these 25 patients were followed up and correlated with therapeutic outcome retrospectively. RESULTS: The 146 lesions were classified as osteolytic (77), osteoblastic (41), mixed-pattern (11), or no change/negative (17) on CT. The majority of the osteolytic (72; 93.5%) and mixed-pattern lesions (nine; 81.8%), but fewer of the osteoblastic lesions (25; 61%), showed increased [(18)F]FDG uptake. After treatment, 58 osteolytic lesions (80.5%) became [(18)F]FDG negative and osteoblastic on CT and only 14 relatively large lesions (19.5%) remained [(18)F]FDG avid. Of the 25 [(18)F]FDG-avid osteoblastic lesions, 13 (52%) became [(18)F]FDG negative, but 12 (48%) remained [(18)F]FDG avid and increased in size on CT. Five of the mixed-pattern lesions remained [(18)F]FDG avid after treatment. All 17 CT-negative lesions became [(18)F]FDG negative; however, nine of them became osteoblastic. None of the initially [(18)F]FDG-negative lesions showed [(18)F]FDG avidity during follow-up. CONCLUSION: [(18)F]FDG uptake reflects the immediate tumor activity of bone metastases, whereas the radiographic morphology changes vary greatly with time among patients.

Esplen, M. J., B. Toner, et al. (2000). "A supportive-expressive group intervention for women with a family history of breast cancer: results of a phase II study." Psychooncology **9**(3): 243-52.

BACKGROUND: Evidence suggests that there are significant psychological and behavioural sequelae associated with having a family history of breast cancer (BC) which can interfere with comprehension of risk estimates. PURPOSE: The purpose of this study was to develop, standardize and do preliminary testing of a group intervention designed to address the emotional impact of having a family history of BC. METHODS: This study is a single-arm pilot design with pre- and post-measures of perceived risk, psychosocial distress, knowledge and screening practices. RESULTS: The primary study outcome measure of risk comprehension was significantly improved by 70%, according to our predetermined criteria for success. In addition, the most important secondary measures of psychosocial functioning, such as cancer-related distress (p=0.025), depression (p=0.05), anxiety (p=0.005) and unresolved grief (p=0.034) were significantly improved. CONCLUSION: The results of this initial pilot study are encouraging; however, further research is required, using a randomized controlled study design to evaluate the relative contribution of this intervention to the successful modification of risk comprehension, enhanced psychological functioning, and to promote optimal screening adherence.

Fang, C. Y., S. M. Miller, et al. (2003). "Psychosocial correlates of intention to undergo prophylactic oophorectomy among women with a family history of ovarian cancer." Prev Med **37**(5): 424-31.

BACKGROUND: The purpose of this study was to examine sociodemographic and psychosocial correlates of intention to undergo prophylactic oophorectomy among women with a family history of ovarian cancer. METHODS: Participants were 76 women enrolled in a familial cancer risk assessment program. Psychosocial assessments were collected upon entry into the program and included measures of perceived risk of developing ovarian cancer, perceived benefits and limitations of prophylactic oophorectomy, and psychological distress. In addition, respondents were asked whether they intended to undergo prophylactic oophorectomy in the following 12 months. RESULTS: Thirty-four percent reported intention to have surgery within 12 months. Logistic regression analyses indicated that intention to undergo surgery was associated with several psychosocial factors including greater perceived risk of developing ovarian cancer and greater perceived benefits of surgery. CONCLUSIONS: Women who have heightened risk perceptions and who perceive there to be many benefits of surgery may be more inclined to undergo the procedure, possibly without fully considering the potential limitations and consequences of surgery. These findings suggest the need for education and risk counseling designed to facilitate informed decision making among not only high-risk women, but also women who perceive themselves to be at increased risk.

Farley, M., J. M. Golding, et al. (2002). "Is a history of trauma associated with a reduced likelihood of cervical cancer screening?" J Fam Pract **51**(10): 827-31.

OBJECTIVE: We tested the hypothesis that a history of trauma (especially sexual trauma) was

associated with a reduced likelihood of having had medically appropriate cervical cancer screening. STUDY DESIGN: A case-control study using mailed self-report questionnaires. POPULATION: The questionnaires were completed by an age-stratified random sample of adult women members of a large health maintenance organization. The sample included 364 women who had received medically appropriate cervical cancer screening and 372 who had not. OUTCOMES MEASURED: We defined cases as women who, according to their medical record, had not had cervical cancer screening within 2 years before the study. Controls were defined as women who had been screened. We evaluated exposures to trauma that we hypothesized to be associated with the case/control state. RESULTS: Women who had been sexually abused in childhood were less likely to have had a Pap smear within the past 2 years (36.0% vs. 50.4%, P =.050). Other traumatic events were associated with Pap testing in bivariate analyses but not when demographic characteristics and clinic location were controlled. Childhood sexual abuse remained associated with reduced odds of Pap screening in logistic regression analyses that controlled for clinic location, demographics, attitudes about Pap screening, and posttraumatic stress disorder symptoms (adjusted OR = 0.56, 95% CI 0.34 to 0.91). CONCLUSIONS: These findings suggest that childhood sexual abuse may lead to decreased probability of screening for cervical cancer, potentially contributing to the poorer health seen in other studies of women who have been sexually abused.

Figueiredo, J. C., M. Ennis, et al. (2007). "Influence of young age at diagnosis and family history of breast or ovarian cancer on breast cancer outcomes in a population-based cohort study." Breast Cancer Res Treat **105**(1): 69-80.

PURPOSE: The objective of this study was to examine the association of: (i) diagnosis at age </=35, (ii) first-degree family history of breast or ovarian cancer (BOC) and (iii) a research based definition of genetic risk, with tumor characteristics, treatment and survival in breast cancer (BC). PATIENTS AND METHODS: Consenting female participants in the population-based Ontario Familial Breast Cancer Registry diagnosed with primary invasive BC between 1996 and 1998 were followed prospectively until 2005. RESULTS: Among 967 women, 105 were </=35 years old at diagnosis and 686 were classified as genetic risk cases, including 349 with a first-degree family history. Individuals diagnosed at age </=35 were more likely to self-detect tumors, to present with inflammatory BC, to have invasive ductal carcinoma of no special type, high T stage, and tumors with lymphovascular invasion (LVI), high grade and negative estrogen receptors. Younger women were more likely to receive chemotherapy and less likely to receive hormonal therapy. Diagnosis </=35 years old was associated with significantly reduced distant recurrence free survival, an effect that did not persist after adjustment for tumor and treatment related variables. Poor outcomes were restricted to younger women with hormone responsive BC. Family history was associated with increased rates of mammographic detection of BC, lower tumor stage and less frequent inflammatory BC, but had no association with BC outcomes. CONCLUSION: Women diagnosed with BC at age </=35 have more aggressive tumors; these adverse tumor characteristics, rather than age, lead to poor outcomes. Family history was not associated with survival.

Foo, W., J. M. Young, et al. (2009). "Family history? The forgotten question in high-risk colorectal cancer patients." Colorectal Dis **11**(5): 450-5.

AIM: The aim of the study was to investigate the frequency and detail of family history recorded for patients diagnosed with potentially high-risk colorectal cancer, and to determine the proportion of these patients referred to a high-risk assessment clinic. METHOD: Medical records of patients diagnosed with colorectal cancer under the age of 50 admitted to a major Sydney teaching hospital were reviewed. The proportion of records containing information about family history was calculated. Associations between recording of family history and demographic and clinical characteristics of patients were investigated. Logistic regression modelling was performed to identify significant, independent predictors of study outcomes. RESULTS: Of 113 patients with colorectal cancer diagnosed under the age of 50 years, 61 (54%, 95% CI: 44-63%) had an entry in their hospital medical record about family history. Family history was significantly less likely to be recorded for females, for those admitted via the Emergency Department, and for those with shorter lengths of stay. A significant family history was found in 51% of the 61 patients who had a family history recorded. Records of patients attending specialist colorectal surgeons were significantly more likely to contain information about family history than those who attended other specialists (P = 0.04). Only 14 patients (12%, 95% CI: 7-20%) were formally referred for further genetic assessment. CONCLUSION: These results suggest that family history is still being neglected in routine clinical practice, and high-risk assessment services are underutilized, implying the need for further dissemination of guidelines with

regard to the recognition and management of hereditary colorectal cancer.

Fujino, Y., A. Tamakoshi, et al. (2004). "Prospective study of transfusion history and thyroid cancer incidence among females in Japan." Int J Cancer **112**(4): 722-5.

A link between hepatitis C virus (HCV) infection and thyroid cancer was recently reported in a series of case-control studies in southern Italy. A prospective study could reinforce these findings. However, cohort studies that began before 1990 rarely assessed serological HCV infection. In addition, thyroid cancer is rare and generally has a good prognosis. Therefore, incidence outcome data are required, rather than mortality data, to evaluate the risk of thyroid cancer. Blood transfusion history might be a possible substitute measure to evaluate the cancer risks associated with HCV infection because blood transfusions were the major HCV transmission route in Japan until 1992. The purpose of our study was therefore to examine the association between transfusion history and thyroid cancer. A baseline survey of members of the JACC Study was conducted from 1988 until 1990, which involved 110,792 participants from 45 areas throughout Japan. Data were collected from a total of 37,983 women with no history of cancer at the baseline (337,906 person-years) and 79 cases of thyroid cancer were identified among this group. A history of blood transfusion marginally increased the risk of thyroid cancer [risk ratio (RR)=1.77, 95% confidence interval (CI)=0.95-3.30], and a history of transfusion and/or liver disease significantly increased the thyroid cancer risk (RR=1.84, 95% CI=1.07-3.16). These results indirectly support an association between HCV and thyroid cancer. In addition, our data reveal an association between blood transfusion and thyroid cancer, which might be facilitated by transfusion-associated immunomodulation.

Ganz, P. A. (2006). "Monitoring the physical health of cancer survivors: a survivorship-focused medical history." J Clin Oncol **24**(32): 5105-11.

Cancer survivors frequently visit their primary-care physicians, as well as oncology specialists, for follow-up care. There is a need to monitor these survivors for the late physical effects of cancer, yet few health care providers have received training in how to do this. This article provides guidance on how to take a cancer survivor-directed medical history to facilitate the elicitation of relevant exposures, family history, and symptoms that may be related to the late effects of cancer therapy.

Gao, Y., N. Hu, et al. (2009). "Family history of cancer and risk for esophageal and gastric cancer in Shanxi, China." BMC Cancer **9**: 269.

BACKGROUND: Family history (FH) by different relative types and risk of upper gastrointestinal (UGI) cancers has been only rarely reported; the data on UGI cancer survival are sparse. METHODS: 600 esophageal squamous cell carcinoma (ESCC) cases, 598 gastric cardia adenocarcinoma cases, and 316 gastric non-cardia adenocarcinoma cases, and 1514 age-, gender-, and neighborhood-matched controls were asked for FH in first degree relatives and non-blood relatives. Odds ratios (ORs) and 95% confidence intervals (CIs) from logistic regressions, and hazard ratios (HRs) from Cox proportional hazard regressions were estimated. RESULTS: Increased ESCC risk was associated with FH of any cancer (OR = 1.72, 95% CI = 1.39-2.12), FH of any UGI cancer (OR = 2.28, 95%CI = 1.77-2.95) and FH of esophageal cancer (OR = 2.84, 95%CI = 2.09-3.86), but not FH of non-UGI cancer. Individuals with two or more affected first-degree relatives had 10-fold increased ESCC risk. FH of gastric cardia cancer was associated with an increased risk of all three cancers. Cancer in non-blood relatives was not associated with risk of any UGI cancer. FH of UGI cancer was associated with a poorer survival rate among younger ESCC cases (HR = 1.82, 95%CI = 1.01-3.29). CONCLUSION: These data provide strong evidence that shared susceptibility is involved in esophageal carcinogenesis and also suggest a role in prognosis.

Garavello, W., E. Negri, et al. (2005). "Family history of cancer, its combination with smoking and drinking, and risk of squamous cell carcinoma of the esophagus." Cancer Epidemiol Biomarkers Prev **14**(6): 1390-3.

We analyzed the association between history of cancer in first-degree relatives and the risk of squamous cell carcinoma of the esophagus (SCCE) using data from three case-control studies conducted in Italy and Switzerland on 805 incident, histologically confirmed SCCE, and 3,461 hospital controls. The alcohol- and tobacco-adjusted odds ratio (OR) for a family history of esophageal cancer was 3.2 [95% confidence interval (CI), 1.7-6.2], and the OR was higher when the affected relative was a brother or was diagnosed at age <55 years. Compared to subjects without family history of esophageal cancer, non-current smokers, drinking <49 drinks per week, the OR was 2.9 (95% CI, 1.1-7.5) for family history alone, 15.5 (95% CI, 11.7-20.5) for current smokers drinking > or = 49 drinks per week without family history of esophageal cancer, and 107.0 (95% CI, 13.0-880.2) for current smokers drinking > or = 49

drinks per week who also had a family history of esophageal cancer. The risk of SCCE was also increased in subjects with a family history of cancer of the oral cavity/pharynx (OR, 3.7; 95% CI, 1.5-9.0) and stomach (OR, 2.0; 95% CI, 1.1-3.6), but not of other cancers, nor for a family history of any cancer (OR, 1.0; 95% CI, 0.8-1.4). These data show that, as for many other epithelial cancers, the risk of SCCE is increased in subjects with a family history of the disease, and that--in Western countries--avoidance of alcohol and tobacco is also the best way to prevent SCCE in subjects with a family history of the disease.

Geller, A. C., D. R. Brooks, et al. (2006). "Sun protection practices among offspring of women with personal or family history of skin cancer." Pediatrics **117**(4): e688-94.

OBJECTIVE: Family history of skin cancer is an important determinant of skin cancer risk for offspring. No previous study of the effect of personal or family history of skin cancer on the sun protection behaviors of the offspring has been published. METHODS: A retrospective study was conducted of the sun protection behaviors of the adolescent participants in the Growing Up Today Study (GUTS), who were offspring of mothers from the Nurses Health Study II. Adolescents' surveys were matched with their mothers' reports of a personal or family history of skin cancer and compared with adolescents whose mothers did not report a personal or family history of skin cancer. The outcome measures were (1) occurrence of frequent sunburns during the past summer, (2) use of a tanning bed during the past year, and (3) routine use of sunscreen. Frequent sunburns were defined as the report of > or = 3 sunburns during the past summer. We compared those who reported having used a tanning bed in the past year at least once with those who reported no tanning bed use in the past year. Routine use of sunscreen was defined as a respondent who replied that he or she "always" or "often" used sunscreen with sun protection factor of 15 or more when he or she was outside for > 15 minutes on a sunny day during the past summer. General estimating equations were used to calculate odds ratios and 95% confidence intervals adjusted for gender, age, color of untanned skin, and number of friends who were tanned. We also conducted an additional analysis restricted to children whose mothers had received a diagnosis of skin cancer in which we assessed sun protection behaviors according to the child's age and mother's age at the time of the mother's diagnosis and the number of years that had passed since the diagnosis of the mother's skin cancer. RESULTS: In 1999, 9943 children reported their sun protection behaviors; 8697 of their mothers had not received a diagnosis of skin cancer or reported a family history of melanoma, 463 participants' mothers had received a diagnosis of skin cancer, and 783 participants' mothers reported a family history of melanoma. Between 1989 and 1999, 371 mothers of GUTS participants received a diagnosis of skin cancer: melanoma (n = 44), squamous cell (n = 39), and basal cell cancer (n = 311); 23 mothers received a diagnosis of > 1 type of skin cancer. Because GUTS includes siblings from the same family, the 371 mothers with skin cancer had 463 offspring in GUTS. Offspring of mothers with skin cancer were slightly more likely to report frequent sunburns in the past year compared with those with neither maternal diagnosis nor family history (39% vs 36%). Tanning bed use was not significantly different among those with either a maternal diagnosis of skin cancer or family history of melanoma as compared with nonaffected adolescents (8% vs 9% vs 10%). Sunscreen use among offspring of mothers with skin cancer was higher than among those whose mothers had a family history of melanoma or mothers with no personal history of skin cancer (42% vs 33% vs 34%). Tan-promoting attitudes were also similar across all groups. Only 25% thought that a natural skin color was most attractive, and on average, 25% in each group agreed that it was worth burning to get a tan. Children of mothers who had received a diagnosis > 2 years in the past were less likely to use sunscreen, more likely to sunburn, and more likely to use tanning beds than children of mothers with a more recent diagnosis, although the results did not reach statistical significance. CONCLUSION: Frequent sunburns, suboptimal sunscreen use, and high rates of tanning bed use are commonplace even among the children of health professionals who are at risk for developing skin cancer themselves as a result of personal or family history. With new information on family risk, pediatricians can use the potential of a teachable moment to ensure optimal sun protection for children who are at risk.

Goldberg, R. M., D. J. Sargent, et al. (2002). "Early detection of toxicity and adjustment of ongoing clinical trials: the history and performance of the North Central Cancer Treatment Group's real-time toxicity monitoring program." J Clin Oncol **20**(23): 4591-6.

Prospective clinical trials are the gold standard for evidence-based methodology used to support changes in the practice of medicine. Clinical researchers, regulatory agencies, payers, and the public embrace the conduct of phase I, II, and III clinical trials as integral to improving patient care. The National Cancer Institute (NCI) funds a number of cooperative oncology groups to conduct such clinical trials in the United States. In order to protect

enrolling patients, the NCI requires expedited reporting to allow rapid identification of severe side effects on NCI-sponsored clinical trials. However, chemotherapy drugs frequently cause predictable side effects, the rapid reporting of which would potentially overwhelm the system. This article describes the development and documents the performance of a real-time toxicity reporting system implemented by the North Central Cancer Treatment Group. The goal of this system is to supplement the currently required NCI adverse event monitoring procedures and to permit study teams to identify the need to modify ongoing clinical trials. The system has proven its value in the monitoring of phase II and III trials, including trial N9741, a three-arm, phase III, advanced colorectal cancer chemotherapy study exploring combinations of irinotecan, oxaliplatin, and fluorouracil. We believe the methods described present opportunities for improving patient safety in clinical research.

Goldie, S. J., D. Grima, et al. (2003). "A comprehensive natural history model of HPV infection and cervical cancer to estimate the clinical impact of a prophylactic HPV-16/18 vaccine." Int J Cancer **106**(6): 896-904.

The object of our study is to project the impact of a prophylactic vaccine against persistent human papillomavirus (HPV)-16/18 infection on age-specific incidence of invasive cervical cancer. We developed a computer-based mathematical model of the natural history of cervical carcinogenesis to incorporate the underlying type-specific HPV distribution within precancerous lesions and invasive cancer. After defining plausible ranges for each parameter based on a comprehensive literature review, the model was calibrated to the best available population-based data. We projected the age-specific reduction in cervical cancer that would occur with a vaccine that reduced the probability of acquiring persistent infection with HPV 16/18, and explored the impact of alternative assumptions about vaccine efficacy and coverage, waning immunity and competing risks associated with non-16/18 HPV types in vaccinated women. The model predicted a peak age-specific cancer incidence of 90 per 100,000 in the 6th decade, a lifetime cancer risk of 3.7% and a reproducible representation of type-specific HPV within low and high-grade cervical precancerous lesions and cervical cancer. A vaccine that prevented 98% of persistent HPV 16/18 was associated with an approximate equivalent reduction in 16/18-associated cancer and a 51% reduction in total cervical cancer; the effect on total cancer was attenuated due to the competing risks associated with other oncogenic non-16/18 types. A vaccine that prevented 75% of persistent HPV 16/18 was associated with a 70% to 83% reduction in HPV-16/18 cancer cases. Similar effects were observed with high-grade squamous intraepithelial lesions (HSIL) although the impact of vaccination on the overall prevalence of HPV and low-grade squamous intraepithelial lesions (LSIL) was minimal. In conclusion, a prophylactic vaccine that prevents persistent HPV-16/18 infection can be expected to significantly reduce HPV-16/18-associated LSIL, HSIL and cervical cancer. The impact on overall prevalence of HPV or LSIL, however, may be minimal. Based on the relative importance of different parameters in the model, several priorities for future research were identified. These include a better understanding of the heterogeneity of vaccine response, the effect of type-specific vaccination on other HPV types and the degree to which vaccination effect persists over time.

Gramling, R., D. Anthony, et al. (2006). "Self-rated breast cancer risk among women reporting a first-degree family history of breast cancer on office screening questionnaires in routine medical care: the role of physician-delivered risk feedback." Genet Med **8**(10): 658-64.

PURPOSE: We investigated whether risk-related feedback delivered by one's primary care physician is associated with self-ratings of risk among women found to have a first-degree family history of breast cancer on office screening questionnaires. METHODS: Design: Mailed survey of women registered with the Cancer Genetics Network having a first-degree family history of breast cancer. Eligibility: Completion of primary care-based family history screening within the past year. Independent variable: presence of physician feedback about breast cancer risk. Dependent variable: self-rated breast cancer risk. Modifying variable: trust in one's doctor. RESULTS: Three hundred one women met eligibility criteria (73% minimum response rate); feedback was associated with rating one's risk to be "high" in both crude and multivariate analysis. (ORadj = 2.38; 95% CI = 1.30, 4.38). Higher levels of trust in the physician were associated in a dose-dependent fashion with the strength of association between feedback and self-rating one's risk to be high. CONCLUSIONS: Physician feedback following the identification of a first-degree family history of breast cancer appears to influence whether or not women categorize themselves to be at high risk and trust is an important modifier of this association.

Gramling, R., C. B. Eaton, et al. (2009). "Hormone replacement therapy, family history, and breast cancer risk among postmenopausal women." Epidemiology **20**(5): 752-6.

BACKGROUND: Evidence is mixed regarding how familial predisposition to breast cancer affects the relation between hormone replacement therapy and risk of postmenopausal breast cancer. We investigated whether the risk difference for invasive breast cancer attributable to estrogen plus progesterone replacement therapy is greater among women with a first-degree family history of the disease. METHODS: This study is a longitudinal follow-up of 16,608 postmenopausal women aged 50-79 years who were enrolled between 1993 and 2002 in the Women's Health Initiative randomized trial of estrogen plus progesterone replacement therapy versus placebo. RESULTS: Three hundred forty-nine cases of invasive breast cancer occurred during a mean follow-up period of 5.6 years. The invasive breast cancer risk difference attributable to the hormone therapy was 0.007 among women with first-degree family history and 0.005 among the others, resulting in a negligible interaction contrast (IC = 0.002; 95% confidence interval = -0.014 to 0.018). The interaction contrast restricted to estrogen-receptor-positive invasive breast cancers was also negligible (IC = -0.006; 95% CI = -0.021 to 0.008). CONCLUSION: Family history and estrogen plus progesterone replacement therapy have independent and noninteracting effects on the risk of invasive breast cancer among participants in the Women's Health Initiative randomized trial.

Green, B. L., J. L. Krupnick, et al. (2000). "Trauma history as a predictor of psychologic symptoms in women with breast cancer." J Clin Oncol **18**(5): 1084-93.

PURPOSE: To identify predictors of psychiatric problems in women with early-stage breast cancer. PATIENTS AND METHODS: One hundred sixty women with early-stage breast cancer were recruited from three treatment centers. They filled out self-report questionnaires, including a medical history and demographic survey, the Trauma History Questionnaire, Life Event Questionnaire, Brief Symptom Inventory, Beck Depression Inventory, and Duke-UNC Functional Social Support Questionnaire, and were evaluated using the Structured Clinical Interview for DSM-III-R. RESULTS: Hierarchical regression analyses indicated that four of five variable sets made a significant incremental contribution to outcome prediction, with 35% to 37% of the variance explained. Outcomes were predicted by demographic variables, trauma history variables, precancer psychiatric diagnosis, recent life events, and perceived social support. Cancer treatment variables did not predict outcome. CONCLUSION: The findings highlight the important roles of trauma history and recent life events in adjustment to cancer and have implications for screening and treatment.

Greendale, G. A., L. Petersen, et al. (2001). "Factors related to sexual function in postmenopausal women with a history of breast cancer." Menopause **8**(2): 111-9.

BACKGROUND: The normal life expectancy of survivors of early-stage breast cancer (BCS) underscores the need to address long-term quality of life issues in these women. Sexual dysfunction persists after breast cancer treatment, despite recovery in other domains. OBJECTIVE: To examine associations between a broad array of characteristics and sexuality in BCS. PARTICIPANTS: Sixty-one postmenopausal BCS who were participants in a randomized, controlled trial of nonhormonal interventions for menopause symptoms and who had a partnered, intimate relationship. METHODS: Cross-sectional analysis of baseline trial data. Outcomes were standardized scales of sexual interest, dysfunction, and satisfaction. Candidate predictors included demographic, anatomical, medical, psychological, sociocultural, and hormonal characteristics. Forward, stepwise regression was used. RESULTS: Relationship quality, vaginal discomfort, education, and hot flashes were each associated with two of the three domains of sexuality assessed. Ten other factors entered predictive models: age, time since diagnosis, breast conservation, comorbidity, urinary incontinence, perceived health, body image, bioavailable testosterone, luteinizing hormone, and sex hormone binding globulin. Each of these 10 factors was associated with only one sexuality domain. CONCLUSIONS: In this small sample of BCS, we found multiple correlates of sexuality. Most seem to impact uniquely on individual domains of sexual function. Several characteristics are modifiable and could be targets for intervention.

Griffith, G. L., R. T. Edwards, et al. (2004). "Estimating the survival benefits gained from providing national cancer genetic services to women with a family history of breast cancer." Br J Cancer **90**(10): 1912-9.

The aim of this paper is to compare a service offering genetic testing and presymptomatic surveillance to women at increased risk of developing breast cancer with its predecessor of no service at all in terms of survival and quality-adjusted survival (QALYs) by means of a Markov cohort chain simulation model. Genetic assessment and presymptomatic care provided between 0.07-1.61 mean additional life years and 0.05-1.67 mean QALYs over no services. Prophylactic surgery and

surveillance extended mean life expectancy by 0.41-1.61 and 0.32-0.99 years, respectively over no services for high-risk women. Model outcomes were sensitive to all the parameters varied in the sensitivity analysis. Providing cancer genetic services increase survival and as long as services do not induce adverse psychological effects they also provide more QALYs. The greatest survival and QALY benefits were found for women with identified mutations. As more cancer genes are identified, the survival and cost-effectiveness of genetic services will improve. Although mastectomy provided most additional life years, when quality of life was accounted for oophorectomy was the optimal strategy. Delayed entry into coordinated genetic services was found to diminish the average survival and QALY gains for a woman utilising these services.

Griffith, K. A., D. B. McGuire, et al. (2008). "Influence of family history and preventive health behaviors on colorectal cancer screening in African Americans." Cancer **113**(2): 276-85.

BACKGROUND: African Americans (AAs) have low rates of colorectal cancer (CRC) screening. To the authors' knowledge, factors that influence their participation, especially individuals with a family history of CRC ("family history"), are not well understood. METHODS: A secondary analysis of the 2002 Maryland Cancer Survey data examined predictors of risk-appropriate, timely CRC screening ("screening") in AAs with a family history and in individuals without a family history. Predictors that were evaluated included age, sex, family history, mammogram or prostate-specific antigen (PSA) screening, body mass index, activity, fruit/vegetable consumption, alcohol, smoking, perceived risk of cancer, education, employment, insurance, access to a healthcare provider, and healthcare provider recommendation of fecal occult blood test (FOBT) and/or sigmoidoscopy/colonoscopy. RESULTS: In individuals without a family history of CRC (N = 492), recommendation for FOBT (odds ratio [OR] of 11.90; 95% confidence interval [95% CI], 6.84-20.71) and sigmoidoscopy/colonscopy (OR of 7.06; 95% CI, 4.11-12.14), moderate/vigorous activity (OR of 1.74; 95% CI, 1.06-2.28), and PSA screening history (OR of 2.68; 95% CI, 1.01-7.81) were found to be predictive of screening. In individuals with a family history (N = 88), recommendation for sigmoidoscopy/colonscopy (OR of 24.3; 95%, CI 5.30-111.34) and vigorous activity (OR of 5.21; 95% CI, 1.09-24.88) were found to be predictive of screening. However, family history did not predict screening when the analysis was controlled for age, education, and insurance. AAs who had a family history were less likely to screen compared with their white counterparts (N = 293) and compared with AAs who were at average risk for CRC ($P < .05$). CONCLUSIONS: Regardless of family history, healthcare provider recommendation and activity level were important predictors of screening. Lower screening rates were observed in AAs who had a family history compared with individuals who did not. The authors believe that, for AAs who have a family history, further examination of barriers and facilitators to CRC screening within the cultural context is warranted.

Gunduz, E., M. Gunduz, et al. (2009). "Downregulation of TESTIN and its association with cancer history and a tendency toward poor survival in head and neck squamous cell carcinoma." Arch Otolaryngol Head Neck Surg **135**(3): 254-60.

OBJECTIVE: To examine the role of TESTIN as a candidate tumor suppressor gene in head and neck carcinogenesis. DESIGN: Mutation and messenger RNA (mRNA) expression analyses. SETTING: Academic research. PATIENTS: Paired normal and tumor samples were obtained from 38 patients with primary head and neck squamous cell carcinoma. MAIN OUTCOME MEASURES: Analysis and comparison of TESTIN gene mRNA expression and its relationship to clinicopathologic variables. RESULTS: Mutation analysis showed a nucleotide and amino acid change in 6 of the 38 tumor samples (16.0%). Semiquantitative mRNA expression analysis of TESTIN revealed a decreased expression in approximately 50% of the tumors compared with their matched normal controls. Interestingly, comparison of clinicopathologic variables to mRNA expression status of TESTIN revealed a significant difference in terms of cancer history ($P = .03$). Moreover, a higher smoking ratio and a family cancer history were also associated with downregulation of TESTIN, although the difference was not statistically significant ($P = .43$ and $P = .16$, respectively). Kaplan-Meier survival analysis demonstrated a worse survival rate among the patients with low TESTIN expression compared with the patients with normal-high TESTIN expression. CONCLUSIONS: Our findings suggest that inactivation of TESTIN is involved in head and neck carcinogenesis through its downregulation. Further studies in various human cancer tissues using a large sample size and in vitro functional studies as well as clinical comparison research studies would give us a better evaluation of TESTIN's role and its possible future application in molecular diagnosis and treatment of different cancer types, including head and neck squamous cell carcinoma.

Guzzo, T. J., A. Kutikov, et al. (2008). "The clinical and pathological history of prostate cancer progression in men with a prior history of high grade prostatic

intraepithelial neoplasia." Can J Urol **15**(4): 4174-8; discussion 4179.

OBJECTIVES: The natural history of high grade prostatic intraepithelial neoplasia (HGPIN) is incompletely understood limiting evidence based recommendations regarding screening and repeat biopsy intervals. Our objective was to evaluate the natural history of HGPIN to better assess the time frame to disease progression and the pathological findings at the time of progression to cancer. METHODS AND MATERIALS: We retrospectively reviewed 74 consecutive patients with an initial diagnosis of HGPIN. The number and timing of all biopsies leading to the diagnosis of cancer were assessed. Clinical and pathological features of those patients with eventual disease progression were evaluated. RESULTS: The mean number of biopsies performed before subsequent cancer diagnosis was 5 (range: 3-13). The mean time to the diagnosis of cancer was 29 months (range: 7-83). Men with a history of HGPIN had lower percent positive biopsies at the time of cancer diagnosis ($p < 0.001$) and smaller volume tumors on final pathology ($p = 0.041$) compared to men without a history of HGPIN. CONCLUSIONS: Patients with an initial diagnosis of HGPIN on transrectal ultrasound (TRUS) guided biopsy progressed to cancer at a mean of 29 months. The vast majority of patients that progressed to prostate cancer had low volume disease at the time of diagnosis and definitive treatment. Our data indicate the importance of re-evaluation in HGPIN patients and suggest a trend toward low volume disease in carefully followed patients. Prospective data is warranted to adequately define an evidence based biopsy regimen in men with HGPIN.

Habel, L. A., A. Pressman, et al. (2006). "Use of raloxifene among women with a history of breast cancer." Breast Cancer Res Treat **96**(2): 123-9.

PURPOSE: To examine raloxifene use among women with a history of breast cancer. METHODS: Kaiser Permanente tumor registry and membership files were used to identify women diagnosed with breast cancer after 1994 who were health plan members in 1998 or later, when raloxifene became available. Information on raloxifene treatment was obtained from computerized pharmacy records. Treatment patterns were examined and the characteristics of those who did and did not receive raloxifene were compared. RESULTS: Among the 17,968 women with a history of breast cancer, 711 (4.0%) had at least one prescription for raloxifene. Use among these women was more common than among similarly aged women in the health plan without a history of breast cancer, especially among those less than age 60 years. Among women with a history of breast cancer, raloxifene users were more than twice as likely as non-users to have had a bone mineral density test (60 versus 26%, $p<0.0001$) and, if tested, were more likely to have osteopenia or osteoporosis (80 versus 63%, $p<0.0001$). Compared to non-users, users had earlier stage breast cancer at diagnosis (80% versus 71% with local disease, $p<0.0001$). Raloxifene use was largely restricted to women whose initial breast cancer had not been treated with adjuvant tamoxifen or who had received less than 5 years of tamoxifen therapy. CONCLUSION: In this setting, raloxifene use among women with a history of breast cancer is related to stage at diagnosis and bone mineral density and is rare among women who have completed a 5-year course of adjuvant tamoxifen.

Hemminki, K., H. Zhang, et al. (2008). "Modification of risk for subsequent cancer after female breast cancer by a family history of breast cancer." Breast Cancer Res Treat **111**(1): 165-9.

An increased risk of second primary cancers may depend on many reasons, including therapy for the first cancer and heritable causation. Population level data are not available exploring the risks of subsequent cancers after breast cancer considering a familial history of breast cancers. We used the nation-wide Swedish Family-Cancer Database to investigate such risks, based on 43,398 first invasive female breast cancers. Standardized incidence ratios (SIRs) were calculated for the second cancer after breast cancer using rates for first cancer as a reference. Many cancers at discordant sites were increased after breast cancer. SIRs for subsequent neoplasms in women who had a family history of breast cancer were increased for ovarian (2.0) and endometrial (1.8) cancers and for acute lymphoid leukemia (12.7) and myelofibrosis (9.4). The data suggest that the familial aggregation of breast and endometrial cancers may be explained by yet unidentified heritable causes. The remarkably high risks for second acute lymphoid leukemia and myelofibrosis, both characterized by chromosomal aberrations, in women with a family history of breast cancer may signal heritable defects in the ability to process DNA damage caused by ionizing radiation and chemotherapy.

Hernandez, D. J., M. E. Nielsen, et al. (2008). "Natural history of pathologically organ-confined (pT2), Gleason score 6 or less, prostate cancer after radical prostatectomy." Urology **72**(1): 172-6.

OBJECTIVES: Men with pathologically organ-confined, Gleason score 6 or less prostate cancer are considered to have an excellent prognosis after surgery as definitive monotherapy. We determined the incidence of biochemical recurrence

(BR), local recurrence (LR), distant metastasis (DM), and prostate cancer-specific mortality (PCSM) among this low-risk cohort. METHODS: A retrospective search of our radical prostatectomy database identified 6081 men with pathologically organ-confined (pT2), Gleason score 6 or less prostate cancer treated from 1983 to 2005. Of these, 2551 (42%) had adequate follow-up information and were assessed for BR, LR, DM, and PCSM. The pathologic specimens of men with disease progression were reevaluated by an experienced genitourinary pathologist, and the patients with disease that was upgraded or upstaged (n = 25) were excluded from additional analysis, resulting in a final study cohort of 2526. The actuarial probabilities of BR and LR were estimated using the Kaplan-Meier method. RESULTS: With a median follow-up of 5.0 years (range 2 to 22), BR occurred in 13 patients (0.5%). The 5, 10, and 15-year actuarial probability of BR was 0.3%, 0.9%, and 1.3%, respectively. Five patients (0.2%) developed LR, four of whom received salvage radiotherapy with a subsequently undetectable prostate-specific antigen level. The 5, 10, and 15-year actuarial probability of LR was 0.1%, 0.5%, and 0.5%, respectively. No DM or PCSM occurred. CONCLUSIONS: With postoperative follow-up for more than 2500 patients with pathologically organ-confined, Gleason score 6 or less prostate cancer, BR and LR after radical prostatectomy were extremely rare, and no patients experienced DM or PCSM.

Hill, D. A., S. Preston-Martin, et al. (2002). "Medical radiation, family history of cancer, and benign breast disease in relation to breast cancer risk in young women, USA." Cancer Causes Control **13**(8): 711-8.

OBJECTIVE: In previous studies breast cancer risk has been increased among women who received high doses (above 100-200 cGy) of ionizing radiation or those exposed to lower doses prior to age 20. Some evidence suggests that such risk may be distinctly elevated among women with a family history of breast or ovarian cancer (probably only carriers of specific gene mutations) and women with benign breast disease (BBD). METHODS: A population-based case-control study in Los Angeles County obtained interview data from 744 women who were aged 40 or younger and diagnosed with breast cancer during 1983-1988, and from 744 matched controls. Women with a positive family history of breast or ovarian cancer reported cancer in a mother, sister, or grandmother. Women with BBD reported a physician diagnosis. Radiation exposure was defined as a history of either radiation therapy or moderate exposure to medical radiography. RESULTS: Breast cancer risk was elevated among women exposed to medical radiation prior to age 20 years (odds ratio (OR) = 1.4, 95% confidence interval (CI) = 1.2-1.8), relative to unexposed women. This increased risk was observed only among women with a history of BBD (OR = 2.4, 95% CI = 1.6-3.7). Overall, risk was not associated with exposure to medical radiation after age 20 years, although among women with a positive family history of breast or ovarian cancer, exposed women had an increased risk (OR= 1.8, 95% CI = 1.0-3.1). Breast cancer risk was not increased among women with a family history of breast/ovarian cancer exposed to medical radiation before age 20 years or those with BBD exposed to medical radiation after age 20 years. DISCUSSION: Study participants may have received radiation doses that are no longer common, hampering study generalizability. Although differences in recall between cases and controls cannot be completely excluded, women with BBD or a family history of breast cancer appear to have greater breast cancer risk following relatively low ionizing radiation exposure than other women in this study.

Holly, E. A., C. A. Eberle, et al. (2003). "Prior history of allergies and pancreatic cancer in the San Francisco Bay area." Am J Epidemiol **158**(5): 432-41.

Data from a large population-based case-control study conducted in the San Francisco Bay Area between 1994 and 2001 were analyzed to examine the association between pancreatic cancer and history of allergic conditions. Pancreatic cancer cases (n = 532) had to be 21-85 years of age and were identified using rapid case ascertainment. Random digit dialing and Health Care Financing Administration lists (age, > or = 65 years) were used to obtain 1,701 controls who were frequency-matched to cases by sex and age within 5 years. In-person interviews were conducted and detailed allergy history data were obtained for all participants. Prior history of any allergy was associated with a reduced risk estimate for pancreatic cancer (odds ratio (OR) = 0.77, 95% confidence interval (CI): 0.63, 0.95). Inverse associations were observed for common allergens, including house dust (OR = 0.72, 95% CI: 0.54, 0.94), cats (OR = 0.59, 95% CI: 0.41, 0.85), plants (OR = 0.77, 95% CI: 0.62, 0.96), and mold (OR = 0.49, 95% CI: 0.32, 0.75), and for all allergic symptoms, although some confidence intervals included unity. Trends were observed for decreased risks associated with increasing number of allergies (p = 0.0006) and severity of allergic symptoms (p = 0.003). These results provide support for the plausibility that immune function in relation to allergies may play a role in the etiology of pancreatic cancer.

Huang, X. E., K. Hirose, et al. (2004). "Comparison of lifestyle risk factors by family history for gastric,

breast, lung and colorectal cancer." Asian Pac J Cancer Prev **5**(4): 419-27.

To assess the theoretical impact of lifestyle of a cancer family history in first-degree relatives (CFH) and clarify interactions between CFH and lifestyle factors, hospital-based comparison and case-reference studies were conducted in Nagoya, Japan. Totals of 1988 gastric, 2455 breast, 1398 lung and 1352 colorectal cancer patients, as well as 50,706 non-cancer outpatients collected from 1988 to 1998, were checked for lifestyle factors, which included dietary and physical exercise habits, as well as smoking/drinking status. General lifestyle factors with non-cancer outpatients did not differ by the CFH status. Case-reference analyses showed that frequent intake of fruits, raw vegetables, carrots, pumpkin, cabbage and lettuce, as well as frequent physical exercise, were associated with decreased risk for all four sites of cancer, while habitual smoking increasing the risk of gastric, and more particularly, lung cancer. Interestingly, the study revealed the magnitude of odds ratios for the above lifestyle factors obtained from CFH positives to be similar to those from CFH negatives for these four sites of cancer. There were no significant interactions between CFH and any particular lifestyle factor. In conclusion, our results suggest no appreciable influence of CFH on lifestyle related risk factors for gastric, breast, lung, and colorectal cancer. Habitual smoking increased, while frequent physical exercise and raw vegetables intake decreased cancer risk, regardless of the CFH status.

Huber, A., E. K. Bentz, et al. (2005). "Ten polymorphisms of estrogen-metabolizing genes and a family history of colon cancer--an association study of multiple gene-gene interactions." J Soc Gynecol Investig **12**(7): e51-4.

Estrogen replacement therapy is associated with a reduced risk of colon cancer. Therefore, we evaluated the following ten estrogen metabolism-associated single-nucleotide polymorphisms (SNPs) by sequencing-on-chip technology using solid-phase polymerase chain reaction (PCR) on oligonucleotide microarrays: catechol-O-methyltransferase (COMT) Val158Met G-->A, 17-beta-hydroxysteroid dehydrogenase type 1 (HSD17) vlV A-->C, cytochrome P-450 (CYP) 17 A2 allele T-->C, CYP1A1 MspI RFLP T-->C, CYP1A1 Ile462Val A-->G, CYP19 Arg264Cys C-->T, CYP19 C1558T C-->T, CYP 1B1 Leu432Val, CYP1B1 Asn453Ser, and estrogen receptor (ER) alpha IVS1 -401-->C in 76 patients with a family history of colon cancer and 722 healthy controls. Using stepwise logistic regression models, we found that none of the investigated SNPs is associated with a family history of colon cancer in a univariate and multivariate logistic regression model. In addition, when all two-way interactions of the investigated SNPs were ascertained, no significant interactions between SNPs were observed. In conclusion, we found no association between the carriage of one or multiple SNPs of the estrogen metabolism and a family history of colon cancer.

Hurley, K. E., S. M. Miller, et al. (2001). "Anxiety/uncertainty reduction as a motivation for interest in prophylactic oophorectomy in women with a family history of ovarian cancer." J Womens Health Gend Based Med **10**(2): 189-99.

Most women at familial risk for ovarian cancer must decide about prophylactic oophorectomy without conclusive genotypic information about their risk level. Some women with relatively low-risk profiles seek prophylactic oophorectomy or are recommended the procedure by their physicians, if they appear "cancerphobic." This study investigated the desire to reduce anxiety in relation to other factors associated with interest in prophylactic oophorectomy in a group of women with varying degrees of familial risk for ovarian cancer. Ninety-four women enrolled in an ongoing program for women with a family history of ovarian cancer received personalized risk counseling and were classified as having a sporadic, familial, or putative hereditary pedigree by a genetics counselor. Eligible enrollees were interviewed by telephone about current and future interest in prophylactic oophorectomy, perceived risk of ovarian cancer, severity of cancer anxiety, stress-related ideation, and reasons for and against surgery. Reduction of anxiety/uncertainty was the factor most strongly associated with current interest in prophylactic oophorectomy, independent of objective risk classification, perceived risk, severity of cancer anxiety, intrusive ideation, or other variables. Future interest in prophylactic oophorectomy was predicted by other perceived benefits of surgery. Current, but not future, interest in prophylactic oophorectomy appears motivated in part by seeking immediate relief from anxiety. Interest in prophylactic oophorectomy may fluctuate based on varying exposure to cues that trigger anxiety. Women seeking prophylactic oophorectomy, particularly those with lower-risk family pedigrees, should be offered options for anxiety management as part of informed consent for prophylactic oophorectomy.

Isaacs, C., B. N. Peshkin, et al. (2002). "Breast and ovarian cancer screening practices in healthy women with a strong family history of breast or ovarian cancer." Breast Cancer Res Treat **71**(2): 103-12.

Studies in women with a family history of cancer demonstrate a wide variability in the uptake of cancer screening measures. Little data exist regarding

the breast and ovarian cancer screening practices of women who are members of hereditary breast cancer families. In order to address this issue, we examined the screening behaviors and the determinants of screening in a clinic based group of 216 women with a strong family history of breast or ovarian cancer who were participating in a free genetic counseling and testing research program. At baseline, prior to obtaining genetic counseling or testing, 50% of women ages 30-39, 83% of those age 40-49, 69% of those 50-64, and 53% of those >65 reported having a mammogram in the prior year. Adherence to mammography recommendations was correlated with age, number of relatives with breast cancer, and income. Twenty percent of participants had at least one CA- 125 performed and 31 % had ever obtained a screening ultrasound. Having at least one relative with ovarian cancer was very strongly associated with ovarian cancer screening [OR = 12.3, 95% CI = 4.6-33 for CA-125; OR=4.9, 95% CI=2.4, 10.1 for ultrasound]. No association between cancer worries/distress and either breast or ovarian cancer screening was found. In conclusion, the breast and ovarian screening uptake in healthy women from hereditary breast cancer families is suboptimal, even for women over age 50, for whom annual mammography is clearly indicated. These findings indicate a need for better education about screening guidelines for high-risk women.

Jacobson, J. S., A. B. Troxel, et al. (2001). "Randomized trial of black cohosh for the treatment of hot flashes among women with a history of breast cancer." J Clin Oncol **19**(10): 2739-45.

PURPOSE: Most breast cancer survivors experience hot flashes; many use complementary or alternative remedies for these symptoms. We undertook a randomized clinical trial of black cohosh, a widely used herbal remedy for menopausal symptoms, among breast cancer patients. PATIENTS AND METHODS: Patients diagnosed with breast cancer who had completed their primary treatment were randomly assigned to black cohosh or placebo, stratified on tamoxifen use. At enrollment, patients completed a questionnaire about demographic factors and menopausal symptoms. Before starting to take the pills and at 30 and 60 days, they completed a 4-day hot flash diary. At the final visit, they completed another menopausal symptom questionnaire. Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels were measured in a subset of patients at the first and final visits. RESULTS: Of 85 patients (59 on tamoxifen, 26 not on tamoxifen) enrolled in the study, 42 were assigned to treatment and 43 were assigned to placebo; 69 completed all three hot flash diaries. Both treatment and placebo groups reported declines in number and intensity of hot flashes; the differences between the groups were not statistically significant. Both groups also reported improvements in menopausal symptoms that were, for the most part, not significantly different. Changes in blood levels of FSH and LH also did not differ in the two groups. CONCLUSION: Black cohosh was not significantly more efficacious than placebo against most menopausal symptoms, including number and intensity of hot flashes. Our study illustrates the feasibility and value of standard clinical trial methodology in assessing the efficacy and safety of herbal agents.

Johansson, J. E., O. Andren, et al. (2004). "Natural history of early, localized prostate cancer." Jama **291**(22): 2713-9.

CONTEXT: Among men with early prostate cancer, the natural history without initial therapy determines the potential for survival benefit following radical local treatment. However, little is known about disease progression and mortality beyond 10 to 15 years of watchful waiting. OBJECTIVE: To examine the long-term natural history of untreated, early stage prostatic cancer. DESIGN: Population-based, cohort study with a mean observation period of 21 years. SETTING: Regionally well-defined catchment area in central Sweden (recruitment March 1977 through February 1984). PATIENTS: A consecutive sample of 223 patients (98% of all eligible) with early-stage (T0-T2 NX M0 classification), initially untreated prostatic cancer. Patients with tumor progression were hormonally treated (either by orchiectomy or estrogens) if they had symptoms. MAIN OUTCOME MEASURES: Progression-free, cause-specific, and overall survival. RESULTS: After complete follow-up, 39 (17%) of all patients experienced generalized disease. Most cancers had an indolent course during the first 10 to 15 years. However, further follow-up from 15 (when 49 patients were still alive) to 20 years revealed a substantial decrease in cumulative progression-free survival (from 45.0% to 36.0%), survival without metastases (from 76.9% to 51.2%), and prostate cancer-specific survival (from 78.7% to 54.4%). The prostate cancer mortality rate increased from 15 per 1000 person-years (95% confidence interval, 10-21) during the first 15 years to 44 per 1000 person-years (95% confidence interval, 22-88) beyond 15 years of follow-up (P =.01). CONCLUSION: Although most prostate cancers diagnosed at an early stage have an indolent course, local tumor progression and aggressive metastatic disease may develop in the long term. These findings would support early radical treatment, notably among patients with an estimated life expectancy exceeding 15 years.

Kabat, G. C., A. B. Miller, et al. (2008). "Oral contraceptive use, hormone replacement therapy, reproductive history and risk of colorectal cancer in women." Int J Cancer **122**(3): 643-6.

Evidence from epidemiologic studies suggests a possible role of exogenous and endogenous hormones in colorectal carcinogenesis in women. However, with respect to exogenous hormones, in contrast to hormone replacement therapy, few cohort studies have examined oral contraceptive use in relation to colorectal cancer risk. We used data from a large cohort study of Canadian women enrolled in a randomized controlled trial of breast cancer screening to assess the association of oral contraceptive use, hormone replacement therapy and reproductive factors with risk of colorectal cancer, overall and by subsite within the colorectum. Cancer incidence and mortality were ascertained by linkage to national databases. Among 89,835 women aged 40-59 at enrollment and followed for an average of 16.4 years, we identified 1,142 incident colorectal cancer cases. Proportional hazards models were used to estimate the associations between the exposures of interest and risk of colorectal cancer. Ever use of oral contraceptives at baseline was associated with a modest reduction in the risk of colorectal cancer (hazard ratio 0.83, 95% confidence interval 0.73-0.94), with similar effects for different subsites within the colorectum. No trend was seen in the hazard ratios with increasing duration of oral contraceptive use. No associations were seen with use of hormone replacement therapy (ever use or duration of use) or reproductive factors. Our results are suggestive of an inverse association between oral contraceptive use and colorectal carcinogenesis. However, given the lack of a dose-response relationship and the potential for confounding, studies with more complete assessment of exogenous hormone use throughout the life course are needed to clarify this association.

Karlsson, C. T., B. Malmer, et al. (2006). "Breast cancer as a second primary in patients with prostate cancer--estrogen treatment or association with family history of cancer?" J Urol **176**(2): 538-43.

PURPOSE: In a large population based study we reported an increased risk of male breast cancer after prostate cancer. In the current study we performed a comprehensive investigation of whether treatment for prostate cancer and/or family history is responsible for the excess risk. MATERIALS AND METHODS: This study had 2 parts. 1) We performed a nested case-control study in 41 men who had previously been identified with first prostate cancer, followed by male breast cancer and in 81 matched controls with prostate cancer only. The medical records of these men were retrieved and clinical data such as stage, grade and treatment were extracted. 2) We also performed a family study including relatives of men with a diagnosis of prostate as well as breast cancer, irrespective of which was first. The 878 relatives were identified through parish offices and linked to the Swedish Cancer Registry to evaluate the occurrence of breast, prostate and other cancers and calculate if there were any excess risks for different cancers. RESULTS: Cases with prostate plus breast cancer received estrogen treatment more often than controls with prostate cancer only ($p = 0.03$). The period of estrogen treatment was longer in the cases, although it was not statistically significant. Mean time from prostate cancer diagnosis to breast cancer diagnosis was 47.6 months. Cases and controls did not differ in grade or stage. In the family study an increased risk of prostate cancer was found in relatives (SIR 2.14, 95% CI 1.09 to 3.18). For other cancers no significantly increased risks were found. In 2 families pedigree analysis using the BRCAPRO program (http://www3.utsouthwestern.edu/cancergene/) revealed an estimated 100% and 49% probability in families 1 and 2, respectively, that the proband was a BRCA2 carrier. CONCLUSIONS: Our data suggest that most of the increased risk of breast cancer following prostate cancer can be explained by estrogen treatment. However, in a small number of men with prostate as well as breast cancer pedigree analysis suggests that BRCA2 mutation might be the underlying cause.

Kawai, H., A. Tada, et al. (2005). "Smoking history before surgery and prognosis in patients with stage IA non-small-cell lung cancer--a multicenter study." Lung Cancer **49**(1): 63-70.

The prognosis of lung cancer patients with surgically resected non-small-cell lung cancer (NSCLC) can be predicted generally from age, sex, histologic type, stage at diagnosis, and additional treatment. Nine studies have reported that a history of smoking before diagnosis influences the prognosis of the disease in lung cancer patients. In this study, a total of 3082 patients who underwent surgery and were diagnosed with primary pathological stage IA NSCLC at 36 national hospitals from 1982 to 1997 were analyzed for the effect of smoking on survival. Smoking history and other factors influencing either the overall survival or the disease-specific survival rates of patients were estimated with the Cox proportional hazards model. Multivariate analysis demonstrated significant associations between overall survival and age ($P < 0.0001$), sex ($P = 0.0002$), and performance status (PS) ($P < 0.0001$). Disease-specific survival was associated with age ($P = 0.0063$), sex (0.00161), and PS ($P = 0.0029$). In males, disease-

specific survival was associated with age (P = 0.0120), PS (P = 0.0022), and pack-years (number of cigarette packs per day, and years of smoking) (P = 0.0463). These results indicate that smoking history (pack-years) is important clinical prognostic factor in estimating disease-specific survival, in male patients with stage IA primary NSCLC that has been surgically resected.

Kelly, K. M., R. Shedlosky-Shoemaker, et al. (2007). "Cancer family history reporting: impact of method and psychosocial factors." J Genet Couns **16**(3): 373-82.

Family history is one the greatest risk factors for disease and one of the most important informational tools in medical genetics for the purpose of diagnosis, risk assessment, prevention and treatment. However, research is needed on the comparability of different methods of cancer family history assessment and the influence of psychosocial factors in family history reports. The purpose of this study was to determine if individuals had discrepancies between written and interview reports of cancer family history and the role of psychosocial factors in these discrepancies. Oncology patients (n=104) were administered a survey to assess psychosocial factors (i.e., information-seeking, worry, perceived risk, and health literacy) and were asked to provide family history in a written and an interview form. Randomization determined which form individuals received first. No differences in the amount of missing data or the amount of unspecified data were noted between the written and interview method. Psychosocial factors did not differentiate between those who had discrepancies in family history reports and those who did not have discrepancies in family history reports; although there was a trend for those with lower literacy and those who were blunters to be more discrepant on type of cancer diagnosis. In sum, this preliminary study indicates that written and interview methods of family history assessment for first degree relatives may be used interchangeably. The ability to use written methods will facilitate collection of basic family history information in the oncology clinic.

Kessler, B. and P. Albertsen (2003). "The natural history of prostate cancer." Urol Clin North Am **30**(2): 219-26.

Predicting the long-term outcome of patients who choose watchful waiting as initial therapy for prostate cancer is difficult. The wide variation in disease progression, the impact of competing medical hazards, and the potential impact of early hormonal therapy that is characteristic of contemporary patients all conspire to compromise survival estimates dating from the pre-PSA era. The survival analysis figure developed by Albertsen et al (Fig. 1) estimates a 15-year survival rate based on patient age and Gleason score at diagnosis from patients diagnosed in the pre-PSA era. Although no effort was made to adjustfor competing medical hazards, patients and clinicians can adjust a patient's chronological age to match his "physiological" age. The advent of widespread PSA testing appears to have advanced the date of diagnosis by approximately 5 years and the onset of secondary treatment by at least as many years. Therefore, the figure describing the natural history of prostate cancer most likely underestimates rather than overestimates survival among men with newly diagnosed, localized prostate cancer who select watchful waiting as their treatment choice. As contemporary databases of men with localized prostate cancer mature, more data on the natural history of this disease will become available. Only time will tell how the use of PSA has altered the precision of historic case-series data.

Kim, J. J., K. M. Kuntz, et al. (2007). "Multiparameter calibration of a natural history model of cervical cancer." Am J Epidemiol **166**(2): 137-50.

The objective of this study was to develop a comprehensive natural history model of human papillomavirus (HPV) and cervical cancer using a two-step approach to model calibration. In the first step, the authors utilized primary epidemiologic data from a longitudinal study of women in Brazil and identified a plausible range for each input parameter that produced model output within the 95% confidence intervals of the data. In the second step, they performed a simultaneous search over all input parameters to identify parameter sets that produced output consistent with data from multiple sources. A goodness-of-fit score was computed for 555,000 unique parameter sets using a likelihood-based approach, and a sample of good-fitting parameter sets was used in the model to illustrate the advantage of the calibration approach by projecting a range of benefits associated with cervical cancer prevention policies. The calibrated model had reasonable fit to the data in terms of duration and prevalence of HPV infection for high-risk types, prevalence of precancerous lesions, and incidence of cancer. The authors found that leveraging primary data from longitudinal studies provides unique opportunities for model parameterization of the unobservable nature of HPV infection and its role in the development of cervical cancer.

Kim, K. I., G. R. Klein, et al. (2007). "Uncemented total hip arthroplasty in patients with a history of pelvic irradiation for prostate cancer." J Bone Joint Surg Am **89**(4): 798-805.

BACKGROUND: Pelvic irradiation for a malignant tumor may cause osteonecrosis of the acetabulum. The purpose of this study was to evaluate the outcome of uncemented total hip arthroplasty in patients with a history of pelvic irradiation for the treatment of prostate cancer. METHODS: We performed a retrospective review of the clinical records and radiographs of fifty-eight patients (sixty-six hips) who had had radiation therapy for prostate cancer and had subsequently undergone an elective primary uncemented total hip arthroplasty at our institution. The mean age of the patients at the time of the index operation was seventy-four years. The mean duration of follow-up was 4.8 years (range, two to 7.5 years). RESULTS: At the time of the final follow-up, fifty-one patients (fifty-eight hips) who were still living and had been followed for a minimum of two years had a well-ingrown and functioning replacement. The mean Harris hip score had significantly improved from 47 points preoperatively to 90 points at the time of the final follow-up ($p < 0.05$). The mean scores on the physical and mental health measures of the Short Form-36 had also improved significantly from 45.1 and 65.3 points, respectively, before the operation to 73.4 and 83.7 points postoperatively ($p < 0.05$ for both). There was no aseptic loosening of either component in any of the hips. Two hips had revision of the femoral component; one was revised because of a periprosthetic fracture of the femur and the other because of subsidence of the femoral component. CONCLUSIONS: Uncemented total hip arthroplasty can be a successful option for the treatment of coxarthrosis in patients with a history of pelvic irradiation for prostate cancer. Osseointegration of uncemented components does not seem to be compromised in these patients in the short term. LEVEL OF EVIDENCE: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.

Klotz, L. (2004). "Active surveillance with selective delayed intervention: using natural history to guide treatment in good risk prostate cancer." J Urol **172**(5 Pt 2): S48-50; discussion S50-1.

PURPOSE: This article reviews the data supporting an approach of active surveillance with selective delayed intervention for good risk localized prostate cancer. The challenge is to identify those patients who are not likely to experience significant progression, while offering radical therapy to those who are at risk. MATERIALS AND METHODS: A prospective phase 2 study of active surveillance with selective delayed intervention was initiated in 1995. Patients were treated initially with surveillance, while those who had a prostate specific antigen (PSA) doubling time (DT) of 2 years or less, or grade progression on re-biopsy were offered radical intervention. The remainder were closely monitored. RESULTS: The cohort consisted of 299 patients with good risk prostate cancer or intermediate risk prostate cancer in men older than 70 years. Median PSA DT was 7.0 years and 35% of the men had a PSA DT of greater than 10 years. The majority of patients remain on surveillance. At 8 years overall actuarial survival was 85% and disease specific survival was 99%. CONCLUSIONS: Most men with favorable risk prostate cancer will die of unrelated causes. The approach of active surveillance with selective delayed intervention based on PSA DT represents a practical compromise between radical therapy in all, which results in overtreatment in patients with indolent disease, and watchful waiting with palliative therapy only, which results in under treatment in those with aggressive disease. Results at 8 years are favorable. Longer followup will be required to confirm the safety of this approach in men with long (greater than 15-year) life expectancy.

Koga, T., Y. Horio, et al. (2004). "Identification of MGB1 as a marker in the differential diagnosis of lung tumors in patients with a history of breast cancer by analysis of publicly available SAGE data." J Mol Diagn **6**(2): 90-5.

The risk of developing second primary cancers is increased in patients with breast cancer. The lung is one of the major target organs, and therefore a differential diagnosis between primary and metastatic cancers is required for the treatment of lung tumors in patients with a history of breast cancer. However, biopsy specimens frequently result in small, fragmented tissues containing only a few, degenerated cancer cells. We attempted to find a useful marker for differential diagnosis, using the online SAGE database. We selected three molecules, small breast epithelial mucin (SBEM), prostate epithelium-specific Ets transcription factor (PDEF), and mammaglobin (MGB1), as potential markers for breast cancer. SBEM and PDEF proved of no use for practical differential diagnosis because they are expressed in the normal bronchus. In contrast, expression of MGB1 was detected in all 22 primary breast cancers, but not in 22 normal lung tissues. Furthermore, all 12 metastatic breast cancers examined demonstrated positive MGB1 transcripts, whereas one of 48 primary lung adenocarcinomas expressed MGB1. This suggests that MGB1 can serve as a differential molecular marker. In practice, prospective examination, using the nine cases with a history of breast cancer, confirmed the usefulness of MGB1 in differential diagnosis.

Kote-Jarai, Z., T. J. Powles, et al. (2007). "BRCA1/BRCA2 mutation status and analysis of cancer family history in participants of the Royal Marsden Hospital tamoxifen chemoprevention trial." Cancer Lett **247**(2): 259-65.

We have analysed the pedigrees of all 70 women who developed cancer in the Royal Marsden Hospital (RMH) tamoxifen chemoprevention trial, using the Claus model, to assess breast cancer susceptibility heterozygote risk (HR) and screened the entire coding regions of BRCA1 and 2 genes in 62 of these cases. We found a reduced incidence of breast cancers developing on tamoxifen in women who have a lower HR, but not in women with higher HR. There were too few BRCA1/2 mutations (4 cases) to be able to determine the efficacy of tamoxifen by BRCA status. Immunohistochemical analysis showed a significantly lower frequency of median ER (p=0.03) in the cancers developing in tamoxifen-treated patients. These results suggest that tamoxifen is less likely to be effective at reducing breast cancers which are ER negative and also in some individuals at higher HR.

Laing, S. S. and K. Makambi (2008). "Predicting regular breast cancer screening in African-American women with a family history of breast cancer." J Natl Med Assoc **100**(11): 1309-17.

OBJECTIVE: To evaluate the impact of socioeconomic, personal and affective factors on regular breast cancer screening in at-risk African-American women. METHODS: The study was a cross-sectional analysis assessing socioeconomic and affective predictors of breast cancer screening practices. Unaffected African-American women ages 40-64 with a family history of breast cancer were recruited from community settings. The main outcome measures were recent mammography, regular mammography and regular breast self-examinations. RESULTS: The majority of women reported having a recent mammogram (73%) and yearly mammograms (71%). More than half (56%) reported monthly breast self-examinations (BSEs). Available health insurance and risk perception had significant independent associations with regular mammography screening so that women having a mammogram every 6-12 months were more likely to have health insurance [odds ratio (OR)=4.99, 95% confidence interval (CI): 1.05-23.52], and women not engaged in regular screenings were less likely to perceive future breast cancer risk (OR=0.10, 95% CI: 0.01-0.96). Access to regular healthcare had a significant independent association with recent mammography so that women having a mammogram in the past 12 months were more likely to have access to regular healthcare (OR=6.59, 95% CI: 1.01-42.79). CONCLUSIONS: A significant majority of this subset of African-American women engage in repeat mammography screenings with cognitive and economic factors predicting noncompliance. Additional research with repeat mammography users is required so that regular screening practices can be encouraged among all at-risk women.

Lee, K. L., J. B. Marotte, et al. (2005). "Positive family history of prostate cancer not associated with worse outcomes after radical prostatectomy." Urology **65**(2): 311-5.

OBJECTIVES: To determine the clinical outcomes in men with (FH) and without (NFH) a family history of prostate cancer after radical prostatectomy. METHODS: We performed a retrospective analysis of 557 men with localized prostate cancer treated by radical prostatectomy between 1989 and 2000. We defined a positive FH as having one or more first-degree relatives such as a father or brother with prostate cancer. The clinical and pathologic features, as well as biochemical disease-free survival, defined as an undetectable prostate-specific antigen level (less than 0.2 ng/mL), were compared between the FH and NFH groups. RESULTS: Compared with the NFH group, the FH men were younger at surgery (median 62 years versus 64 years, P = 0.01), had a lower median preoperative prostate-specific antigen level (7.2 ng/mL versus 7.8 ng/mL, P = 0.05), and were more likely to have only low-grade disease at the final pathologic evaluation (26.2% versus 17.8%, P = 0.05). At a median follow-up of 7.5 years (mean 7.6 +/- 2.9 years), 17% of the FH group had biochemical disease recurrence compared with 30% in the NFH group. The actuarial disease-free survival rate at 5 and 10 years for the two groups was 86% and 80% compared with 73% and 66%, respectively (P = 0.01). When controlled for pathologic variables in a multivariate analysis, FH was not an independent predictor of disease-free survival. CONCLUSIONS: The association of improved disease-free survival in the FH patients may have been driven by an earlier age at diagnosis and more favorable pathologic features.

Legge, F., M. Petrillo, et al. (2008). "Epithelial ovarian cancer relapsing as isolated lymph node disease: natural history and clinical outcome." BMC Cancer **8**: 367.

BACKGROUND: Several evidences suggested that ovarian cancer (OC) patients showing isolated lymph node recurrence (ILNR) have an indolent evolution. The aim of the study was to retrospectively review ILNR observed in our Institution over the past 11 years in order to investigate: the pattern of disease progression after the

first diagnosis of ILNR, and their clinical outcome. METHODS: Between September 1995 and September 2006, 523 epithelial OC were diagnosed in our centers, and 301 of these relapsed. Cases with a diagnosis of ILNR, and at least 12 months of follow up after the diagnosis of ILNR were included. Post-relapse survival (PRS) was recorded from the date of the diagnosis of ILNR to the date of death or date last seen. Survival probabilities were estimated according to the method of Kaplan and Meier and compared by the log rank test. Cox's regression model with stepwise variable selection was used to analyse the role of clinico-pathological parameters as prognostic factors for PRS. RESULTS: Thirty-two cases were identified as ILNR (10.6% of the recurrences, and 6.1% of the OC population). Most of the patients continued to exhibit the same pattern of progression during follow up, with 75% of the patients free from peritoneal disease after 2 years from the diagnosis of ILNR. Median Post-Relapse Survival (PRS) was 37 months, and median Overall Survival (OS) was 109 months, with all patients surviving more than 2 years after the initial diagnosis. In multivariate analysis only Platinum-Free Interval (PFI) retained a prognostic role for PRS (p value = 0.033). CONCLUSION: ILNR represents a less aggressive pattern of OC relapse which keeps progressing in the lymph nodes in a relatively high percentage of cases. On the other hand, the occurrence of peritoneal spreading after ILNR is associated with a rapidly fatal outcome.

Lindqvist, P. G., C. Hellsten, et al. (2008). "Screening history of women in Malmo with invasive cervical cancer." Eur J Obstet Gynecol Reprod Biol **137**(1): 77-83.

OBJECTIVES: Cervical cancer is one of the most common forms of cancer among women. Cytological screening and follow-up are potentially effective procedures for preventing the development of - and mortality from - cervical cancer. The purpose of this study was to investigate the screening history of women diagnosed with cervical cancer with the aim of improving the screening programme. STUDY DESIGN: All of the 187 women diagnosed with invasive cervical cancer in Malmo between 1991 and 2000 were identified, and those below 61 years of age (n=130) were included in the analysis. The cytological and histological screening history of these women prior to their diagnosis was scrutinized. We analyzed shortcomings related to the cervical screening with special attention to participation defined as having had a cervical smear within 1 year of the scheduled time. RESULTS: Of the non-participants who developed cervical cancer (n=70), roughly one-third "never participated," half were "sub-optimal participants," and one-sixth were "decliners," i.e., women who declined the recommended measures. Among participants (n=60), 80% were either "unexplained" (n=35) or "misread as normal" (n=13). The 9.5% subgroup of non-participants was at an 11-fold increased risk of being diagnosed with invasive cervical cancer. CONCLUSION: The greatest reduction in cervical cancer would be realized if non-participants could be brought into the screening program.

Longo, D. R., T. B. Patrick, et al. (2001). "The natural history of the use of healthcare information by women with breast cancer: a conceptual model." Proc AMIA Symp: 413-7.

The overall goal of our research agenda is to contribute to improved quality of healthcare by identifying factors that foster or inhibit the use of healthcare information by patients to make informed healthcare decisions. We propose to study the natural history of the use of healthcare information by women with breast cancer to support decisions about health care. To do so in this paper we propose a conceptual model developed based on an extensive literature review and critique that describes patients' health information use over the disease course. It will guide our further investigation of the complex relationships among patients' personal circumstances, the progress of their medical treatment, and their satisfaction and empowerment as informed decision-makers. The model will help policy makers and health professionals identify the best means to provide patients with useful information, and help all stakeholders in health care acquire information needed to improve healthcare quality.

Lykins, E. L., L. O. Graue, et al. (2008). "Beliefs about cancer causation and prevention as a function of personal and family history of cancer: a national, population-based study." Psychooncology **17**(10): 967-74.

OBJECTIVE: Research suggests individuals possess multifaceted cognitive representations of various diseases. These illness representations consist of various beliefs, including causal attributions for the disease, and are believed to motivate, guide, and shape health-related behavior. As little research has examined factors associated with beliefs about cancer causation, this study examined the relationship between personal and family history of cancer and beliefs about the causes and prevention of malignant disease. METHODS: Data were obtained from 6369 adult respondents to the 2003 Health Information National Trends Survey, a national population-based survey. Information about personal and family history of cancer and beliefs regarding cancer causation and prevention was obtained. RESULTS: Results showed

both a personal and family history of cancer were associated with differences in beliefs about the causes of cancer. In general, a personal history of cancer was not significantly linked to causal attributions for cancer relative to those without a personal history. In contrast, a family history of cancer tended to increase the likelihood a respondent viewed a particular cause as increasing cancer risk. Thus, personal and vicarious experience with cancer had dramatically diverging influences on attributions of cancer causation, which may be due to differing self-protection motives. CONCLUSION: Results support the belief that illness representations, in this case the causal belief component, are influenced by both personal and vicarious experience with a disease and also suggest illness representations may influence receptivity to messages and interventions designed to increase appropriate cancer risk reduction behavior.

Lynch, H. T. and J. F. Lynch (2002). "Hereditary cancer: family history, diagnosis, molecular genetics, ecogenetics, and management strategies." Biochimie **84**(1): 3-17.

The translation of knowledge about hereditary breast cancer and its improved control, as well as prevention through prophylactic surgery, has been significantly accelerated through the veritable explosive discoveries in molecular genetics inclusive of BRCA1 and BRCA2 germline mutations. Needed however, among the physician community, medical geneticists, and genetic counselors, is a raised level of knowledge about hereditary breast cancer syndromes. Particular attention needs to be given to their extant genotypic and phenotypic heterogeneity, their natural history, and foremost, the requirement of a sufficiently detailed family history, with knowledge as to how to interpret its significance so that hereditary cancer syndrome can be diagnosed, should it, in fact, exist in the particular family. Collectively, surveillance and management programs can then be developed for the patient and his or her high-risk relatives. We believe very firmly that this knowledge needs to be extended to the individual patient(s), first- and second-degree relatives so that they can benefit from this knowledge.

Macefield, R. C., J. A. Lane, et al. (2009). "Do the risk factors of age, family history of prostate cancer or a higher prostate specific antigen level raise anxiety at prostate biopsy?" Eur J Cancer **45**(14): 2569-73.

To date, little is known of the impact knowledge of personal risk factors has on anxiety in men undergoing biopsy tests for prostate cancer. This analysis explores anxiety scores of men at higher risk due to age, family history of prostate cancer and a higher prostate specific antigen (PSA) level when proceeding from PSA test to prostate biopsy. A prospective cohort of 4198 men aged 50-69 years with a PSA result of >3ng/ml was studied, recruited for the Prostate testing for cancer and Treatment study (ProtecT). Anxiety scores at the time of biopsy were lower in older men ($p<0.001$). No age group showed an increase in anxiety as the men proceeded from PSA testing to biopsy, although older men did not show the same level of decrease in anxiety as younger men ($p=0.035$). There was no difference in anxiety scores at biopsy between men with or without a family history of prostate cancer ($p=0.68$), or between those with a raised PSA of 10-<20ng/ml compared to a PSA result of 3-<10ng/ml ($p=0.46$). Change in scores since the initial PSA test appeared unaffected by family history ($p=0.995$) or by PSA result ($p=0.76$). Within the context of a research study, the increased risk of prostate cancer through older age, having a family history of prostate cancer, or having a significantly elevated PSA level appears to have no detrimental effect on men's anxiety level when proceeding to biopsy.

Madanat, L. M., P. M. Lahteenmaki, et al. (2007). "The natural history of thyroid function abnormalities after treatment for childhood cancer." Eur J Cancer **43**(7): 1161-70.

The aim of the study was to find out which of childhood cancer survivors are at higher risk of thyroid dysfunction, and the timeframe for its development. The consequences of different treatments, particularly chemotherapy, were of interest. Follow-up data for 291 patients from a cohort of 360 patients were available and analysed in this retrospective study. Impaired thyroid function occurred in 71/291 (24%) patients: brain tumours 30/65 (46%), Hodgkin's disease (HD) 10/21 (48%), leukaemia/non Hodgkin's lymphoma (NHL) 19/140 (14%) and others 12/65 (18%). Patients with brain tumours had a higher hazard ratio (HR) over leukaemia/NHL (HR 7.47) but not over HD (HR 1.57). These patients also developed thyroid hypofunction earlier than patients with HD or leukaemia/NHL. Age at diagnosis did not have an effect on the occurrence or timeframe of development of thyroid hypofunction. Radiotherapy (HR 4.68) and radiotherapy combined with chemotherapy (HR 2.90) were associated with a higher risk than chemotherapy alone. Chemotherapy added to radiotherapy tended to increase risk (HR 2.42 95% confidence interval (CI) 1.00-5.87). Craniospinal irradiation did not differ significantly from total body irradiation (TBI) (HR 1.09 95%CI 0.25-4.76) or direct thyroid irradiation (HR 0.81 95%CI 0.32-2.06), but cranial irradiation (CIR) (HR 0.18 95%CI 0.08-0.38) was less harmful to thyroid function. Girls were more prone to effects of irradiation (HR 2.10 95%CI 1.15-3.82). All

treatments, excluding surgery, predispose to thyroid dysfunction. Suggestions for follow-up of thyroid function are made.

Madlensky, L., S. W. Flatt, et al. (2005). "Is family history related to preventive health behaviors and medical management in breast cancer patients?" Breast Cancer Res Treat **90**(1): 47-54.

INTRODUCTION: Women diagnosed with breast cancer who also have a family history of the disease are at increased risk of developing additional primary breast or ovarian cancers. We investigated whether a relationship exists between family history and health behaviors in a cross-sectional study of breast cancer survivors. METHODS: Participants in the Women's Healthy Eating and Living (WHEL) Study (a randomized trial designed to test the effect of a plant-based diet on breast cancer recurrence) completed baseline questionnaires about their family history and health behaviors. Medical records and self-reports provided treatment data. Participants were defined as having a family history (FH+) if they met specific family history criteria (n=195), and were compared with women having no family history (FH-) of breast cancer (n=1736). RESULTS: The mean age of breast cancer diagnosis was 51.2 years for both groups, but FH+ women were more likely to be diagnosed before age 40. FH+ and FH- women had similar dietary patterns, alcohol intake, exercise patterns, body mass index and smoking histories. However, FH+ women were more likely to have undergone prophylactic contralateral mastectomy (OR=3.6, 95% CI=2.2 - 6.2) and bilateral oophorectomy (OR=1.6; 95% CI=1.0 - 2.3) following diagnosis, adjusted for age and time since diagnosis. The FH+ and FH- groups had similar patterns of use of anti-estrogen medications and frequency of medical follow-up. CONCLUSIONS: Breast cancer survivors with a strong family history of breast cancer are more likely to undergo surgical preventive measures to reduce their risk of additional cancer, but do not report undertaking more preventive lifestyle behaviors compared to breast cancer survivors without a family history.

Maheu, C. (2009). "Implications of living with a strong family history of breast cancer." Can J Nurs Res **41**(2): 100-12.

The findings presented here are from a qualitative study in which data were gathered from 20 women who had received inconclusive genetic testing results for inherited breast cancer susceptibility. Before describing the significance, for them, of their genetic test results, all of the participants related what it was like to live with a strong family history of breast cancer. The focus of this article is the women's experience of living with a personal and strong family history of breast cancer. For these women, having such a history had become a fact of life that could not be ignored.Three themes were identified in the data: expecting and dealing with a diagnosis of breast cancer protecting oneself and others, and increasing exposure to cancer screening procedures. These themes address the underlying reality that having a personal and family history of breast cancer is not an isolated situation but part of one's journey in choosing to undergo genetic testing for inherited breast cancer susceptibility.

Major, P. P., R. J. Cook, et al. (2009). "Natural history of malignant bone disease in breast cancer and the use of cumulative mean functions to measure skeletal morbidity." BMC Cancer **9**: 272.

BACKGROUND: Bone metastases are a common cause of skeletal morbidity in patients with advanced cancer. The pattern of skeletal morbidity is complex, and the number of skeletal complications is influenced by the duration of survival. Because many patients with cancer die before trial completion, there is a need for survival-adjusted methods to accurately assess the effects of treatment on skeletal morbidity. METHODS: Recently, a survival-adjusted cumulative mean function model has been generated that can provide an intuitive graphic representation of skeletal morbidity throughout a study. This model was applied to the placebo-control arm of a pamidronate study in patients with malignant bone disease from breast cancer. RESULTS: Analysis by bone lesion location showed that spinal metastases were associated with the highest cumulative mean incidence of skeletal-related events (SREs), followed by chest and pelvic metastases. Metastases located in the extremities were associated with an intermediate incidence of SREs, and those in the skull were associated with the lowest incidence of SREs. CONCLUSION: Application of this model to data from the placebo arm of this trial revealed important insight into the natural history of skeletal morbidity in patients with bone metastases. Based on these observations, treatment for the prevention of SREs is warranted regardless of lesion location except for metastases on the skull.

Makarov, D. V., E. B. Humphreys, et al. (2008). "The natural history of men treated with deferred androgen deprivation therapy in whom metastatic prostate cancer developed following radical prostatectomy." J Urol **179**(1): 156-61; discussion 161-2.

PURPOSE: We report on the natural history and factors influencing the prognosis of a cohort of hormone naive, prostate specific antigen era patients in whom metastatic prostate cancer developed after radical prostatectomy who were followed closely and

treated with deferred androgen deprivation therapy at the time of metastasis. MATERIALS AND METHODS: A total of 3,096 men underwent radical prostatectomy performed by a single surgeon at Johns Hopkins Hospital between 1987 and 2005. Of these men 422 had prostate specific antigen failure. Distant metastasis developed in 123 patients, of whom 91 with complete data formed the study cohort initially treated during the prostate specific antigen era (1987 to 2005) and receiving androgen deprivation therapy after documented metastasis. A total of 41 men died of prostate cancer. Median survival times were estimated by Kaplan-Meier analysis. Prognostic impact was estimated as the hazard ratio derived from the Cox proportional hazards model. RESULTS: Median followup from radical prostatectomy was 120 months (range 24 to 216). Kaplan-Meier median (range) times to failure were 24 months (12 to 144) from radical prostatectomy to prostate specific antigen failure, 36 months (0 to 132) from prostate specific antigen failure to metastasis, 84 months (12 to 180) from metastasis to death and 168 months (24 to 216) from radical prostatectomy to death. Statistically significant univariate risk factors for prostate cancer specific mortality at the time of metastasis were pain at diagnosis of metastases ($p = 0.002$), time from radical prostatectomy to metastasis ($p = 0.024$) and prostate specific antigen doubling time less than 3 months during the 24 months before metastasis ($p = 0.016$). Multivariable analysis demonstrated independent predictors of prostate cancer specific mortality at the time of metastasis, namely pain (HR 3.5, $p = 0.003$) and prostate specific antigen doubling time less than 3 months (HR 3.4, $p = 0.017$). CONCLUSIONS: Men treated with deferred androgen deprivation therapy for the development of metastasis after radical prostatectomy may have a long life span, 169 months after radical prostatectomy (range 24 to 216). The presence of pain and short prostate specific antigen doubling time predicted an unfavorable outcome.

Makinen, T., T. L. Tammela, et al. (2002). "Family history and prostate cancer screening with prostate-specific antigen." J Clin Oncol **20**(11): 2658-63.

PURPOSE: Early detection of prostate cancer has been recommended for men with affected first-degree relatives despite the lack of evidence for mortality reduction. We therefore evaluated the impact of family history in the Finnish prostate cancer screening trial. PATIENTS AND METHODS: Approximately 80,000 men were identified from the population register for the first screening round. Of the 32,000 men randomized to the screening arm, 30,403 were eligible at the time of invitation. A blood sample was drawn from the participants (n = 20,716), and serum prostate-specific antigen (PSA) was determined. Men with a PSA level > or = 4.0 ng/mL were referred for prostate biopsy. Information on family history was obtained through a self-administered questionnaire at baseline. RESULTS: A total of 964 (5%) of the 20,716 screening participants had a positive family history, and 105 (11%) were screening-positive. Twenty-nine tumors were diagnosed, corresponding to a detection rate of 3.0% (29 of 964) and a positive predictive value of 28% (29 of 105). Of the 19,347 men without a family history, 1,487 (8%) had a PSA level > or = 4.0 ng/mL. The detection rate was 2.4% (462 of 19,347) and the positive predictive value was 31% (462 of 1,487). The risk associated with a positive family history was not substantially increased (rate ratio, 1.3; 95% confidence interval, 0.9 to 1.8). The results were not affected by the age of the screenee or age at diagnosis of the affected relative. The program sensitivity was 6% (29 of 491) (ie, selective screening policy would have missed 94% of cancers in the population). No differences were seen in the characteristics of screen-detected cancers by family history. CONCLUSION: Our findings provide no support for selective screening among men with affected relatives.

Mann, B. S., J. R. Johnson, et al. (2005). "Letrozole in the extended adjuvant treatment of postmenopausal women with history of early-stage breast cancer who have completed 5 years of adjuvant tamoxifen." Clin Cancer Res **11**(16): 5671-7.

PURPOSE: To present the basis of the decision of the Food and Drug Administration to grant accelerated approval for letrozole for extended adjuvant treatment of early-stage breast cancer in postmenopausal women after completion of adjuvant tamoxifen. EXPERIMENTAL DESIGN: The Food and Drug Administration reviewed the data from the MA17 trial, a single, multinational, randomized, double-blind, and placebo-controlled trial, submitted by the applicant to support the proposed new indication. RESULTS: MA17 consisted of a core study and Lipid and Bone Mineral Density safety substudies. It enrolled 5,187 patients. In the core study, median treatment duration was 24 months and median follow-up duration was 27.4 months. Using a conventional definition of disease-free survival, 122 events on letrozole and 193 events on placebo were observed (hazard ratio, 0.62; 95% confidence interval, 0.49-0.78; P = 0.00003). Distant disease-free survival also improved with letrozole, 55 versus 92 events (hazard ratio, 0.61; 95% confidence interval, 0.44-0.84; P = 0.003). No statistically significant improvement in overall survival was observed. Hot flushes, arthralgia/arthritis, myalgia, and new diagnosis of osteoporosis were more common on letrozole. Frequency of fractures and cardiovascular

ischemic events was not significantly different. A statistically significant mean decrease in bone mineral density in the hip occurred at 24 months on letrozole. CONCLUSIONS: Letrozole administration led to a statistically significant prolongation in disease-free survival. Fractures and cardiovascular events were similar to placebo; however, new diagnoses of osteoporosis were more frequent. Short duration of treatment and follow-up precluded assessment of long-term safety and efficacy. Thus, accelerated approval was granted instead of regular approval.

Maradiegue, A., K. Jasperson, et al. (2008). "Scoping the family history: assessment of Lynch syndrome (hereditary nonpolyposis colorectal cancer) in primary care settings--a primer for nurse practitioners." J Am Acad Nurse Pract **20**(2): 76-84.

PURPOSE: To describe and discuss the characteristic features and red flags of Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer, that warrants referral for genetic cancer risk assessment (GCRA). A focus on the nurse practitioner's (NP) role in familial risk assessment, physical examination, initiation of genetic referrals, and issues related to the genetic counseling process are also discussed. DATA SOURCES: A review and synopsis of professional guidelines, clinical articles, and research studies on Lynch syndrome and the genetics of inherited cancer syndromes associated with colorectal cancer. Online resources from the American Gastroenterological Association, American Medical Association, the American Nurses Association, the National Comprehensive Cancer Network, the National Cancer Institute, the National Cancer Institute-Physician Data Query, the National Coalition of Health Professional Education in Genetics, the National Human Genome Research Institute, the National Society of Genetic Counselors, International Society of Nurses in Genetics, and the Oncology Nursing Society. CONCLUSIONS: Approximately 5% of all colon cancers are because of a germ line mutation predisposing individuals and their family members to colorectal and other cancers. Although the efficacy of screening modalities is established, healthcare providers often fail to identify those at greatest risk for disease. The extended family history is the first step in recognition of individuals "suspect" for hereditary colon cancers such as Lynch syndrome. Early-age onset of Lynch syndrome-associated cancers, an autosomal-dominant pattern, multiple primary tumors in an individual or multiple family members with Lynch syndrome-associated cancers, characteristic pathological features of colon cancer, or a known germ line Lynch syndrome mutation in a family member are "red flags" that will aid NPs in identifying individuals who may benefit from GCRA. IMPLICATIONS FOR NURSE PRACTITIONER PRACTICE: The importance of enhanced surveillance for early diagnosis and prevention of disease is a critical part of primary care. Thus, it is imperative that NPs obtain a minimum of a three-generation pedigree, recognize hereditary cancer patterns, and provide referral counseling for consideration of genetic testing of individuals suspect for Lynch syndrome.

Margolin, S., H. Johansson, et al. (2006). "Family history, and impact on clinical presentation and prognosis, in a population-based breast cancer cohort from the Stockholm County." Fam Cancer **5**(4): 309-21.

BACKGROUND: The aim of the present study was to define the proportion of different levels of family history in a cohort of consecutive breast cancer patients from the Stockholm region, and to assess whether familial breast cancer has phenotypic traits different from those of sporadic patients. METHODS: All incident breast cancer patients in a 19-month period were eligible for the study and 70% (489/696) participated. The family history and clinical parameters were obtained from questionnaires and medical records. RESULTS: In total 35% had a family history. Age at onset was 58.9 years in the familial group vs. 60.7 years in the sporadic patients (P = 0.14) and 8% of the familial patients had bilateral breast cancer compared to 4% in the sporadic group (P = 0.08). There were 31% node positive tumors in the sporadic group vs. 22% in the cases with family history (P = 0.04). Hormonal background, treatment and prognosis (median follow-up 4.7 years) were not related to family history. CONCLUSION: In addition to high-risk familial breast and breast-ovarian cancer, constituting about 10% of all breast cancer cases, another 25% of the breast cancer cases have a family history, a group hypothetically valuable for association studies on low-risk genes. In contrast to previous reports, we did not observe a relationship between family history and phenotypic traits. A possible explanation for this can be different study design. The considerable heterogeneity in familial breast cancer means that different criteria for familiality can influence the result. Furthermore, our study was prospective and population based and included paternal inheritance.

Markman, M. (2006). "Management of ovarian cancer. An impressive history of improvement in survival and quality of life." Oncology (Williston Park) **20**(4): 347-54; discussion 354, 357-8, 364 passim.

Over the past 2 decades, we have seen major progress in the management of women with ovarian

cancer, with improvements in both overall survival and quality of life. To truly appreciate this progress, it is important to understand the state of affairs regarding the treatment of ovarian cancer in the early 1980s. This paper will discuss that historical background, describe the increasingly favorable impact of evolving treatment paradigms in ovarian cancer, and note future directions for clinical research in this complex disease process.

Martin, W. and L. Degner (2006). "Perception of risk and surveillance practices of women with a family history of breast cancer." Cancer Nurs **29**(3): 227-35.

A retrospective study was designed to examine the relationship between perception of risk and surveillance activities (mammography and clinical breast examination) in women with a family history of breast cancer. The Revised Susceptibility, Benefits, and Barriers Scale for Mammography Screening, the Centre for Epidemiology Studies--Depression Scale (CES-D), and a demographic form were administered to a convenience sample of 56 women. There were no significant relationships between perceived risk and screening activities. No significant correlations were found between age or depressive symptoms with either perceived risk or screening behaviors. Women with postsecondary qualifications were more likely to obtain regular mammograms. A substantial portion (34.5%) of participants reported depressive symptoms at a level associated with clinically significant levels of depression (>or=16 on the CES-D). Women over age 50 reported significantly more depressive symptoms than younger women. Perceived risk was not associated with screening; however, depression should be considered closely when dealing with women with higher-than-average risk of breast cancer.

Marttunen, M. B., P. Hietanen, et al. (2001). "A prospective study on women with a history of breast cancer and with or without estrogen replacement therapy." Maturitas **39**(3): 217-25.

OBJECTIVE: Because a categorical refusal of estrogen replacement therapy (ERT) from postmenopausal patients with a history of breast cancer is not based on any research evidence and may be more harmful than beneficial, we evaluated the safety and efficacy of ERT in these women. METHODS: We recruited 131 patients who had been treated for breast cancer for a mean of 4.2 years (range 1 month to 20 years) before. Eighty-eight decided to use ERT, whereas 43 refused or had no need for ERT. At recruitment, the patients were carefully examined for breast and gynaecologic findings. Non-hysterectomized patients wishing to receive ERT (n=54) then started using estradiol as oral tablets (2 mg/day) (n=44) or as transdermal gel (1.5 mg/day) (n=10) in combination with 10-day courses of oral medroxyprogesterone acetate at 4-week intervals, whereas hysterectomized patients (n=34) used only estradiol, orally (2 mg/day) (n=31) or transdermally (1.5 mg/day) (n=3). The patients using ERT were carefully examined 6 and 12 months later, and then annually at a specific outpatient department, and the mean follow-up time is now 2.5 years (range from 1 month to 5.2 years, 216 woman-years). The 43 patients not wishing to receive ERT were followed annually at the oncologic department for a mean of 2.6 years (range from 1 month to 4.7 years), and served as a control group. RESULTS: ERT significantly reduced climacteric symptoms, and the Kupperman score fell by 63%, from 26.9+/-8.6 to 9.9+/-6.7 (mean+/-SD). In non-hysterectomized women, medroxyprogesterone acetate triggered withdrawal bleeding in all except seven women. Seven patients (13%) experienced spotting during ERT. In 27 women, endometrial thickness exceeded 10 mm, and two of the total of 54 patients (3.7%) had simple hyperplasia. This vanished spontaneously in 3-6 months. Ten patients terminated the use of ERT within the first 12 to 39 months due to the lack of severe vasomotor symptoms (n=4) or due to the recurrence of breast cancer or to cancer of the contralateral breast (n=6). Eighty-one of the 88 patients (92%) using ERT showed no evidence of recurrence, whereas five patients (5.7%) had recurrence in 12-36 months and two patients (2.3%) developed a cancer of the contralateral breast in 14-24 months; another one of those wanted to continue with ERT. Thus the combined risk of recurrence or a new cancer of the contralateral breast in ERT users was 7/216 woman-years (3% per year). In the control group, 38 of 43 patients (88.4%) showed no evidence of recurrence or contralateral cancer, whereas four patients had recurrence and one developed a contralateral breast cancer (5/112 woman-years, 4% per year). CONCLUSIONS: Symptomatic climacteric patients with a history of breast cancer benefited from ERT without increasing their risk of recurrence, but the short follow-up and the small number of patients limit any definitive recommendations.

Matloff, E. T., A. Moyer, et al. (2006). "Healthy women with a family history of breast cancer: impact of a tailored genetic counseling intervention on risk perception, knowledge, and menopausal therapy decision making." J Womens Health (Larchmt) **15**(7): 843-56.

BACKGROUND: Women with a family history of breast cancer have several menopausal therapy options, including tamoxifen, hormone therapy (HT), alternative medications, or no treatment. This complex decision should be based on each

woman's risk to develop breast cancer, menopausal symptoms, preferences, and risks for other conditions. The authors determined the effects of a personalized risk assessment and genetic counseling intervention on knowledge, risk perception, and decision making in a group of healthy women who had a first-degree relative with breast cancer. METHODS: Forty-eight cancer-free menopausal women age > or =40 years who had at least one first-degree relative with breast cancer were randomized to a genetic counseling intervention or control. Intervention participants were given a personalized risk assessment for breast cancer, heart disease, osteoporosis, and uterine cancer based on family history and personal health data. Knowledge, risk perception, and medication usage were measured at baseline, 1 month, and 6 months. RESULTS: Knowledge was higher in the intervention group at both follow-up time points postintervention. Perceived risk for developing breast cancer was significantly lower and more accurate in the intervention group at 1 and 6 months postintervention than at baseline, as was perceived risk of developing heart disease. Although the counseling intervention did affect both knowledge and risk perception, overall, both groups were reluctant to take any form of menopausal therapy. CONCLUSIONS: A personalized risk assessment and genetic counseling intervention improves patient knowledge and risk perception; however, it is unclear that the intervention influenced menopausal treatment decisions.

McCredie, M. R., K. J. Sharples, et al. (2008). "Natural history of cervical neoplasia and risk of invasive cancer in women with cervical intraepithelial neoplasia 3: a retrospective cohort study." Lancet Oncol **9**(5): 425-34.

BACKGROUND: The invasive potential of cervical intraepithelial neoplasia 3 (CIN3; also termed stage 0 carcinoma) has been poorly defined. At the National Women's Hospital, Auckland, New Zealand, treatment of CIN3 was withheld from a substantial number of women between 1965 and 1974 as part of an unethical clinical study. The resulting variation in management allows comparison of the long-term risk of invasive cancer of the cervix in women whose lesion was minimally disturbed with those who had adequate initial treatment followed by conventional management. We aimed to estimate the long-term risk of invasive cancer in these two groups of women. A judicial inquiry referred for independent clinical review in 1988 all women for whom there remained doubt about the adequacy of their management. METHODS: Between February, 2001, and December, 2004, medical records, cytology, and histopathology were reviewed for all women with CIN3 diagnosed between 1955 and 1976, whose treatment was reviewed by judicial inquiry and whose medical records could be located, and linkages were done with cancer and death registers and electoral rolls. To take into account the probability that the CIN3 lesion had been completely removed, we classified adequacy of treatment by type of procedure, presence of CIN3 at the excision margin, and subsequent cytology. The primary outcome was cumulative incidence of invasive cancer of the cervix or vaginal vault. Follow-up continued until death or Dec 31, 2000, whichever came first. Analyses accounted for procedures during follow-up. FINDINGS: 1229 women whose treatment was reviewed by the judicial inquiry in 1987-88 were included. Of these, 48 records (4%) could not be located and 47 women (4%) did not meet the inclusion criteria. At histopathological review, a further 71 (6% of 1134) women were excluded because the review diagnosis was not CIN3. We identified outcomes in the remaining 1063 (86% of 1229) women diagnosed with CIN3 at the hospital in 1955-76. In 143 women managed only by punch or wedge biopsy, cumulative incidence of invasive cancer of the cervix or vaginal vault was 31.3% (95% CI 22.7-42.3) at 30 years, and 50.3% (37.3-64.9) in the subset of 92 such women who had persistent disease within 24 months. However, cancer risk at 30 years was only 0.7% (0.3-1.9) in 593 women whose initial treatment was deemed adequate or probably adequate, and whose treatment for recurrent disease was conventional. INTERPRETATION: This study provides the most valid direct estimates yet available of the rate of progression from CIN3 to invasive cancer. Women with untreated CIN3 are at high risk of cervical cancer, whereas the risk is very low in women treated conventionally throughout.

McDonnell, S. K., D. J. Schaid, et al. (2001). "Efficacy of contralateral prophylactic mastectomy in women with a personal and family history of breast cancer." J Clin Oncol **19**(19): 3938-43.

PURPOSE: To estimate the efficacy of contralateral prophylactic mastectomy in women with a personal and family history of breast cancer. PATIENTS AND METHODS: We followed the course of 745 women with a first breast cancer and a family history of breast and/or ovarian cancer who underwent contralateral prophylactic mastectomy at the Mayo Clinic between 1960 and 1993. Family history information and cancer follow-up information were obtained from the medical record, a study-specific questionnaire, and telephone follow-up. Life-tables for contralateral breast cancers, which consider age at first breast cancer, current age, and type of family history, were used to calculate the number of breast cancers expected in our cohort had they not had a prophylactic mastectomy. RESULTS: Of the 745

women in our cohort, 388 were premenopausal (age < 50 years) and 357 were post- menopausal. Eight women developed a contralateral breast cancer. Six events were observed among the premenopausal women, compared with 106.2 predicted, resulting in a risk reduction of 94.4% (95% confidence interval [CI], 87.7% to 97.9%). For the 357 postmenopausal women, 50.3 contralateral breast cancers were predicted, whereas only two were observed, representing a 96.0% risk reduction (95% CI, 85.6% to 99.5%). CONCLUSION: The incidence of contralateral breast cancer seems to be reduced significantly after contralateral prophylactic mastectomy in women with a personal and family history of breast cancer.

McKean-Cowdin, R., H. S. Feigelson, et al. (2001). "Risk of endometrial cancer and estrogen replacement therapy history by CYP17 genotype." Cancer Res **61**(3): 848-9.

Common variants among genes coding for enzymes in sex steroid biosynthetic pathways may influence the risk of endometrial cancer. We examined the association between endometrial cancer risk and estrogen replacement therapy (ERT) by CYP17 genotype using 51 incident cases and 391 randomly selected controls from a multiethnic cohort in Hawaii and Los Angeles, California. The relative risk of endometrial cancer was calculated for ever use versus never use of ERT by CYP17 genotype (TT, TC, and CC). We found that women who reported ever taking ERT were more than twice as likely to develop endometrial cancer as women who never took ERT [odds ratio (OR), 2.24; 95% confidence interval (CI), 1.19-4.23]. Among these women, the risk of endometrial cancer was higher for women homozygous for the CYP17 T allele (OR, 4.10; 95% CI, 1.64-10.3), but not for women with the C allele (OR, 1.31; 95% CI, 0.53-3.21). These preliminary findings suggest that CYP17 or other variants in estrogen biosynthesis or metabolism pathways may be potential markers of endometrial cancer susceptibility due to ERT.

Mehdipour, P., M. Atri, et al. (2003). "Laddering through pedigrees: family history of malignancies in primary breast cancer patients." Asian Pac J Cancer Prev **4**(3): 185-92.

A family history (FH) of breast cancer (BC) is a long recognized risk factor for developing the disease. Also, there have been some reports of links between an FH and some other malignancies (mostly uterus, ovary, and prostate cancers), and an increased risk of developing BC. In this paper we present descriptive report of the occurrence pattern of malignancies in families of BC afflicted patients through 4 generations. Patients included 542 Iranian primary BC cases, presenting at an outpatient clinic for treatment and follow-up. Detailed pedigrees were drawn for each patient, and data for a total of 6220 relatives were gathered. Among the probands, 29.9% and 53.9% had a positive FH of BC and other malignancies (OM) respectively. Mean number of breast cancers was nearly double in maternal-lines versus paternal-line relatives. Also, occurrence of brain, uterus, and colorectal cancers was significantly higher in maternal-line relatives, but conversely, liver cancer showed a tendency toward paternal-line relatives (1st degree relatives excluded). The highest frequency of BC involvement was noted in 2nd degree/2nd generation, and 3rd degree/3rd generation relatives. For OMs, although gastric cancer was by far the most frequent OM across pedigrees, uterus cancer, and hematopoeitic system lesions (leukemia) predominated over gastric cancer through the 3rd and 4th generations respectively. We did not find any relation between having a positive FH of BC, and developing early-onset BC. The findings discussed in this paper were partially presented at the 18th UICC International Cancer Congress, Oslo-Norway, 30 June-5 July 2002.

Metcalfe, K. A., W. D. Foulkes, et al. (2008). "Family history as a predictor of uptake of cancer preventive procedures by women with a BRCA1 or BRCA2 mutation." Clin Genet **73**(5): 474-9.

Women with a BRCA1 or BRCA2 mutation are at an elevated risk of developing breast and ovarian cancer; however, it is unclear to what extent family history influences the uptake of cancer prevention options. Women with a BRCA1/2 mutation completed a follow-up questionnaire that assessed uptake of cancer preventive options. The pedigree of each woman was reviewed, and information was recorded on cancers diagnosed in relatives. Five hundred and seventeen women were included in the study. Women with a sister with breast cancer were more likely to have a prophylactic mastectomy than those without a sister with breast cancer [odds ratios (OR) = 2.4, p = 0.003]. Uptake of prophylactic mastectomy was significantly lower in women with a mother with ovarian cancer compared with those whose mother did not have ovarian cancer (OR = 0.4, p = 0.01). Having a mother or sister with ovarian cancer significantly predicted the uptake of prophylactic oophorectomy (OR = 1.6, p = 0.04). Women with a BRCA2 mutation were less likely to have a prophylactic oophorectomy than those with a BRCA1 mutation (OR = 0.49, p = 0.0004). Among women with a BRCA1 or BRCA2 mutation, family history predicts the uptake of prophylactic mastectomy and prophylactic oophorectomy.

Miller, V. A., M. G. Kris, et al. (2004). "Bronchioloalveolar pathologic subtype and smoking history predict sensitivity to gefitinib in advanced non-small-cell lung cancer." J Clin Oncol **22**(6): 1103-9.

PURPOSE: Gefitinib, an inhibitor of the epidermal growth factor receptor tyrosine kinase, induces radiographic regressions and symptomatic improvement in patients with non-small-cell lung cancer (NSCLC). Phase II trials suggested female sex and adenocarcinoma were associated with response. We undertook this analysis to identify additional clinical and pathologic features associated with sensitivity to gefitinib. PATIENTS AND METHODS: We reviewed medical records, pathologic material, and imaging studies of all 139 NSCLC patients treated on one of three consecutive studies of gefitinib monotherapy performed at our institution. We identified patients experiencing a major objective response and compared their clinical and pathologic features with the others. Univariate and multivariable analyses were performed on potential predictive features associated with sensitivity to gefitinib. RESULTS: Of 139 patients, 21 (15%; 95% CI, 9% to 21%), experienced a partial radiographic response. Variables identified as significant in univariate analysis included adenocarcinoma versus other NSCLC (19% v 0%; P=.004), adenocarcinoma with bronchioloalveolar features versus other adenocarcinomas (38% v 14%; P<.001), never smoker status versus former/current (36% v 8%; P<.001), and Karnofsky performance status > or =80% versus < or =70% (22% v 8%; P=.03). Multivariable analysis revealed the presence of adenocarcinoma with any bronchioloalveolar features (P=.004) and being a never smoker (P=.006) were independent predictors of response. CONCLUSION: Our data suggest that individuals in whom gefitinib is efficacious are more likely to have adenocarcinomas of the bronchioloalveolar subtype and to be never smokers. These observations may provide clues to mechanisms determining sensitivity to this agent and suggest that NSCLC has a different biology in patients who never smoked and those with bronchioloalveolar carcinoma.

Ming, M. E., R. M. Levy, et al. (2004). "Validity of patient self-reported history of skin cancer." Arch Dermatol **140**(6): 730-5.

OBJECTIVE: To determine the validity of patient self-report of skin cancer history. DESIGN: A cohort of patients was randomly selected from the case group in a prior case-control study involving skin cancer, and a second cohort was randomly selected from the controls of that study. Patient self-reported history (as determined by responses to a survey) was compared with the gold standard of chart documentation of a pathology report or a procedure note from Mohs micrographic surgery demonstrating skin cancer. SETTING: University-based outpatient dermatology clinic. PATIENTS: Three hundred patients were selected. MAIN OUTCOME MEASURES: Patients were considered to have correctly classified their skin cancer history if their self-reported history was consistent with chart documentation. RESULTS: We obtained chart information for 258 patients.Of those patients, 183 (70.9%) had chart documentation of nonmelanoma skin cancer, and 16 (6.2%) had chart documentation of a melanoma. Using chart documentation as the gold standard, we found that patients correctly identified their basal cell carcinoma status in 84.3% of cases; their squamous cell carcinoma status in 81.5% of cases; their overall nonmelanoma skin cancer status in 91.8% of cases; their melanoma status in 94.8% of cases; and their overall skin cancer status in 92.6% of cases. Patients' self-reported history of skin cancer of any type had a positive predictive value of 95.1% and a negative predictive value of 85.9%. CONCLUSIONS: Self-reported history of skin cancer had a high degree of sensitivity and specificity and a high positive and negative predictive value within the study population. Obtaining medical information by patient report appears to be a useful tool for determining medical history of skin cancer.

Mohr, S. B. (2009). "A brief history of vitamin d and cancer prevention." Ann Epidemiol **19**(2): 79-83.

PURPOSE: To review the history of vitamin D and its use in cancer prevention. METHODS: The literature on published studies of vitamin D and its role in human health was reviewed and summarized. RESULTS: The modern history of vitamin D began in the mid-1800s, when it was noticed that city children were more likely to have rickets than rural children. Half a century later, Palm reported that children raised in sunny climates virtually never developed rickets. McCollum isolated vitamin D, and Windaus its precursors, receiving the Nobel Prize. Other scientists later observed that people with skin cancer had lower prevalence of nonskin cancers, and that lower overall mortality rates from all internal cancers combined existed in sunnier areas. These observations went largely unnoticed, and the field stagnated until 1970, when maps were created of cancer mortality rates. Through study of these maps, Cedric and Frank Garland of Johns Hopkins University reported a strong latitudinal gradient for colon cancer mortality rates in 1980, and hypothesized that higher levels of vitamin D compounds in the serum of people in the south were responsible, and that calcium intake also would reduce incidence. Edward Gorham and

colleagues carried out cohort and nested studies, including the first study that found an association of a serum vitamin D compound with reduced cancer risk. William B. Grant then carried out numerous ecologic studies that extended the vitamin D-cancer theory to other cancers. CONCLUSIONS: The history of the role of vitamin D in human health is rich and much of that history is yet to be written not only by scientists, but by policy makers with the vision and leadership necessary to bridge the gap between research and policy.

Morgan, M. A. (2009). "Cancer survivorship: history, quality-of-life issues, and the evolving multidisciplinary approach to implementation of cancer survivorship care plans." Oncol Nurs Forum **36**(4): 429-36.

PURPOSE/OBJECTIVES: To discuss the history of cancer survivorship, related quality-of-life issues, and cancer survivorship care plans (CSCPs). DATA SOURCES: CINAHL, PubMed, published articles, and Web sites. DATA SYNTHESIS: A cancer survivor is an individual who has been diagnosed with cancer, regardless of when that diagnosis was received, who is still living. Cancer survivorship is complex and involves many aspects of care. Major areas of concern for survivors are recurrence, secondary malignancies, and long-term treatment sequelae that affect quality of life. Four essential components of survivorship care are prevention, surveillance, intervention, and coordination. A CSCP should address the survivor's long-term care, such as type of cancer, treatments received, potential side effects, and recommendations for follow-up. It should include preventive practices, how to maintain health and well-being, information on legal protections regarding employment and health insurance, and psychosocial services in the community. CONCLUSIONS: Survivorship care for patients with cancer requires a multidisciplinary effort and team approach. Enhanced knowledge of long-term complications of survivorship is needed for healthcare providers. Further research on evidence-based practice for cancer survivorship care also is necessary. IMPLICATIONS FOR NURSING: Nurses can review CSCPs with patients, instruct them when to seek treatment, promote recommended surveillance protocols, and encourage behaviors that lead to cancer prevention and promote well-being for cancer survivors.

Murff, H. J., D. Byrne, et al. (2004). "Cancer risk assessment: quality and impact of the family history interview." Am J Prev Med **27**(3): 239-45.

BACKGROUND: Identification of individuals at high risk for colon and breast cancer requires an adequate family history assessment and can influence cancer screening and genetic testing decisions. Little data exist that evaluate the completeness of the family history interview in primary care. METHODS: Retrospective chart review of 995 new patient visits to 28 primary care physicians evaluating the completeness of the family cancer history for colon or breast cancer. Family history information was evaluated for inclusion of age at diagnosis, degree of kinship, and specification of disease of interest. RESULTS: Family history information on cancer diagnoses was collected on 679 (68%) of the patients. Specific information regarding the individual affected and the cancer diagnosis was present in 414 (61%) of the records. Affected first-degree relatives were more likely to have their age of cancer diagnosis recorded than second-degree relatives (39%, 95% confidence interval [CI]=34%-44% vs 16%, 95% CI=12%-20%). Age at diagnosis of cancer in first-degree relatives was documented in 51% of colon cancers, 38% of breast cancers, and 27% of ovarian cancers. Only 17% of individuals who meet criteria for early-onset breast cancer genetic testing were referred for genetic services. CONCLUSIONS: Adequate cancer risk assessment using family history information requires age at cancer diagnosis and specification of a cancer diagnosis. Age at diagnosis was frequently missing from family history assessments, which could have a potential impact on identification of high-risk individuals. When family history information does identify high-risk individuals, only the minority are referred for genetic services.

Ness, K. K., J. M. Oakes, et al. (2005). "Prevalence of the metabolic syndrome in relation to self-reported cancer history." Ann Epidemiol **15**(3): 202-6.

PURPOSE: To estimate the prevalence of metabolic syndrome in persons with a history of cancer from a population-based sample of adults, and compare that prevalence to persons without a history of cancer. METHODS: Data from the Third National Health and Nutrition Examination Survey were analyzed to compare prevalence and prevalence differences of the metabolic syndrome, as defined by Adult Treatment Panel III criteria, between 486 persons with a reported history of cancer and 12,526 persons with no reported history of cancer. RESULTS: The prevalence of metabolic syndrome was 258/1000 persons for those with a cancer history and 184/1000 persons among those without, resulting in a prevalence difference of 74/1000 persons (95% CI, 38-110). Prevalence differences varied substantially by age at interview. The prevalence difference was highest among those aged 40 to 49 years (112/1000 persons) and 50 to 59 years (73/1000

persons), while those in younger (18-39 years) and older (: 60 years) age groups had a moderately higher prevalence among those without a cancer history. CONCLUSION: These results add to the emerging concern that metabolic syndrome and associated risks for cardiovascular disease and type 2 diabetes may be an adverse late effect of cancer and/or its treatment.

Newcomb, P. A., A. Trentham-Dietz, et al. (2001). "Fracture history and risk of breast and endometrial cancer." Am J Epidemiol **153**(11): 1071-8.

Fractures in postmenopausal women may serve as a surrogate measure of bone density, reflecting long-term lower estrogen levels, and lower estrogen levels appear to be inversely associated with breast and endometrial cancer. Breast cancer cases aged 50-79 years (n = 5,559) and endometrial cancer cases aged 40-79 years (n = 739) were enrolled in a US case-control study in 1992-1994 to evaluate the relation between fractures and risk of breast and endometrial cancer. Controls for the breast cancer analysis (n = 5,829) and the endometrial cancer analysis (n = 2,334) were randomly selected from population lists (driver's license and Medicare files). Information on fracture history and other risk factors was obtained by telephone interview. Compared with women without a fracture in the past 5 years, the odds ratios for women with a history of fracture were 0.80 (95% confidence interval (CI): 0.68, 0.94) for breast cancer and 0.59 (95% CI: 0.40, 0.89) for endometrial cancer. Height loss (> or =2.5 cm) and recent fracture history were associated with the lowest risk of breast cancer (odds ratio = 0.62, 95% CI: 0.46, 0.83) and endometrial cancer (odds ratio = 0.15, 95% CI: 0.05, 0.43). These data suggest that the endogenous hormonal factors associated with increased fracture risk are also related to decreased breast cancer risk and, more strongly, to endometrial cancer risk.

Nicoletto, M. O., R. Bertorelle, et al. (2009). "Family history of cancer rather than p53 status predicts efficacy of pegylated liposomal doxorubicin and oxaliplatin in relapsed ovarian cancer." Int J Gynecol Cancer **19**(6): 1022-8.

BACKGROUND: The aim of the study was to assess the efficacy of pegylated liposomal doxorubicin (PLD) and oxaliplatin in patients affected by relapsed epithelial ovarian cancer with a family history of BRCA and p53 mutations. METHODS: Seventy-two women received a median of 7.5 courses of PLD at 30 to 35 mg/m2 plus oxaliplatin at 70 mg/m2, and associations between BRCA1/2 and TP53 status and overall survival (OS) were determined. Thirty-eight had a short platinum-free interval (PFI; <12 months), and 34 had a long PFI (> or =12 months). RESULTS: Nine patients had BRCA1 mutations, and 1 had a BRCA2 mutation. Platinum sensitivity was associated with OS (P = 0.0001). At a median follow-up of 9.3 months, objective response rate, median time to progression, and OS were 47.3%, 5.8 months, and 12.9 months, respectively, in short PFI compared with the 76.5%, 11.5 months, and 47.7 months in long PFI. p53 status did not correlate to these parameters. The median time to progression was 11.5 months for high-risk patients versus 6.5 months for patients with sporadic cancer (P = 0.0188), and the median OS from the start of treatment was 48.7 and 16.2 months (P = 0.0032), respectively. Toxicity was mostly grade 1 or 2. CONCLUSIONS: High response rates in the long-PFI patients indicate that this treatment is beneficial and well tolerated. Platinum sensitivity and positive family history and/or a BRCA1/BRCA2 mutation are a useful predictor of response.

Nikander, E., M. Metsa-Heikkila, et al. (2004). "Effects of phytoestrogens on bone turnover in postmenopausal women with a history of breast cancer." J Clin Endocrinol Metab **89**(3): 1207-12.

High phytoestrogen intake among Asian women has been thought to explain the low risk of bone fractures in these populations. In a randomized placebo-controlled trial we studied the effects of isoflavonoids on urinary output of the N-terminal cross-linked telopeptide of type I collagen, pyridinoline (Pyr), and deoxypyridinoline (Dpyr) (bone resorption markers) and serum levels of bone-specific alkaline phosphatase and N-terminal and C-terminal procollagen type I (bone formation markers). Fifty-five postmenopausal women with a history of breast cancer used phytoestrogens (114 mg of isoflavonoids) or placebo tablets daily for 3 months; the treatment regimens were then crossed over after a 2-month washout period. The markers were measured before and on the last day of each treatment period. Bone resorption was reduced during phytoestrogen use, as reflected in falls in the urinary output of Pyr (9%; P = 0.001) and Dpyr (5%; P = 0.008). Compared with the placebo group, the fall in Dpyr was significant (P = 0.022) and the falls in Pyr (P = 0.084) and N-terminal cross-linked telopeptide of type I collagen (P = 0.082) showed a trend toward significance. Bone formation markers were not affected by this regimen. Thus, isoflavonoid-induced inhibition of bone resorption may contribute to the low risk of osteoporosis in Asian women.

Norman, P. and K. Brain (2005). "An application of an extended health belief model to the prediction of breast self-examination among women with a family history of breast cancer." Br J Health Psychol **10**(Pt 1): 1-16.

OBJECTIVES: This study reports an application of the health belief model (HBM) to the prediction of breast self-examination (BSE) among women with a family history of breast cancer. The study also considered the influence of breast cancer worries and past behaviour. METHODS: Eight hundred and thirty-three women completed questionnaires, based on the HBM, to assess their beliefs about breast cancer and BSE. Of these women, 567 were followed-up at 9 months when BSE frequency was assessed. RESULTS: Discriminant function analysis was employed to discriminate among infrequent, appropriate and excessive BSE. Two functions were calculated which were predictive of group membership. The first function maximally discriminated between the infrequent BSE group and the other two groups, with infrequent selfexaminers reporting a greater number of self-efficacy and emotion barriers, fewer benefits and less frequent BSE at Time 1. The second function maximally discriminated between the excessive BSE group and the appropriate BSE group, with excessive selfexaminers reporting higher levels of breast cancer worries and perceived severity and fewer self-efficacy barriers. CONCLUSIONS: The results highlight the importance of focusing on excessive as well as infrequent BSE. Interventions designed to enhance women's confidence in their ability to perform BSE, coupled with attempts to reduce breast cancer worries, may encourage more appropriate and effective BSE.

Noronha, V., N. Berliner, et al. (2006). "Treatment-related myelodysplasia/AML in a patient with a history of breast cancer and an oligodendroglioma treated with temozolomide: case study and review of the literature." Neuro Oncol **8**(3): 280-3.

The emergence of temozolomide as an effective alkylating agent with little acute toxicity or cumulative myelosuppression has led to protracted courses of chemotherapy for many patients with gliomas. Secondary, or treatment-related, myelodysplasia (t-MDS) and acute myelogenous leukemia (t-AML) are life-threatening complications of alkylating chemotherapy and have been reported in patients with primary brain tumors. We describe a case of temozolomide-related t-MDS/AML and discuss the clinical features of this condition. Administration of an alkylating agent in patient populations with long median survivals must be undertaken with an understanding of the potential for this treatment complication.

O'Donnell, H. and C. Parker (2008). "What is low-risk prostate cancer and what is its natural history?" World J Urol **26**(5): 415-22.

This article reviews the definition, incidence, pathological characteristics and natural history of low risk localised prostate cancer. Low risk disease is typically defined as clinical stage T1/T2a, biopsy Gleason score </=6, PSA < 10. This risk classification has provided a useful system for reporting of outcomes and for the production of clinical guidelines. However, the low-risk disease is a broad category with a range of pathological characteristics and clinical behaviour. Many, but not all, low-risk prostate cancers are clinically insignificant, destined never to cause any harm. The challenge of managing low risk localized prostate cancer is to distinguish patients with clinically relevant cancers, who may benefit from radical treatment, from the remainder who do not need any intervention. The natural history of untreated low-risk localised prostate cancer has not been well studied, partly because it is a relatively recent entity, and partly because it has been standard practice for men with low risk disease to receive treatment. Data from watchful waiting in the pre-PSA era, modelling studies to take account of the lead time and overdiagnosis associated with PSA testing, and the early results of active surveillance can all provide insights into the likely natural history of low risk disease. There remains a major unmet need for markers of individual prostate cancer behaviour within the low-risk category. Such markers could be used to distinguish those men with truly indolent disease, suitable for observation, from those with significant prostate cancer that stand to benefit from treatment.

Okamoto, N. (2008). "A history of the cancer registration system in Japan." Int J Clin Oncol **13**(2): 90-6.

In Japan, the first actual survey of morbidity from cancer was conducted by Dr. Mitsuo Segi in Miyagi Prefecture from 1951 to 1953. Population-based cancer registries were started in 1957 in Hiroshima and 1958 in Nagasaki for the follow-up of survivors of the atomic bombings. Public population-based cancer registries, under the cancer control programs of the prefectural governments, were started in Aichi and Osaka prefectures in 1962. After the Law on Health and Medical Services for the Aged was enacted in 1983, population-based cancer registries were initiated promptly in many prefectures. As of 2007, there were population-based cancer registries in 35 of Japan's 47 prefectures and in one city. The Research Group for Population-Based Cancer Registration in Japan was organized by Dr. Isaburo Fujimoto, the chairperson in 1975, with a grant-in-aid from the National Cancer Research Promotion Program. This research group has continued until now and has been making continuous efforts. To promote standardization of the registry process and to improve

the quality of registry data, the Japanese Association of Cancer Registries (JACR) was organized in 1992. The Japanese government Third-Term 10-Year Comprehensive Strategy for Cancer Control was launched in 2004, with the slogan "Targeting a drastic reduction in cancer morbidity and mortality." This strategy includes not only promoting cancer research but also promoting cancer prevention, improving the quality of cancer care, promoting social support systems, and promoting effective systems for monitoring cancer incidence and survival.

Osman, I., H. I. Scher, et al. (2001). "HER-2/neu (p185neu) protein expression in the natural or treated history of prostate cancer." Clin Cancer Res **7**(9): 2643-7.

PURPOSE: Amplification of HER-2/neu gene and overexpression of its encoded product, the p185neu (HER-2/neu) tyrosine kinase membrane receptor, have been associated with tumor progression in certain neoplasms. We conducted this study to investigate patterns of HER-2/neu protein expression in prostate cancer, analyzing different points in the natural and treated history of the disease. EXPERIMENTAL DESIGN: Radical prostatectomy cases (83) and 20 metastatic lesions were studied for the association between HER-2/neu protein overexpression detected by immunohistochemistry and clinicopathological parameters, including time to prostate-specific antigen (PSA) relapse. RESULTS: HER-2/neu protein overexpression, defined as complete membrane staining in >10% of tumor cells using the Food and Drug Administration-approved Dako kit, was found in 9 of 45 (20%) of evaluable hormone naive primary tumors and 23 of 34 (67%) primary tumors after androgen-deprivation therapy (P = 0.0001). Of the 20 metastatic lesions, positivity was noted in 16 (80%) of the cases. On univariate analysis, HER-2/neu overexpression was associated with pretreatment PSA (P = 0.011) and time to PSA relapse (P = 0.02). After controlling for pretreatment PSA, the association between hormone treatment and HER-2/neu was still observed. No association was found between HER-2/neu overexpression and Gleason score, capsular invasion, and tumor proliferative index determined by Ki67. CONCLUSIONS: These data suggest that there is significant HER-2/neu overexpression in primary tumors that persist after androgen deprivation. It also emphasizes the importance of characterizing tumors at determined points in the natural or treated history of prostate cancer when targeting treatment to specific biological processes.

Ozono, S., S. Hinotsu, et al. (2001). "Treated natural history of superficial bladder cancer." Jpn J Clin Oncol **31**(11): 536-40.

BACKGROUND: The present study was conducted to examine the natural history of superficial bladder cancer. METHODS: One hundred and forty-four patients with superficial bladder cancer who had been treated with transurethral resection of bladder tumor (TURBt) alone were analyzed. RESULTS: The non-recurrence rate was 64.8% at 36 months and 61.2% at 60 months after TURBt. When the non-recurrence rate after TURBt was analyzed by background variables, the rate differed significantly between the solitary tumor group and the multiple tumor group. The tumor recurrence hazard curves for the entire population had one high peak before 500 days and another slight peak around 1500 days after TURBt. CONCLUSIONS: These results will provide basic information useful when evaluating new regimens of intravesical instillation therapy for prophylaxis of superficial bladder cancer after our complete TURBt in the Nara Uro-Oncology Research Group.

Panchal, S., O. Shachar, et al. (2009). "Breast cancer in a BRCA2 mutation carrier with a history of prostate cancer." Nat Rev Clin Oncol **6**(10): 604-7.

BACKGROUND: A 49-year-old patient with high-risk prostate cancer presented to a specialist. He was treated with neoadjuvant hormonal therapy for 6 months, followed by conformal radiotherapy. Three years later, he had a biochemical recurrence and commenced continuous luteinizing hormone-releasing hormone analog and antiandrogen therapy as part of a clinical trial. Aside from notable gynecomastia, he remained asymptomatic. He has a strong family history of breast cancer with multiple sisters affected. INVESTIGATIONS: At 58 years of age, the patient underwent BRCA2 germline testing and was found to be a mutation carrier. Following post-test counseling, he was offered clinical breast examination, which was unremarkable except for gynecomastia. Baseline screening mammography identified a 4 mm cluster of microcalcifications and ductal carcinoma in situ (DCIS) was confirmed by stereotactic biopsy. DIAGNOSIS: DCIS in a male BRCA2 mutation carrier undergoing androgen deprivation therapy for prostate cancer. MANAGEMENT: The patient was treated with bilateral mastectomy and no additional systemic therapy was recommended. This case report illustrates the importance of implementing screening mammography in male BRCA mutation carriers, particularly in those with a BRCA2 mutation.

Parker, C., D. Muston, et al. (2006). "A model of the natural history of screen-detected prostate cancer, and

the effect of radical treatment on overall survival." Br J Cancer **94**(10): 1361-8.

The lead time and over-detection associated with prostate-specific antigen (PSA) screening, and generational improvements in all-cause mortality, make prostate cancer outcome studies from the pre-PSA era difficult to interpret in a contemporary setting. We developed a competing-risks hazard model to estimate the natural history of screen-detected prostate cancer, and the impact of radical treatment on overall survival. The model of hazard of mortality was fitted to clinical outcome data from the pre-PSA era, and the effects of screening, generational mortality improvements and radical treatment were incorporated. Sensitivities to the choice of baseline data and values of key parameters were assessed. Lead-time estimates in men diagnosed aged 55-59 years were 14.1, 9.3 and 5.0 years for men with Gleason scores <7, 7 and >7, respectively, assuming biennial screening with 100% attendance. Central estimates of 15-year prostate cancer mortality for conservative management of screen-detected prostate cancer ranged from 0 to 2% for Gleason scores <7, 9 to 31% for Gleason score 7 and 28-72% for Gleason scores >7. For men aged 55-59 years at diagnosis, the predicted absolute 15-year survival benefit from curative treatment was 0, 12 and 26% for men with Gleason scores <7, 7 and >7, respectively. Estimates of the survival benefit of radical treatment were relatively insensitive to values of key parameters. The case for curative treatment, rather than conservative management, of screen-detected localised prostate cancer is strongest in men with high-grade disease. This conclusion contrasts with current patterns of care.

Peters, C. A., R. G. Stock, et al. (2009). "Effect of family history on outcomes in patients treated with definitive brachytherapy for clinically localized prostate cancer." Int J Radiat Oncol Biol Phys **73**(1): 24-9.

PURPOSE: To determine the impact familial prostate cancer has on prognosis in men treated with brachytherapy for clinically localized prostate cancer. METHODS AND MATERIALS: A total of 1,738 consecutive patients with prostate cancer (cT1-3, N0/X, M0) received low-dose-rate brachytherapy alone or in combination with external beam radiation therapy or hormone ablation from 1992 to 2005. The primary end-point was freedom from biochemical failure (FFBF) using the Phoenix definition. Minimum follow-up was 2 years and the median follow-up was 60 months (range, 24-197 months). RESULTS: A total of 187 of 1,738 men (11%) had a family history of prostate cancer in a first-degree relative. For the low-risk patients, both groups had similar actuarial 5-year FFBF (97.2% vs. 95.5%, p = 0.516). For intermediate-risk patients, there was a trend toward improved biochemical control in men positive for family history (5-yr FFBF 100% vs. 93.6%, p = 0.076). For the high-risk patients, men with a positive family history had similar 5-year FFBF (92.8% vs. 85.2%, p = 0.124). On multivariate analysis, family history was not significant; use of hormones, high biologic effective dose, initial prostate-specific antigen value, and Gleason score were the significant variables predicting biochemical control. CONCLUSIONS: This is the first study to examine the relationship of familial prostate cancer and outcomed in men treated with brachytherapy alone or in combination therapy. Men with a positive family history have clinicopathologic characteristics and biochemical outcomes similar to those with sporadic disease.

Petrisek, A., S. Campbell, et al. (2000). "Family history of breast cancer. Impact on the disease experience." Cancer Pract **8**(3): 135-42.

PURPOSE: Family history is the most prominent risk factor, besides advanced age, for the incidence of breast cancer among women. This study investigates differences in the experiences of women in the detection, diagnosis, and treatment of early-stage disease. The purpose of this research is to obtain a more comprehensive understanding of the impact of family history on the overall illness experience. DESCRIPTION OF STUDY: Self-report retrospective data obtained from in-depth interviews with a convenience sample of 179 women who had recently received a diagnosis of nonrecurrent stage 0 to IIIA breast cancer are used to compare the experiences of women with and without a family history of breast cancer (FHOBC). The authors examine differences in screening behavior, method of detection, diagnostic processes, treatment decision making, and therapy receipt, and they report the results of bivariate analyses. RESULTS: The results suggest that women with FHOBC have a different disease experience than those without an affected relative. Women with FHOBC were more likely than their counterparts to comply with screening guidelines, to seek more timely care, to consult with specialists, to be influenced by the experiences of others, to feel comfortable with treatment decisions, and to receive adjuvant therapy. CLINICAL IMPLICATIONS: Healthcare providers should be aware that compliance with mammography and therapy guidelines may vary with FHOBC. Because the better health-related behavior reported by women with affected relatives suggests that they may have higher perceived risk, physicians should be sensitive to potentially elevated levels of anxiety, provide accurate information about relative risk, put patient concerns in the proper perspective, and include

family members in treatment discussions. Alternatively, women without an FHOBC appear to have less favorable screening, detection, diagnosis, and treatment decision-making behavior. Because family doctors play an important role in the care of these patients, they may need to provide special education and counseling regarding the importance of adherence to screening guidelines, recognition of relevant symptoms, initiation of timely examinations, consultation with cancer specialists, and compliance with treatment recommendations.

Powles, T. J., A. Howell, et al. (2008). "Red clover isoflavones are safe and well tolerated in women with a family history of breast cancer." Menopause Int **14**(1): 6-12.

OBJECTIVE: To assess the safety and tolerability of a standardized 40 mg red clover isoflavone dietary supplement (Promensil, Novogen) in women with a family history of breast cancer to evaluate the feasibility of using the supplement for prevention of breast cancer in healthy women. STUDY DESIGN: Healthy women aged 35-70 years (n = 401) with at least one first-degree relative with breast cancer received red clover isoflavones or placebo for three years in a randomized, double-blind, placebo-controlled pilot trial. Participants were assessed clinically and blood samples taken for biochemical analysis every six months. In addition, study participants underwent mammography, bone density and transvaginal ultrasound (postmenopausal women only) once per year. RESULTS: No significant differences in breast density, endometrial thickness, serum cholesterol, follicle stimulating hormone levels and bone mineral density were detected between those taking red clover isoflavones and placebo. In postmenopausal women, some significant differences in bone marker levels were seen between active and placebo groups, at six months and at 12 months. The adverse event profile was similar across all red clover isoflavone and placebo groups. CONCLUSION: This three-year study supports the growing body of evidence that treatment with red clover isoflavones is safe and well tolerated in healthy women. Supplements containing red clover isoflavones did not adversely affect breast density, skeletal strength or cardiovascular status. In postmenopausal women, endometrial status was not adversely affected. The adverse event profile was similar between red clover isoflavones, and placebo and endocrine status did not differ.

Purdue, M. P., P. J. Mink, et al. (2005). "Hormone replacement therapy, reproductive history, and colorectal adenomas: data from the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial (United States)." Cancer Causes Control **16**(8): 965-73.

OBJECTIVE: Findings from some epidemiologic studies of colorectal cancer and adenoma suggest that the protective effect of post-menopausal hormone replacement therapy (HRT) may differ across categories of age and body mass index (BMI). We conducted an analysis of women participating in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial to investigate the relationship between HRT use and prevalent adenoma, both overall and across different population subgroups. METHODS: Women aged 55-74 were randomized to screening by flexible sigmoidoscopy at ten PLCO screening centers between September 1993 and September 2001. We identified 1468 women with at least one left-sided adenoma and 19,203 without adenoma or colorectal cancer. Information about HRT and reproductive factors was obtained from a self-administered questionnaire. RESULTS: Compared to never use of HRT, current use was associated with a decreased prevalence of left-sided adenoma (odds ratio (OR) 0.85; 95% confidence interval (CI) 0.75-0.97). We found no evidence of dose-response with increasing duration of use for current or former users. The association with current HRT use was stronger among women aged 65+ (OR 0.69; 95% CI 0.56-0.84), with a BMI<30 (OR 0.82; 95% CI 0.71-0.95) and who regularly use aspirin or ibuprofen (OR 0.77; 95% CI 0.65-0.91). Other reproductive factors were not significantly associated with adenoma prevalence. CONCLUSIONS: Our findings suggest that current HRT use may protect against colorectal adenoma, and that this protective effect is short-lived following cessation of use.

Ramsey, S. D., P. Yoon, et al. (2006). "Population-based study of the prevalence of family history of cancer: implications for cancer screening and prevention." Genet Med **8**(9): 571-5.

PURPOSE: Family history assessment is gaining importance as a potential public health tool to help determine susceptibility to common cancers. Population-based data on the prevalence of having a family history of common cancers are scant. METHODS: We queried survey questions from the National Health Interview Survey, an annual nationwide survey of approximately 36,000 households in the United States, to determine the prevalence of persons reporting one or more first-degree relatives with breast, colorectal, lung, prostate, or ovarian cancer. RESULTS: Breast cancer was the most common condition noted for family members (7.74% of respondents), followed by lung cancer (7.10%), colorectal cancer (4.96%), prostate cancer (4.68%), and ovarian cancer (1.79%). A family history

of cancer was more commonly reported by older persons, whites, women, and high-income groups. CONCLUSION: A substantial proportion of persons in the United States report having a close family member with cancer, and thus may be eligible for earlier or more aggressive cancer screening services.

Ravdin, P. M. (2004). "Managing the risk of osteoporosis in women with a history of early breast cancer." Oncology (Williston Park) **18**(11): 1385-90, 1393; discussion 1394.

Estrogen is known to play an important role in skeletal health. Female breast cancer patients who receive treatments that reduce estrogen levels, such as aromatase inhibitors, may increase their risk of developing osteoporosis and their risk of fracture. Clinical guidelines enable the physician to assess the risk of osteoporosis by patient history and physical examination. For patients identified as being at risk, it is necessary to test bone mineral density (BMD), using the result to determine which patients require treatment. Two groups can be identified as requiring BMD assessment according to general guidelines: patients < 45 years old who become menopausal due to treatment, and breast cancer patients receiving aromatase inhibitors. Bisphosphonates appear to be the logical treatment of choice for breast cancer patients, as they do not interact with the estrogen receptor. Although not all women receiving aromatase inhibitors will require additional treatment for bone health, postmenopausal women with a history of breast cancer at risk of osteoporosis should be identified, monitored, and managed according to practice guidelines.

Raz, D. J., J. A. Zell, et al. (2007). "Natural history of stage I non-small cell lung cancer: implications for early detection." Chest **132**(1): 193-9.

BACKGROUND: Concern has been raised that early detection of lung cancer may lead to the treatment of clinically indolent cancers. No population-based study has examined the natural history of patients with stage I NSCLC who receive no surgery, chemotherapy, or radiation therapy. Our hypothesis is that long-term survival in patients with untreated stage I non-small cell lung cancer (NSCLC) is uncommon. METHODS: A total of 101,844 incident cases of NSCLC in the California Cancer Center registry between 1989 and 2003 were analyzed; 19,702 patients had stage I disease, of whom 1,432 did not undergo surgical resection or receive treatment with chemotherapy or radiation. Five-year overall survival (OS) and lung cancer-specific survival were determined for this untreated group, for subsets of patients who were recommended but refused surgical resection, and for T1 tumors. RESULTS: Only 42 patients with untreated stage I NSCLC were alive 5 years after diagnosis. Five-year OS for untreated stage I NSCLC was 6% overall, 9% for T1 tumors, and 11% for patients who refused surgical resection. Five-year lung cancer-specific survival rates were 16%, 23%, and 22%, respectively. Among these untreated patients, median survival was 9 months overall, 13 months for patients with T1 disease, and 14 months for patients who refused surgical resection. CONCLUSION: Long-term survival with untreated stage I NSCLC is uncommon, and the vast majority of untreated patients die of lung cancer. Given that median survival is only 13 months in patients with T1 disease, surgical resection or other ablative therapies should not be delayed even in patients with small lung cancers.

Reed, V. K., S. Krishnan, et al. (2008). "Incidence, natural history, and patterns of locoregional recurrence in gastric cancer patients treated with preoperative chemoradiotherapy." Int J Radiat Oncol Biol Phys **71**(3): 741-7.

PURPOSE: To retrospectively determine the incidence and patterns (in-field, marginal, or out-of-field) of locoregional gastric cancer recurrence in patients who received preoperative chemoradiotherapy and to determine the outcome in these patients. METHODS AND MATERIALS: Between 1994 and 2004, 149 patients with gastric carcinoma were treated according to institutional protocols with preoperative chemoradiotherapy. Ultimately, 105 patients had an R0 resection. Of these 105 patients, 65 received preoperative chemotherapy followed by chemoradiotherapy and 40 received preoperative chemoradiotherapy. Most (96%) of these patients received 5-fluorouracil-based chemotherapy during radiotherapy, and the median radiation dose was 45 Gy. We retrospectively identified and classified the patterns of locoregional recurrence. RESULTS: The 3-year actuarial incidence of locoregional recurrence was 13%, with locoregional disease recurring as any part of the failure pattern in 14 patients. Most (64%) of the evaluable locoregional recurrences were in-field. Of the 4 patients with a marginal recurrence, 2 had had inadequate coverage of the regional nodal volumes on their oblique fields. The pathologic complete response rate was 23%. A pathologic complete response was the only statistically significant predictor of locoregional control. CONCLUSION: Patients with gastric cancer who received preoperative chemoradiotherapy had low rates of locoregional recurrence. This strategy merits prospective multi-institutional and randomized evaluation.

Reedy, J., P. S. Haines, et al. (2005). "Qualitative comparison of dietary choices and dietary supplement use among older adults with and without a history of colorectal cancer." J Nutr Educ Behav **37**(5): 252-8.

OBJECTIVE: To explore colorectal cancer survivors' beliefs about diet, dietary supplements, health, and cancer in relation to beliefs of a similar group without colorectal cancer. DESIGN: In-depth, semistructured, open-ended interviews were used to examine perceptions. PARTICIPANTS: Twenty-two participants (10 colorectal cancer survivors and 12 from a comparison group) from the North Carolina Strategies for Improving Diet, Exercise, and Screening Study. ANALYSIS: Verbatim interview transcripts were coded and analyzed. Comparisons were made between colorectal cancer survivors and the comparison group. RESULTS: Three main themes emerged: the influence of significant life events on dietary change, concerns about contaminants in the food supply, and a lack of physician guidance in dietary supplement selection. CONCLUSION AND IMPLICATIONS: The experience of colorectal cancer is significant and may lead to dietary change among some survivors, but these findings do not suggest that it is necessarily more influential than other life events. Participants sought to control diet (for coping or survival) and also felt that diet cannot be controlled (due to the contamination of the food supply). Although many lacked guidance from physicians about dietary supplements, they were comfortable making their own decisions to self-treat. Enhanced understanding of the themes that guide selection of diet and dietary supplements can provide a context for dietitians in practice and researchers conducting behavioral interventions.

Rees, G., P. R. Martin, et al. (2008). "Screening participation in individuals with a family history of colorectal cancer: a review." Eur J Cancer Care (Engl) **17**(3): 221-32.

Literature regarding screening behaviour in individuals with a family history of colorectal cancer was reviewed, in order to determine the prevalence of screening in this population and identify factors associated with screening participation. Four electronic databases were searched from 1994. Thirty papers met the inclusion criteria, including 3 community surveys, 13 studies on first-degree relatives of colorectal cancer patients, and 14 studies on genetic services for colorectal cancer risk assessment. Individuals with a family history of colorectal cancer, who have not received risk assessment, frequently have never had any form of screening for colorectal cancer. Uptake of endoscopic screening when offered to individuals identified as being at increased risk was generally high (often >60% participation). Having a medical recommendation to screen, a stronger family history and perceiving fewer barriers to screening were identified as predictors of screening behaviour. Existing data suggest that use of screening tests in individuals with a family history of colorectal cancer is variable, and our understanding of factors associated with screening behaviour is limited. A number of methodological problems in research to date were identified, and further research is needed in order to inform interventions to support sustained screening participation in this population.

Reis, M. M., M. Tavakoli, et al. (2009). "Evaluation of a surveillance programme for women with a family history of breast cancer." J Med Genet **46**(5): 319-23.

AIM: To establish health related costs and benefits of clinical services for women at increased familial risk of breast cancer. METHODS: Analysis of costs and outcomes for one UK regional service, supplemented with data from a multinational collaborative study. Main outcome measures were aggregate costs for regular clinical examination, mammographic screening and further investigations; breast cancer incidence; proportion of cancers detected at "early" or "late" stage, compared with corresponding data for unscreened women of comparable age; survival in relation to stage at diagnosis; itemised and aggregate costs of management for "early" and "late" stage breast cancer; hence direct health care costs per quality adjusted life-year (QALY) gained. RESULTS: The surveillance programme costs pound1500 (euro1600, US$2100) per woman (over 15 years). Breast cancer incidence is close to 6 per thousand examinations; 75% of tumours are detected through screening and 77% are "early" (path stage 1 or 2). Corresponding figures for unscreened women (including relatives of those attending the breast cancer family clinic) indicate that surveillance achieves a beneficial "stage shift", with reduction in treatment costs and improvement in survival, in about 22% of cases. CONCLUSIONS: The current clinical service for women at familial risk of breast cancer costs about pound4800 (euro5200, US$6800) per QALY gained. That figure is sensitive to the rate of detection of breast cancer and the degree of beneficial stage shift achieved. Within the realistic range of estimates for these two parameters, the cost per QALY may be as high as pound14,000 (euro15,300, US$20,000) or as low as pound1000 (euro1100, US$1400).

Renzi, C., S. Mastroeni, et al. (2008). "Skin cancer knowledge and preventive behaviors among patients with a recent history of cutaneous squamous cell carcinoma." Dermatology **217**(1): 74-80.

AIMS: To evaluate skin cancer knowledge and preventive behaviors of patients recently treated for cutaneous squamous cell carcinoma (SCC) and to examine the factors associated with the adoption of preventive behaviors. METHODS: Telephone survey on 315 SCC patients treated at a large dermatological hospital in Italy, evaluating skin cancer knowledge, sun protection and skin examination practices as well as medical recommendations received after SCC removal. RESULTS: Skin cancer knowledge was fair/low for 48.9% of the participants. Doctors were the main source of skin cancer information for 24.4% of the patients. Of the patients assessed >or=12 months after SCC removal, 32.7% reported a total skin examination after removal. Of the participants, 41.6% never/rarely used sunscreens. In a multivariate analysis, the likelihood of having complete skin examinations was associated with a doctor's advice to have an examination (odds ratio, OR = 2.29; 95% confidence interval, CI = 1.2-4.4), a higher knowledge level (OR = 2.05; 95% CI = 1.1-3.8) and past skin examinations (OR = 3.62; 95% CI = 1.9-7.0). Doctor's recommendations increased the likelihood of adopting preventive behaviors. CONCLUSIONS: We found substantial knowledge gaps and limited adoption of skin cancer prevention, highlighting the need for interventions promoting knowledge and preventive behaviors, particularly among higher-risk patients.

Rini, C., L. Jandorf, et al. (2008). "Distress among inflammatory bowel disease patients at high risk for colorectal cancer: a preliminary investigation of the effects of family history of cancer, disease duration, and perceived social support." Psychooncology **17**(4): 354-62.

Patients with inflammatory bowel disease (IBD) are one of only three groups at high risk for colorectal cancer (CRC), a leading cause of cancer-related mortality. Yet, no research has examined psychological effects of their high-risk status. The present study offered an initial investigation of three potential predictors of patient distress: disease duration, family history of cancer, and perceived social support. Longer disease duration and stronger family history of cancer are associated with elevated CRC risk in this already high-risk population. Perceived support was conceptualized as a resource that could decrease vulnerability to distress or buffer adverse psychological effects of disease duration and family history. Men and women (n = 223) with IBD participating in a colon disease family registry completed measures for this cross-sectional study. Family history of CRC and non-colorectal cancers among first-degree relatives (FDRs) and more distant relatives (DRs) was examined separately. Hierarchical multiple regression analyses revealed that having greater perceived support predicted lower generalized distress ($p<0.001$). Having an FDR history of CRC predicted higher CRC-specific distress ($p = 0.02$). Having a DR history of CRC also predicted higher CRC-specific distress, but only among patients diagnosed more recently ($p = 0.03$). Clinical implications of these findings are discussed along with future research directions.

Rock, C. L., S. W. Flatt, et al. (2008). "Reproductive steroid hormones and recurrence-free survival in women with a history of breast cancer." Cancer Epidemiol Biomarkers Prev **17**(3): 614-20.

Epidemiologic studies fairly consistently show in postmenopausal women that reproductive steroid hormones contribute to primary breast cancer risk, and this association is strongly supported by experimental studies using laboratory animals and model systems. Evidence linking sex hormone concentrations with risk for recurrence in women diagnosed with breast cancer is limited; however, beneficial effects of antiestrogenic therapy on recurrence-free survival suggest that these hormones affect progression and risk for recurrence. This study examined whether baseline serum concentrations of estradiol, testosterone, and sex hormone binding globulin were associated with recurrence-free survival in a nested case-control cohort of women from a randomized diet trial (Women's Healthy Eating and Living Study) who were followed for >7 years after diagnosis. In 153 case-control pairs of perimenopausal and postmenopausal women in this analysis, total estradiol [hazard ratio (HR), 1.41 per unit increase in log concentration; 95% confidence interval (95% CI), 1.01-1.97], bioavailable estradiol (HR, 1.26; 95% CI, 1.03-1.53), and free estradiol (HR, 1.31; 95% CI, 1.03-1.65) concentrations were significantly associated with risk for recurrence. Recurred women had an average total estradiol concentration that was double that of nonrecurred women (22.7 versus 10.8 pg/mL; P = 0.05). Testosterone and sex hormone binding globulin concentrations did not differ between cases and controls and were not associated with risk for recurrence. Although genetic and metabolic factors likely modulate the relationship between circulating sex hormones and risk, results from this study provide evidence that higher serum estrogen concentration contributes to risk for recurrence in women diagnosed with early stage breast cancer.

Rock, C. L., S. W. Flatt, et al. (2005). "Plasma carotenoids and recurrence-free survival in women with a history of breast cancer." J Clin Oncol **23**(27): 6631-8.

PURPOSE: Previous studies suggest that diet may affect recurrence or survival rates in women who

have been diagnosed with breast cancer. The purpose of this study was to examine the relationship between plasma carotenoid concentration, as a biomarker of vegetable and fruit intake, and risk for a new breast cancer event in a cohort of women with a history of early-stage breast cancer. METHODS: Participants were 1,551 women previously treated for breast cancer who were randomly assigned to the control arm of a diet intervention trial between March 1995 and November 2000. Outcome events were probed during semiannual interviews and verified by medical record review. During the period under study, 205 women had a recurrence or new primary breast cancer. Plasma carotenoid concentrations were measured in baseline blood samples. Hazard ratios (HR) and 95% CIs by quartiles of plasma carotenoids were computed, controlling for tumor stage, grade, and hormone receptor status; chemotherapy and tamoxifen therapy; clinical site; age at diagnosis; body mass index; and plasma cholesterol concentration. RESULTS: Women in the highest quartile of plasma total carotenoid concentration had significantly reduced risk for a new breast cancer event (HR, 0.57; 95% CI, 0.37 to 0.89), controlled for covariates influencing breast cancer prognosis. CONCLUSION: Plasma carotenoids are a biologic marker of intake of vegetables and fruit, so this observation supports findings from previous studies that have linked increased vegetable and fruit intake with greater likelihood of recurrence-free survival in women who have been diagnosed with early-stage breast cancer.

Rohrmann, S., W. W. Roberts, et al. (2003). "Family history of prostate cancer and obesity in relation to high-grade disease and extraprostatic extension in young men with prostate cancer." Prostate **55**(2): 140-6.

BACKGROUND: Little is known about predictors of prostate cancer severity in young men. Therefore, we examined whether family history and obesity influence risk of high-grade disease and extraprostatic extension in men < 55-years old. METHODS: Four hundred ninety-eight men aged < 55 years who had had a radical prostatectomy (1992-1999) by one surgeon were mailed a survey in 2000 to assess family history of PCa and anthropometrics. Body mass index (BMI = kg/m(2)) was calculated as an indicator of obesity. Logistic regression was used to compute odds ratios (OR) for high-grade disease (Gleason score > or = 7) and extraprostatic extension. RESULTS: Of the 363 respondents, 35.8% had at least one first-degree relative with PCa. Men with a family history were younger at surgery than those without a family history (48.8 vs. 50.1 years, P < 0.001). After controlling for age, cigarette smoking, and race/ethnicity, men with an affected father had a lower risk of high-grade disease compared to those without an affected father (OR = 0.42, 95% CI 0.23-0.76). Risk of high-grade disease increased with increasing BMI, especially in men < 50-years old (P-trend = 0.02). Family history and BMI were not clearly associated with extraprostatic extension. CONCLUSIONS: After taking into account a younger age at presentation among men with a family history, young men with a family history of PCa were less likely to have high-grade disease. Obesity may be associated with a poorer histology in young men with PCa, especially in men younger than 50 years of age.

Ruo, L., C. Cellini, et al. (2001). "Limitations of family cancer history assessment at initial surgical consultation." Dis Colon Rectum **44**(1): 98-103; discussion 103-4.

PURPOSE: Although important for the diagnosis of familial clustering of colorectal cancer and hereditary nonpolyposis colorectal cancer, the accuracy of familial cancer history assessment in the office setting has been questioned. Furthermore, there are few publications describing the optimal method for accurately capturing a family cancer history. The purpose of this study was to determine how well family cancer history is assessed in patients with early age-of-onset colorectal cancer at initial surgical consultation compared with a telephone interview and mailed questionnaire. METHODS: Medical records of patients 40 years old or younger at the time of colorectal cancer surgery were reviewed for documentation of family cancer history at initial surgical consultation. In addition, family cancer history was solicited from surviving patients or their next of kin by telephone and a mailed questionnaire. The kappa coefficient was used to measure degree of correlation between family cancer history obtained at initial surgical consultation and subsequent telephone interview and questionnaire. RESULTS: One hundred twenty-five patients were available for analysis. Family cancer history was documented on the initial surgical consultation report in 78 percent of cases. Although 31.2 percent were identified as having no family cancer history at initial surgical consultation, this proportion decreased to 13.5 percent after telephone interviews and questionnaires. Family history assessment at initial surgical consultation also failed to identify 7 of 11 individuals meeting Amsterdam criteria for hereditary nonpolyposis colorectal cancer and 10 of 16 individuals meeting modified clinical criteria for hereditary nonpolyposis colorectal cancer. CONCLUSIONS: Although family cancer history was commonly obtained during the initial surgical consultation of patients with colorectal cancer, there was a tendency to underestimate the extent of familial cancer. A telephone interview and

questionnaire conducted at a later date may reveal a more comprehensive family cancer history. This is an important observation, because individuals identified as high-risk for hereditary nonpolyposis colorectal cancer or familial clustering of colorectal cancer require special consideration with respect to screening, surveillance, and surgical management.

Ryan, C. J. and T. M. Beer (2007). "Prostate specific antigen only androgen independent prostate cancer: natural history, challenges in management and clinical trial design." J Urol **178**(3 Pt 2): S25-9.

PURPOSE: There is no current standard of care for patients with nonmetastatic androgen independent prostate cancer, a condition defined by increasing serum prostate specific antigen despite anorchid testosterone levels and no radiographic evidence of metastases. A consensus panel was convened to review data and propose a strategy for trial design and prioritization. MATERIALS AND METHODS: Published literature on the natural history of nonmetastatic androgen independent prostate cancer was reviewed. A panel discussion was held, focusing on reviewing current and past trials, and the development of research priorities for patients in this disease state. RESULTS: Based on 1 report the natural history of nonmetastatic androgen independent prostate cancer is relatively long but heterogeneous. External validation of these published findings has not been performed. Clinical trial design in this setting is impeded by heterogeneity and lack of knowledge about the natural history, prolonged time to clinical end points, such as the development of metastases or death, and a lack of knowledge about how intermediate end points, eg the development of bone metastases, are related to the long-term outcome, eg survival. In clinical practice a reluctance to use therapies with substantial toxicity as well as a lack of outcome data on such patients leaves a vacuum in which there is no standard of care, although secondary hormonal manipulations are widely used. CONCLUSIONS: Further research is needed to define the natural history of this disease state, educate patients and clinicians about its distinct natural history and develop informative clinical trial designs suited to this patient population.

Schilsky, R. L., O. R. McIntyre, et al. (2006). "A concise history of the cancer and leukemia group B." Clin Cancer Res **12**(11 Pt 2): 3553s-5s.

A formal National Cancer Institute Clinical Trials Cooperative Group Program was conceived in 1955 when Dr. Sidney Farber, Mary Lasker, and others approached Congress with a proposal to increase support for studies of chemotherapy of cancer. In response, Congress awarded US $5 million to the National Cancer Institute to establish the Chemotherapy National Service Center. The founders of the Cancer and Leukemia Group B, James Holland and Emil (Tom) Frei, III, envisioned that successful chemotherapy for leukemia and other hematologic malignancies could be expeditiously realized through carefully designed clinical trials executed uniformly as a cooperative effort among several institutions. In 1956, the group was designated the Acute Leukemia Group B by the Chemotherapy National Service Center Clinical Studies Panel, and Frei was elected chairman. In the ensuing 50 years, the Cancer and Leukemia Group B has expanded to national and even international membership, and its research programs have expanded to include all of the common adult solid tumors and hematologic malignancies in a multidisciplinary effort to improve the outcomes for patients with cancer and to better understand the biology of malignant disease.

Sellers, T. A., D. M. Grabrick, et al. (2004). "Does folate intake decrease risk of postmenopausal breast cancer among women with a family history?" Cancer Causes Control **15**(2): 113-20.

BACKGROUND: Several recent studies suggest that adequate dietary folate may attenuate the risk of breast cancer associated with intake of alcohol. We examined whether the putative benefit extends to women with a family history (FH) of breast cancer using a cohort of 33,552 postmenopausal women aged 55-69 years in 1986. METHOD: Folate and alcohol intake was estimated from a food frequency questionnaire completed at baseline. Folate was categorized as upper 50th, 31st-50th, 11th-30th, and <10th percentiles. Alcohol use was initially classified into three levels; never drinkers, less than the median and greater than the median. Subsequent models collapsed levels of intake to any versus none. Occurrence of breast cancer was determined through linkage to the Iowa SEER registry. Multivariate-adjusted relative risks (RR) and 95% confidence intervals (CI) were estimated through Cox proportional hazards regression, stratified on FH using non-drinkers with high folate and no FH as the referent group. RESULTS: Through 14 years, 1823 incident cases were identified, 308 among FH+ women. Among FH- women, low folate was not a risk factor among non-drinkers (RR = 0.96, CI = 0.73-1.26), but was among drinkers (RR = 1.40, CI = 1.05-1.86). Drinkers with high folate were not at elevated risk (RR = 1.03, CI = 0.89-1.19). Among FH+ women, low folate was a risk factor among drinkers (RR = 2.21, CI = 1.43-3.41) and non-drinkers (RR = 2.39, CI = 1.36-4.20). Further, drinkers with high folate remained at increased risk (RR = 1.67, CI= 1.30-2.14). However, FH+ women with high folate

who did not drink alcohol had no elevated risk. CONCLUSION: These results suggest that folate may attenuate the risks of postmenopausal breast cancer associated with family history, but only if alcohol use is avoided or minimized.

Shiffman, M. L. (2003). "Natural history and risk factors for progression of hepatitis C virus disease and development of hepatocellular cancer before liver transplantation." Liver Transpl **9**(11): S14-20.

1. Chronic infection with hepatitis C virus (HCV) is the leading cause of cirrhosis and the most common indication for liver transplantation in many countries throughout the world. 2. The most significant factors leading to fibrosis progression in patients with chronic HCV infection include the degree of inflammation present on liver biopsy and ongoing alcohol use. 3. Patients with cirrhosis secondary to chronic HCV infection are at increased risk for developing hepatocellular carcinoma (HCC). 4. Achieving a sustained virological response after treatment with interferon, with or without ribavirin, is associated with a reduced risk for the development of cirrhosis and HCC and prolonged survival.

Simone, J. V. (2006). "History of the treatment of childhood ALL: a paradigm for cancer cure." Best Pract Res Clin Haematol **19**(2): 353-9.

The history of the treatment of childhood leukemia from 1950 to the present is reviewed here. Particular emphasis is placed on the 'Total Therapy' studies conducted at St Jude Children's Research Hospital in Memphis, Tennessee. Under the guidance of Donald Pinkel, MD, the first medical director of St Jude, variations in chemotherapy and craniospinal irradiation were tried, and by Study XV, begun in 2000, a 4-year event-free survival of 92+/-7% had been achieved. Strengths and weaknesses in the current treatment of childhood leukemia are discussed as well as possibilities for the future.

Smith, E. L., C. Skosey, et al. (2006). "The cancer and leukemia group B oncology nursing committee (1983-2006): a history of passion, commitment, challenge, and accomplishment." Clin Cancer Res **12**(11 Pt 2): 3638s-41s.

The Cancer and Leukemia Group B (CALGB) Oncology Nursing Committee (ONC) was initially established in 1983 as a working group with the specific aim of promoting protocol compliance through collaboration, communication, and education to enhance the scientific goals of the Group. Due to the efforts of its members, the committee gained full committee status. ONC members now serve as principal investigators and coinvestigators on research studies, continue to sponsor biannual educational sessions individually and in concert with other CALGB committees, and continue to develop tools to enlighten patients about their disease and the clinical trial process. The ONC, an administrative group of 12 members, provides leadership within CALGB. Although ONC members have always acted as liaisons to the disease and modality committees, three positions have recently been designated specifically for doctorally prepared nurse scientists. Since its inception, general nurse membership within the group has more than doubled to a total of more than 500 members.

Smith, M. R., F. Kabbinavar, et al. (2005). "Natural history of rising serum prostate-specific antigen in men with castrate nonmetastatic prostate cancer." J Clin Oncol **23**(13): 2918-25.

PURPOSE: To describe the natural history of nonmetastatic prostate cancer and rising prostate-specific antigen (PSA) despite androgen deprivation therapy. PATIENTS AND METHODS: The 201 patients in this report were the placebo control group from an aborted randomized controlled trial to evaluate the effects of zoledronic acid on time to first bone metastasis in men with prostate cancer, no bone metastases, and rising PSA despite androgen deprivation therapy. Relationships between baseline covariates and clinical outcomes were assessed by Cox proportional hazard analyses. Covariates in the model were baseline PSA, Gleason sum, history of bilateral orchiectomies, regional lymph node metastases at diagnosis, prior prostatectomy, time from androgen deprivation therapy to random assignment, time from diagnosis to random assignment, and PSA velocity. RESULTS: At 2 years, 33% of patients had developed bone metastases. Median bone metastasis-free survival was 30 months. Median time to first bone metastases and overall survival were not reached. Baseline PSA level greater than 10 ng/mL (relative risk, 3.18; 95% CI, 1.74 to 5.80; $P < .001$) and PSA velocity (4.34 for each 0.01 increase in PSA velocity; 95% CI, 2.30 to 8.21; $P < .001$) independently predicted shorter time to first bone metastasis. Baseline PSA and PSA velocity also independently predicted overall survival and metastasis-free survival. Other covariates did not consistently predict clinical outcomes. CONCLUSION: Men with nonmetastatic prostate cancer and rising PSA despite androgen deprivation therapy have a relatively indolent natural history. Baseline PSA and PSA velocity independently predict time to first bone metastasis and survival.

Somers, T. J., J. C. Michael, et al. (2009). "Cancer genetics service interest in women with a limited

family history of breast cancer." J Genet Couns **18**(4): 339-49.

Women with a limited family history of breast cancer may be interested in cancer genetics information although their objective risk of breast cancer may not indicate routine referral to cancer genetics services. This study examined factors related to interest and use of cancer genetics services in a community sample of women with a limited family history of breast cancer (N = 187) who had no previous contact with cancer genetics services. Participants provided demographic information and ratings of perceived risk, cancer distress, attitudes, and intentions to initiate cancer genetics services. Participants were given information about a cancer genetics clinic that served women having concerns about their breast cancer risk. Women were contacted within 6 weeks and 8 months following their study appointment. Six weeks following their study appointment, 25% of women had initiated cancer genetics services. Eight months following their study appointment, 18% of women reported having completed a cancer genetics service appointment. Baseline intentions independently predicted both initiation at 6 weeks and appointment at 8 months. Cancer distress was positively associated with cancer genetics service initiation and appointment. Results suggest that some women with a limited family history of breast cancer are interested in seeking out cancer genetics information. Women with a limited family history of breast cancer may benefit from the availability of cancer genetics information provided through primary healthcare settings.

Spangler, E., C. M. Zeigler-Johnson, et al. (2005). "Association of prostate cancer family history with histopathological and clinical characteristics of prostate tumors." Int J Cancer **113**(3): 471-4.

Genetic factors may be used not only to assess risk of prostate cancer development but also to evaluate prostate cancer outcomes including clinical prognosis, treatment methods, and treatment response. To assess the role of family history on prostate cancer outcomes, we evaluated tumor characteristics, diagnostic precursors and biochemical (prostate specific antigen) relapse-free survival in men with and without a family history of prostate cancer. A total of 684 prostate cancer cases unselected for family history were identified from an ongoing hospital based prostate cancer case-control study between 1995 and 2002. Self-reported family history was grouped within the following categories: none, any, moderate (one affected first or second degree relative) and high (2 or more affected first or second degree relatives). We further considered groups defined by early (before age 60) and late (after age 60) age at diagnosis. Overall, tumor stage was not significantly associated with any (odds ratio [OR] = 1.43 95% confidence interval [CI] = 1.00-2.05) or moderate (OR = 1.48, 95% CI = 1.0-2.19) family histories. Men diagnosed before age 60, however, had higher tumor stages if they had any (OR = 2.19, 95% CI = 1.28-3.75) or moderate (OR = 2.15, 95% CI = 1.2-3.9) family histories. Men diagnosed after age 60 with any family history were significantly more likely to experience biochemical (PSA) failure (Hazard ratio [HR] = 2.60, 95%CI = 1.08-6.25). Men with any and moderate family histories were at significantly increased risk of biochemical failure (HR = 2.49, 95%CI = 1.25-4.95 and HR = 2.46, 95% CI = 1.17-5.16, respectively). Moderate family history increased probability of seminal vesicle invasion (OR = 2.14, 95%CI = 1.06-4.34). Our results suggest that a family history of prostate cancer may be associated with predictors of clinical outcome in prostate cancer cases unselected for a family history of prostate cancer.

Srivastava, A. R. and D. Dalela (2004). "Prostate cancer: altering the natural history by dietary changes." Natl Med J India **17**(5): 248-53.

The importance of diet on the development and progression of prostate cancer was initially suggested by epidemiological studies. Since then, there has been a vast amount of research in this field. Compelling evidence now provides hope that evidence-based dietary alterations may markedly alter the natural history of this disease. Is there enough evidence for clinicians to be able to advise dietary modifications? The preliminary results no doubt are encouraging, but at present there seems to be no evidence to justify the widespread use of these proposed dietary interventions. However, as public awareness increases, all physicians involved with the care of patients with cancer of the prostate will need to be better armed with the current updates and advice on this issue.

Stadler, W. (2007). "Chromosomes, hypoxia, angiogenesis, and trial design: a brief history of renal cancer drug development." Clin Cancer Res **13**(6): 1630-3.

Stein, K., G. Lewendon, et al. (2005). "Improving uptake of cervical cancer screening in women with prolonged history of non-attendance for screening: a randomized trial of enhanced invitation methods." J Med Screen **12**(4): 185-9.

OBJECTIVE: To compare the effectiveness and cost-effectiveness of three methods of inviting women with a long history of non-attendance to undergo cervical screening. METHODS: Randomized controlled trial and cost-effectiveness analysis. In all,

1140 women were identified from routine NHS screening records as having no smear for at least 15 years and randomly allocated to receive a telephone call from a nurse, a letter from a well-known celebrity (Claire Rayner) or letter from the local NHS Cervical Screening Commissioner. Uptake of screening was measured using routine data and attributed to interventions if occurring within three months. Uptake was compared with a control group. Costs of carrying out the interventions were noted from the perspective of the NHS and cost-effectiveness, as cost per additional attender, calculated. RESULTS: Uptake following all interventions was low: telephone call (1.4, 95% confidence interval [CI] 0.38-3.6%); celebrity letter (1.8, 95% CI 0.57-4.0%); commissioner letter (4.6, 95% CI 2.5-7.7%); control group (1.8, 95% CI 0.57-4.0%). There were no significant differences between groups. Telephone intervention was not possible in a quarter of women whose numbers were unlisted. Telephone intervention was the most expensive and least effective of the interventions. The commissioner letter yielded an additional attender within three months at an incremental cost of 23.21 pounds compared with taking no action. CONCLUSIONS: Neither a telephone call from a nurse nor a letter from a celebrity to encourage attendance for cervical screening were effective or cost-effective in women with a prolonged history of non-participation in the screening programme. A letter from the local cervical screening programme commissioner resulted in a small, non-significant increase in uptake. The low cost and ease of implementation of this intervention supports further research into its use in routine practice.

Sugano, H. (1999). "The cancer problem--carcinogenesis and prevention from the viewpoint of the natural history of cancer." Anticancer Res **19**(5A): 3787-90.

Cancer is mostly environmental in origin and therefore is theoretically preventable by control of environmental conditions. From the viewpoint of the natural history of cancer, the multi-step nature of neoplasia and the generally long latent period are stressed. The molecular biology of cancer tells us that neoplasia is a disease of the genes, with each tumor having its own series of gene alterations. Numerous carcinogens, mutagens and others, have been identified, and we are now in a good position to promote cancer prevention. The aim is to postpone clinical manifestation of latent cancer to an older age, and has two aspects: one is elimination of carcinogens from the environment and the other is active efforts to improve the lifestyle and develop effective chemopreventive agents. For understanding of prevention, elucidation of molecular mechanisms of interactions between genes and environmental or dietary compounds for each cancer is essential.

Sylvester, R. J. (2006). "Natural history, recurrence, and progression in superficial bladder cancer." ScientificWorldJournal **6**: 2617-25.

Superficial bladder cancer encompasses patients with stage Ta T1 tumors and patients with carcinoma in situ (CIS). The natural history or treatment-related prognosis of these patients varies considerably from one patient to the next based on the patient's clinical and the tumor's pathological characteristics. Based on a review of the literature, the most important prognostic factors for recurrence are the prior recurrence rate, number of tumors, and tumor size; whereas for progression, the most important prognostic factors are the T category, grade, and presence of CIS. Treatment with intravesical bacillus Calmette-Guerin reduces both the risk of recurrence and the risk of progression, and is the treatment of choice in high-risk papillary tumors and in patients with CIS. Assessment of a patient's prognostic factors and his or her risk of recurrence and progression is a prerequisite for determining the most appropriate treatment and frequency of follow-up for a given patient.

Szelei-Stevens, K. A., R. R. Kuske, et al. (2000). "The influence of young age and positive family history of breast cancer on the prognosis of ductal carcinoma in situ treated by excision with or without radiation therapy or by mastectomy." Int J Radiat Oncol Biol Phys **48**(4): 943-9.

BACKGROUND: Several recent studies have investigated the influence of family history on the progression of DCIS patients treated by tylectomy and radiation therapy. Since three treatment strategies have been used for DCIS at our institution, we evaluated the influence of family history and young age on outcome by treatment method. METHODS: Between 1/1/82 and 12/31/92, 128 patients were treated for DCIS by mastectomy (n = 50, 39%), tylectomy alone (n = 43, 34%), and tylectomy with radiation therapy (n = 35, 27%). Median follow-up is 8.7 years. Thirty-nine patients had a positive family history of breast cancer; 26 in a mother, sister, or daughter (first-degree relative); and 26 in a grandmother, aunt, or cousin (second-degree relative). Thirteen patients had a positive family history in both first- and second-degree relatives. RESULTS: Six women developed a recurrence in the treated breast; all of these were initially treated with tylectomy alone. There were no recurrences in the mastectomy group or the tylectomy patients treated with postoperative radiation therapy. Patients with a positive family

history had a 10.3% local recurrence rate (LRR), vs. a 2.3% LRR in patients with a negative family history (p = 0.05). Four of 44 patients (9.1%) 50 years of age or younger recurred, compared to two of 84 patients (2.4%) over the age of 50 (p = 0.10). Fifteen patients had both a positive family history and were 50 years of age or younger. Among these women, the recurrence rate was 20%. Women in this group treated by lesionectomy alone had a LRR of 38% (3 of 8). CONCLUSION: The most important determinant of outcome was the selection of treatment modality, with all of the recurrences occurring in the tylectomy alone group. In addition to treatment method, a positive family history significantly influenced LRR in patients treated by tylectomy, especially in women 50 years of age or younger. These results suggest that DCIS patients, particularly premenopausal women with a positive family history, benefit from treatment of the entire breast, and raise concerns about treating patients with a possible genetic susceptibility to breast cancer with tylectomy alone.

Talman, M. L., B. B. Rasmussen, et al. (2008). "Estrogen Receptor analyses in the Danish Breast Cancer Cooperative Group. History, methods, prognosis and clinical implications." Acta Oncol **47**(4): 789-94.

INTRODUCTION: Estrogen receptor (ER) is a prognostic and predictive biomarker, which has been known for 40 years. The detection method has developed over the years from different biochemical assays (BCA) to immunohistochemistry (IHC) on paraffin embedded tissue. The aim of the present study is to describe the development in ER analysis in the Danish Breast Cancer cooperative Group (DBCG), in the period of 1977 to 2006, regarding quantity and method of analyses. To compare BCA with IHC, and to report the prognosis for low-risk breast cancer patients. PATIENTS AND METHODS: In the period of 1991-1993, BCA and IHC were both performed on 2 364 tumours from breast cancer patients in Denmark. Three central laboratories in Copenhagen, Aarhus and Aalborg, respectively, performed BCA, while IHC was done in each of the pathology departments participating in the study. Data on ER status, clinical variables and prognostic factors were obtained from the DBCG database. Prognosis is calculated from the DBCG protocol 89a, regarding recurrence free survival (RFS) and overall survival (OS). RESULTS: We find an increasing frequency of ER positive tumours over time, with correlation to patient age. There is a better RFS and OS for tumours positive in both ER determinations. However, BCA is more sensitive than IHC. We find a significant correlation between positive ER status and other low risk factors, except lymph node status. DISCUSSION: Immunohistochemistry has several advantages compared with BCA; it is decentralised, only requiring small amounts of tumour tissue, with direct light microscopic interpretation of invasive tumour cells. It is less expensive and more rapid than BCA. Results in this study show the same RFS in both ER determinations. We conclude that IHC in analysing ER is a rapid, reliable and easy method, and we recommend the use of external quality control programme.

Tavani, A., E. Ricci, et al. (2000). "Influence of menstrual and reproductive factors on ovarian cancer risk in women with and without family history of breast or ovarian cancer." Int J Epidemiol **29**(5): 799-802.

BACKGROUND: As women with a family history of ovarian and/or breast cancer possibly inherit genetic changes that alter their risk of ovarian cancer, other established risk factors for ovarian cancer may influence the risk differently in women with and without a family history of the disease. METHODS: Case-control study conducted between 1983 and 1991 in Northern Italy. Cases were 971 women, under 75 years, with incident, histologically confirmed epithelial ovarian cancer, and controls were 2758 women, under 75 years, admitted to hospitals for non-malignant, non-hormone-related conditions, who had not undergone bilateral oophorectomy. Of these, 93 cases and 139 controls had a family history of ovarian and/or breast cancer. RESULTS: The risk of ovarian cancer increased with irregular menstrual cycles, late age at menopause, natural menopause, nulliparity, never use of oral contraceptives and use of hormone replacement therapy. We computed an 'adult life risk score' (ALRS) considering the combined effect of these factors. Compared to women without a family history and a low ALRS, the OR was 1.7 for women without family history and high ALRS, 1.4 for women with a family history and low ALRS, and 3.5 for women with a family history and high ALRS. CONCLUSIONS: Intervention on selected hormonal risk factors for ovarian cancer might be important for women with a family history of the disease.

Torgenson, M. J., J. E. Shea, et al. (2008). "Natural history of pancreatic cancer recurrence following "curative" resection in athymic mice." J Surg Res **149**(1): 57-61.

OBJECTIVE: We present a mouse model of pancreatic cancer recurrence following "curative" resection using a novel technique of implanting red fluorescent protein transfected tumor cells within a hyaluronan-based synthetic extracellular matrix into the distal pancreas of nude mice. Following "curative" pancreatic resection, we demonstrate postoperative

disease recurrence by fluorescence imaging. METHODS: Forty athymic nude mice underwent pancreatic injection with red fluorescent protein transfected MiaPaCa-2 or AsPc-1 cells suspended in a synthetic extracellular matrix. In 20 animals, the distal pancreas and primary tumor were resected at 2 or 5 wk following injection. The remaining 20 mice underwent sham resection. Eight weeks following resection, necropsy and fluorescence imaging were performed to assess disease recurrence. RESULTS: At exploration, 39 of 40 mice had primary tumors. Eighteen of 20 mice were eligible for curative resection. Eight weeks following "curative" resection, 10 of 18 mice had recurrent disease. Of these, six developed local recurrence, two had distant metastases, and two had both. CONCLUSIONS: Using an orthotopic animal model, we are able to reliably develop primary tumors, safely perform "curative" resection, and demonstrate a 56% recurrence rate 8 wk following resection. We confirmed disease-free resection using fluorescence imaging. This model may prove useful for preclinical adjuvant therapeutic trials.

Tracy, K. A., J. M. Quillin, et al. (2008). "The impact of family history of breast cancer and cancer death on women's mammography practices and beliefs." Genet Med **10**(8): 621-5.

PURPOSE: To summarize the impact of a family history of breast cancer on mammography practices and beliefs. METHOD: Survey data concerning breast health practices and beliefs were utilized for a cross-sectional analysis. Participants were 899 racially diverse nonpregnant women 40 years and older without breast cancer. The impact of various aspects of cancer family history on mammography, perceived barriers to and benefits of screening, and perceived breast cancer risk was assessed. RESULTS: More women with a first-degree relative with breast cancer reported a mammogram within the past year and rated their breast cancer risk higher. Death of a first-degree relative impacted the belief that breast cancer can be cured with early detection. Degree of relatedness of affected relative impacted mammography practice and risk perceptions. CONCLUSION: Family history of breast cancer impacted mammography adherence, beliefs about outcomes with early detection, and risk perceptions. Breast cancer death in a family may be a better predictor of beliefs about breast cancer detection and cure than family history of cancer alone. These findings have implications for how screening recommendations and risk information are communicated to patients with different familial cancer experiences.

Traina, T. A., I. Poggesi, et al. (2008). "Pharmacokinetics and tolerability of exemestane in combination with raloxifene in postmenopausal women with a history of breast cancer." Breast Cancer Res Treat **111**(2): 377-88.

PURPOSE: Raloxifene is a second-generation selective estrogen receptor modulator that reduces the incidence of breast cancer in postmenopausal women. Exemestane, a steroidal aromatase inhibitor, decreases contralateral new breast cancers in postmenopausal women when taken in the adjuvant setting. Preclinical evidence suggests a rationale for coadministration of these agents to achieve complete estrogen blockade. EXPERIMENTAL DESIGN: We tested the safety and tolerability of combination exemestane and raloxifene in 11 postmenopausal women with a history of hormone receptor-negative breast cancer. Patients were randomized to either raloxifene (60 mg PO daily) or exemestane (25 mg PO daily) for 2 weeks. Patients then initiated combination therapy at the same dose levels for a minimum of 1 year. Pharmacokinetic and pharmacodynamic data for plasma estrogens, raloxifene, exemestane, and their metabolites were collected at the end of single-agent therapy and during combination therapy. RESULTS: Plasma concentration-time profiles for each drug were unchanged with monotherapy versus combination therapy. Raloxifene did not affect plasma estrogen levels. Plasma estrogen concentrations were suppressed below the lower limit of detection by exemestane as monotherapy and when administered in combination with raloxifene. The most common adverse events of any grade included arthralgias, hot flashes, vaginal dryness and myalgias. CONCLUSIONS: In this small study, coadministration of raloxifene and exemestane did not affect the pharmacokinetics or pharmacodynamics of either agent to a significant degree in postmenopausal women. The combination of estrogen receptor blockade and suppression of estrogen synthesis is well tolerated and warrants further investigation.

Trudeau, M. E., K. I. Pritchard, et al. (2005). "Prognostic factors affecting the natural history of node-negative breast cancer." Breast Cancer Res Treat **89**(1): 35-45.

PURPOSE: We undertook a natural history investigation of a broad selection of prognostic factors in a cohort of women with node-negative breast cancer. PATIENTS AND METHODS: The cohort consisted of 415 consecutive histologic node-negative (T1-3, M0) patients, operated on for primary breast cancer at Women's College Hospital, Toronto, Canada, between 1977 and 1986. Only 7% of these patients were given adjuvant systemic therapy;

further, for the 48% of women who underwent lumpectomy, only 29% received adjuvant radiotherapy to the breast. Paraffin-embedded tumour tissue was available for the majority of patients. The following factors were examined for their univariate and multivariate effects on time to recurrence outside the breast (DFI) and survival from breast cancer (DSS): age, weight, tumour size, estrogen receptor, progesterone receptor, histologic type, tumour grade, nuclear grade, lymphovascular invasion, overexpression of neu oncoprotein, DNA ploidy, % cells in S-phase, and adjuvant therapy. Multivariate analyses utilized a Cox model with a step-wise factor selection for the 260 patients with complete information. RESULTS: A worse prognosis was indicated when there was lymphovascular invasion (for DFI, $p < 0.001$; for DSS, $p = 0.0046$), high %S-phase (for DFI, $p = 0.08$; for DSS, $p = 0.02$), high tumour grade (for DFI, $p = 0.02$; for DSS, $p = 0.03$), and overexpression of neu oncoprotein (for DSS, $p = 0.07$). CONCLUSIONS: In our natural history investigation, two factors, lymphovascular invasion and tumour grade, are of particular interest since they may be readily incorporated into clinical practice. Overexpression of neu oncoprotein may also play a role in determining prognosis for women administered adjuvant systemic therapy.

Tsukuma, H., A. Oshima, et al. (2000). "Natural history of early gastric cancer: a non-concurrent, long term, follow up study." Gut **47**(5): 618-21.

BACKGROUND: Controversy has arisen on the natural history of early gastric cancer (EGC). While some emphasise the effectiveness of early detection in reducing mortality from gastric cancer, others insist that EGC is a pseudo-cancer. AIMS/PATIENTS/METHODS: To elucidate the natural history of EGC, a non-concurrent, long term, follow up study was conducted in 71 patients who were diagnosed endoscopically as having EGC, which was confirmed as cancer on biopsy, but in whom surgical resection was not conducted or delayed by more than six months. RESULTS: The natural course of EGC was observed in 56 cases. Over a period of 6-137 months, 20 remained in the early stage while 36 progressed to the advanced stage. The proportion remaining in the early stage consistently decreased with time. Median duration of those who remained in the early stage was estimated as 44 months. The cumulative five year risk for progressing to the advanced stage was 63.0%. In 38 cases there was no evidence for undergoing surgical resection for gastric cancer. The cumulative five year corrected survival was estimated as 62.8% among those unresected. Hazard rate ratio for gastric cancer mortality was 0.65 ($p=0.34$) for screening detected versus non-screening detected. Hazard rate ratio for gastric cancer mortality was 0.51, significantly lower for patients whose operations were delayed compared with those unresected. CONCLUSIONS: Although EGC showed a relatively long natural history in general, it progressed to the advanced stage with time and led to death from gastric cancer for the most part if left untreated.

Tyndel, S., J. Austoker, et al. (2007). "What is the psychological impact of mammographic screening on younger women with a family history of breast cancer? Findings from a prospective cohort study by the PIMMS Management Group." J Clin Oncol **25**(25): 3823-30.

PURPOSE: Studies are underway to establish the clinical effectiveness of annual mammographic screening in women younger than 50 years with a family history of breast cancer. This study investigated both the positive and negative psychological effects of screening on these women. PATIENTS AND METHODS: Women who received an immediate all-clear result after mammography (n = 1,174) and women who were recalled for additional tests before receiving an all-clear result (false positive; n = 112) completed questionnaires: 1 month before mammography, and 1 and 6 months after receiving final results. The questionnaires included measures of cancer worry, psychological consequences, and perceived benefits of breast screening. RESULTS: Women who received an immediate all-clear result experienced a decrease in cancer worry and negative psychological consequences immediately after the result, whereas women who were recalled for additional tests did not. By 6 months this cancer-specific distress had reduced significantly in both groups. Changes in levels of distress were significantly different between the two groups, but in absolute terms the differences were not large. Recalled women reported significantly greater positive psychological consequences of screening immediately after the result, and were also more positive about the benefits of screening compared with women who received an immediate all-clear result. CONCLUSION: For women receiving an immediate all-clear result, participating in annual mammographic screening is psychologically beneficial. Furthermore, women who are recalled for additional tests do not appear to be harmed by screening: these women's positive views about mammography suggest that they view any distress caused by recall as an acceptable part of screening.

Underwood, S. M., K. Richards, et al. (2008). "Pilot study of the breast cancer experiences of African American women with a family history of breast

cancer: implications for nursing practice." Abnf J **19**(3): 107-13.

Experts in the area of breast cancer detection and control recommend that women at increased risk discuss their risk status and risk management with their health care providers. In spite of the excessive breast cancer burden borne by African American women, little attention has been given to studying breast cancer risk communication and/or breast cancer risk management in this at-risk population group. This report summarizes the outcomes of a study undertaken to explore the degree to which breast cancer, breast cancer risk, and breast cancer risk management were discussed by African American women and their health care providers Targeted for inclusion in the study were African American women who had a first degree relative or multiple second degree relatives that had been diagnosed with pre-menopausal breast cancer. Of particular interest was the extent to which African American women with a family history of breast cancer perceived themselves to be at risk for developing breast cancer and the extent to which they discussed their family history, their breast cancer risk, and, breast cancer risk management with their providers.

Vassilopoulou-Sellin, R. and M. J. Klein (2002). "Health care priorities for menopausal women with a history of breast cancer." South Med J **95**(11): 1269-75.

BACKGROUND: The opinion of breast cancer survivors and their physicians about long-term health, especially menopause, is not well understood. METHODS: Seventy-three patients and 22 physicians answered questions regarding medical follow-up and menopause. RESULTS: One third of specialists preferred follow-up of 5 years or less, while 59% preferred 10 years or longer; 46% of patients preferred follow-up for 10 years or longer. Physicians preferred that primary care physicians supervise menopausal health (55%), but patients disagreed (30%). Physicians cited heart health most important, followed by skeletal health and climacteric symptoms. Physicians believed that climacteric symptoms were patients' leading concern, but patients cited heart health, followed by skeletal health and cognitive dysfunction. Neither patients nor physicians advocated estrogen use. CONCLUSIONS: Differences of opinion exist between breast cancer patients and specialists regarding follow-up and management of menopause. However, both patients and physicians prefer prolonged surveillance by a cancer specialist, with attention to heart and skeletal health issues.

Venkitaraman, R., K. Thomas, et al. (2008). "Baseline urinary phytoestrogen levels and the natural history of untreated, localised prostate cancer in a British population." Int J Biol Markers **23**(3): 192-7.

AIM: To determine whether urinary concentrations of phytoestrogens are associated with the rate of disease progression in men with untreated, localised prostate cancer. PATIENTS AND METHODS: Patients with untreated, localised prostatic adenocarcinoma on a prospective clinical study of active surveillance had urine samples collected at baseline. Patients underwent monitoring with serial PSA levels and repeat octant prostate biopsies. Disease progression was defined as either adverse histology on repeat biopsy (primary Gleason grade >or= 4, or >50% positive cores) or radical treatment for PSA velocity >1 ng/mL/year. Time to disease progression was analysed with respect to baseline urinary levels of genistein, enterolactone, daidzein and equol, assayed using liquid chromatography/tandem mass spectrometry. RESULTS: 191 patients were evaluable, with a median follow-up of 2.5 years. 71 patients experienced disease progression. No significant association was seen between time to disease progression and baseline urinary levels of daidzein (p=0.85), genistein (p=0.81), enterolactone (p=0.085) or equol (p=0.33). No significant association was seen between adverse histology on repeat biopsy and urinary levels of either daidzein (p=0.85), genistein (p=0.58), enterolactone (p=0.88) or equol (p=0.71). There was no significant correlation between PSA velocity and urinary levels of daidzein (p=0.90), genistein (p=0.98), enterolactone (p=0.10) or equol (p=0.60). CONCLUSION: These data do not support the hypothesis that phytoestrogens prevent disease progression in men with localised prostate cancer.

Verkooijen, H. M., E. Rapiti, et al. (2009). "Impact of a positive family history on diagnosis, management, and survival of breast cancer: different effects across socio-economic groups." Cancer Causes Control **20**(9): 1689-96.

BACKGROUND: This study aims to investigate whether increased awareness of breast cancer, due to a positive family history (FH), reduces diagnostic, therapeutic, and survival differences between women of low versus high socio-economic status (SES). METHODS: All breast cancer patients registered between 1990 and 2005 at the population-based Geneva Cancer Registry were included. With multivariate logistic and Cox regression analysis, we estimated the impact of SES and FH on method of detection, treatment, and mortality from breast cancer. RESULTS: SES discrepancies in method of detection and suboptimal treatment, as seen among women without a FH, disappeared in the presence of a positive FH. SES differences in stage and survival

remained regardless of the presence of a positive FH. Overall, positive FH was associated with better survival. This effect was the strongest in women of high SES (age-adjusted Hazard Ratio [HR(ageadj)] 0.54 [0.3-1.0]) but less pronounced in women of middle (0.77 [0.6-1.0]), and absent in women of low SES (0.80 [0.5-1.2]). CONCLUSION: A positive FH of breast cancer may reduce SES differences in access to screening and optimal treatment. However, even with better access to early detection and optimal treatment, women of low SES have higher risks of death from their disease than those of high SES.

Viana, D. V., J. R. Goes, et al. (2008). "Family history of cancer in Brazil: is it being used?" Fam Cancer **7**(3): 229-32.

In developing countries, low budgets make the issue of integrating genetics into clinical practice a challenge, a situation in which the use of family history (FH) becomes important for patient care, as it is a low cost strategy and a risk assessment tool. The purpose of this study was to review medical records of patients with colorectal cancer (CRC) seen in a public University Hospital and evaluate how often FH of cancer is registered. Initially we searched a database for patients who were seen in our hospital between 2002 and 2004 with the diagnosis of CRC. We found 415 patients, 104 of whom were excluded. A total of 311 charts were reviewed and classified into 3 groups. Group A: no FH documented; group B: FH was documented, but FH of cancer was not collected; and group C: FH of cancer was documented. We also investigated what type of information was recorded, in order to verify if important elements were assessed. Ninety-eight charts (31.5%) were classified in group A, 20 (6.5%) in group B, and 193 (62%) in group C. In addition, we observed that important information regarding affected relatives was not collected in most of the charts. In conclusion, we found that although FH of cancer was recorded in 62% of charts of patients with CRC, information that could be relevant for risk assessment and management of at-risk families was missing. Our findings expose an important problem in health education that could reflect negatively in the quality of medical assistance to individuals at risk for familial cancer.

Wakelee, H. A., P. Bernardo, et al. (2006). "Changes in the natural history of nonsmall cell lung cancer (NSCLC)--comparison of outcomes and characteristics in patients with advanced NSCLC entered in Eastern Cooperative Oncology Group trials before and after 1990." Cancer **106**(10): 2208-17.

BACKGROUND: Demographic factors and treatment regimens were evaluated in relation to differences in outcome between patients with advanced nonsmall cell lung cancer (NSCLC) who were diagnosed and treated on Eastern Cooperative Oncology Group Phase II and III trials from 1981 to 1990 and from 1991 to 2000. METHODS: In this retrospective analysis, 6 advanced NSCLC trials were identified between 1981 and 1990, and 3 trials were identified after 1990. Patient characteristics (n = 3398 patients) and other clinical outcomes were analyzed, including progression-free survival (PFS) and overall survival (OS). RESULTS: Patients who entered on trials after 1990 more likely were women, received a cisplatin-containing regimen, had a performance status of 0 or 1, had Stage IIIB (vs. Stage IV) disease, had tumors with adenocarcinoma histology, had weight loss < or = 10%, and had pulmonary-only metastases (although more total metastases and brain metastases) compared with patients who were diagnosed before 1990. OS was longer post-1990 than pre-1990 (8.2 months vs. 5.8 months pre-1990), and PFS was longer post-1990 (3.5 months vs. 2.6 months pre-1990; P<.001 for both). In addition, the median interval from the date of disease progression to death increased by nearly 62% in the later decade. CONCLUSIONS: Improved survival in more recent NSCLC trials was explained in part by the enrollment of patients with more favorable prognostic factors. A change in the natural history of the disease was reflected by some of these changes, including increased numbers of women with the disease and changes in the patterns of metastases. Changes in eligibility criteria also accounted for some improvements in prognostic factors and improved second line therapies in the later decade. Thus, the survival improvements are likely to be multifactorial, with improved therapies also playing a major role.

Walker, G. R., J. J. Schlesselman, et al. (2002). "Family history of cancer, oral contraceptive use, and ovarian cancer risk." Am J Obstet Gynecol **186**(1): 8-14.

OBJECTIVE: The purpose of this study was to determine whether women with a family history of ovarian cancer are at reduced risk of ovarian cancer from the use of oral contraceptives and to compare their risk with that of women with no family history of ovarian cancer. STUDY DESIGN: A population-based case-controlled study was conducted from May 1994 through July 1998 in which 767 women aged 20 to 69 years with a diagnosis of epithelial ovarian cancer were ascertained from 39 hospitals in 3 northeastern states. Personal interviews with the women and 1367 control subjects provided data that allowed us to estimate the relative risk of ovarian cancer in relation to a family history of cancer and total duration of oral contraception. RESULTS: Among the 33 case patients and 24 control subjects

with a first-degree family history of ovarian cancer, risk of ovarian cancer declined with increasing duration of oral contraception (P =.01). Risk reduction from short-term use of oral contraceptives (< or = 48 months) did not differ significantly by family history (combined estimate of odds ratio, 0.72; 90% CI, 0.59%-0.87%). Risk reduction from long-term use of oral contraceptives (>48 months) was greater in women with a positive family history of ovarian cancer (odds ratio, 0.12) than in women with a negative family history of ovarian cancer (odds ratio, 0.51; test of interaction, P =.04; 692 case patients, 1279 control subjects). CONCLUSION: Four to 8 years of oral contraception may substantially reduce the risk of ovarian cancer by age 70 years in women with a family history of the disease, from approximately 4 women per 100 women who did not use oral contraceptives to only 2 women per 100 women who did use oral contraceptives.

Warner, E., J. C. Carroll, et al. (2003). "Educating women about breast cancer. An intervention for women with a family history of breast cancer." Can Fam Physician **49**: 56-63.

OBJECTIVE: To evaluate an "information aid" for women with a family history of breast cancer. DESIGN: Before-after descriptive study. SETTING: Family practices in Ontario. PARTICIPANTS: Of 405 randomly selected Ontario physician members of the College of Family Physician's of Canada's National Research System, 97 agreed to participate and to recruit three consecutive female patients with any family history of breast cancer. INTERVENTIONS: Patients completed a baseline questionnaire and, after reviewing the information aid, a satisfaction questionnaire. Four weeks later, they completed a third questionnaire. MAIN OUTCOME MEASURES: Patient satisfaction, knowledge, worries related to breast cancer, risk perception, and attitudes toward screening. RESULTS: Of 203 patients recruited, 160 (79%) completed all three questionnaires. The information aid was rated excellent or very good by 91% of the women; 99% would recommend it to other women. Knowledge improved significantly; worry about breast cancer did not increase. CONCLUSION: The information aid is a useful resource for women and primary care physicians and could facilitate appropriate risk assessment and management of women with a family history of breast cancer.

Warner, E., R. E. Heisey, et al. (1999). "Hereditary breast cancer. Risk assessment of patients with a family history of breast cancer." Can Fam Physician **45**: 104-12.

OBJECTIVES: To assist family physicians in stratifying women with a family history of breast cancer as being at low, moderate, or high risk of hereditary breast cancer (HBC). To present guidelines for managing each of these risk groups. QUALITY OF EVIDENCE: A MEDLINE search was conducted from January 1976 to December 1997 using key words related to breast cancer risk factors, risk assessment, prevention, and screening. Risk stratification criteria were derived empirically and assessed using retrospective chart review. MAIN FINDINGS: Although up to 20% of women in the general population have a family history of breast cancer, less than 5% are at high risk for HBC. Certain features in a family history suggest increased risk. Women with none of these features are at low risk for HBC and should have annual clinical breast examinations and mammography at least every 2 years starting at age 50. Women with one or more features of increased risk who do not meet criteria for referral to a familial cancer clinic are at moderate risk for HBC and should begin annual mammography and clinical breast examination at age 40. Women who meet referral criteria are at high risk for HBC and should be counseled regarding referral to a familial cancer clinic for more detailed risk assessment and consideration for genetic testing. All women should be taught proper breast self-examination technique and encouraged but not pressured to practise it monthly for life. CONCLUSION: A simple algorithm can assist physicians in stratifying women into low, moderate, and high HBC risk groups. Management strategies for each group are given in this article and the two following (Heisey et al page 114 and Carroll et al page 126).

Wasserman, L., S. W. Flatt, et al. (2004). "Correlates of obesity in postmenopausal women with breast cancer: comparison of genetic, demographic, disease-related, life history and dietary factors." Int J Obes Relat Metab Disord **28**(1): 49-56.

BACKGROUND: Obesity in women has been associated with a variety of factors, including genetic predisposition, social class, early age at menarche, exercise, alcohol consumption and diet. Obesity is a risk factor for the occurrence and the recurrence of breast cancer in postmenopausal women, perhaps because of increased exposure to estrogen, insulin and insulin-like growth factors (IGFs). The progesterone receptor (PR) and the steroid hormone receptor coactivator pCIP/ACTR/AIB1/TRAM1/RAC3 (AIB1) are hypothesized to mediate signaling crosstalk between these hormonal pathways. Polymorphisms in both genes have been described and their association with breast cancer risk reported. If genetic factors contribute to obesity, and the PR and AIB1 genes influence estrogenic, insulin and IGF pathways, then

genetic patterns resulting from PR and AIB1 polymorphisms may be associated with obesity in postmenopausal women. OBJECTIVE: We compared the PR and AIB1 genotypes of postmenopausal women with breast cancer with demographic, disease-related, reproductive, lifestyle and dietary variables in terms of the strength of their relationship with obesity (BMI> or =30 kg/m2). SUBJECTS: A total of 301 postmenopausal women previously diagnosed with Stage I, II or IIIA breast cancer, who are enrolled in the Women's Healthy Eating and Living (WHEL) study (age: 34.5-70.8 y, BMI: 17.8-54.6 kg/m2). MEASUREMENTS: The PR polymorphism PROGINS was identified by PCR. The length of the AIB1 polyglutamine repeat was determined by PCR and nondenaturing gel electrophoresis or DNA sequencing. BMI was obtained at the baseline clinic visit upon entry into the WHEL study. Information about date of diagnosis, stage of disease, tumor hormone receptor status and adjuvant treatment received were obtained from medical records. Reproductive, menstrual history, demographic, family history of cancer, smoking history and exercise frequency and intensity information were obtained from questionnaires. Dietary and alcohol intake data came from four 24-h telephone recalls of food intake obtained at the study entry. RESULTS: The combined inheritance of PROGINS A1/A1 and AIB1 28/29, 28/30, 28/31, 29/29 or 29/30 (AIB1 LG) genotypes (adjusted odds ratio (OR)=2.22 (95% confidence interval 1.25-3.93)) and early age at menarche (<12 y) (adjusted OR=2.34 (1.12-4.86)) were each associated with the risk for obesity. Current use of tamoxifen (adjusted OR=0.49 (0.28-0.87)) and an alcohol intake > or =10 g/day (adjusted OR=0.28 (0.11-0.77)) were inversely associated with BMI > or =30 kg/m2. CONCLUSION: Early age at menarche and a PROGINS A1/A1+AIB1 LG genetic pattern had comparable levels of association with obesity in this cross-sectional sample of postmenopausal women with breast cancer. Since this was a cross-sectional rather than a case-control design, the association between PROGINS and AIB1 genotype and obesity found in this sample should be considered preliminary, and must be re-evaluated with a new and larger sample.

Weiss, R. B., S. H. Woolf, et al. (2003). "Natural history of more than 20 years of node-positive primary breast carcinoma treated with cyclophosphamide, methotrexate, and fluorouracil-based adjuvant chemotherapy: a study by the Cancer and Leukemia Group B." J Clin Oncol **21**(9): 1825-35.

PURPOSE: Breast cancer heterogeneity dictates lengthy follow-up to assess outcomes. Efficacy differences for three regimens that are based on adjuvant cyclophosphamide, methotrexate, and fluorouracil (CMF) are presented in this article, but cancer recurrence sites, time of relapse, subsequent primary cancers, and causes of death in the natural history of node-positive breast cancer are emphasized. PATIENTS AND METHODS: Beginning in 1975, 905 patients with node-positive cancer were randomly assigned to receive CMF or two regimens of CMF plus other agents. Median follow-up is 22.6 years. The natural-history analysis was performed on a subset of 814 patients. RESULTS: Eighty percent of the 599 women known to have died, died of metastatic breast cancer. Only 8.5% of the deceased women died of a cause other than breast cancer, a second or third cancer, or adjuvant chemotherapy toxicity. One hundred five women (12.8%) developed other primary cancers, with 49 (46.6%) occurring in the contralateral breast. Therapeutic efficacy differences of the CMF regimens reported earlier have been maintained more than 20 years later. For certain subsets, the five-drug regimen had advantages over CMF. Bone was the most common recurrence site. The longest interval to relapse has been 23.5 years, and 18% of those who relapsed did so more than 10 years later. CONCLUSION: Despite adjuvant chemotherapy, a large majority (80%) of women with node-positive breast cancer die of the disease, and many recurrences develop more than 10 years later. CMF plus vincristine and prednisone provides a benefit compared with CMF, but the magnitude varies with the number of involved nodes. Outcome trends in earlier analyses of this study were maintained even years later.

West, D. S., P. G. Greene, et al. (2003). "The impact of a family history of breast cancer on screening practices and attitudes in low-income, rural, African American women." J Womens Health (Larchmt) **12**(8): 779-87.

BACKGROUND: Women with a family history of breast cancer are at increased risk for developing cancer and, therefore, might be expected to engage in early detection practices more actively than women without a family history. Alternatively, women with a family history may avoid thinking about cancer and have attitudes and practices that do not promote early detection. METHODS: This study examined breast cancer attitudes and practices among African American women aged >or=50 who had not had a mammogram in the last 2 years. RESULTS: Phone survey data from 320 female clients of low-income, rural primary care clinics (91% African American) indicated that 15% self-reported a family history of breast cancer (FH(+)). Half of the FH(+) women did not know their relative risk of developing breast cancer. Of those providing a risk estimate, 67%

perceived themselves at low risk compared with other women their age. Perceived relative risk was comparable between FH(+) and FH(-) women. Further, FH(+) women did not indicate greater worry about breast cancer, nor did they have more accurate knowledge of mammography recommendations than FH(-) women. Two thirds of FH(+) women had never had a mammogram. Monthly breast self-examination did not differ between FH(+) and FH(-) women. CONCLUSIONS: Thus, neither knowledge of a positive family history nor perceived relative risk of breast cancer was associated with either increased or decreased early detection practices among these low-income, rural, African American women who have underused mammography. Furthermore, a substantial proportion of FH(+) women had not ever participated in screening mammography. Interventions to increase mammography rates in this population of underusers are indicated.

Wilson, B., N. Qureshi, et al. (2009). "Clinical utility of cancer family history collection in primary care." Evid Rep Technol Assess (Full Rep)(179): 1-94.

OBJECTIVES: This systematic review aimed to evaluate, within unselected populations: the (1) performance of family history (FHx)-based models in predicting cancer risk; (2) overall benefits and harms associated with established cancer prevention interventions; (3) impact of FHx-based risk information on the uptake of preventive interventions; and (4) potential for harms associated with collecting cancer FHx. DATA SOURCES: MEDLINE, EMBASE, CINAHL, Cochrane Central, Cochrane Database of Systematic Reviews, and PsycINFO were searched from 1990 to June 2008 inclusive. Cancer guidelines and recommendations were searched from 2002 forward and systematic reviews from 2003 to June 2008. REVIEW METHODS: Standard systematic review methodology was employed. Eligibility criteria included English studies evaluating breast, colorectal, ovarian, or prostate cancers. Study designs were restricted to systematic review, experimental and diagnostic types. Populations were limited to those unselected for cancer risk. Interventions were limited to collection of cancer FHx; primary and/or secondary prevention interventions for breast, colorectal, ovarian, and prostate cancers. RESULTS: Accuracy of models. Seven eligible studies evaluated systems based on the Gail model, and on the Harvard Cancer Risk Index. No evaluations demonstrated more than modest discriminatory accuracy at an individual level. No evaluations were identified relevant to ovarian or prostate cancer risk. Efficacy of preventive interventions. From 29 eligible systematic reviews, seven found no experimental studies evaluating interventions of interest. Of the remaining 22, none addressed ovarian cancer prevention. The reviews were generally based on limited numbers of randomized or controlled clinical trials. There was no evidence either to support or refute the use of selected chemoprevention interventions, there was some evidence of effectiveness for mammography and fecal occult blood testing. Uptake of intervention. Three studies evaluated the impact of FHx-based risk information on uptake of clinical preventive interventions for breast cancer. The evidence is insufficient to draw conclusions on the effect of FHx-based risk information on change in preventive behavior. Potential harms of FHx taking. One uncontrolled trial evaluated the impact of FHx-based breast cancer risk information on psychological outcomes and found no evidence of significant harm. CONCLUSIONS: Our review indicates a very limited evidence base with which to address all four of the research questions: 1) the few evaluations of cancer risk prediction models do not suggest useful individual predictive accuracy; 2) the experimental evidence base for primary and secondary cancer prevention is very limited; 3) there is insufficient evidence to assess the effect of FHx-based risk assessment on preventive behaviors; 4) there is insufficient evidence to assess whether FHx-based personalized risk assessment directly causes adverse outcomes.

Woolley, T., P. G. Buettner, et al. (2002). "Sun-related behaviors of outdoor working men with a history of non-melanoma skin cancer." J Occup Environ Med **44**(9): 847-54.

The present study describes sun exposure and sun protection behaviors of northern Australian outdoor workers with previous non-melanoma skin cancer (NMSC). In 1999 a cross-sectional study of northern Australian men with previous NMSC was conducted by self-administered questionnaire. Compared to other men, outdoor workers spent more time in the sun on average working days and days off ($P < 0.0001$, respectively), and outdoor workers with sun-sensitive skin reported that more skin lesions had been removed ($P = 0.0461$). The workplace did not reinforce sun-safe practices of 36.8% of workers who spent half their time or more outdoors. Sun-protective behaviors were not different between in- and outdoor workers. Outdoor workers experienced high levels of sun exposure, however, sun-protective behavior was similar to other workers. Workplaces should be targeted to reinforce sun-safe policies.

Woolley, T., P. G. Buettner, et al. (2003). "Sunburn in Australian men with a history of non-melanoma skin cancer." Am J Health Behav **27**(3): 195-207.

OBJECTIVE: To identify predictors of recent sunburn in north Australian men with a history of non-melanoma skin cancer (NMSC). METHODS: A survey of men with previous NMSC was conducted (n = 300, response rate 62%). RESULTS: Fifty-four percent of participants reported recent sunburn. Predictors identified included younger age, belief that NMSC is caused by childhood sun exposure, belief that sun protection will not help prevent further NMSC, wearing of casual clothes, and use of shade as the main sun-protection strategy. CONCLUSION: Health promotion messages should emphasize the importance of sun protection throughout life and the use of stringent sun-protection measures.

Yagyu, K., Y. Lin, et al. (2004). "Bowel movement frequency, medical history and the risk of gallbladder cancer death: a cohort study in Japan." Cancer Sci **95**(8): 674-8.

Few risk factors for gallbladder cancer have been identified with sufficient statistical power, because this cancer is rare. The present study was conducted to evaluate the association of bowel movement frequency and medical history with the risk of death from gallbladder cancer using the data set from a large-scale cohort study. A total of 113,394 participants (42.0% males), aged 40 to 89 years, were followed up for 11 years. Information on the medical history of selected diseases, history of blood transfusions, frequency of stools, and tendency toward diarrhea at baseline was collected through a self-administered questionnaire. The Cox proportional hazard model was used to estimate the hazard ratio (HR). During the follow-up period, a total of 116 deaths (46 males, 70 females) from gallbladder cancer were identified. After adjustments for age and gender, history of hepatic disease (HR: 2.28; 95% confidence intervals (95% CI): 1.24-4.21), frequency of stool, and tendency toward diarrhea (HR: 0.26; 95% CI: 0.08-0.83) were found to be significantly associated with the risk of death from gallbladder cancer. Compared with those who had a stool at least once a day, the HR was 2.06 (95% CI: 0.82-5.18) for those who had a stool less than once in 6 days (P for trend = 0.050). In this prospective study, constipation and a history of hepatic disease were found to elevate the risk of gallbladder cancer death, whereas a tendency toward diarrhea diminished it.

Yang, R. C., P. K. Mills, et al. (2006). "Cancer screening, reproductive history, socioeconomic status, and anticipated cancer-related behavior among Hmong adults." Asian Pac J Cancer Prev **7**(1): 79-85.

In the United States, breast, cervical, colorectal and prostate cancer screening rates are low or non-existent in the Hmong population compared to non-Hispanic Whites. No Hmong adults report ever participating in prostate (male only) and colorectal cancer screening. US-born Hmong women, those living in the US 20 years, and those 39 years old are more likely to be screened for breast and cervical cancer than other women. The Hmong, in general, are a young population (median age = 34 years) with low socioeconomic status. As a function of these characteristics, 52% of Hmong women reported having their first child at 15-19 years old and continued to bear children until 40-54 years old. The combination of young age at first pregnancy and multiparity probably protects Hmong women from breast cancer but elevates cervical cancer risk.

Yossepowitch, O., F. J. Bianco, Jr., et al. (2007). "The natural history of noncastrate metastatic prostate cancer after radical prostatectomy." Eur Urol **51**(4): 940-7; discussion 947-8.

OBJECTIVES: To characterise the natural history of metastatic prostate cancer after radical prostatectomy (RP) in patients followed expectantly for rising prostate-specific antigen (PSA) (noncastrate metastases). METHODS: Cox proportional hazards analyses were used to assess predictors of survival among 95 patients who developed clinically detectable noncastrate metastases after RP. The initial metastatic phenotype was characterised as minimal (nodal or axial skeletal involvement) or extensive (appendicular skeletal involvement or visceral metastases). Estimates of survival after diagnosis of metastases were generated with the Kaplan-Meier method. RESULTS: Median disease-specific survival from diagnosis of noncastrate metastases was 6.6 yr (95% confidence interval [CI], 5.2, 7.9). The initial site of metastatic disease was bone, lymph node, and viscera in 63%, 36%, and 6% of patients, respectively. Thirteen patients (14%) had extensive disease at their first metastatic manifestation. Longer PSA doubling time in the rising PSA state (hazard ratio [HR] 0.8 for each month increase in doubling time; 95%CI, 0.67-0.94) and the initial metastatic phenotype (HR 0.3 for minimal vs. extensive disease; 95%CI, 0.1-0.6) were associated with improved survival. The prostatectomy Gleason score, lymph node status at RP, PSA level at diagnosis of metastases, and interval from surgery to diagnosis of metastases did not correlate with outcome. CONCLUSION: Men who develop noncastrate metastases after RP may have a durable survival. Favourable prognostic indicators include longer PSA doubling time preceding diagnosis of metastases and initial involvement of axial skeleton or lymph nodes.

Yusoff, I. F., N. E. Hoffman, et al. (2002). "Colonoscopic surveillance for family history of

colorectal cancer: are NHMRC guidelines being followed?" Med J Aust **176**(4): 151-4.

OBJECTIVES: To assess whether referrals for surveillance colonoscopy and subsequent follow-up recommendations for patients with a family history of colorectal cancer concurred with the published National Health and Medical Research Council (NHMRC) guidelines. DESIGN: A prospective audit of patients with a family history of colorectal cancer referred for surveillance colonoscopy. Follow-up recommendations were assessed retrospectively. SETTING AND SUBJECTS: All patients referred to a major teaching hospital for surveillance colonoscopy on the basis of a family history of colorectal cancer from 2 January 2000-15 April 2001. MAIN OUTCOME MEASURES: Concurrence of referrals and recommendations with NHMRC guidelines. RESULTS: Of 340 patients referred because of a family history of colorectal cancer, 202 (83 men, 119 women) were asymptomatic. Their mean age was 50 years (95% CI, 48.3-51.6 years). The family history of 95 (47%) of these patients satisfied the NHMRC criteria for colonoscopic surveillance. Another 20 patients (17%) satisfied the criteria, but were referred before the recommended age to commence surveillance. Analysis by referral source showed that the proportion of referrals meeting NHMRC guidelines was higher from specialists than from general practitioners (75% v 45%), and this difference was significant. Follow-up recommendations, when made, concurred with NHMRC guidelines in 81% of cases. CONCLUSIONS: Further education of the medical community is required to increase understanding of colorectal screening strategies and ensure appropriate resource allocation.

Zell, J. A., J. Honda, et al. (2008). "Survival after colorectal cancer diagnosis is associated with colorectal cancer family history." Cancer Epidemiol Biomarkers Prev **17**(11): 3134-40.

BACKGROUND: Colorectal cancer (CRC) family history is a known risk factor for CRC development; however, effects of CRC family history on survival after CRC diagnosis are less well-defined. Our population-based analysis investigates whether familial CRC cases exhibit improved survival compared with sporadic CRC cases. METHODS: Cases enrolled in the University of California Irvine Gene-Environment Study of Familial Colorectal Cancer from 1994 to 1996 were analyzed, with follow-up through December 2006. Cases were categorized as familial or sporadic based on self-reported CRC family history in a first-degree relative. Univariate and multivariate survival analyses with Cox proportional hazards ratios were done for overall survival (OS) and CRC-SS (CRC-SS). RESULTS: One thousand one hundred fifty-four CRC cases were analyzed, including 781 colon cancer and 373 rectal cancer cases. Nineteen percent of colon cases had family history of CRC in a first-degree relative, compared with 16% of rectal cancer cases. No statistically significant differences between familial and sporadic colon or rectal cancer cases were detected for age, gender, ethnicity, stage, tumor location, histology, tumor grade, or stage-specific treatment rendered. Among colon cancer cases, family history of CRC (versus no family history as a reference group) was associated with improved OS (adjusted hazard ratio, 0.760; 95% confidence interval, 0.580-0.997), but not with CRC-SS (hazard ratio, 0.880; 95% confidence interval, 0.621-1.246). No OS or CRC-SS differences were detected for rectal cancer cases. CONCLUSIONS: CRC cases with family history of the disease have improved overall survival compared with sporadic CRC cases, a finding that is independent of other relevant clinical factors.

Zell, J. A., A. J. McEligot, et al. (2007). "Differential effects of wine consumption on colorectal cancer outcomes based on family history of the disease." Nutr Cancer **59**(1): 36-45.

Potentially favorable effects of wine consumption on colorectal cancer (CRC) incidence have been reported, but effects on clinical outcomes are unknown. This case-only analysis was designed to investigate outcomes among familial (n = 141) and sporadic (n = 358) CRC patients enrolled in the University of California Irvine CRC gene-environment study during 1994-1996 based on their reported frequency of wine consumption in the year prior to diagnosis. Cases were categorized as either regular or infrequent wine consumers. Univariate survival rate analyses were estimated using the Kaplan and Meier method and log-rank test. Multivariate survival analyses were performed using Cox proportional hazards ratios (HRs). Earlier stage at presentation (P = 0.034) was noted for familial (but not sporadic) CRC cases reporting regular wine consumption. An overall survival (OS) benefit was observed for familial (but not sporadic) CRC cases that were regular (10-yr OS = 75%) versus infrequent wine consumers (10-yr OS = 47%; P = 0.002). This survival improvement for familial CRC cases remained after adjustment for age, stage, treatment, and other clinically relevant factors (HR = 0.50, 95% confidence interval = 0.25-0.99). Our findings implicate favorable effects of wine consumption on stage at presentation and survival in CRC, selectively among familial CRC cases.

Ziv, E., J. Shepherd, et al. (2003). "Mammographic breast density and family history of breast cancer." J Natl Cancer Inst **95**(7): 556-8.

The association between mammographic breast density and breast cancer risk may be the result of genetic and/or environmental factors that determine breast density. We reasoned that if the genetic factors that underlie breast density increase breast cancer risk, then breast density should be associated with family history of breast cancer. Therefore, we determined the association between mammographic density and family history of breast cancer among women in the San Francisco Mammography Registry. Mammographic density was classified using the four BI-RADS criteria: 1 = almost entirely fatty, 2 = scattered fibroglandular tissue, 3 = heterogeneously dense, and 4 = extremely dense. We adjusted for age, body mass index, hormone replacement therapy use, menopause status, and personal history of breast cancer. Compared with women with BI-RADS 1 readings, women with higher breast density were more likely to have first-degree relatives with breast cancer (BI-RADS 2, odds ratio [OR] = 1.37, 95% confidence interval [CI] = 0.96 to 1.89; BI-RADS 3, OR = 1.70, 95% CI = 1.19 to 2.40; BI-RADS 4, OR = 1.70, 95% CI = 1.05 to 2.71). Thus, the genetic factors that determine breast density may determine breast cancer risk.

Zubor, P., K. Kajo, et al. (2006). "Repetitive demand for radical cancer risk reduction surgery in a young BRCA1 mutation carrier with strong family history of BRCA linked malignancies." Ginekol Pol **77**(7): 543-9.

It is known that BRCA genes play central roles in hereditary breast and ovarian cancers. BRCA1 mutation carriers face a cumulative lifetime risk of ovarian and breast cancer development. We report on a case of a strong family prevalence of BRCA1 linked malignancies as an immense psychological encumbrance and reason of demand for radical prophylactic risk decreasing surgeries in a 29 year-old healthy woman with proved 3889delAG BRCA1 gene mutation on exon 11, codon 1265 in effort to prevent possible malignant changes in the ovaries and the breast. Problems regarding the management of asymptomatic BRCA mutation carriers, time and impact of early prophylactic surgery in young women are discussed with a review of recent literature.

Zucchetto, A., L. Dal Maso, et al. (2007). "History of treated hypertension and diabetes mellitus and risk of renal cell cancer." Ann Oncol **18**(3): 596-600.

BACKGROUND: An increased risk of renal cell cancer (RCC) has been reported in subjects with hypertension. Whether this association may vary according to sex, smoking, obesity, or RCC clinical presentation is unclear. Results on the link between diabetes mellitus and RCC are inconclusive. PATIENTS AND METHODS: We conducted an Italian multicenter case-control study, including 767 (494 men, 273 women) incident cases of RCC, under 80 years of age, and 1534 hospital controls, frequency-matched to cases. Multiple logistic regression models, conditioned to center, sex, and age, and adjusted for period of interview, education, smoking, and body mass were used to estimate odds ratios (OR). RESULTS: Compared with subjects never treated, patients with a history of treated hypertension [OR = 1.7, 95% confidence interval (CI) 1.4-2.1] reported an excess risk of RCC. This pattern was confirmed in different strata of sex, education, smoking habits, body mass, tumor histological type, stage, or grade. The attributable risk of RCC for treated hypertension in this population was 16%. A slight, nonsignificant increased risk was found for history of diabetes mellitus (OR = 1.3, 95% CI 0.9-1.7). CONCLUSION: A possible causal role of hypertension in renal cell carcinogenesis is supported by the consistency of the direct association.

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