

Cancer History Research Literatures

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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 article introduces recent research reports as references in the cancer history related studies.

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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. This article introduces recent research reports as references in the related studies.

The following introduces recent reports as references in the related studies.

Alcalay, R. N., L. N. Clark, et al. "Lack of association between cancer history and PARKIN genotype: a family based study in PARKIN/Parkinson's families." *Genes Chromosomes Cancer*. 2012 Dec;51(12):1109-13. doi: 10.1002/gcc.21995. Epub 2012 Aug 24.

A number of publications have attributed a tumor suppressive (TS) function to PARKIN, a gene associated with recessive familial early onset Parkinson's disease (EOPD). Discoveries of PARKIN deletions and point mutations in tumors, functional studies, and data from mouse models have been presented to support the hypothesis. We have asked whether PARKIN mutations are associated with history of cancer in humans. We interviewed 431 participants who were screened for PARKIN mutations, including 149 EOPD cases and their family members, who were unaware of mutation status. We found no significant difference in self-reported history of cancer among carriers of one or two PARKIN mutations and noncarriers, odds ratio 0.75 (95%

confidence interval 0.27-1.83). In particular, no increase in cancer history was seen among homozygous and compound heterozygous mutation carriers compared to noncarriers. Therefore, we hypothesize that published studies attributing TS capability to PARKIN merit further exploration and we present a reevaluation of these data with respect to patterns of mutation frequencies in normal and cancer cells. We conclude that although Parkin may exert a suppressive effect in mice, further studies are required prior to assigning a TS function to PARKIN in humans.

Bakir, T., G. Can, et al. "Stomach cancer history in the siblings of patients with gastric carcinoma." *Eur J Cancer Prev*. 2000 Dec;9(6):401-8.

A case-control study in the population of the Eastern Black Sea region of Turkey was conducted to learn the incidence of stomach cancer in the siblings of patients with gastric carcinoma. Among 1240 patients with gastric carcinoma, 168 had sibling(s) with a history of stomach cancer versus 19 cases in the control group matched according to age and gender (OR 10.07, $P < 0.0001$). The frequency of a history of stomach cancers and cancer of other organs in first- to third-degree relatives was 60.7% and 38.0%, respectively, of 168 sibling cases with gastric carcinoma ($P < 0.0001$). Fifty-two point three per cent of sibling cases having a history of cancer in other organs in their relatives also reported stomach cancer in the same-degree relatives. The number of stomach cancers in the first- to third-degree relatives of sibling cases was higher than the number of other organ cancers in the same-degree relatives ($P < 0.01$). Familial clustering of stomach cancer was reported in 12.5% of sibling cases. The study of stomach cancer history in the siblings suggests: the presence of a genetic susceptibility, high risk of the disease

occurrence in the siblings of patients, higher predisposition to gastric than to other organ cancers in the relatives, and not infrequent familial clustering.

Bardia, A., P. Novotny, et al. "Efficacy of nonestrogenic hot flash therapies among women stratified by breast cancer history and tamoxifen use: a pooled analysis." Menopause. 2009 May-Jun;16(3):477-83. doi: [10.1097/gme.0b013e31818c91ca](https://doi.org/10.1097/gme.0b013e31818c91ca).

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.

Beaugerie, L. "Management of inflammatory bowel disease patients with a cancer history." Curr Drug Targets. 2014;15(11):1042-8.

In inflammatory bowel disease (IBD) patients, thiopurines promote carcinogenesis of Epstein-Barr Virus (EBV)-related lymphomas, non-melanoma skin cancers and urinary tract cancers, while anti-TNF agents could promote carcinogenesis of melanomas. Patients with IBD and previous cancer are at a higher risk of developing new or recurrent cancer than IBD patients without a history of cancer, irrespective of the use of immunosuppressants. In transplant recipients, the use of thiopurines is

associated with a high rate of cancer recurrence, particularly within the first two years following transplantation. In patients with chronic inflammatory disease, limited data suggest that no dramatic incidence of cancer recurrence is associated with the use of thiopurines or anti-TNF agents. However, there is a rationale for a two-year drug holiday from immunosuppressants after the diagnosis and treatment of the majority of incident cancers, as often as possible. Extending the duration of the immunosuppressant drug holiday to 5 years in patients with previous cancers associated with a high risk of recurrence in the post-transplant state should be considered. The immunosuppressants that can be initiated or resumed after cancer treatment should be chosen according to the type of the previous cancer. All individual decisions should be made on a case-by-case basis, together with the oncologist, according to characteristics and expected evolution of the index cancer, expected impact of the immunosuppressants on cancer evolution, and intrinsic severity of IBD, with its associated risks.

Bendell, J. and R. M. Goldberg "Targeted agents in the treatment of pancreatic cancer: history and lessons learned." Curr Opin Oncol. 2007 Jul;19(4):390-5.

PURPOSE OF REVIEW: The treatment of pancreatic cancer is an ongoing challenge with minimal substantive improvement in patient outcomes despite many randomized phase III clinical trials evaluating multiple agents, both alone and in combination. Such disappointing outcomes clearly call for broadening the scope of pharmacologic approaches to managing this disease. With increasing insight into pathways within tumor cells that are related to tumor growth and spread, and development of 'targeted therapies' against these pathways, much attention has turned to the use of these agents, alone or coupled with chemotherapy, in the treatment of pancreatic cancer. **RECENT FINDINGS:** Several targeted agents have been studied in patients with pancreatic cancer. Of the agents studied, the only agent that has shown to provide a modest but significant benefit in survival for these patients is erlotinib, an epidermal growth factor receptor tyrosine kinase inhibitor. **SUMMARY:** From trials done to date, minimal benefit has been found with the addition of targeted agents in the treatment of pancreatic cancer. More potential pathways remain to be targeted, however, and there are a plethora of new agents to be tested. Due to the likelihood that different pathways drive the development and growth of different tumors of the same site of origin the inclusion of biomarker studies to correlate with treatment effect may be a necessary component of clinical trials to learn how to best tailor therapy to the patient.

Bertino, J. R. "Chemotherapy of colorectal cancer: history and new themes." Semin Oncol. 1997 Oct;24(5 Suppl 18):S18-3-S18-7.

Since the clinical introduction of 5-fluorouracil (5-FU) in 1958, improvements in the treatment of advanced colorectal cancer have been modest. However, improvements in response rates have been demonstrated when 5-FU is administered in conjunction with leucovorin, and when methotrexate or trimetrexate is administered preceding 5-FU, indicating that higher response rates could be achieved by biomodulating the activity of 5-FU. Thus, significant emphasis has been placed on designing more effective 5-FU-based combination regimens. Novel agents, including the thymidylate synthase inhibitor raltitrexed and the topoisomerase I inhibitor irinotecan, also have demonstrated activity in colorectal cancer. Other new approaches include the administration of oral 5-FU prodrugs. The development of novel agents, new therapeutic approaches, and the refinement of existing agents and regimens in the clinic will likely improve response rates and, ultimately, patient survival. The history, current treatment options, and future opportunities for advances in chemotherapy for the treatment of colorectal cancer are discussed.

Bodurtha, J. N., D. McClish, et al. "The KinFact intervention - a randomized controlled trial to increase family communication about cancer history." J Womens Health (Larchmt). 2014 Oct;23(10):806-16. doi: 10.1089/jwh.2014.4754.

BACKGROUND: Knowing family history is important for understanding cancer risk, yet communication within families is suboptimal. Providing strategies to enhance communication may be useful. **METHODS:** Four hundred ninety women were recruited from urban, safety-net, hospital-based primary care women's health clinics. Participants were randomized to receive the KinFact intervention or the control handout on lowering risks for breast/colon cancer and screening recommendations. Cancer family history was reviewed with all participants. The 20-minute KinFact intervention, based in communication and behavior theory, included reviewing individualized breast/colon cancer risks and an interactive presentation about cancer and communication. Study outcomes included whether participants reported collecting family history, shared cancer risk information with relatives, and the frequency of communication with relatives. Data were collected at baseline, 1, 6, and 14 months. **RESULTS:** Overall, intervention participants were significantly more likely to gather family cancer information at follow-up (odds ratio [OR]: 2.73; 95% confidence interval [CI]: 2.01, 3.71) and to share familial cancer

information with relatives (OR: 1.85; 95% CI: 1.37, 2.48). Communication frequency (1=not at all; 4=a lot) was significantly increased at follow-up (1.67 vs. 1.54). Differences were not modified by age, race, education, or family history. However, effects were modified by pregnancy status and genetic literacy. Intervention effects for information gathering and frequency were observed for nonpregnant women but not for pregnant women. Additionally, intervention effects were observed for information gathering in women with high genetic literacy, but not in women with low genetic literacy. **CONCLUSIONS:** The KinFact intervention successfully promoted family communication about cancer risk. Educating women to enhance their communication skills surrounding family history may allow them to partner more effectively with their families and ultimately their providers in discussing risks and prevention.

Bragado, C., M. J. Hernandez-Lloreda, et al. "[Physical self-concept, anxiety, depression, and self-esteem in children with cancer and healthy children without cancer history]." Psicothema. 2008 Aug;20(3):413-9.

The main purpose of this study is to test if children with cancer receiving chemotherapy show a poorer physical self-concept, less self-esteem and more anxiety and depression than healthy children (with no cancer history) within the same age range (9-16 years old) and social condition. Furthermore, the capacity of self-concept and self-esteem to predict emotional distress is analyzed. The Spanish versions of PSDQ, CDI and STAIC were administered to 30 children with cancer and 90 healthy children. Except for the health and flexibility dimensions in the PSDQ, no significant differences between groups were found. Self-esteem was the best predictor of depression, whereas health and self-concept predicted anxiety.

Brattstrom, C., F. Granath, et al. "Overall and cause-specific mortality in transplant recipients with a pretransplantation cancer history." Transplantation. 2013 Aug 15;96(3):297-305. doi: 10.1097/TP.0b013e31829854b7.

BACKGROUND: It is unclear to what extent cancer history affects posttransplantation mortality in solid organ transplant recipients. **METHODS:** We identified a Swedish population-based cohort of solid organ transplant recipients in the National Patient Register 1970 to 2008 and linked it to the Cancer and Cause-of-Death Register. Overall and cause-specific mortality was estimated using Cox regression. **RESULTS:** Of 10,448 eligible recipients, 416 (4%) had a prior malignancy unrelated to the indication for transplantation diagnosed 2 months or more before surgery (median, 5.7 years). Mortality among cancer

history recipients was 30% increased after transplantation, compared with other recipients (adjusted hazard ratio [HR], 1.3; 95% confidence interval [CI], 1.1-1.5; $P < 0.001$), driven by cancer-specific death with no increase in cardiovascular, infectious, or other noncancer mortality. An increased rate of death due to cancer history was primarily observed among nonkidney recipients (adjusted HR(nonkidney), 1.8; 95% CI, 1.3-2.5; HR(kidney), 1.2; 95% CI, 1.0-1.4). Rates were greatest for patients with waiting times of 5 years or less but persisted with waiting times more than 10 years among kidney and nonkidney recipients with prior aggressive cancer types (gastrointestinal, breast, kidney/urothelial, and hematologic malignancies). **CONCLUSION:** We conclude that organ transplant recipients with cancer history are at a moderately increased rate of death after transplantation, driven primarily by death due to cancer recurrence.

Brown, L. M., G. Gridley, et al. "Family cancer history and susceptibility to oral carcinoma in Puerto Rico." Cancer. 2001 Oct 15;92(8):2102-8.

BACKGROUND: Use of alcohol and tobacco are the major risk factors for cancers of the oral cavity and pharynx in most of the world. A heritable component to oral carcinoma risk also has been suggested, although only limited data are available on familial aggregation of this disease. **METHODS:** A population-based case-control study of 342 subjects with carcinomas of the oral cavity and pharynx (oral carcinoma) and 521 controls was conducted in Puerto Rico. The relation between family history of carcinomas of the oral cavity, the upper aerodigestive tract (UADT), and other selected sites with risk of oral carcinoma was explored using logistic regression modeling techniques. **RESULTS:** Risk of oral carcinoma was elevated for subjects reporting a first-degree relative with carcinoma of the oral cavity (odds ratio [OR], 2.5; 95% confidence interval [CI], 0.8-8.0) or any UADT carcinoma (OR, 2.6; 95% CI, 1.4-4.8). The increased risk associated with family history of UADT carcinoma tended to be greatest for subjects with known risk factors (i.e., heavy consumption of alcohol and/or tobacco and infrequent intake of raw fruits and vegetables) and with oral carcinoma diagnoses at ages younger than 65 years. **CONCLUSIONS:** These findings are consistent with a heritable component to oral carcinoma, although shared lifestyle risk factors may be partially involved.

Carpenter, K. M., S. Eisenberg, et al. "Characterizing biased cancer-related cognitive processing: relationships with BRCA1/2 genetic mutation status, personal cancer history, age, and prophylactic

surgery." Health Psychol. 2014 Sep;33(9):1003-11. doi: 10.1037/a0032737. Epub 2013 Jun 17.

OBJECTIVE: This study evaluated associations of cancer-related cognitive processing with BRCA1/2 mutation carrier status, personal cancer history, age, and election of prophylactic surgery in women at high risk for breast cancer. **METHOD:** In a 2 (BRCA1/2 mutation carrier status) x 2 (personal cancer history) matched-control design, with age as an additional predictor, participants ($N = 115$) completed a computerized cancer Stroop task. Dependent variables were response latency to cancer-related stimuli (reaction time [RT]) and cancer-related cognitive interference (cancer RT minus neutral RT). RT and interference were tested as predictors of prophylactic surgery in the subsequent four years. **RESULTS:** RT for cancer-related words was significantly slower than other word groups, indicating biased processing specific to cancer-related stimuli. Participants with a cancer history evidenced longer RT to cancer-related words than those without a history; moreover, a significant Cancer History x Age interaction indicated that, among participants with a cancer history, the typical advantage associated with younger age on Stroop tasks was absent. BRCA mutation carriers demonstrated more cancer-related cognitive interference than noncarriers. Again, the typical Stroop age advantage was absent among carriers. Exploratory analyses indicated that BRCA+ status and greater cognitive interference predicted greater likelihood of undergoing prophylactic surgery. Post hoc tests suggest that cancer-related distress does not account for these relationships. **CONCLUSIONS:** In the genetic testing context, younger women with a personal cancer history or who are BRCA1/2 mutation carriers might be particularly vulnerable to biases in cancer-related cognitive processing. Biased processing was associated marginally with greater likelihood of prophylactic surgery.

Casey, R., P. Brennan, et al. "Influence of familial cancer history on lymphoid neoplasms risk validated in the large European case-control study epilymph." Eur J Cancer. 2006 Oct;42(15):2570-6. Epub 2006 Aug 22.

Lymphomas have a potentially important familial component; large studies using recent classification systems are lacking. Based on a multicentre case-control study in seven European countries, we recruited 2480 cases of lymphoid neoplasms (LN) and 2540 controls, matched by country, age and sex. Diagnoses were established according to the World Health Organisation (WHO) classification. We estimated odds ratios (OR) and 95% confidence intervals (CI) for cancer in first-degree relatives and for the kind of relative affected. The OR

of LN for a family history of haematological cancer was 1.6 (OR=1.2-2.1). The OR was particularly high for chronic lymphocytic leukaemia (CLL) (OR=2.9 [1.9-4.5]). A familial case of lymphoma increased the risk of Hodgkin's lymphoma (HL) (OR=3.4 [1.5-7.8]). No increased risk was observed for diffuse large B-cell and follicular lymphomas. For CLL and HL, the risk was similar in parents, offspring and siblings. Our study suggests familial aggregation of CLL with a family history of haematological cancer and of HL with a family history of lymphoma. The transmission pattern suggests a dominant model of heredity.

Cessna, J. M., J. Pidala, et al. "Relationships between parenting self-efficacy and distress in parents who have school-aged children and have been treated with hematopoietic stem cell transplant or have no cancer history." *Psychooncology*. 2015 May 12. doi: [10.1002/pon.3848](https://doi.org/10.1002/pon.3848).

OBJECTIVE: Studies demonstrate that parents with cancer experience distress and that parenting self-efficacy (PSE) is related to distress among parents without cancer. However, no study to date has examined the relationships between PSE and psychological distress among parents with cancer. This study sought to address this issue by comparing parents with cancer who had undergone hematopoietic stem cell transplantation (HSCT) to parents without cancer on measures of PSE and psychological distress. **METHODS:** A sample of 57 patients diagnosed with cancer who had undergone HSCT and a control group of 57 parents with no history of cancer were recruited for participation in the study. Medical record reviews assessed clinical variables, and participants filled out self-report measures of demographics, PSE, general self-efficacy, and psychological distress. **RESULTS:** As hypothesized, parents with cancer reported less PSE and more psychological distress than controls (all p -values ≤ 0.05). Furthermore, findings indicated that both PSE and general self-efficacy mediated the relationship between cancer status and psychological distress. **CONCLUSIONS:** Findings expand understanding of the potential sources of distress among parents with cancer who have been treated with HSCT and who have school-aged children. They also suggest that interventions aimed at reducing distress in these individuals should seek to target both parenting and general self-efficacy. Copyright (c) 2015 John Wiley & Sons, Ltd.

Desai, M. M., M. L. Bruce, et al. "Validity of self-reported cancer history: a comparison of health interview data and cancer registry records." *Am J Epidemiol*. 2001 Feb 1;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.

Ferrigno, D., G. Buccheri, et al. "Serum tumour markers in lung cancer: history, biology and clinical applications." *Eur Respir J*. 1994 Jan;7(1):186-97.

The association of biological markers with cancer has been recognized for many decades. Current interest in markers for cancer arose in the mid 1960s, with the discoveries of alpha-fetoprotein and carcinoembryonic antigen. They were called oncofetal proteins, because of their presence in high concentrations during embryonic development, their virtual disappearance in the neonatal period, and their reappearance with cancers of specific cell types. Essentially, any molecular species may be produced in abnormal amounts or under abnormal circumstances by a tumour, and thereby become useful as a tumour marker. Several tumour markers have been studied in lung cancer. Unfortunately, none of these appear to be sufficiently sensitive and specific to be reliable for screening and diagnostic purposes. However, there is a body of evidence which proves that at least some of these substances may be useful in the evaluation of the course and prognosis of the disease. This review presents data concerning the most studied and interesting tumour markers in lung cancer.

Fischereder, M. and K. W. Jauch "Prevalence of cancer history prior to renal transplantation." *Transpl Int*. 2005 Jul;18(7):779-84.

Recurrent and de novo cancers contribute to morbidity and mortality post-transplantation. However, data on cancer prevalence in waiting list patients are lacking. The purpose of this study was to determine the prevalence of malignancy in patients considered for renal transplantation. Records of 382 potential renal transplant recipients were reviewed for the presence of malignant tumours. In 38 patients 45 tumours were detected. Forty-two malignancies were histologically confirmed, in three patients the evaluation was ongoing. Fourteen tumours were diagnosed before and 31 after initiation of dialysis. Overall cancer prevalence was 9.9%. For patients in the waiting list, the mean time from diagnosis of the malignancy was 2.2 years. Twenty of 45 (44%) tumours were located in the urinary system. The majority of malignancies was treated with a curative intention. Thus, 68% of patients with malignancies were listed as 'transplantable' or 'temporarily not transplantable'. From the waiting list, 13% were removed, 8% died and 11% had their evaluation halted because of their malignancy. Four patients received a transplant while eight patients died or were removed permanently from the list prior to transplantation. Death or removal from the list was as frequently related to tumour progression as to other causes (four patients each). A substantial number of waiting list patients had a history of malignancy. Future strategies have to identify patients at risk to assure intensive monitoring for recurrence, selection of patients who do not benefit from deferred transplantation and consideration of specific immunosuppressive protocols.

Ghiorzo, P., L. Pastorino, et al. "Prevalence of the E318K MITF germline mutation in Italian melanoma patients: associations with histological subtypes and family cancer history." *Pigment Cell Melanoma Res.* 2013 Mar;26(2):259-62. doi: 10.1111/pcmr.12047. Epub 2012 Dec 10.

A French and an Australian study have recently identified a rare germline functional variant in the microphthalmia-associated transcription factor (MITF) (E318K) that predisposes to familial and sporadic melanoma and to renal cell carcinoma (RCC), showing a new link between two tumour types with different risk factors and between deregulated sumoylation and cancer. The aim of this study was to test the prevalence of the MITF E318K mutation in 667 Italian melanoma patients. We observed significant associations between histological subtypes and family cancer history. Carriers exhibited a nearly threefold higher risk of developing melanoma compared with controls. Carriers were also more likely to have developed multiple primary melanomas (6.40-fold), compared with wt patients. Carriers with a

personal and/or family history of pancreatic cancer and kidney cancer had a nearly 31- and eightfold higher risk of developing melanoma compared with wt patients. Our findings further support MITF as a medium-penetrance melanoma susceptibility gene, highlight a potential association with histological subtypes and suggest that MITF may predispose to pancreatic cancer.

Grover, S., E. M. Stoffel, et al. "Physician assessment of family cancer history and referral for genetic evaluation in colorectal cancer patients." *Clin Gastroenterol Hepatol.* 2004 Sep;2(9):813-9.

BACKGROUND AND AIMS: An accurate family history is an essential component of cancer risk assessment. Our aim was to determine the concordance of family history assessments made by physicians with patients' self-reports and the frequency of referral for genetic evaluation in high-risk colorectal cancer (CRC) patients. **METHODS:** A self-administered family cancer history questionnaire was completed by 387 consecutive CRC patients at their first visit to a gastroenterology cancer clinic. Physician notes from the first visit were reviewed to determine the concordance of the family cancer history with patients' self-reported history. Prevalence of individuals that satisfied the Bethesda guidelines for hereditary colon cancer were compared with actual rates of referral. Regression analyses were used to determine factors associated with a comprehensive physician evaluation of family history. **RESULTS:** Oncologists documented a comprehensive family history in 59% (184 of 311) of patients with a first- or second-degree relative with cancer. Young age at diagnosis and a first-degree relative with CRC were not associated with a more comprehensive family history assessment. An increasing number of cancers per family was a strong predictor of a less comprehensive family history assessment (odds ratio = 0.63; $P < 0.0001$). Seventy-five of 387 (19%) CRC patients met Bethesda guidelines for genetics assessment, however, only 13 of 75 (17%) were referred. **CONCLUSIONS:** Increased complexity in family cancer history leads to a decrease in accuracy of family history, suggesting the need for systematic approaches to facilitate family history assessment. Familial cancer risk remains largely unrecognized and referral rates for genetic evaluation for CRC syndromes are low.

Gunduz, E., M. Gunduz, et al. "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.* 2009 Mar;135(3):254-60. doi: 10.1001/archoto.2008.560.

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.

Hamann, H. A., T. J. Somers, et al. "Posttraumatic stress associated with cancer history and BRCA1/2 genetic testing." *Psychosom Med.* 2005 Sep-Oct;67(5):766-72.

OBJECTIVE: A subset of women who are at elevated cancer risk due to family history exhibit evidence of cancer-specific distress. These stress responses may represent symptoms of posttraumatic stress disorder (PTSD). The present study assessed rates of PTSD related to personal or family cancer history and BRCA1/2 testing. **METHODS:** Participants were 84 women enrolled in a larger project focused on genetic testing decisions. Semistructured diagnostic interviews were used to identify instances of threshold and subthreshold PTSD. **RESULTS:** Results indicated that 16.7% of the women reported current threshold or subthreshold PTSD related to personal or family cancer history. An additional 26.2% reported past-only cancer-related

threshold or subthreshold PTSD. Of the 65 women who received BRCA1/2 results and completed the test-related PTSD module, only 7.7% reported threshold or subthreshold PTSD related to the genetic testing process. However, when rates were examined based on carrier status, 25.0% of BRCA1/2 carriers reported test-related threshold or subthreshold PTSD compared with only 10.0% of variants and 2.3% of noncarriers. **CONCLUSIONS:** Results from this study suggest that both personal and family cancer diagnoses can be significant stressors for a subset of high-risk women. Rates of threshold and subthreshold PTSD related to genetic testing appear to be less common, although carriers may be at higher risk for significant posttraumatic symptoms.

Hasenbring, M. I., N. Kreddig, et al. "Psychological impact of genetic counseling for hereditary nonpolyposis colorectal cancer: the role of cancer history, gender, age, and psychological distress." *Genet Test Mol Biomarkers.* 2011 Apr;15(4):219-25. doi: 10.1089/gtmb.2010.0165. Epub 2010 Dec 31.

AIMS: We prospectively examined the impact of an initial interdisciplinary genetic counseling (human geneticist, oncologist, and psycho-oncologist) on feelings of anxiety with a special focus on subgroups related to personal cancer history, gender, age, and education. **RESULTS:** At baseline, cancer-affected men revealed a significantly higher level of anxiety than unaffected men ($p < 0.05$), whereas history of cancer did not play a role in women. Furthermore, a significant interaction between time, gender, and age was identified for change of anxiety. While women in general and men above 50 years revealed a significant reduction in anxiety, younger men did not show any change over time. A logistic regression indicated that clinical Hospital Anxiety and Depression Scale-A cases can be predicted by general distress (Brief Symptom Inventory) as well as by hereditary nonpolyposis colorectal cancer-related cognitions of intrusion and avoidance (impact of event scale) with a correct classification of 86%. **CONCLUSIONS:** Although initial hereditary nonpolyposis colorectal cancer counseling leads to an overall reduction of anxiety, differential effects of cancer history, gender, and age focus on subgroups of cancer-affected men, who may display unexpectedly high anxiety scores at baseline. Especially younger men do not seem to reduce this high anxiety level. Baseline anxiety was mainly determined by maladaptive situation-specific cognitions. Therefore, counselors should be more aware of anxiety-related cognitions in cancer-affected younger men.

Horn, L. C., G. Raptis, et al. "Familial cancer history in patients with carcinoma of the cervix uteri." Eur J Obstet Gynecol Reprod Biol. 2002 Feb 10;101(1):54-7.

OBJECTIVES: Several cancers show the tendency to aggregate in families. But the contribution of heredity to the causation of sporadic malignancies, like cervical cancer is unclear. **STUDY DESIGN:** Seven hundred and thirty-seven women with operative treated cervical cancer (CX) were searched for familiar history of malignant tumours. Positive familial history was stated, if one first degree relative was affected by malignant tumour. The site of malignant tumour was stated and the mean age was compared. **RESULTS:** Twenty-two percent of the women had malignancies at different sites in first degree relatives. In about one-half the mother, in 30% the father and in 11% more than one first degree relative was affected. Overall, first degree relatives of 21 patients (13%) had malignancies of the lungs or the oro-pharynx. Thirty-seven women had malignant tumours of the lower genital tract and 11 had invasive cervical cancer. Mean age of patients with positive familial history was the same as those without (43 versus 42 years) it. But, women whose first degree female relatives had cervical cancer were significantly younger than those with extragenital malignancies (37 versus 45 years). The mean 5-year survival rate was higher in patients with a positive familial cancer history (85.6% versus 74.6%; $P=1.7$). **CONCLUSIONS:** The data suggest, that a small number of patients have a familial susceptibility for cervical cancer and probably for HPV-associated neoplasms. Further studies establishing the immune status and the search for genetic polymorphisms of these patients are required.

Hsieh, C. B., C. Tzao, et al. "APACHE II score and primary liver cancer history had risk of hospital mortality in patients with pyogenic liver abscess." Dig Liver Dis. 2006 Jul;38(7):498-502. Epub 2006 May 15.

BACKGROUND: The Acute Physiology and Chronic Health Evaluation II classification system has been extensively used for predicting the patient mortality in various diseases. However, its utilisation on the pyogenic liver abscess has not yet been well studied. **AIMS:** The purpose of this study was to validate this system on this high death rate disease. **PATIENTS:** A retrospective study was conducted to assess 314 patients with pyogenic liver abscesses admitted to tertiary medical centre in past 12 years. **METHODS:** The outcome measurement was the in-hospital mortality. A multiple logistic regression model was used to assess the association between mortality and Acute Physiology and Chronic Health Evaluation II score while controlling for the potential

confounding factors. **RESULTS:** The overall in-hospital mortality was 8.3%. The mean Acute Physiology and Chronic Health Evaluation II score of the expired patients was higher ($P<0.0001$). The mortality rate increased rapidly when Acute Physiology and Chronic Health Evaluation II score ≥ 15 . After controlling for the potential confounding factors, patient with high admission Acute Physiology and Chronic Health Evaluation II score ≥ 15 had a higher chance of in-hospital mortality ($P<0.01$). In addition, the primary liver cancer history is also a risk factor ($P=0.03$). **CONCLUSIONS:** The Acute Physiology and Chronic Health Evaluation II score and the primary liver cancer history predict the in-hospital mortality of the pyogenic liver abscess patient.

Kastrinos, F., E. W. Steyerberg, et al. "The PREMM(1,2,6) model predicts risk of MLH1, MSH2, and MSH6 germline mutations based on cancer history." Gastroenterology. 2011 Jan;140(1):73-81. doi: 10.1053/j.gastro.2010.08.021. Epub 2010 Aug 19.

BACKGROUND & AIMS: We developed and validated a model to estimate the risks of mutations in the mismatch repair (MMR) genes MLH1, MSH2, and MSH6 based on personal and family history of cancer. **METHODS:** Data were analyzed from 4539 probands tested for mutations in MLH1, MSH2, and MSH6. A multivariable polytomous logistic regression model (PREMM(1,2,6)) was developed to predict the overall risk of MMR gene mutations and the risk of mutation in each of the 3 genes. The discriminative ability of the model was validated in 1827 population-based colorectal cancer (CRC) cases. **RESULTS:** Twelve percent of the original cohort carried pathogenic mutations (204 in MLH1, 250 in MSH2, and 71 in MSH6). The PREMM(1,2,6) model incorporated the following factors from the probands and first- and second-degree relatives (odds ratio; 95% confidence intervals [CIs]): male sex (1.9; 1.5-2.4), a CRC (4.3; 3.3-5.6), multiple CRCs (13.7; 8.5-22), endometrial cancer (6.1; 4.6-8.2), and extracolonic cancers (3.3; 2.4-4.6). The areas under the receiver operating characteristic curves were 0.86 (95% CI, 0.82-0.91) for MLH1 mutation carriers, 0.87 (95% CI, 0.83-0.92) for MSH2, and 0.81 (95% CI, 0.69-0.93) for MSH6; in validation, they were 0.88 for the overall cohort (95% CI, 0.86-0.90) and the population-based cases (95% CI, 0.83-0.92). **CONCLUSIONS:** We developed the PREMM(1,2,6) model, which incorporates information on cancer history from probands and their relatives to estimate an individual's risk of mutations in the MMR genes MLH1, MSH2, and MSH6. This Web-based decision making tool can be used to assess

risk of hereditary CRC and guide clinical management.

Makitaro, R., P. Paakko, et al. "An epidemiological study of lung cancer: history and histological types in a general population in northern Finland." *Eur Respir J.* 1999 Feb;13(2):436-40.

A prospective epidemiological study was conducted to assess the incidence, diagnosis, histology and surgical treatment of lung cancer in northern Finland. The results were compared with those obtained in a similar survey 20 yrs earlier. Most of the patients with a suspected lung tumour were interviewed (72%) and the information was combined with that obtained from the national cancer registry. All pathological specimens were re-evaluated by a pathologist. A total of 602 new lung cancer cases (85% male, 15% female) were diagnosed during the years 1990-1992, the annual incidence per 100,000 being 63 for males and 9.5 for females. The number not reported to the Finnish Cancer Registry was low (<1%). Lung cancer was confirmed histologically in 381 cases (63%) and in addition cytologically in 135 cases (23%). Squamous cell carcinoma was the most common histological type (40%), the proportion of adenocarcinoma being 26%, small cell carcinoma 24% and large cell carcinoma 4%. The incidence of lung cancer had decreased significantly among males (from 87 to 63 per 100,000) compared with 20 yrs earlier but had increased among females (from 4.1 to 9.5), chiefly on account of adenocarcinoma. The findings of this prospective study show an increase in the incidence of lung adenocarcinoma among females, a histological type which is less closely related to smoking than the other cancers. This suggests that other risk factors may play an increasing role in the aetiology of lung cancer.

Marino, J. L., C. M. Saunders, et al. "Nature and severity of menopausal symptoms and their impact on quality of life and sexual function in cancer survivors compared with women without a cancer history." *Menopause.* 2014 Mar;21(3):267-74. doi: 10.1097/GME.0b013e3182976f46.

OBJECTIVE: After cancer treatment, troublesome menopausal symptoms are common but poorly understood. Using standardized instruments, we measured differences in symptom nature, severity, impact on quality of life, and sexual function between cancer survivors and noncancer participants. **METHODS:** The Menopause Symptoms After Cancer Clinic operates within the general menopause service in a large women's hospital, providing menopause advice and management to women with menopausal symptoms and a cancer history. Menopausal symptoms were recorded using the Greene Climacteric Scale, past-week symptoms were recorded using the

Functional Assessment of Cancer Therapy breast cancer subscale and endocrine symptom subscale, and sexual symptoms were recorded using Fallowfield's Sexual Activity Questionnaire. **RESULTS:** Cancer survivors (n = 934) and noncancer participants (n = 155) did not significantly differ by age at menopause (46 y) or age at first clinic visit (51 y). Cancer survivors were more likely than noncancer participants to be severely troubled by vasomotor symptoms (hot flushes and night sweats; odds ratio, 1.71; 95% CI, 1.06-2.74) and reported more frequent (6.0 vs 3.1 in 24 h; P < 0.001) and more severe (P = 0.008) hot flushes. In contrast, cancer survivors were significantly less troubled by psychological and somatic symptoms and reported better quality of life than noncancer participants. Groups did not differ significantly in physical or functional well-being, gynecologic symptom severity, or sexual function. **CONCLUSIONS:** Cancer survivors are more troubled by vasomotor symptoms than noncancer participants, but noncancer participants report greater psychological symptoms. Sexual function does not differ. An improved understanding of the nature and impact of menopause on cancer survivors can be used to direct management protocols.

Maruyama, A., T. Saito, et al. "Cancer history and loss of MSH2 and MLH1 protein expression in patients with endometrial hyperplasia." *Int J Gynecol Cancer.* 2003 May-Jun;13(3):352-60.

In order to evaluate the hereditary background of endometrial hyperplasia patients in relation to protein expression of DNA mismatch repair genes, we evaluated 69 patients with endometrial hyperplasia and 18 patients with normal endometrium having both a personal and family history of cancer (two hereditary nonpolypoid colorectal cancer (HNPCC) patients). We obtained personal and family histories of cancer for all patients. MSH2 and MLH1 protein expression was investigated by immunohistochemical methods. In the endometrial hyperplasia patients, 11 had personal histories and 40 had family histories of cancer. Among the 11 endometrial hyperplasia patients with a personal history of cancer, most cancers were breast or colorectal cancers (82%). In the 40 patients with a family history of cancer, colorectal cancer (33%) was the most frequent. The incidence of loss of expression of MSH2 and/or MLH1 protein in endometrial hyperplasia patients with personal (64%) or family (40%) histories was significantly higher than that in patients without such history (no personal: 21% and no family: 10%; P = 0.0035 and 0.0065). No protein loss was detected in any of the cases with normal endometrium having either a personal or family history of cancer. Our results suggest that a portion of

endometrial hyperplasia cases having a personal or family history of cancer may belong to HNPCC, and that in these cases, abnormality of the mismatch repair system may be an early event in endometrial carcinogenesis.

Mathur, A. P., A. Saini, et al. "Diagnostic accuracy retrospectively of electrocardiographic findings and cancer history for tamponade in patients determined to have pericardial effusion by transthoracic echocardiogram." Am J Cardiol. 2013 Apr 1;111(7):1062-6. doi: 10.1016/j.amjcard.2012.11.064. Epub 2013 Jan 22.

Unexpected pericardial effusions are often found by frontline providers who perform computed tomography. To study the hypothesis that electrocardiographic findings and whether cancer is known or suspected importantly change the likelihood of tamponade for such providers, all unique patients with moderate or large pericardial effusions determined by transthoracic echocardiography during a 6-year period were retrospectively identified. Electrocardiograms were evaluated by blinded investigators for electrical alternans (total and QRS), low voltage (limb leads only, precordial leads only, and both), and tachycardia (>100 QRS complexes/min). Medical records were reviewed to determine whether cancer was known or suspected and whether tamponade was diagnosed. Tamponade was present in 66 patients (27% of 241) with moderate or large pericardial effusions. No tachycardia lowered the odds of tamponade the most (likelihood ratio 0.4, 95% confidence interval 0.3 to 0.6) but by a degree less than any single diagnostic element increased it when present. The combined presence of all 3 electrocardiographic findings and cancer increased the odds of tamponade 63-fold (likelihood ratio 63, 95% confidence interval 33 to 150), whereas their combined absence decreased the odds only fivefold (likelihood ratio 0.2, 95% confidence interval 0.2 to 0.3). In conclusion, electrocardiography findings and cancer rule in tamponade better than they rule it out. Combining these diagnostic elements improves their discriminatory power but not sufficiently enough to rule out tamponade in patients with moderate or large pericardial effusions.

Mayne, S. T., J. Buenconsejo, et al. "Familial cancer history and lung cancer risk in United States nonsmoking men and women." Cancer Epidemiol Biomarkers Prev. 1999 Dec;8(12):1065-9.

The authors conducted a population-based case-control study of lung cancer in nonsmoking men and women in New York State from 1982 to 1984. Nonsmokers included both never smokers (45%) and former smokers who had quit at least 10 years before

diagnosis/interview (55%). In-person interviews were completed for 437 lung cancer cases and 437 matched population controls. Cases and controls were asked to report on their family history of cancer, as well as smoking status of family members. Cases were significantly more likely than controls to report having a paternal history of any cancer [odds ratio (OR), 1.67] and aerodigestive tract cancers (OR, 2.78); a maternal history of breast cancer (OR, 2.00); a history of any cancer in brothers (OR, 1.58) and sisters (OR, 1.66); and a nearly significant excess of lung cancer (OR, 4.14; P = 0.07), aerodigestive tract cancer (OR, 3.50; P = 0.06), and breast cancer (OR, 2.07; P = 0.053) in sisters. The excess risk in relatives of cases as compared to relatives of controls also was evident in a cohort analysis of the relatives. These results support the hypothesis of a genetic susceptibility to various cancers in families with lung cancer in nonsmokers.

Milliron, B. J., M. Z. Vitolins, et al. "Usual dietary intake among female breast cancer survivors is not significantly different from women with no cancer history: results of the National Health and Nutrition Examination Survey, 2003-2006." J Acad Nutr Diet. 2014 Jun;14(6):932-7. doi: 10.1016/j.jand.2013.08.015. Epub 2013 Oct 26.

Dietary intake is a modifiable behavior that may reduce the risk of recurrence and death among breast cancer survivors. Cancer survivors are encouraged to consume a diet rich in fruit, vegetables, and whole grains and limit red meat, processed meat, and alcohol intake. Using data from the National Health and Nutrition Examination Survey (2003-2006), this study examined whether breast cancer survivors and women with no history of cancer differed in the distribution of usual intake of foods included in the dietary recommendations for preventing cancer and recurrences. Participants completed one or two 24-hour dietary recalls. The food groups included in this analysis were whole fruit; total vegetables; dark green and orange vegetables; whole grains; red meat; processed meat; alcohol; and calories from solid fat, alcohol, and added sugar. The National Cancer Institute Method was used to estimate the distribution of usual intake and to compare breast cancer survivors (n=102) to noncancer respondents (n=2,684). Using age and cancer survivor as covariates, subgroup estimates of usual intake were constructed. No significant group differences were found, except that survivors reported a greater intake of whole grains. More than 90% of both groups did not meet recommendations for fruits, vegetables, and whole grains; 75.4% and 70.2%, respectively, consumed less than the red meat recommendation; and <10% of either group met the recommendation for percent energy from solid fat, alcohol, and added

sugar. The diet of breast cancer survivors was not significantly different from women with no history of cancer.

Murabito, J. M., J. C. Evans, et al. "Family breast cancer history and mammography: Framingham Offspring Study." Am J Epidemiol. 2001 Nov 15;154(10):916-23.

The authors examined mammography use according to family cancer history and identified predictors of recent use (≤ 2 years). Framingham Offspring Study participants in Framingham, Massachusetts, aged 40-79 years, completed a breast health questionnaire in 1996-1997. The study sample of women included 141 with a first-degree relative with breast cancer, 221 with a mother or sister(s) with other cancers, and 331 with a mother and sister(s) who participate in the Framingham Heart Study and did not report a history of cancer. Stepwise logistic regression analysis was used to identify predictors of recent mammography use. Among women with a family breast cancer history, 98% reported mammography use compared with 95% of other women. Recent mammography use was higher in women with a family breast cancer history (93%) compared with women with a family history of other cancer (80%) and women without a family history of cancer (84%) ($p = 0.004$). Odds ratios and 95% confidence intervals for significant predictors of recent mammography use were as follows: family history of breast cancer, 3.2 (95% confidence interval (CI): 1.4, 7.7); recent clinical breast examination, 17.4 (95% CI: 9.2, 32.8); and smoking, 0.4 (95% CI: 0.2, 0.7). Mammography use was high among women with a family breast cancer history.

Murff, H. J., R. A. Greevy, et al. "The comprehensiveness of family cancer history assessments in primary care." Community Genet. 2007;10(3):174-80.

BACKGROUND: Accurate family history information is required for adequate breast and colorectal cancer risk assessments. Few studies have examined the comprehensiveness of the family medical history interview in primary care. **METHODS:** We compared family cancer history information collected through a self-completed survey with that documented within medical charts for 310 patients. **RESULTS:** Forty-three percent (18/42) of individuals at increased risk for breast or colorectal cancer based on their family history had documentation of this risk within their chart. Age of cancer diagnosis was recorded for 40% (50/124) of affected relatives identified by chart review compared with 81% (203/252) identified through the survey ($p < 0.0001$). **CONCLUSIONS:** Over half of the

individuals at increased risk for breast or colorectal cancer based on their family history did not have documentation of this risk within their medical record, and the age of relatives at diagnosis was frequently missing.

Ness, K. K., J. M. Oakes, et al. "Prevalence of the metabolic syndrome in relation to self-reported cancer history." Ann Epidemiol. 2005 Mar;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.

Nudelman, K. N., S. L. Risacher, et al. "Association of cancer history with Alzheimer's disease onset and structural brain changes." Front Physiol. 2014 Oct 31;5:423. doi: 10.3389/fphys.2014.00423. eCollection 2014.

Epidemiological studies show a reciprocal inverse association between cancer and Alzheimer's disease (AD). The common mechanistic theory for this effect posits that cells have an innate tendency toward apoptotic or survival pathways, translating to increased risk for either neurodegeneration or cancer. However, it has been shown that cancer patients experience cognitive dysfunction pre- and post-treatment as well as alterations in cerebral gray matter density (GMD) on MRI. To further investigate these issues, we analyzed the association between cancer history (CA \pm) and age of AD onset, and the relationship between GMD and CA \pm status across diagnostic groups in the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort study. Data was analyzed

from 1609 participants with information on baseline cancer history and AD diagnosis, age of AD onset, and baseline MRI scans. Participants were CA+ (N = 503) and CA- (N = 1106) diagnosed with AD, mild cognitive impairment (MCI), significant memory concerns (SMC), and cognitively normal older adults. As in previous studies, CA+ was inversely associated with AD at baseline (P = 0.025); interestingly, this effect appears to be driven by non-melanoma skin cancer (NMSC), the largest cancer category in this study (P = 0.001). CA+ was also associated with later age of AD onset (P < 0.001), independent of apolipoprotein E (APOE) epsilon4 allele status, and individuals with two prior cancers had later mean age of AD onset than those with one or no prior cancer (P < 0.001), suggesting an additive effect. Voxel-based morphometric analysis of GMD showed CA+ had lower GMD in the right superior frontal gyrus compared to CA- across diagnostic groups (P crit < 0.001, uncorrected); this cluster of lower GMD appeared to be driven by history of invasive cancer types, rather than skin cancer. Thus, while cancer history is associated with a measurable delay in AD onset independent of APOE epsilon4, the underlying mechanism does not appear to be cancer-related preservation of GMD.

Olson, S. H., S. Iyer, et al. "Cancer history and other personal factors affect quality of life in patients with hepatitis C." *Health Qual Life Outcomes*. 2005 Jun 16;3:39.

BACKGROUND: Although patients with chronic hepatitis C (CHC) have been found to have reduced quality of life, little is known about how other characteristics affect their quality of life. The purpose of this study was to investigate the effect of other characteristics, including history of cancer, on quality of life in patients with CHC. **METHODS:** One hundred forty patients from clinics at three hospitals in New York City completed a detailed epidemiologic interview about demographic and lifestyle characteristics and the SF-36 measuring health-related quality of life. We compared results from our patients to normative data using t-tests of differences between means. We used multivariate analyses to determine other personal and health-related factors associated with quality of life outcomes. **RESULTS:** Compared to normative data, these patients had reduced quality of life, particularly on physical functioning. The summary Physical Component Score (PCS) was 45.4 +/- 10.6 and the Mental Component Score (MCS) was 48.2 +/- 11.1, vs norms of 50 +/- 10.0; p-values were < 0.0001 and < 0.05, respectively. In multivariate analyses, the PCS was significantly lower among those with cancer history, > or = 2 other chronic conditions, less education, low physical activity, and higher

alanine aminotransferase (ALT) levels. Cancer was more important for men, while other chronic conditions were more important for women. On the MCS, history of depression, low physical activity, alcohol use, and female gender were independently associated with poorer scores. **CONCLUSION:** Several health and lifestyle factors independently influence quality of life in CHC patients. Different factors are important for men and women.

Pacheco-Figueiredo, L., L. Antunes, et al. "Health-related behaviours in the EpiPorto study: cancer survivors versus participants with no cancer history." *Eur J Cancer Prev*. 2011 Jul;20(4):348-54. doi: 10.1097/CEJ.0b013e328345f923.

Cancer survivors are at an increased risk of a second primary cancer, partly due to unhealthy behaviours. In a cohort of adults (recruitment: 1999-2003; follow-up - linkage with population-based cancer registry: up to 2009) we compared the baseline exposure to smoking, alcohol and dietary intake and physical activity between: cancer survivors (CS) - cancer diagnosis before baseline (n=53); no cancer (NC) participants - without cancer diagnosis at baseline or during follow-up (n=2261); latent cancer (LC) participants - without cancer diagnosis at baseline but diagnosed during follow-up (n=139). Age-, sex- and education-adjusted prevalences and means were computed, as applicable. The prevalence of current smoking was nearly 20% among CS and NC (approximately four cigarettes per day) and 30% in LC (seven cigarettes per day). LC had the highest average alcohol intake (25.5 g/day) and NC the lowest (17.0 g/day). The proportion of participants reporting sports practice was higher for CS (50%) than for NC or LC (approximately 33%). CS and NC had higher fruit/vegetable consumption than LC (4.2 and 4.4 vs. 3.8 servings per day). In a composite index on health behaviours (including smoking, physical activity and alcohol and fruit/vegetable intake) the highest and lowest scores were 1.74 for NC and 1.52 for LC respectively, whereas CS scored 1.63. The exposure to each risk factor appeared comparable in CS and NC, whereas LC tended to have unhealthier behaviours. This may be partially explained by the acquisition of healthier habits by CS after diagnosis, but there still remains scope for improvement, as revealed by the low scores observed for the joint exposure to the main risk factors.

Peker, S., U. Abacioglu, et al. "Gamma knife radiosurgery for cavernous sinus plasmacytoma in a patient with breast cancer history." *Surg Neurol*. 2005 Feb;63(2):174-6; discussion 176-7.

BACKGROUND: Multiple myeloma (MM) presentation with cerebral mass lesion is unusual.

Gamma knife radiosurgery for plasmacytoma has not been reported so far. CASE REPORT: We report a 70-year-old female with a medical history of infiltrative ductal carcinoma of the breast. She developed cavernous sinus syndrome (CSS) 5 months before admission to the hospital. The magnetic resonance imaging revealed an isointense solitary mass in the left cavernous sinus in noncontrast T1-weighted images. The lesion was highly enhancing with gadolinium-diethylenetriaminopentaacetic acid. She was operated by using Dolenc technique, and the tumor was partially resected. The pathological examination of the tumor tissue revealed a plasmacytoma. Systemic evaluation was positive for the diagnosis of MM. She underwent gamma knife radiosurgery for the residual cavernous sinus tumor. Chemotherapy with prednisolone and melphalan was given. Follow-up magnetic resonance images 6 months after the treatment demonstrated complete tumor disappearance. However, she died of sepsis 26 months after the diagnosis. CONCLUSION: This is an unusual MM case with a history of breast cancer, which had CSS and which demonstrated an excellent response to gamma knife radiosurgery.

Pisano, M., V. Mezzolla, et al. "A new mutation of BRCA2 gene in an Italian healthy woman with familial breast cancer history." Fam Cancer. 2011 Mar;10(1):65-71. doi: 10.1007/s10689-010-9389-7.

Heterozygous germ line mutations in the Breast CAncer1 (BRCA1) and BRCA2 genes can lead to a high risk of breast and ovarian cancer, in addition to a significantly increased susceptibility of pancreatic, prostate and male breast cancer. The BRCA2 belongs to the tumor suppressor gene family and the protein encoded by this gene is involved in the repair of chromosomal damage, with an important role in the error-free repair of DNA double strand breaks. After complete sequencing of coding regions and splice junctions of both genes, in a family with breast cancer history, a non previously reported heterozygous mutation in BRCA2 was detected and studied in an Italian healthy female. The direct sequencing disclosed, on exon 15, an insertion (7525_7526insT). The frame shift mutation of BRCA2 causes a disruption of the translational reading frame, resulting in a stop codon 29 amino acids downstream, in the 2538 position of the BRCA2 protein. The mutated allele codifies a truncated protein, lacking the two putative nuclear localization signals (NLSs) that reside within the extreme C-terminal domain of BRCA2. Since this mutant protein not performs a translocation into the nucleus, it is fully non-functional.

Polednak, A. P. Regarding "prevalence of the metabolic syndrome in relation to self-reported cancer

history", Ann Epidemiol. 2006 Dec;16(12):877-9. Epub 2006 Aug 1.

Quillin, J. M., J. N. Bodurtha, et al. "The effect of a school-based educational intervention on gender differences in reported family cancer history." J Cancer Educ. 2008;23(3):180-5. doi: 10.1080/08858190802235395.

BACKGROUND: Gender differences in reported family cancer history could reduce the effectiveness of genetic screening for cancer risk. METHODS: We randomized 6 schools to teach ninth graders about health genealogy through workshops or offered a delayed intervention. We assessed the effect of the intervention on reported family history of various cancers along with gender and side of the family from which cancer was reported. RESULTS: Girls reported more breast cancer in the family. Both sexes reported more maternal relatives with breast cancer. There were no treatment group effects. CONCLUSIONS: There are gender differences in reported family history of breast cancer.

Rabin, C., M. L. Rogers, et al. "Effect of personal cancer history and family cancer history on levels of psychological distress." Soc Sci Med. 2007 Jan;64(2):411-6. Epub 2006 Oct 24.

This study examined the impact of personal and family cancer history on psychological distress. Regression analyses were conducted on a nationally representative sample of adult individuals who participated in the 2000 National Health Interview Survey, USA. Effects on distress of a personal cancer history, any family cancer history, or mother, father, sister or brother with a cancer history were examined. The interaction of personal and family cancer histories and three-way interactions with gender were also assessed. Analyses indicate that having either a personal or family cancer history is linked with significantly greater psychological distress and there is evidence of an interaction. Three-way interactions with gender were not found. Consistent with prior research, results demonstrated that cancer survivors are more distressed than the general population. Results extend prior research by indicating that having a first-degree relative with cancer increases risk for distress, and having personal and family cancer histories may exert a synergistic effect on distress.

Rena, O., F. Davoli, et al. "The solitary pulmonary nodule in patients with previous cancer history: results of surgical treatment." Eur J Surg Oncol. 2013 Nov;39(11):1248-53. doi: 10.1016/j.ejso.2013.08.014. Epub 2013 Aug 24.

BACKGROUND: The present study was carried out to evaluate the characteristics of solitary

pulmonary nodule (SPN) in patients with previous cancer(s) and to analyse the outcome of its surgical treatment. **METHODS:** We retrospectively analysed 131 patients with history of previous malignancy submitted to lung surgery for new identified SPN between January 2004 and December 2009. **RESULTS:** The diagnosis was metastasis in 65 patients, primary lung cancer in 57, benign lesion in 9. Primary lung cancers were significantly larger, had higher maxSUV at CT-PET scanning, occurred after a longer disease-free interval in patients older and with worse lung function when compared with metastatic lesions. Overall survival at 5-year was 67% for benign lesions, 62% for primary lung cancer, 48% for metastatic disease. Histological subtype, SPN diameter less than 2 cm and DFI >36 months were factors influencing long-term prognosis of metastatic patients. Histological subtype and pathological staging were factors influencing long-term outcome of primary lung cancer patients. **DISCUSSION:** Surgical resection of solitary pulmonary nodule is essential in patients with history of previous cancer to rule out benign lesions, to offer diagnostic confirmation and local control of the disease in metastatic tumours and to correctly stage and treat primary lung cancer.

Tehranifar, P., H. C. Wu, et al. "Validation of family cancer history data in high-risk families: the influence of cancer site, ethnicity, kinship degree, and multiple family reporters." *Am J Epidemiol.* 2015 Feb 1;181(3):204-12. doi: 10.1093/aje/kwu258. Epub 2015 Jan 7.

Information on family cancer history (FCH) is often collected for first-degree relatives, but more extensive FCH information is critical for greater accuracy in risk assessment. Using self-reported diagnosis of cancer as the gold standard, we examined differences in the sensitivity and specificity of relative-reported FCH by cancer site, race/ethnicity, language preference, and kinship degree (1,524 individuals from 557 families; average number of relatives per family = 2.7). We evaluated the impact of FCH data collected in 2007-2013 from multiple relatives by comparing mean values and proportions for the number of relatives with any cancer, breast cancer, or ovarian cancer as reported by a single relative and by multiple relatives in the same family. The sensitivity of FCH was lower in Hispanics, Spanish-speaking persons, and third-degree relatives (e.g., for all cancers, sensitivities were 80.7%, 87.4%, and 91.0% for third-, second-, and first-degree relatives, respectively). FCH reported by multiple relatives included a higher number of relatives with cancer than the number reported by a single relative (e.g., mean increase of 1.2 relatives with any cancer), with more relatives diagnosed with any cancer, breast cancer, and ovarian cancer in 52%,

36% and 12% of families, respectively. Collection of FCH data from multiple relatives may provide a more comprehensive picture of FCH and may potentially improve risk assessment and preventive care.

Theis, B., N. Boyd, et al. "Accuracy of family cancer history in breast cancer patients." *Eur J Cancer Prev.* 1994 Jul;3(4):321-7.

We assessed the validity of information reported by patients with breast cancer on cancer in first- and second-degree relatives. In Toronto, Canada, 165 patients completed mailed questionnaires about cancer in relatives and were then interviewed in person. Their reports were compared with relatives' hospital records, cancer registry or death records for presence of cancer, site and age at diagnosis. Questionnaire and interview reports agreed with records for 82-96% of reports on first-degree and 48-80% on second-degree relatives. Proband reports of cancer sites in first-degree relatives were generally accurate (breast 99%, ovary 100%, prostate 85%, colon 93%). Reports of cancer sites in second-degree relatives were accurate for prostate cancer but only for 85% of breast and 72% of colon cancers. Age at diagnosis of breast cancer was correct in 92% of cases in first-degree and 54% in second-degree relatives. The interview contributed additional information about the presence of cancer in second-degree relatives, and the site and age at diagnosis in first- and second-degree relatives. In a similar population the questionnaire alone should yield adequate data for identifying families that warrant further investigation.

Tilkin, C., M. Toucheque, et al. "[Quality of life in children with cancer history and parental adaptation]." *Rev Med Liege.* 2014 Nov;69(11):622-7.

This study assesses quality of life (Qol) in children with cancer history as well as Qol of their parents and examines the relationship between parental adjustment and children Qol. Two groups were formed: an experimental group composed by children with cancer antecedents and their parents and a control group with healthy children and their parents. Children have filled a questionnaire about their Qol. Parents have completed questionnaires about their coping, their illness perceptions, their parenting stress and their Qol. The results show that Qol was satisfactory and similar in both groups. Significant correlations were found between parental illness representations (threat and personal control) and children Qol as well as between coping strategies based on maintaining family cohesion and children Qol. This study highlights the need to assess the adjustment of parents after child cancer and to develop interventions targeting parental representations and coping strategies.

Vitaliano, P. P., J. M. Scanlan, et al. "Psychosocial stress moderates the relationship of cancer history with natural killer cell activity." Ann Behav Med. 1998 Summer;20(3):199-208.

Data suggest that both cancer history and psychosocial stress may be associated with reductions in natural killer cell activity (NKA). Therefore, we tested whether individual differences in cancer history, chronic/perceived stress, and their interactions would be associated with decreased levels of NKA. We tested these hypotheses in 80 spouse caregivers of victims of Alzheimer's Disease (AD) (persons known to report high levels of psychosocial stress) and in 85 age- and sex-matched spouses of non-demented controls. Participants were assessed at study entry (Time 1) and 15-18 months later (Time 2). Individuals with cancer histories (N = 43) had not been treated with immune altering medications within the last year. At both Times 1 and 2, cross-sectional main effects were weak or absent for cancer history, perceived stress (e.g. high hassles, low uplifts), and caregiver status; however, interactions occurred between cancer history and perceived stress, such that persons with cancer histories and high hassles/low uplifts had the lowest NKA values ($p < .05$). These results occurred even after controlling for age, gender, beta-blocker use, hormone replacement therapy, alcohol, and exercise. At Time 1, an interaction also occurred between caregiver status and cancer history--caregivers with cancer histories had lower NKA than did controls with cancer histories and caregivers/controls without cancer histories ($p < .05$). At Time 2, this interaction only showed a trend ($p < .08$), primarily because caregivers with cancer histories experienced increases in NKA ($p < .05$) from Time 1 to Time 2, whereas in the other three groups NKA did not change. Importantly, in caregivers with cancer histories, high perceived stress at Time 1 predicted low NKA at Time 2 ($p < .05$). This research suggests that the combinations of biological vulnerabilities and chronic/perceived stress may have interactive effects resulting in reduced NKA.

Wenzel, J., D. Tormo, et al. "Toll-like receptor-agonists in the treatment of skin cancer: history, current developments and future prospects." Handb Exp Pharmacol. 2008;(183):201-20.

This review will briefly cover some important aspects of skin structure and function before touching upon fundamental principles of neoplastic cell growth in the skin and some of the important molecular pathways involved. After presenting evidence for a role of the immune system in shaping the development of skin cancer, concepts for tumor immunotherapy with TLR-agonists are introduced from a historical point of view. Subsequently, the use of synthetic

DNA, synthetic RNA and synthetic small immunostimulatory molecules for immunotherapy of early forms of epithelial carcinoma (actinic keratoses) and melanoma (lentigo maligna), as well as for advanced metastatic melanoma, is comprehensively presented. Finally, current developments and future prospects for immunotherapy of occult or unresectable melanoma metastases, the most important clinical problem today, are discussed.

Westman, J., H. Hampel, et al. "Efficacy of a touchscreen computer based family cancer history questionnaire and subsequent cancer risk assessment." J Med Genet. 2000 May;37(5):354-60.

OBJECTIVE: A computer based touchscreen family cancer history questionnaire was developed and implemented to facilitate the provision of cancer risk assessments for the ambulatory and outpatient populations of a free standing cancer hospital. **METHODS:** A questionnaire consisting of a series of branched point decision making screens was developed which enables the participant to enter demographic data, personal cancer history, and cancer histories for first and second degree relatives. A freestanding touchscreen computer kiosk system was used to place the questionnaire in public areas of the cancer hospital and clinic. Genetic professionals analysed the data received, using published criteria, and provided a basic cancer risk assessment and surveillance recommendations within 10 business days. A survey was completed by a small random group of users ($n = 59$) three to six months after receipt of their risk assessment. **RESULTS:** After 11 months, 1440 people had entered information and received a written communication. Only 2% of completed questionnaires contained insufficient information to provide a basic risk assessment. Of the small group of participants surveyed, almost all (95%) felt "very comfortable" using the system, 93% remembered receiving the risk assessment letter when queried three to six months later, 42% felt their perceptions about cancer risk had changed, and 20% had made changes in their or their family's cancer surveillance practices. **CONCLUSION:** The touchscreen computer family history questionnaire allows easy collection of family history information, provision of risk assessments to a broad population, and promotes increased awareness of familial risk and appropriate surveillance.

Widschwendter, A., T. Brunhuber, et al. "Detection of human papillomavirus DNA in breast cancer of patients with cervical cancer history." J Clin Virol. 2004 Dec;31(4):292-7.

BACKGROUND: Recent studies have revealed a possible role for the human papillomavirus

(HPV) in the pathogenesis of breast cancer. In this study, patients having both a history of invasive cervical cancer and breast cancer as second primary cancer were selected for enrolment in a study of breast carcinomas for the presence of HPV. **METHODS:** Paraffin-embedded tissue from cervical cancer, pelvic lymph nodes, breast cancer and axillary lymph nodes of eleven patients were examined for the presence of HPV DNA using a polymerase chain reaction - enzyme immuno assay. DNA extraction was performed with the "QIAamp Tissue Kit" according to the manufacturer's instructions. Additionally, serum samples taken between diagnosis of cervical and breast cancer, were analyzed for the presence of HPV DNA to examine a possible haematogenous spread of oncogenic HPV DNA. **RESULTS:** All cervical carcinomas were HPV-positive. HPV DNA was detected in seven out of eleven cases in breast cancer and/or axillary lymph node tissue. Six patients had the same HPV type (HPV-16) in cervical cancer and in the corresponding breast cancer/lymph node tissue. In one case, the same HPV DNA type (HPV 16) was detected in cervical cancer, breast cancer and serum sample. **CONCLUSION:** These results suggest that HPV DNA might be transported from the original site of infection to the breast tissue by the bloodstream, and that it is possibly involved in the carcinogenesis of breast neoplasia in some patients.

Wozniak, A., K. Szyfter, et al. "[Head and neck cancer-history]." *Przegl Lek.* 2012;69(10):1079-83.

According to epidemiological data head and neck cancers constitute for 12% of all malignancies in the world. It is estimated that a total of 400 000 cases of the mouth and throat and of 160 000 cases of laryngeal cancer, 300 000 people die each year. History of head and neck cancers developed and underwent many changes at the turn of the century. Treatment, pathogenesis and possessed state of knowledge on the subject has changed. Starting from the ancient times there were texts on how to treat and examine patients. The Edwin Smith and Ebers Papyrus are two of the oldest medical documents describing the treatment of cancer patients. Hippocrates was the first person who used the word "cancer" and probably he was the first who divided the tumors into benign and malignant. In a document known as the Doctrine of Hippocrates he described skin cancer and cancer treatments. Over the next centuries, medical science did not develop because of religious concerns about autopsy and surgical procedures. The 17th century is a period in which there were a lot of new information about how to treat such oral cancer. Cancer of the tongue was removed by cauterization, which in the 18th century was replaced by the use of surgical instruments. In the same age glossectomy has been

accepted as the treatment of choice performed in the treatment of cancer. The 19th century brought a major breakthrough in the treatment of surgical, diagnostic, anesthetic techniques and understanding of the pathological mechanisms. Histological evaluation of tumors has become mandatory and standard practice in the assessment of cancer. Laryngectomy and neck lymph nodes removal has become commonplace. Modified Radical Neck Dissection (MRND), became popularized as another cancer treatment technique. Describing ways to treat cancer, radiotherapy can not be ignored - there are several new techniques such as Intensity Modulated Radiotherapy (IMRT) and hypofractionation currently used. Chemotherapy and the introduction of many new drugs have changed the outlook for patients suffering from cancer. Recently there are expectations about the targeted therapy, especially in medicaments blocking epidermal growth factor receptor (EGFR).

Yazici, H., H. Tigli, et al. "Are CYP17 genotypes a biomarker for ovarian cancer in patients with cancer history in their family?" *Oncol Res.* 2006;16(1):43-7.

BRCA1 and BRCA2 genes are responsible for 5-10% of breast and ovarian cancer cases. However, the vast majority of ovarian and breast cancer cases do not display the hereditary form of the disease. Estrogen-metabolizing genes may also contribute to the predisposition of breast or ovarian cancer. Polymorphic variants of the estrogen-metabolizing gene, CYP17, have been associated with the risk of hormone-related cancers. In this study we investigated the CYP17 polymorphisms in ovarian cancer patients harboring mutations in the BRCA1 and BRCA2 genes, patients displaying familial characteristics but not carrying mutations and patients with sporadic ovarian cancer. Association between the allele frequencies, the CYP17 genotype and tumor characteristics or clinical parameters was evaluated. Our data suggest evidence for an association between ovarian cancer risk and the CYP17 genotype in the subgroup of patients with familial disease in whom no mutations in the BRCA genes are found. Although there were no statistically significant differences in the genotype distribution between the control group and the subgroup of patients with BRCA mutations, the frequency of the CYP17 A2 allele was significantly higher in the subgroup of patients without BRCA mutations. We found a four- to eightfold higher risk in ovarian cancer patients with family history but without BRCA mutations. Our data indicate that the CYP17 A2 allele polymorphism may confer an increased risk and can provide a biomarker for ovarian cancer patients in whom no mutations in the BRCA genes are observed.

Zick, C. D., R. N. Mayer, et al. "Putting it off: family breast cancer history and women's retirement planning." *Psychooncology*. 2015 Jan 29. doi: [10.1002/pon.3759](https://doi.org/10.1002/pon.3759).

OBJECTIVE: Cancer diagnoses have significant consequences that extend beyond the individual to family members. Our research builds on prior research by examining how a family history of breast cancer is related to women's retirement preparations. **METHODS:** Taking guidance from the stress process model, we generate and test hypotheses using multivariate logistic regression and unique data on retirement planning and familial cancer histories for 467 women. We supplement this analysis with the qualitative findings from two focus groups. **RESULTS:** We find consistent evidence that women with a mother and/or sister who had a breast cancer diagnosis are significantly less likely to engage in retirement preparation activities than otherwise similar women with no family history. The same effect is not observed when other first-degree relatives have different cancer diagnoses. The face validity of these quantitative findings is confirmed by the focus group analysis. **CONCLUSIONS:** Our research suggests that the stressors experienced by close female relatives of women who have had breast cancer may lead to behaviors and attitudes that have consequences for their post-retirement quality of life. Copyright (c) 2015 John Wiley & Sons, Ltd.

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