Cancer and Epidemiology literature

Mark H Smith

Queens, New York 11418, USA
mark20082009@gmail.com

Abstract: Cancer is the cells that grow out of control. Cancer cells can also invade other tissues. Growing out of control and invading other tissues are what makes a cell a cancer cell. Involved in more than 100 diseases, the cancer can cause serious illness and death. Normally, the cells become cancer cells because of DNA damage. This material is a literature collection of the researches on the cancer and the epidemiology.
[Smith MH. **Cancer and Epidemiology literature.** *Cancer Biology* 2012;2(1):35-73]. (ISSN: 2150-1041). http://www.cancerbio.net. 4

Keywords: cancer; biology; life; disease; research; literature; epidemiology

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

Adlercreutz, H. (1995). "Phytoestrogens: epidemiology and a possible role in cancer protection." Environ Health Perspect **103 Suppl 7**: 103-12.

Because many diseases of the Western Hemisphere are hormone-dependent cancers, we have postulated that the Western diet, compared to a vegetarian or semivegetarian diet, may alter hormone production, metabolism, or action at the cellular level by some biochemical mechanisms. Recently, our interest has been mainly focused on the cancer-protective role of some hormonelike diphenolic phytoestrogens of dietary origin, the lignans and the isoflavonoids. The precursors of the biologically active compounds originate in soybean products (mainly isoflavonoids), whole grain cereal food, seeds, and probably berries and nuts (mainly lignans). The plant lignan and isoflavonoid glycosides are converted by intestinal bacteria to hormonelike compounds with weak estrogenic but also antioxidative activity; they have now been shown to influence not only sex hormone metabolism and biological activity but also intracellular enzymes, protein synthesis, growth factor action, malignant cell proliferation, differentiation, and angiogenesis in a way that makes them strong candidates for a role as natural cancer-protective compounds. Epidemiologic investigations strongly support this hypothesis because the highest levels of these compounds in the diet are found in countries or regions with low cancer incidence. This report is a review on recent results suggesting that the diphenolic isoflavonoids and lignans are natural cancer-protective compounds.

Ahlgren, J. D. (1996). "Epidemiology and risk factors in pancreatic cancer." Semin Oncol **23**(2): 241-50.

Pancreatic cancer is one of the most lethal neoplasms. Incidence in the United States has remained fairly stable over the past 25 years, with about 25,000 cases annually. Almost 100% of cases are fatal. Incidence in the developed world parallels that in the United States. Incidence in undeveloped nations is lower but may be underreported. Worldwide incidence is about 185,000 cases per year. There are no striking environmental risk factors, and geographic variation is less than with other gastrointestinal cancers. The most significant risk appears to be cigarette smoking, with a risk ratio of about 2. Alcohol and coffee consumption have been reported as possible risks in some (but not in most) studies. Diet is probably a significant factor, but is difficult to evaluate quantitatively. Other putative associations, including diabetes, probably are unimportant.

Akslen, L. (1994). "Thyroid-cancer - some aspects of epidemiology and etiologic factors, pathological features and tumor biology." Int J Oncol **4**(4): 931-42.

Malignant tumours specific for the thyroid gland originate from either the follicular cells (papillary, follicular undifferentiated carcinomas) or the parafollicular C-cell system (medullary carcinomas). Regarding the follicle derived carcinomas, various types of data indicate that radiation exposure, for example therapeutic radiation given to children for benign disorders in the head and neck area, is an important risk factor. Dietary

components may also be relevant. The marked female predominance. which is not specific for malignant tumours, is probably the result of hormonal cofactors and differences in growth promotion of early lesions (microcarcinomas). Further development of follicle derived tumours is characterized by decreasing tumour cell dependence of TSH, along with the introduction of autocrine loops, e.g. expression of the TGF alpha/EGF-receptor system. and such mechanisms may in part explain the development of autonomous growth. In parallel with these phenotypic changes, several alterations have also been described in various thyroid tumours, including the medullary carcinomas, for example in the ras and ret genes. Activation of some oncogenes, like the EGF-receptor system, may also be relevant for late tumor progression and hence of prognostic value. to-ether with other factors like p53 and nm23. In addition to classical clinocopathological features, molecular data are of increasing importance in biological grading of thyroid tumours.

Alberg, A. J., A. P. Lam, et al. (1999). "Epidemiology, prevention, and early detection of breast cancer." Curr Opin Oncol **11**(6): 435-41.

Globally, breast cancer is the third most common form of cancer and the most common among women. The age-adjusted incidence rates of breast cancer are 176% higher in developed than in developing nations. Male breast cancer is rare, but important studies provided risk factor information for comparison with studies of female breast cancer. There has been considerable interest in a possible role of organochlorines and polychlorinated biphenyls in the etiology of breast cancer, but the results of several null studies indicate the likelihood of such associations is extremely remote, providing reassuring news for the public. Prophylactic mastectomy was observed to significantly reduce a woman's chances of developing breast cancer, but it does not lower the risk to zero. Tamoxifen was found to be an effective chemopreventive agent in the Breast Cancer Prevention Trial, but this result was not replicated in two randomized trials in Europe. Striking reductions in the risk for breast cancer were observed for raloxifene in a randomized, placebo-controlled trial that had been designed for the prevention of osteoporosis. A large-scale, randomized trial of tamoxifen-verus-raloxifene among women at increased risk for developing breast cancer is now underway.

Alberg, A. J., K. Visvanathan, et al. (1998). "Epidemiology, prevention, and early detection of breast cancer." Curr Opin Oncol **10**(6): 492-7.

The evidence that alcohol consumption increases a woman's chances of getting breast cancer is now more persuasive. Higher blood concentrations of organochlorine compounds were not associated with increased risk of breast cancer in recent studies. The relationship of exogenous estrogen use to breast cancer risk is now clarified: current users of both oral contraceptives and hormone replacement therapy experience a slightly elevated risk that dissipates after cessation of use. Alcohol consumption and hormone replacement therapy are both associated with slightly increased breast cancer risk, but the overall health benefits of hormone replacement therapy and low levels of alcohol consumption appear to outweigh the risks in the general population. These circumstances underscore the complex decisions facing women and the need to consider individual risk factor profiles. For the genes BRCA1 and BRCA2, more data are needed to understand the risks associated with specific mutations, optimal implementation of genetic testing, and prevention and early detection strategies for women who have positive test results. Interesting leads in identifying women at increased risk for breast cancer have been generated via the study of genetic polymorphisms. The results of tamoxifen in the Breast Cancer Prevention Trial have made the possibility of chemoprevention for breast cancer a reality. Raloxifene, another antiestrogen, has emerged as a potential chemopreventive agent. Its efficacy in reducing breast cancer risk will be compared with that of tamoxifen in a randomized trial.

Ali, O., P. Cohen, et al. (2003). "Epidemiology and biology of insulin-like growth factor binding protein-3 (IGFBP-3) as an anti-cancer molecule." Horm Metab Res **35**(11-12): 726-33.

The Insulin-like Growth Factor (IGF) signaling system plays a central role in cellular growth, differentiation and proliferation. IGFBP-3 is the most abundant IGF binding protein in human serum and has been shown to be a growth inhibitory, apoptosis-inducing molecule, capable of acting via IGF-dependent and IGF-independent mechanisms. Over the last decade, several clinical studies have proposed that individuals with IGFBP-3 levels in the upper range of normal may have a decreased risk for certain common cancers. This includes evidence of a protective effect against breast cancer, prostate cancer, colorectal cancer, and lung cancer. In addition, a series of in vitro studies and animal experiments point towards an important role for IGFBP-3 in the regulation of cell growth and apoptosis. In this brief review, we discuss the biological role of IGFBP-3 and summarize the epidemiological and experimental evidence suggesting a role for IGFBP-3 as an anti-cancer molecule.

Al-Zahrani, A. S. and K. Ravichandran (2007). "Epidemiology of thyroid cancer: a review with special reference to Gulf Cooperation Council (GCC) states." Gulf J Oncolog(2): 17-28.

A wide variation in incidence of thyroid cancer according to age, sex, ethnicity and geographic region was observed. In general, it occurs more frequently in women than men and a substantially higher rate was observed particularly during fertile period of women compared with men of the same age. Papillary carcinoma is the most prevalent histological type, irrespective of gender and conditions like iodine level. Over the years the incidence of thyroid cancer, especially papillary type, increases around the world. Ionizing radiation, in particular radiotherapy to head and neck region was the most established risk factor for thyroid cancer. Goiter, miscarriage or abortion (particularly in the first pregnancy) may also predispose to thyroid cancer risk. Cigarette smoking and use of contraceptives may be modifier of thyroid cancer risk. In all the GCC states thyroid cancer is the second most common cancer except in Babrain and Kuwait (where it stands third). During the five year peribd (1998-2002) 549 male and 1898 female thyroid caneers were diagnosed in all the GCC states. Papillary carcinoma is the predominant histological type followed by follicular carcinoma in both genders. Among females, Qatar has the highest incidence with an age standardized incidence rate of 13.5 per 100,000 followed by Kuwait (7.7), Bahrain (7.6), Emirates (6.0), Oman (5.9), and Saudi Arabia (5.0). There were at least 2.6 female thyroid cancer cases (in Kuwait) for each male thyroid cancer case and this goes up to 6.6 in Babrain. Incidence of thyroid cancer in the GCC states is closer or higher than that of some of the developed countries.

Anderson, W. F., N. Chatterjee, et al. (2002). "Estrogen receptor breast cancer phenotypes in the Surveillance, Epidemiology, and End Results database." Breast Cancer Res Treat **76**(1): 27-36.

BACKGROUND: Researchers question whether estrogen receptor alpha-negative (ERN) and -positive (ERP) represent different stages of one disease or different breast cancer types. OBJECTIVE: To further examine ERalpha phenotypes, we stratified incident tumor characteristics in the Surveillance, Epidemiology, and End Results (SEER) Database (n = 82,488) by ERN and ERP. METHODS: Study variables included black-white race, age-at-diagnosis, and standard incident tumor characteristics. These characteristics were arbitrarily dichotomized into good versus poor prognostic factor groups, for example, good (tumor size < or = 2.0 cm, negative axillary lymph nodes, and good histologic grade) versus poor (tumor size > 2.0 cm, positive nodes, and poor grade). Age frequency density plots were generated from the corresponding age-at-diagnosis frequency histograms. Average annual age-specific incidence rates (or risks) were adjusted to the 1970 United States standard female population. RESULTS: Age frequency density plots demonstrated bimodal premenopausal and postmenopausal breast cancer populations. ERN was correlated with premenopausal disease, black race, and poor prognostic factor groups, whereas ERP was associated with postmenopausal disease, white race, and favorable tumor characteristics. ERN rates increased premenopausally and then flattened to a nearly constant level after 50 years of age. ERP risk rose for most of a woman's lifetime with the greatest risk occurring between 75 and 79 years. CONCLUSIONS: ERalpha exhibited bimodal age frequency distribution with a dichotomous pattern for age-specific rates, racial, and prognostic factor profiles. Menopause had a greater effect on ERN than ERP. Possible implications for breast carcinogenesis and cancer prevention are discussed in the text.

Arab, L. and D. Il'yasova (2003). "The epidemiology of tea consumption and colorectal cancer incidence." J Nutr **133**(10): 3310S-3318S.

This manuscript provides a brief synopsis of 30 studies aimed at examining tea consumption as a factor in the incidence of colon and rectal cancers. The 30 papers examine populations in 12 countries and provide data on consumption of both black and green tea. These studies do not provide consistent evidence to support the theory from animal studies and basic research that tea is a potent chemopreventive agent. Details of the studies are presented, and the potential impact of measurement error, publication bias, the form of tea consumed, the appropriateness of the outcomes studied and the adjustment of confounders related to both tea consumption and risk of colorectal cancer or polyps in various countries are explored. In general, the data are not more consistent for green than for black tea. Particularly with green tea, the doses consumed do get into a perceived protective range in a significant subset of the population. A negative association is stronger in observational epidemiologic studies of rectal cancer than in colon cancer. There is no consistent adjustment for important potential confounders of any tea relationship, such as coffee and alcohol consumption and physical activity levels. Finally, the assessment of tea in most of these studies was based on a single question and therefore may have significant measurement error compared with more recent studies specifically aimed at assessing tea consumption.

Badar, F., N. Anwar, et al. (2005). "Geographical variation in the epidemiology of esophageal cancer in Pakistan." Asian Pac J Cancer Prev **6**(2): 139-42.

STUDY OBJECTIVES: To evaluate whether factors such as the geographic area of residence, sex, and anatomic subsite of esophagus can prognosticate the histologic subtype of esophagus cancer. DESIGN: To study the major histologic subtypes of esophagus cancer stratified by various factors through multivariate analyses using morphology as the dependent factor and gender, province, and subsite of esophagus as independent factors. SETTING: A tertiary care cancer hospital situated in the city of Lahore in Pakistan. PATIENTS: Three hundred and thirty five patients diagnosed either with esophageal squamous cell carcinoma or adenocarcinoma, from December 1994 to April 2004, were included. Subjects were residents of either Punjab or the Northwest Frontier Province in Pakistan. MAIN RESULTS: An excessive likelihood of development of squamous cell carcinoma versus adenocarcinoma was established for the Northwest Frontier Province as compared to Punjab (odds ratio 2.7, 95 percent confidence interval: 1.2, 6.2, p = 0.02), and in the upper-third of the esophagus relative to the lower-third of the organ (odds ratio 8.8, 95 percent confidence interval: 2.8, 28.3, p < 0.001). CONCLUSIONS: This histologic variation may be explained by environmental and lifestyle factors peculiar to geographical regions.

Baquet, C. R. and P. Commiskey (1999). "Colorectal cancer epidemiology in minorities: a review." J Assoc Acad Minor Phys **10**(3): 51-8.

Colorectal cancer is the second leading cause of cancer death in the United States. In 1997, more than 131,000 new cases and more than 54,000 deaths were estimated. Racial and ethnic disparities in incidence, mortality and survival rates, and trends exist for this disease. Differences in colorectal cancer screening, early detection, and treatment in minority communities are related to therapeutic outcomes. Age-adjusted incidence rates for men with colorectal cancer are highest for Alaskan native men, followed by Japanese, then African-American men. For women, the incidence is highest for Alaskan native women, followed by African-American, then Japanese women. Mortality rates in men are highest for African Americans, followed by Alaskan natives and then Hawaiians. In women, mortality rates are highest for Alaskan natives, then African Americans and whites. Colorectal cancer screening rates vary by race, income, and education. It is interesting that, when compared with whites, African-American men demonstrate the higher reported rate of screening for this disease. In addition, site specificity is different for African Americans compared with whites. Findings also reveal that stage at diagnosis is an influential factor with regard to mortality and survival. This may be related in part to socioeconomic factors, differences in anatomic site, and treatment differences in African Americans. Risk factor data for this disease are scarce for minority populations. Documented differences in colorectal cancer incidence, mortality, and survival rates exist between minorities and whites. Additional research is needed on risk factors specific to African Americans and other minorities, differences in treatment, and the role of socioeconomic status.

Bedwani, R., F. el-Khwsky, et al. (1997). "Epidemiology of bladder cancer in Alexandria, Egypt: tobacco smoking." Int J Cancer **73**(1): 64-7.

The relationship between smoking and bladder cancer risk was investigated using data from a case-control study conducted between January 1994 and July 1996 in Alexandria, Egypt. Cases were 151 males with incident, histologically confirmed invasive cancer of the bladder, and controls were 157 males admitted to hospital for acute, non-neoplastic, non-urinary tract, non-smoking-related conditions. With reference to never smokers, ex-smokers had a multivariate odds ratio (OR) of 4.4 [95% confidence interval (CI) 1.7-11.7] and current smokers of 6.6 (95% CI 3.1-13.9). The ORs were 5.4 for < 20 and 7.6 for > or = 20 cigarettes per day. After adjustment for cigarette smoking, the ORs were 0.8 for waterpipe and 0.4 for hashish smokers. The risk was significantly related to duration of smoking (OR of 16.5 for > 40 years), and inversely related to age at starting (OR of 8.8 for starting < 20 years), and inversely related to time since quitting smoking. Compared with never smokers who did not report a clinical history of schistosomiasis, the OR was 9.4 for smokers with a history of schistosomiasis, and 10.7 for smokers ever employed in high-risk occupations compared with non-smokers not reporting such a history. Thus, our results, while not giving indications of an increased bladder cancer risk with habits other than cigarette smoking, found a remarkably strong association with various measures of cigarette smoking that could explain 75% of bladder cancer cases among males from Alexandria. The prevalence of smoking was very low among women, and consequently tobacco was not a relevant risk factor for female bladder cancer.

Bernstein, L. (2002). "Epidemiology of endocrine-related risk factors for breast cancer." J Mammary Gland Biol Neoplasia **7**(1): 3-15.

Ovarian and other hormones are major determinants of breast cancer risk. Particularly important is the accumulative exposure of the breast to circulating levels of the ovarian hormones estradiol

and progesterone. A number of breast cancer risk factors can be understood in light of how they affect women's hormone profiles. Age is a marker for the onset and cessation of ovarian activity. Racial differences in hormone profiles correlate with breast cancer incidence patterns. Age at menarche not only serves as the chronological indicator of the onset of ovarian activity, but as a predictor of ovulatory frequency during adolescence and hormone levels in young adults, and has a long-lasting influence on risk. Age at menopause, another established breast cancer risk factor, marks the cessation of ovarian activity. Pregnancy history and lactation experience also are hormonal markers of breast cancer risk. Postmenopausal obesity, which is associated with higher levels of estrogen following cessation of ovarian activity, increases breast cancer risk, whereas physical activity, which can limit menstrual function, reduces risk. A relatively recent area of investigation is prenatal exposures like preeclampsia and low birth weight; both may be associated with lower in utero exposure to estrogen and also may predict lower breast cancer risk as an adult. Improved understanding of these exposures and their potential interactions with breast cancer susceptibility genes may, in the future, improve our prospects for breast cancer prevention.

Blot, W. J. and J. K. McLaughlin (1999). "The changing epidemiology of esophageal cancer." Semin Oncol **26**(5 Suppl 15): 2-8.

The patterns of esophageal cancer are dramatically changing in the United States. Three decades ago the large majority of these cancers were squamous cell carcinomas, but the incidence of esophageal adenocarcinoma has been steadily increasing. By the early 1990s, adenocarcinoma had become the most common cell type of esophageal cancer among white patients, although squamous cell cancers still predominated among black patients. The trends are not simply due to gastric cardia cancers now being called esophageal adenocarcinomas, because the rates of tumors appearing just below the esophageal-gastric junction are also increasing. Tobacco and alcohol consumption are the primary causes of squamous cell carcinomas of the esophagus. The causes of esophageal adenocarcinoma are not well known; thus, reasons for the increasing incidence are not clear. Tobacco smoking has now been established as a risk factor, but there appears to be little link to alcohol consumption. One of the strongest emerging risk factors, however, is obesity. Increases in the prevalence of obesity and the incidence of esophageal adenocarcinoma are parallel, and several epidemiologic studies have shown upwards of threefold excess risks among overweight individuals. Further research into the causes of these usually fatal cancers may help identify other potential determinants and provide needed information to help stem their increase.

Brenner, H., D. Rothenbacher, et al. (2009). "Epidemiology of stomach cancer." Methods Mol Biol **472**: 467-77.

Despite a major decline in incidence and mortality over several decades, stomach cancer is still the fourth most common cancer and the second most common cause of cancer death in the world. There is a 10-fold variation in incidence between populations at the highest and lowest risk. The incidence is particularly high in East Asia, Eastern Europe, and parts of Central and South America, and it is about twice as high among men than among women. Prognosis is generally rather poor, with 5-year relative survival below 30% in most countries. The best established risk factors for stomach cancer are Helicobacter pylori infection, the by far strongest established risk factor for distal stomach cancer, and male sex, a family history of stomach cancer, and smoking. While some factors related to diet and food preservation, such as high intake of salt-preserved foods and dietary nitrite or low intake of fruit and vegetables, are likely to increase the risk of stomach cancer, the quantitative impact of many dietary factors remains uncertain, partly due to limitations of exposure assessment and control for confounding factors. Future epidemiologic research should pay particular attention to differentiation of stomach cancer epidemiology by subsite, and to exploration of potential interactions between H. pylori infection, genetic, and environmental factors.

Broeders, M. J. and A. L. Verbeek (1997). "Breast cancer epidemiology and risk factors." Q J Nucl Med **41**(3): 179-88.

Breast cancer is the most common malignancy among women in the Western society. Over the past decades it has become apparent that breast cancer incidence rates are increasing steadily, whereas the mortality rates for breast cancer have remained relatively constant. Information through the media on this rising number of cases has increased breast health awareness but has also introduced anxiety in the female population. This combination of factors has made the need for prevention of breast cancer an urgent matter. Breast cancer does not seem to be a single disease entity. A specific etiologic factor may therefore have more influence on one form of breast cancer than another. So far though, as shown in our summary of current knowledge on established and dubious risk factors, no risk factors have been identified that can explain a major part of the incidence. Efforts to identify other ways for primary

prevention have also been discouraging, even though breast cancer is one of the most investigated tumours world-wide. Thus, at this point in time, the most important strategy to reduce breast cancer mortality is early detection through individual counselling and organised breast screening programs. The recent isolation of breast cancer susceptibility genes may introduce new ways to reduce the risk of breast cancer in a small subset of women.

Bucsky, P. and T. Parlowsky (1997). "Epidemiology and therapy of thyroid cancer in childhood and adolescence." Exp Clin Endocrinol Diabetes **105 Suppl 4**: 70-3.

Thyroid cancer is a rare disease in childhood and adolescence. However, it represents the most frequent cancer type in this age group. Thyroid cancer amounts about 0.5%-1.5% of all malignancies in children and adolescents. In Germany 10-30 cases could be expected in a year. The most common histologic type for this age group is the differentiated thyroid cancer (DTC), i.e. the papillary and follicular subtypes (90%). In 10% of patients medullary thyroid cancer (MTC) will be diagnosed. DTC occur more often in girls than in boys (female/male-ratio 2:1), with a median age of about 12-13 years (yrs). An important aetiological factor of DTC is a former exposition to different kinds of radiation. In childhood and adolescence MTC mostly appears in patients suffering from the syndrome MEN-2, whereas the sporadic form is rare. As in DTC, more girls than boys can be diagnosed for MTC (female/male-ratio 2-3:1), with a median age about 10 yrs. The anaplastic/undifferentiated subtype occurs extremely rare. For all types of thyroid cancer the most important therapeutic approach is the surgical intervention. In most cases of DTC an optimal disease control could be achieved by radioiodine therapy. Prognosis of DTC in children and adolescents is favourable. However, therapeutic strategies and modalities reported in the literature are very different. In contrast, prognosis of MTC is rather poor, that of the anaplastic type is infaust. No other effective therapy option than surgery is available. To evaluate the therapeutic efficacy of a combined modality therapy by both radiotherapy and cytostatic drugs in children and adolescents with poor prognosis types of thyroid cancer, an interdisciplinary multicenter therapy study will now be started in Germany.

Caporaso, N. E. and M. T. Landi (1994). "Molecular epidemiology: a new perspective for the study of toxic exposures in man. A consideration of the influence of genetic susceptibility factors on risk in different lung cancer histologies." Med Lav **85**(1): 68-77.

This data in the aggregate suggests that the 3 best studied genetic susceptibility factors (CYP2D6 extensive metabolizers, GST mu null phenotype, and CYP1A1 "mutant" alleles in Asians only) constitute greater risk factors for the more smoking related histologies of lung cancer, but not for adenocarcinoma. The epidemiologic evidence for a these genetic susceptibility factors in tobacco-related cancer is suggestive but not determinant. A consensus estimate of relative risk for extensive metabolizers of debrisoquine is around 2. Variability in study results depend on a number of factors which include: assay misclassification, non-correspondence of phenotype/genotype in certain subjects, disease heterogeneity, exposure variation, ethnic and racial variation. Future studies should emphasize: a high quality approach to data gathering, careful attention to epidemiologic design, and the use of intermediate markers where feasible. Investigators should consider the use of multiple genetic markers since PCR approaches can make this an efficient approach. A meta-analysis may serve to illuminate points of heterogeneity between studies. New discoveries should provide opportunities to explore for analogous associations in other malignancies. It may be speculated that the "specificity" of the association observed for each of the genetic factors tends to support the general causal nature of the hypothesis. The fact that each shares the histologic preference at least suggests that a common mechanism may be operative. The observation that the tobacco-cancer association, though clearly present, is weaker for adenocarcinoma than for the other lung cancer histologies, suggests that the underlying mechanism involves some interaction of the genetic trait with exposure to tobacco smoking, and suggests further attention to this factor to elucidate differences in risk estimates for genetic susceptibility factors among different studies.

Ceschi, M., F. Gutzwiller, et al. (2007). "Epidemiology and pathophysiology of obesity as cause of cancer." Swiss Med Wkly **137**(3-4): 50-6.

According to World Health Organisation estimates 1.1 billion people were overweight or obese worldwide in the year 2000 with the prevalence rapidly increasing. Compelling evidence suggests that excess body weight is a risk factor for several cancer types including cancer of the colon, breast, endometrium, kidney, oesophagus, as well as possibly additional sites. According to previous meta-analyses and systematic literature reviews, an important proportion of cancer has been estimated to be attributable to excess body weight. The extrapolation of a European meta-analysis [1] to the Swiss situation broadly estimates that around 700 cancers could be

prevented in the absence of overweight and obesity in this country. The data presented highlights the public health relevance of preventing excess body weight. Several interacting metabolic and hormonal pathways seem to underlie the association between being overweight and cancer with insulin-resistance playing a central role. Since evidence is mounting that excess body weight can also adversely affect cancer prognosis, obesity is a primary target for cancer control programs.

Chan, J. M., M. J. Stampfer, et al. (1998). "What causes prostate cancer? A brief summary of the epidemiology." Semin Cancer Biol **8**(4): 263-73.

In recent decades, prostate cancer has emerged as one of the most common diseases among older men, particularly in Western society. Several years ago, only age, race, and family history were known risk factors for this disease. However, today, much progress has been made towards discovering nutritional and hormonal risk factors for prostate cancer. Biomarkers, including testosterone and insulin-like growth factor, and nutritional factors, especially meat, fat, and dairy intake, have been linked to greater risk of disease. Higher consumption of selenium and vitamin E, fructose/fruits, and tomatoes all have been associated with reduced occurrence of prostate cancer, but as yet their efficacy for prevention remains unproven. The challenge of understanding the enigmas of this disease will continue into future decades, as we convert current knowledge into preventive and therapeutic recommendations.

Chen, W. Y. and G. A. Colditz (2007). "Risk factors and hormone-receptor status: epidemiology, risk-prediction models and treatment implications for breast cancer." Nat Clin Pract Oncol **4**(7): 415-23.

It is increasingly being recognized that breast cancer does not represent a single homogeneous disease; instead, the hormone-receptor status defines important clinical and etiologic differences. We review the epidemiologic data on differences in risk-factor associations by hormone-receptor status and highlight major trends in the literature. We discuss the development and evaluation of breast cancer risk models, with a focus on the Rosner and Colditz model, which can separately estimate the risk of hormone-receptor-positive and hormone-receptor-negative breast cancers. We also discuss the clinical implications of accounting for hormone-receptor status in breast cancer risk-prediction models.

Chen, Y. C. and D. J. Hunter (2005). "Molecular epidemiology of cancer." CA Cancer J Clin **55**(1): 45-54; quiz 57.

Epidemiology is very successful in identifying environmental and lifestyle factors that increase or reduce risk of specific cancers, leading to cancer prevention strategies. However, the etiology of many types of cancer is still poorly understood, despite extensive use of questionnaires and interview-based approaches in conventional epidemiologic studies. The integration of molecular techniques into epidemiology studies may provide new insights and has been referred to as molecular epidemiology. For instance, our ability to make connections between lifestyle and cancer risk is limited by difficulty in accurately measuring exposure to many carcinogens-newer molecular markers of exposure may provide better information. The completion of the Human Genome Project gives us knowledge of the genetic variations that presumably underlie the fact that a family history of cancer is a risk factor for most cancer types. Some of this excess risk has been explained over the last decade by identification of mutations in genes that give rise to a very high familial risk. Molecular epidemiologists are searching for genes that may give rise to much smaller increases in individual risk, but account for much of the residual risk associated with family history. These genes may also interact with environment and lifestyle factors such that cancer risk is not equally elevated in all persons exposed to an environmental factor (but not genetically susceptible), or all gene carriers (but not exposed to the environmental factor). Molecular markers may help to differentiate tumors with the same histologic appearance into different etiologic subtypes. Finally, response to treatment may be determined by molecular subtypes of the tumor, or inherited variation in drug metabolism. Examples will be given of how use of molecular techniques is informative in epidemiological studies of cancer and is predicted to lead to improvements in cancer incidence, early detection, and mortality.

Chhabra, S. K., V. L. Souliotis, et al. (1996). "Nitrosamines, alcohol, and gastrointestinal tract cancer: recent epidemiology and experimentation." In Vivo **10**(3): 265-84.

Recent epidemiological and experimental data continues to implicate nitrosamines in causation of gastrointestinal cancers. The evidence is strong for pharynx, esophagus, and stomach, and more problematic for liver, pancreas, and colorectum. Substantial levels of the promutagenic DNA adduct, Ob-methylguanine, in DNA from these organs in patas monkeys after a low dose of N-nitrosodimethylamine confirms the capacity for activation of environmental nitrosamines in these primate tissues. Alcohol is both an independent and a tobacco-interactive risk factor, influencing cancer incidence for oropharynx and

esophagus strongly, and for stomach, colorectum, and liver more moderately. In a tabulation of experimental effects of ethanol potentially related to cancer-enhancing effects, toxicokinetic inhibition of hepatic first-pass clearance of nitrosamines is quantitatively greatest, and may be a major part of the mechanism of alcohol's effect on cancer risk for oropharnx, esophagus, and colon. Other operative mechanisms supported by experimental data are induction of activating enzymes, inhibition of DNA repair, and tumor promotion.

Christiani, D. C. (2000). "Smoking and the molecular epidemiology of lung cancer." Clin Chest Med **21**(1): 87-93, viii.

Lung carcinogenesis in humans requires exposure to environmental agents, including the inhalation of tobacco smoke, radioactive compounds, asbestos, heavy metals, and petrochemicals. Tobacco smoking is the risk factor with the highest attributable lung cancer risk worldwide. This article discusses occupational carcinogen exposure and exposure from tobacco use, and the lung-cancer risk associated with these types of exposure.

Chuang, S. C., C. La Vecchia, et al. (2009). "Liver cancer: descriptive epidemiology and risk factors other than HBV and HCV infection." Cancer Lett **286**(1): 9-14.

The incidence of liver cancer is high in all low-resource regions of the world, with the exception of Northern Africa and Western Asia. The estimated worldwide number of new cases of liver cancer in 2002 is 600,000, of which 82% are from developing countries. Given the poor survival from this disease, the estimated number of deaths is similar to that of new cases. Hepatocellular carcinoma (HCC) is the main form of liver cancer. A part from chronic infections with Hepatitis B and Hepatitis C viruses, which are the main causes of HCC, contamination of foodstuff with aflatoxins, a group of mycotoxins produced by the fungi Aspergillus flavus and Aspergillus parasiticus, is an important contributor to HCC burden in many low-income country. Alcoholic cirrhosis is an important risk factor for HCC in populations with low prevalence of HBV and HCV infection, and the association between tobacco smoking and HCC is now established. Diabetes is also related to an excess risk of HCC and the increased prevalence of overweight and obesity likely contributes to it. The second most important type of liver cancer is cholangiocarcinoma, whose main known cause is infestation with the liver flukes, Opistorchis viverrini and Clonorchis sinensis, which is frequent in some areas in South-East Asia. Angiosarcoma is a rare form of liver cancer whose occurence is linked to occupational exposure to vinyl chloride.

Cohen, S. M. and S. L. Johansson (1992). "Epidemiology and etiology of bladder cancer." Urol Clin North Am **19**(3): 421-8.

Urinary bladder cancer has long been associated with specific etiologic factors, and our knowledge of these factors has increased during this century. The most important factor, even in industrialized societies, is cigarette smoking. Specific chemicals have also been identified as causing bladder cancer, as have a variety of occupational exposures to less well-defined specific agents. In other parts of the world, the association of bladder cancer with Balkan nephropathy, endemic blackfoot disease, and schistosomiasis provides additional leads for investigating, and potentially preventing, the process of carcinogenesis in humans. Many of the critical observations in our understanding of bladder cancer have been made by practicing physicians, and this is likely to continue. It is essential that physicians dealing with bladder cancer patients be attuned to potential etiologic factors, including cigarette smoking, various industrial exposures, or drug exposures to further our understanding of this issue. Bladder cancer is a potentially preventable disease and an important one, as indicated by the total number of cases and the extent of morbidity and death attributable to it around the world.

Cote, T. R., A. Manns, et al. (1996). "Epidemiology of brain lymphoma among people with or without acquired immunodeficiency syndrome. AIDS/Cancer Study Group." J Natl Cancer Inst **88**(10): 675-9.

BACKGROUND: In recent years, brain lymphoma incidence has dramatically increased, presumably because of elevated risk of brain lymphoma among persons with acquired immunodeficiency syndrome (AIDS). PURPOSE: The objective of this study was to estimate independent incidence and survival rates of brain lymphoma among persons with or without AIDS and to understand the epidemiologic features of this cancer. METHODS: We linked AIDS and cancer registry reports at nine state and local health departments and compared the demographics, histology, and survival of brain lymphoma cases among persons with or without AIDS. The data were limited to people under 70 years of age. We calculated the incidence of brain lymphoma among persons with AIDS and compared observed cases with those expected. The differences were statistically analyzed using the Poisson test. Epidemiologic features of brain lymphoma in persons with or without AIDS were compared using the chi-squared test, the Student's t test, and the chi-squared

test for linear trend. The logrank test was used to compare survival rates estimated by the Kaplan-Meier technique. All P values were two-sided. RESULTS: We matched 50,989 AIDS registry reports to 859,398 cancer registry reports (data from 1981 to 1990) and found 431 people with both AIDS and brain lymphoma. Among people with AIDS, those developing brain lymphoma versus those without brain lymphoma were more likely to be white (70% versus 59%; P < .001) and had homosexuality as their only human immunodeficiency virus risk factor (75% versus 64%; P < .001). Of the 431 patients, 223 developed brain lymphomas during 47,465 person-years of observation after diagnosis of AIDS. The absolute incidence rate of brain lymphoma among persons with AIDS was 4.7/1000 person-years (95% confidence interval = 4.1-5.3/1000 person-years), 3600-fold higher than the base-line rate in the general population. From 1980 through 1989, overall counts of brain lymphoma increased ninefold. Most of this increase was derived from persons with AIDS, but a substantial increase also occurred among persons without AIDS (0.04/100,000 in 1982 to 0.28/100,000 in 1989) (chi-squared test for trend; P < .05). The median survival was shortest for persons with AIDS and brain lymphoma (2 months), was intermediate for persons with brain lymphoma without AIDS (5-7 months), and was longest for persons with AIDS without brain lymphoma (14 months) (P < .05 for all comparisons). CONCLUSIONS: This analysis distinguishes the separate epidemiologies of brain lymphoma incidence among persons with or without AIDS and shows brain lymphoma incidence among persons with AIDS to be several thousand-fold higher than that in the general population. The study documents the overwhelming effect of AIDS-associated brain lymphoma on the overall rate in the general population and demonstrates a significantly rising trend, although of a lesser magnitude, among persons without AIDS. IMPLICATIONS: This study emphasizes a greater need to bring health care resources to this burgeoning epidemic.

Cresanta, J. L. (1992). "Epidemiology of cancer in the United States." Prim Care **19**(3): 419-41.

Malignant neoplasms are responsible for more than half a million deaths annually and 22.5% of all deaths in the United States. Cancer is the second leading cause of death overall and the leading cause of death among Americans aged 35-64. Within the next decade it may become the leading cause of death. Cancers of digestive and respiratory organs are responsible for 53% of all cancer deaths. Certain subgroups are at elevated risk for various cancers. For example, sun-sensitive or excessively sun-exposed young white adults, young black women, and elderly patients are at increased risk for cutaneous melanoma, breast cancer, and colon cancer, respectively. Black men have the greatest risk for both lung cancer and cancer of the prostate. Acute lymphoblastic leukemia and solid tumors of the brain and nervous system are the most frequent forms of malignancy occurring among children less than or equal to 14 years. Office screening is the traditional method for identifying cancer victims as early as possible. A suitable screening test should be rapid, simple, inexpensive, and impose minimal discomfort. There must be a window of opportunity available to identify the cancer during a detectable preclinical phase, and therapeutic modalities must be available to alter progression. An office screening test for cancer may have any one of four outcomes, and three of them are bad. False negatives are the worst adverse outcome because cancer remains undetected despite screening. An epidemic of lung cancer, caused by cigarette smoking, is occurring in all race and sex groups. If Americans stopped smoking, 87% of lung cancer deaths could be prevented. Tobacco abuse also is a major risk factor for cancer of the esophagus, larynx, and oral cavity. Cigarette smoking is a contributing factor for cancer of the bladder, kidney, and pancreas, and it has been associated with both cervical cancer and cancer of the stomach. Smoking and smokeless tobacco cessation endorsements, messages, and programs must be part of routine disease prevention and health promotion activities in every primary care practice. More than 1 million Americans became new cancer victims last year, and more than 1 million additional cases will be detected this year. Because of the striking variability in state and regional patterns of various forms of cancer, geographic location of a practice may influence the frequency of cancers seen. Four sites (breast, prostate, lung, colon, and rectum) were responsible for 55% of cancer mortality and 56% of all new cases of cancer detected during 1991.(ABSTRACT TRUNCATED AT 400 WORDS)

Crucitti, F., L. Sofo, et al. (1995). "Colorectal cancer. Epidemiology, etiology, pathogenesis and prevention." Rays **20**(2): 121-31.

Colorectal cancer (CRC) is a neoplasm with a steadily growing incidence in Western countries. Moreover the age of 50 and over is a critical risk factor. The relationship between dietary, environmental factors and CRC has been evaluated. At present, a number of genetic risk factors such as the genetic susceptibility, tumor suppressor genes and oncogenes are thought to play a major role. The correlation of CRC with adenomatous polyps and chronic inflammatory disease, ulcerative colitis in particular, has been evaluated. Prevention of CRC is

mainly based on a rational diet and in the adoption of mass screening programmes.

Curado, M. P. and M. Hashibe (2009). "Recent changes in the epidemiology of head and neck cancer." Curr Opin Oncol **21**(3): 194-200.

PURPOSE OF REVIEW: To review the most recent epidemiological studies on head and neck cancer and changes in knowledge about risk factors. The main review concerned the squamous cell carcinoma of the oral cavity, oropharynx, larynx and hypopharynx. RECENT FINDINGS: Overall, the incidence of head and neck cancer is increasing in women, whereas it is decreasing in men. Chewing tobacco is a newly recognized risk factor of great public health concern. Human papillomavirus infection has been found to be a factor of good prognosis for oral cavity and oropharynx squamous cell cancer. The role of tobacco smoking and alcohol in the genesis of this cancer has been reinforced. SUMMARY: The presence or absence of human papillomavirus in patients with squamous cell carcinoma of the head and neck is a new parameter for prediction of long-term outcome of cancer of the oral cavity and of the oropharynx. Head and neck cancer among women in developing countries should deserve more attention, as the mortality rates appear to be higher than those of women in developed countries. For never smokers and never drinkers, more research needs to be done to identify their risk factor patterns.

Damber, J. E. (1998). "Prostate cancer: epidemiology and risk factors." Curr Opin Urol **8**(5): 375-80.

After years of rapid increase, the incidence of prostate cancer has begun to decline in certain areas in the USA. Although these temporal trends are consistent with the impact of screening, it still remains to be shown that early detection programmes and screening will result in a reduced mortality rate from this disease. A positive family history of prostate cancer has been established as an important risk factor, and recent research supports and points to the existence of a subgroup of prostate cancer families with a hereditary form of the disease. Diet is another well-known risk factor. Recently, it has become evident that nutritional factors might both prevent the progression of prostate cancer or induce it.

Dijkman, G. A. and F. M. Debruyne (1996). "Epidemiology of prostate cancer." Eur Urol **30**(3): 281-95.

Prostate cancer is currently one of the most common malignancies worldwide. The incidence of prostate cancer has risen dramatically over the last decade, more so than can be explained by increasing longevity. Mortality rates have also risen, though not as dramatically. There is a wide geographic variation in the incidence of clinical prostate cancer, with higher rates in the United States than in China. One risk factor which could explain this variation is the high fat intake associated with a Western diet. It is also apparent that prostate cancer is now being detected at less advanced stages than in the past. Increased awareness of the disease and improved detection methods are thought to contribute to this earlier detection.

dos Santos Silva, I. and A. J. Swerdlow (1993). "Thyroid cancer epidemiology in England and Wales: time trends and geographical distribution." Br J Cancer **67**(2): 330-40.

Thyroid cancer incidence has been increasing in many countries, whereas mortality has been falling due to better survival. Radiation is the best-established risk factor and there has been concern that recent rises in incidence might be related to fallout radiation from atmospheric nuclear weapon tests. We examined thyroid cancer time trends and geographical distribution in England and Wales and possible interpretations of these. During 1962-84, there were significant increases in incidence ($P < 0.001$) in each sex at ages under 45. Cohort analysis by single year of birth showed an overall increase in incidence risks in women aged 0-44 born since 1920, with a sudden rise in risk for the birth years 1952-55 followed by a lower risk for the more recent cohorts. In men, there was an overall increase in risk at ages 0-44 in successive birth cohorts, but the pattern was irregular. In each sex, the risk in persons aged 45 and over decreased slightly in successive generations. Geographically, highest incidence risks were in countries in North and Mid Wales, in which the risk was almost twice that in the rest of the country. This pattern was present only at ages 45 and over and was most clear in rural areas. The peak of thyroid cancer risk in women born in 1952-55 is consistent with a carcinogenic effect of fallout radiation, since these women were children in the late 1950s and early 1960s when fallout radiation was greatest in England and Wales. The focus of high thyroid cancer risks in Wales was in areas with high levels of fallout radiation. However, thyroid cancer risks in Wales were not high for more recent cohorts (the ones who were exposed to fallout early in life), and a focus on high risk of benign thyroid diseases was present in Wales well before nuclear weapons existed. The distributions of these benign thyroid diseases, or of factors causing them, seem more likely than fallout to explain the high risk areas for thyroid cancer in the country.

Fincham, S. M., A. M. Ugnat, et al. (2000). "Is occupation a risk factor for thyroid cancer? Canadian

Cancer Registries Epidemiology Research Group." J Occup Environ Med **42**(3): 318-22.

A Canadian case-control study explored the etiology of thyroid cancer, including occupational exposure. Analysis of job history from 1272 thyroid cancer patients and 2666 controls revealed statistically significant risks among the following occupations: Wood Processing, Pulp and Papermaking (odds ratio [OR] = 2.54, 95% confidence interval [CI] = 1.11-5.83); Sales and Service (OR = 1.26, 95% CI = 1.05-1.52); and Clerical (OR = 0.81, 95% CI = 0.67-0.97). ORs were adjusted for age, sex, province, cigarette smoking, education, self-reported exposure to radiation at work, and duration of employment. Exposure to ionizing radiation or electromagnetic fields at work (inferred from job histories) did not affect risk, nor did socioeconomic status, measured by education, income, or occupational prestige. Possible explanations for the results and further investigations are discussed.

Friedberg, J. S. and L. R. Kaiser (1997). "Epidemiology of lung cancer." Semin Thorac Cardiovasc Surg **9**(1): 56-9.

Lung cancer is the leading cause of cancer deaths for men and women in the United States, accounting for more cancer deaths since 1930 than all other cancer deaths combined. Whereas primary lung cancer was a relatively rare malignancy in the early 1900s, in 1994 there were approximately 170,000 new cases of lung cancer in the United States, of which roughly 100,000 were in men and 70,000 were in women. Despite numerous medical and surgical advances in the past several decades, there has not been a dramatic increase in the percentage of patients being cured of this lethal disease. Smoking is the primary factor responsible for the lung cancer epidemic, but there are numerous other environmental and genetic factors that have been implicated in the pathogenesis of the disease. Recently, it has become evident that passive smoking may also play a significant role in the development of lung cancer. Although screening has not been proven effective in the past, it may be time to reevaluate this technique because early detection of lung cancer affords the best chance for cure.

Fu, J. B., T. Y. Kau, et al. (2005). "Lung cancer in women: analysis of the national Surveillance, Epidemiology, and End Results database." Chest **127**(3): 768-77.

OBJECTIVES: In order to further characterize the effect of gender on the clinicopathologic features and survival of patients with lung cancer, and to determine gender-associated differences in temporal trends, we analyzed data that had been entered into a population-based cancer database. PATIENTS AND METHODS: Data on demographics, stage at diagnosis, histology, initial therapy, and survival were obtained on all patients with primary bronchogenic carcinoma registered in the national Surveillance, Epidemiology, and End Results database from 1975 to 1999. RESULTS: Of the 228,572 eligible patients, 35.8% were female. The median age at diagnosis was 66 years for both men and women. However, women accounted for 40.9% of patients who were < 50 years of age and for 35.4% of older patients. The incidence of lung cancer in men peaked at 72.5 per 100,000 person-years in 1984 and then declined to 47 per 100,000 person-years by 1999. In women, the incidence continued to rise to a peak of 33.1 per 100,000 person-years in 1991 before reaching a plateau at 30.2 to 32.3 per 100,000 person-years from 1992 to 1999. These changes have resulted in a marked narrowing of the male/female incidence ratio from 3.56 in 1975 to 1.56 in 1999. As initial treatment, women with local disease underwent surgery more frequently than did men. Stage-specific survival rates were better for women at all stages of disease ($p < 0.0001$). In a multivariate analysis, male gender was an independent negative prognostic factor ($p < 0.0001$). CONCLUSION: The incidence rate of lung cancer in women in the United States has reached a plateau. However, women are relatively overrepresented among younger patients, raising the question of gender-specific differences in the susceptibility to lung carcinogens. At each stage of the disease, the relative survival of women is better than that of men, with the largest difference noted in patients with local disease.

Garte, S., C. Zocchetti, et al. (1997). "Gene--environment interactions in the application of biomarkers of cancer susceptibility in epidemiology." IARC Sci Publ(142): 251-64.

Metabolic susceptibility genes are important determinants of individual susceptibility to the effects of environmental carcinogens. These genes follow the form of 'type 2' gene-environment interaction, whereby the polymorphic genetic risk factor functions only in the presence of an environmental exposure. Two different effects of carcinogen dose have been observed for these genes. Sometimes, increasing dose leads to a decreasing interaction, so that cases with the genetic risk factor have lower exposures than those cases without it. Other examples of a direct dose effect, whereby increasing exposure leads to increased interaction, have also been described. We propose a model based on multiple logistic regression to assess the nature of the dose effect in this type of gene-environment interaction. This model allows for distinction between these two dose effects, and other

effects such as protective or non-interactive effects of environmental and genetic risk factors.

Gilbert, S. M. and J. M. McKiernan (2005). "Epidemiology of male osteoporosis and prostate cancer." Curr Opin Urol **15**(1): 23-7.

PURPOSE OF REVIEW: In this review, we will discuss the increasing importance of male osteoporosis, risk factors for the disease, its relationship to prostate cancer and androgen deprivation treatment modalities for prostate cancer, and recent trials describing therapeutic intervention. RECENT FINDINGS: Osteoporosis has become an increasingly important problem in men's health, accounting for significant morbidity in the aging United States male population. Hypogonadism is a major risk factor. Patients treated with androgen deprivation therapy for advanced or metastatic prostate cancer are at risk for both hypogonadism and osteoporosis. These patients may suffer additional morbidity from decreased bone mineralization, such as skeletal fracture. There is a direct association with fracture and decreased quality of life and increased mortality. SUMMARY: Male osteoporosis is an important clinical entity, particularly in aging men and in men with prostate cancer treated with androgen deprivation therapy. No screening recommendations currently exist; however, patients at risk for decreased bone mineralization should be screened and treated to prevent consequent fractures.

Glaser, S. L., C. A. Clarke, et al. (2005). "Cancer surveillance research: a vital subdiscipline of cancer epidemiology." Cancer Causes Control **16**(9): 1009-19.

Public health surveillance systems relevant to cancer, centered around population-based cancer registration, have produced extensive, high-quality data for evaluating the cancer burden. However, these resources are underutilized by the epidemiology community due, we postulate, to under-appreciation of their scope and of the methods and software for using them. To remedy these misperceptions, this paper defines cancer surveillance research, reviews selected prior contributions, describes current resources, and presents challenges to and recommendations for advancing the field. Cancer surveillance research, in which systematically collected patient and population data are analyzed to examine and test hypotheses about cancer predictors, incidence, and outcomes in geographically defined populations over time, has produced not only cancer statistics and etiologic hypotheses but also information for public health education and for cancer prevention and control. Data on cancer patients are now available for all US states and, within SEER, since 1973, and have been enhanced by linkage to other population-based resources. Appropriate statistical methods and sophisticated interactive analytic software are readily available. Yet, publication of papers, funding opportunities, and professional training for cancer surveillance research remain inadequate. Improvement is necessary in these realms to permit cancer surveillance research to realize its potential in resolving the growing cancer burden.

Greenwald, P. and B. K. Dunn (2009). "Landmarks in the history of cancer epidemiology." Cancer Res **69**(6): 2151-62.

The application of epidemiology to cancer prevention is relatively new, although observations of the potential causes of cancer have been reported for more than 2,000 years. Cancer was generally considered incurable until the late 19th century. Only with a refined understanding of the nature of cancer and strategies for cancer treatment could a systematic approach to cancer prevention emerge. The 20th century saw the elucidation of clues to cancer causation from observed associations with population exposures to tobacco, diet, environmental chemicals, and other exogenous factors. With repeated confirmation of such associations, researchers entertained for the first time the possibility that cancer, like many of the infectious diseases of the time, might be prevented. By the mid-20th century, with antibiotics successfully addressing the majority of infectious diseases and high blood pressure treatment beginning to affect the prevalence of heart disease in a favorable direction, the focus of much of epidemiology shifted to cancer. The early emphasis was on exploring, in greater depth, the environmental, dietary, hormonal, and other exogenous exposures for their potential associations with increased cancer risk. The first major breakthrough in identifying a modifiable cancer risk factor was the documentation of an association between tobacco smoking and lung cancer. During the past four decades, epidemiologic studies have generated population data identifying risk factors for cancers at almost every body site, with many cancers having multiple risk factors. The development of technologies to identify biological molecules has facilitated the incorporation of these molecular manifestations of biological variation into epidemiologic studies, as markers of exposure as well as putative surrogate markers of cancer outcome. This technological trend has, during the past two decades, culminated in emphasis on the identification of genetic variants and their products as correlates of cancer risk, in turn, creating opportunities to incorporate the discipline of molecular/genetic epidemiology into the study of cancer prevention. Epidemiology will undoubtedly continue contributing

to cancer prevention by using traditional epidemiologic study designs to address broad candidate areas of interest, with molecular/genetic epidemiology investigations honing in on promising areas to identify specific factors that can be modified with the goal of reducing risk.

Gunter, M. J. and M. F. Leitzmann (2006). "Obesity and colorectal cancer: epidemiology, mechanisms and candidate genes." J Nutr Biochem **17**(3): 145-56.

There is increasing evidence that dysregulation of energy homeostasis is associated with colorectal carcinogenesis. Epidemiological data have consistently demonstrated a positive relation between increased body size and colorectal malignancy, whereas mechanistic studies have sought to uncover obesity-related carcinogenic pathways. The phenomenon of "insulin resistance" or the impaired ability to normalize plasma glucose levels has formed the core of these pathways, but other mechanisms have also been advanced. Obesity-induced insulin resistance leads to elevated levels of plasma insulin, glucose and fatty acids. Exposure of the colonocyte to heightened concentrations of insulin may induce a mitogenic effect within these cells, whereas exposure to glucose and fatty acids may induce metabolic perturbations, alterations in cell signaling pathways and oxidative stress. The importance of chronic inflammation in the pathogenesis of obesity has recently been highlighted and may represent an additional mechanism linking increased adiposity to colorectal carcinogenesis. This review provides an overview of the epidemiology of body size and colorectal neoplasia and outlines current knowledge of putative mechanisms advanced to explain this relation. Family based studies have shown that the propensity to become obese is heritable, but this is only manifest in conditions of excess energy intake over expenditure. Inheritance of a genetic profile that predisposes to increased body size may also be predictive of colorectal cancer. Genomewide scans, linkage studies and candidate gene investigations have highlighted more than 400 chromosomal regions that may harbor variants that predispose to increased body size. The genetics underlying the pathogenesis of obesity are likely to be complex, but variants in a range of different genes have already been associated with increased body size and insulin resistance. These include genes encoding elements of insulin signaling, adipocyte metabolism and differentiation, and regulation of energy expenditure. A number of investigators have begun to study genetic variants within these pathways in relation to colorectal neoplasia, but at present data remain limited to a handful of studies. These pathways will be discussed with particular reference to genetic polymorphisms that have been associated with obesity and insulin resistance.

Gupta, P. C., P. R. Murti, et al. (1996). "Epidemiology of cancer by tobacco products and the significance of TSNA." Crit Rev Toxicol **26**(2): 183-98.

Globally, oral cancer is one of the ten common cancers. In some parts of the world, including the Indian subcontinent, oral cancer is a major cancer problem. Tobacco use is the most important risk factor for oral cancer. The most common form of tobacco use, cigarette smoking, demonstrates a very high relative risk--in a recent cohort study (CPS II), even higher than lung cancer. In areas where tobacco is used in a smokeless form, oral cancer incidence is generally high. In the West, especially in the U.S. and Scandinavia, smokeless tobacco use consists of oral use of snuff. In Central, South, and Southeast Asia smokeless tobacco use encompasses nass, naswar, khaini, mawa, mishri, gudakhu, and betel quid. In India tobacco is smoked in many ways; the most common is bidi, others being chutta, including reverse smoking, hooka, and clay pipe. A voluminous body of research data implicating most of these forms of tobacco use emanates from the Indian subcontinent. These studies encompass case and case-series reports, and case-control, cohort, and intervention studies. Collectively, the evidence fulfills the epidemiological criteria of causality: strength, consistency, temporality, and coherence. The biological plausibility is provided by the identification of several carcinogens in tobacco, the most abundant and strongest being tobacco-specific N-nitrosamines such as N-nitrosonornicotine (NNN) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK). These are formed by N-nitrosation of nicotine, the major alkaloid responsible for addiction to tobacco. The etiological relationship between tobacco use and oral cancer has provided us with a comprehensive model for understanding carcinogenesis.

Hall, J., M. Artuso, et al. (1996). "Molecular epidemiology of skin cancers: DNA repair and non-melanocytic skin cancer." Ann Ist Super Sanita **32**(1): 43-51.

Exposure to sunlight has been clearly associated with non-melanocytic skin cancer, however individual susceptibility differs considerably. Ethnic origin and pigmentary characteristics are generally accepted as risk factors. Another important defense mechanism is the ability to repair DNA photoproducts. In the inherited disorder xeroderma pigmentosum the inability to repair such DNA damage, associated with a high incidence of skin cancers, suggests an important role for DNA repair capacity in the etiology of this cancer. The

development of an in vitro repair assay based on human peripheral blood lymphocytes, has allowed the evaluation of DNA repair capacity as a risk factor in population based studies. This article reviews recent developments in this field.

Hashibe, M., P. Brennan, et al. (2007). "Alcohol drinking in never users of tobacco, cigarette smoking in never drinkers, and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium." J Natl Cancer Inst **99**(10): 777-89.

BACKGROUND: At least 75% of head and neck cancers are attributable to a combination of cigarette smoking and alcohol drinking. A precise understanding of the independent association of each of these factors in the absence of the other with the risk of head and neck cancer is needed to elucidate mechanisms of head and neck carcinogenesis and to assess the efficacy of interventions aimed at controlling either risk factor. METHODS: We examined the extent to which head and neck cancer is associated with cigarette smoking among never drinkers and with alcohol drinking among never users of tobacco. We pooled individual-level data from 15 case-control studies that included 10,244 head and neck cancer case subjects and 15,227 control subjects, of whom 1072 case subjects and 5775 control subjects were never users of tobacco and 1598 case subjects and 4051 control subjects were never drinkers of alcohol. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using unconditional logistic regression models. All statistical tests were two-sided. RESULTS: Among never drinkers, cigarette smoking was associated with an increased risk of head and neck cancer (OR for ever versus never smoking = 2.13, 95% CI = 1.52 to 2.98), and there were clear dose-response relationships for the frequency, duration, and number of pack-years of cigarette smoking. Approximately 24% (95% CI = 16% to 31%) of head and neck cancer cases among nondrinkers in this study would have been prevented if these individuals had not smoked cigarettes. Among never users of tobacco, alcohol consumption was associated with an increased risk of head and neck cancer only when alcohol was consumed at high frequency (OR for three or more drinks per day versus never drinking = 2.04, 95% CI = 1.29 to 3.21). The association with high-frequency alcohol intake was limited to cancers of the oropharynx/hypopharynx and larynx. CONCLUSIONS: Our results represent the most precise estimates available of the independent association of each of the two main risk factors of head and neck cancer, and they exemplify the strengths of large-scale consortia in cancer epidemiology.

Hawk, E. T., P. J. Limburg, et al. (2002). "Epidemiology and prevention of colorectal cancer." Surg Clin North Am **82**(5): 905-41.

CRC, the second-leading cause of cancer death in the United States, is a highly preventable disease. Ironically, available and effective screening technologies are not consistently applied, even as new ones are developed. This discordance between preventive opportunity and practice conveys a sobering message regarding nontechnologic issues that must be addressed if the promise of CRC prevention is to be realized. Our response to this message will determine the public health impact of cancer prevention. In the 1980s, cancer chemoprevention was regarded as scientific speculation. Within the last decade, however, cancer has been recognized as a late, nonobligate stage of carcinogenesis, a chronic process that provides time and targets for preventive intervention. Further advances are emerging out of rigorous clinical testing, which remains the limiting factor in transforming ingenious concepts into useful tools for the prevention of CRC. The challenges and rewards of participation in chemoprevention research--both as patients and health care providers-have never been greater.

Holschneider, C. H. and J. S. Berek (2000). "Ovarian cancer: epidemiology, biology, and prognostic factors." Semin Surg Oncol **19**(1): 3-10.

Ovarian cancer varies widely in frequency among different geographic regions and ethnic groups, with a high incidence in Northern Europe and the United States, and a low incidence in Japan. The majority of cases are sporadic, and only 5% to 10% of ovarian cancers are familial. The etiology of ovarian cancer is poorly understood. Models of ovarian carcinogenesis include the theory of incessant ovulation, in which a person's age at ovulation, i.e., lifetime number of ovulatory cycles, is an index of her ovarian cancer risk. Excessive gonadotropin and androgen stimulation of the ovary have been postulated as contributing factors. Exposure of the ovaries to pelvic contaminants and carcinogens may play a role in the pathogenesis of ovarian cancer. Epidemiologic and molecular-genetic studies identify numerous risk and protective factors. The most significant risk factor is a family history of the disease. Recent advances in molecular genetics have found mutations in the BRCA1 and BRCA2 tumor suppressor genes responsible for the majority of hereditary ovarian cancer. Additional risk factors include nulliparity and refractory infertility. Protective factors include multiparity, oral contraceptives, and tubal ligation or hysterectomy. With five years of oral contraceptive use, women can cut their risk of ovarian

cancer approximately in half; this also holds true for individuals with a family history. Stage at diagnosis, maximum residual disease following cytoreductive surgery, and performance status are the three major prognostic factors. Using a multimodality approach to treatment, including aggressive cytoreductive surgery and combination chemotherapy, five-year survival rates are as follows: Stage I (93%), Stage II (70%), Stage III (37%), and Stage IV (25%).

Hortobagyi, G. N., J. de la Garza Salazar, et al. (2005). "The global breast cancer burden: variations in epidemiology and survival." Clin Breast Cancer **6**(5): 391-401.

Breast cancer is the most common type of cancer and the most common cause of cancer-related mortality among women worldwide. However, the burden is not evenly distributed, and, according to the best available data, there are large variations in the incidence, mortality, and survival between different countries and regions and within specific regions. Many complex factors underlie these variations, including population structure (eg, age, race, and ethnicity), lifestyle, environment, socioeconomic status, risk factor prevalence, mammography use, disease stage at diagnosis, and access to high-quality care. We review recent breast cancer incidence and mortality statistics and explore why these vary so greatly across the world. Further research is needed to fully understand the reasons for variations in breast cancer outcomes. This will aid the development of tailored strategies to improve outcomes in general as well as the standard of care for underserved populations and reduce the burden of breast cancer worldwide.

Igisinov, S., E. Soodonbekov, et al. (2002). "Epidemiology of Esophagus, Lung and Breast Cancer in Mountainous Regions of Kyrgyz Republic." Asian Pac J Cancer Prev **3**(1): 73-76.

Relative incidences of esophagus, lung and breast cancers differ in the various populations in Kyrgyzstan. Esophagus cancer is the most commonly observed among the Turkic groups, especially in Kazakhs, while lung and breast cancer are frequently encountered among the European representatives of the population - Russians in particular. Fluctuation in rates for these cancer forms in the Kyrgyzstan mountain regions is highly dependable on the height above sea level. One potential major factor, which may account for the low cancer frequency in general and influence esophagus, lung and breast cancer forms in particular - is mountain hypoxia. Since, among the native citizens (Kyrgyzes), which are adapted to mountain hypoxia conditions (population adaptation), the indicated cancer forms are not so often than the same forms appearance among the other ethnical groups (long adaptation), especially newcoming ones. Thus, the incidence rates of esophageal cancer in the Kazakh population is about 32,3 (per 100,000), the same sickness in Kyrgyz is about 11,3, the figure for lung cancer among the Russian population is 34,8, while among Kyrgyzes it is 11,2, breast cancer incidence in Russian citizens is 34,8 but only15,1 among Kyrgyz residents. It could be established that the studied forms of cancer are less common in high mountain regions than in the regions with low mountains. To a certain extent, mountain hypoxia may function like a brake for the development of cancer tumors. HGowever, the situation is complex, because of, the presence of the other factors entailed by the demographic, social-economic and other variation.

Jaga, K. and C. Dharmani (2005). "The epidemiology of pesticide exposure and cancer: A review." Rev Environ Health **20**(1): 15-38.

Cancer is a multifactorial disease with contributions from genetic, environmental, and lifestyle factors. Pesticide exposure is recognized as an important environmental risk factor associated with cancer development. The epidemiology of pesticide exposure and cancer in humans has been studied globally in various settings. Insecticides, herbicides, and fungicides are associated with hemopoetic cancers, and cancers of the prostate, pancreas, liver, and other body systems. The involvement of pesticides in breast cancer has not yet been determined. In developing countries, sufficient epidemiologic research and evidence is lacking to link pesticide exposure with cancer development. Agricultural and industrial workers are high-risk groups for developing cancer following pesticide exposure. Children of farm workers can be exposed to pesticides through their parents. Maternal exposure to pesticides can pose a health risk to the fetus and the newborn. The organophosphates are most the commonly used compounds, but the organochlorines are still permitted for limited use in developing countries. Pesticide exposure, independently or in synergism with modifiable risk factors, is associated with several types of cancer.

Jani, A. B., V. A. Master, et al. (2007). "Grade migration in prostate cancer: an analysis using the Surveillance, Epidemiology, and End Results registry." Prostate Cancer Prostatic Dis **10**(4): 347-51.

To utilize the Surveillance, Epidemiology, and End Results (SEER) registry to examine trends in grade assignment. Data from 411 325 patients from 1984 to 2003 were analyzed for grade migration and for cause-specific survival (CSS) as a function of grade. There has been a significant grade migration

during the study period (P<0.001), principally from well-differentiated (WD) to moderately differentiated (MD) disease. Five-year CSS of MD and WD patients have converged, suggesting a decreasing role of grade as a prognostic factor. A grade migration from WD to MD assignment has occurred, suggesting that prognostic categorizations based on grade across eras may be difficult to interpret.

Jarup, L., N. Best, et al. (2002). "Geographical epidemiology of prostate cancer in Great Britain." Int J Cancer **97**(5): 695-9.

Prostate cancer incidence has increased during recent years, possibly linked to environmental exposures. Exposure to environmental carcinogens is unlikely to be evenly distributed geographically, which may give rise to variations in disease occurrence that is detectable in a spatial analysis. The aim of our study was to examine the spatial variation of prostate cancer in Great Britain at ages 45-64 years. Spatial variation was examined across electoral wards from 1975-1991. Poisson regression was used to examine regional, urbanisation and socioeconomic effects, while Bayesian mapping techniques were used to assess spatial variability. There was an indication of geographical differences in prostate cancer risk at a regional level, ranging from 0.83 (95% CI: 0.78-0.87) to 1.2 (95% CI: 1.1-1.3) across regions. There was significant heterogeneity in the risk across wards, although the range of relative risks was narrow. More detailed spatial analyses within 4 regions did not indicate any clear evidence of localised geographical clustering for prostate cancer. The absence of any marked geographical variability at a small-area scale argues against a geographically varying environmental factor operating strongly in the aetiology of prostate cancer.

Johansson, S. L. and S. M. Cohen (1997). "Epidemiology and etiology of bladder cancer." Semin Surg Oncol **13**(5): 291-8.

The incidence of bladder cancer continues to increase, with an estimated 53,000 new cases diagnosed in the United States in 1996-90% of which are transitional cell carcinomas. The male-to-female ratio is 3:1. A number of etiological factors are associated with the development of bladder cancer, but in industrialized countries, cigarette smoking is the most important. Specific chemicals have also been identified as causing bladder cancer, as have a number of occupational exposures to less well-defined specific agents. Treatment with cytostatic drugs, especially cyclophosphamide, is associated with increased risk of bladder cancer, as is treatment with radiotherapy for uterine cancer. In developing countries, especially in the Middle East and parts of Africa, infections with members of the genus Schistosoma are responsible for a high incidence of bladder cancer-75% of which are squamous cell carcinomas. Arsenic has been indicated as a bladder carcinogen in Argentina, Chile, and Taiwan. The reason for the high incidence of urinary tract cancer in individuals suffering from Balkan nephropathy has yet to be determined. A careful history of patients with bladder cancer is an important and useful process in helping to identify causal factor and, in more than one-half the cases, a known relationship is found. Bladder cancer is a potentially preventable disease, with a significant morbidity and mortality in many parts of the world.

Kabat, G. C. (1996). "Aspects of the epidemiology of lung cancer in smokers and nonsmokers in the United States." Lung Cancer **15**(1): 1-20.

While it is well-established that smoking is the predominant risk factor for lung cancer, it is clear that factors other than smoking and occupational exposure play a role in some lung cancers, and particularly adenocarcinoma. Data from a large, hospital-based case-control study are used to examine the association of smoking-related risk factors (amount smoked, filter status, mentholation, and differences in smoking habits between blacks and whites) and selected factors other than smoking (environmental tobacco smoke, previous primary cancer and radiotherapy, reproductive and endocrine factors, and body mass index) with lung cancer. Although smoking shows a dose-response relationship with all major lung cancer cell types, the strength of the relationship is weaker for adenocarcinoma, suggesting that other risk factors must play an important role for this cell type. In blacks and whites of both sexes, odds ratios for lung cancer increased with increasing cumulative tobacco tar intake and decreased with years since quitting smoking. Use of mentholated cigarettes was associated with no greater risk for lung cancer than that associated with the use of nonmentholated cigarettes. Exposure to environmental tobacco smoke generally showed little relation to lung cancer risk. In particular, exposure of nonsmoking wives to a husband's smoking showed no increase in risk. A history of a reproductive primary cancer and a history of radiotherapy were each associated with a fourfold increase in risk in female nonsmokers. An association of lean body mass with lung cancer was observed in current smokers, ex-smokers, and female never smokers. These results are discussed in the context of existing studies. In conclusion, variation in lung cancer rates between populations may be due to: (1) differences in effective exposure to tobacco smoke carcinogens; (2) differences in factors which modify the effect of tobacco smoke, including differences in host

susceptibility and metabolism of carcinogens, or (3) differences in exposure to other independent risk factors for lung cancer.

Kikuchi, S. (2002). "Epidemiology of Helicobacter pylori and gastric cancer." Gastric Cancer **5**(1): 6-15.

Findings in epidemiological studies of the relationship between Helicobacter pylori and gastric cancer have been inconsistent: many studies have yielded a positive relationship, whereas several studies have shown no relationship. The inconsistency arises because of the occurrence of seroreversion during the period between the time that H. pylori exerts a carcinogenic effect and the time of blood sampling. When this seroreversion is taken into account, there is an epidemiologically positive association between H. pylori status and the risk for gastric cancer. In addition to the epidemiological evidence, experimental studies using Mongolian gerbils have shown that H. pylori infection elevates the risk for gastric cancer. It is concluded that H. pylori is a causal factor for gastric cancer. In the creation of preventive strategies against gastric cancer by the eradication of H. pylori, determination of the time at which H. pylori plays a role as a carcinogen is important. Three hypotheses have been proposed in regard to this timing: that H. pylori infection in childhood or the teenage years acts as a factor that produces precancerous lesions with irreversible damage in the gastric mucosa, that in adulthood it acts as an initiator, and also in adulthood, that it acts as a promoter. As these hypotheses are not mutually exclusive, the extent to which each hypothesis plays a part in explaining gastric carcinogenesis should be evaluated. Only a small proportion of subjects infected with H. pylori have gastric cancer during their lifetime. Interleukin-1 polymorphism, a host factor, and CagA, a virulence factor of H. pylori, are suspected to be risk factors for gastric cancer in subjects with H. pylori infection. Dietary factors, especially vitamin C, and patterns of precancerous lesions also seem to influence the relationship between H. pylori and gastric cancer. H. pylori seems to reduce the risk for esophageal and for some gastric cardia adenocarcinomas. This finding, as well as determination of the time at which H. pylori exerts this preventive effect, should be considered in the creation of preventive strategies against gastric cancer that target the eradication of H. pylori.

Knight, J. A., L. Bernstein, et al. (2009). "Alcohol intake and cigarette smoking and risk of a contralateral breast cancer: The Women's Environmental Cancer and Radiation Epidemiology Study." Am J Epidemiol **169**(8): 962-8.

Women with primary breast cancer are at increased risk of developing second primary breast cancer. Few studies have evaluated risk factors for the development of asynchronous contralateral breast cancer in women with breast cancer. In the Women's Environmental Cancer and Radiation Epidemiology Study (1985-2001), the roles of alcohol and smoking were examined in 708 women with asynchronous contralateral breast cancer (cases) compared with 1,399 women with unilateral breast cancer (controls). Cases and controls aged less than 55 years at first breast cancer diagnosis were identified from 5 population-based cancer registries in the United States and Denmark. Controls were matched to cases on birth year, diagnosis year, registry region, and race and countermatched on radiation treatment. Risk factor information was collected by telephone interview. Rate ratios and 95% confidence intervals were estimated by using conditional logistic regression. Ever regular drinking was associated with an increased risk of asynchronous contralateral breast cancer (rate ratio = 1.3, 95% confidence interval: 1.0, 1.6), and the risk increased with increasing duration (P = 0.03). Smoking was not related to asynchronous contralateral breast cancer. In this, the largest study of asynchronous contralateral breast cancer to date, alcohol is a risk factor for the disease, as it is for a first primary breast cancer.

Koc, M. and P. Polat (2001). "Epidemiology and aetiological factors of male breast cancer: a ten years retrospective study in eastern Turkey." Eur J Cancer Prev **10**(6): 531-4.

The aim of this study was to assess the epidemiological and aetiological factors of male breast carcinoma in eastern Turkey. For this purpose we evaluated breast carcinoma patients admitted to our regional hospital from 1990 to 2000. A total of 196 patients were admitted during that time, 11 of whom were male (5%). The average age at presentation was 60.7 +/- 7.5. Infiltrating ductal carcinoma was the most frequent histopathological type; lobular carcinoma was detected in only one of our cases. Right-sided male breast carcinoma was seen in 7 of 11 cases, left-sided in four cases. We detected gynaecomastia in two patients. Other factors were excessive alcohol consumption for 35 years in one patient, family history in one patient and exposure to electromagnetic fields (EMFs) and light at night in four patients. We demonstrated no risk factor in the other three cases. Of the patients in our study, the youngest was 45 years old--the patient with post-pubertal gynaecomastia. The overall rate of male breast carcinoma seen among people who had worked for the Turkish Institution of Electricity in eastern Turkey was 0.3%. In our study we demonstrated a close relation between exposure to EMFs and light at night and male breast carcinoma in eastern Turkey.

We also supposed that not only exposure to EMFs but also the duration of the exposure could affect the risk of development of male breast carcinoma.

Kuijken, I. and J. N. Bavinck (2000). "Skin cancer risk associated with immunosuppressive therapy in organ transplant recipients: epidemiology and proposed mechanisms." BioDrugs **14**(5): 319-29.

The aim of this review is to summarise the available literature regarding the epidemiology and proposed mechanisms of skin cancer development in organ transplant recipients who are receiving lifelong treatment with immunosuppressive therapy and to review the different strategies for managing complications in this group of patients. Organ transplantation is complicated by an increased incidence of certain cancers, of which non-Hodgkin's lymphoma, Kaposi's sarcoma and squamous cell carcinoma are the most common. The most important risk factor for these cancers is immunosuppressive therapy. The relative importance of different immunosuppressive therapy regimens in relation to the development of skin cancer is still unclear. Immunosuppression per se may play the most important role, but other mechanisms, which are independent of host immunity and which may be different for the various agents used, may also be of importance for the increased risk of cancer. Apart from immunosuppressive therapy, exposure to sunlight and infection with human papillomaviruses are believed to be the most important risk factors for the development of cutaneous squamous cell carcinoma in organ transplant recipients. Human papillomaviruses, no doubt, benefit considerably from immunosuppression, as is indicated by the large number of warts found in these patients, but many questions remain unanswered about their significance in cutaneous oncogenesis. The E6 protein from a range of cutaneous human papillomavirus types effectively inhibits apoptosis in response to ultraviolet light damage. It is, therefore, conceivable that the development of skin cancer in organ transplant recipients is the result of a complex interplay between exposure to ultraviolet radiation, human papillomavirus infection and genetic predisposition. Measures for protection from the sun are important for reducing the risk of skin cancer in organ transplant recipients. Regular surveillance of patients with skin problems and easy access to a dermatologist for these patients is advised. Changing the immunosuppressive regimen from azathioprine to cyclosporin or vice versa does not seem to relieve the skin problems. Tapering the immunosuppressive therapy to the lowest possible dose may be of some advantage. Oral retinoids, e.g. acitretin, have some effect in reducing the number of keratotic skin lesions and in the prevention of skin cancer in organ transplant recipients. Resurfacing the back of the hand can be a successful treatment for patients with multiple skin cancers on the back of the hand and can be used prophylactically in patients with severely actinically damaged skin.

Kwan, M. L., L. H. Kushi, et al. (2009). "Epidemiology of breast cancer subtypes in two prospective cohort studies of breast cancer survivors." Breast Cancer Res **11**(3): R31.

INTRODUCTION: The aim of this study was to describe breast tumor subtypes by common breast cancer risk factors and to determine correlates of subtypes using baseline data from two pooled prospective breast cancer studies within a large health maintenance organization. METHODS: Tumor data on 2544 invasive breast cancer cases subtyped by estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (Her2) status were obtained (1868 luminal A tumors, 294 luminal B tumors, 288 triple-negative tumors and 94 Her2-overexpressing tumors). Demographic, reproductive and lifestyle information was collected either in person or by mailed questionnaires. Case-only odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using logistic regression, adjusting for age at diagnosis, race/ethnicity, and study origin. RESULTS: Compared with luminal A cases, luminal B cases were more likely to be younger at diagnosis (P = 0.0001) and were less likely to consume alcohol (OR = 0.74, 95% CI = 0.56 to 0.98), use hormone replacement therapy (HRT) (OR = 0.66, 95% CI = 0.46 to 0.94), and oral contraceptives (OR = 0.73, 95% CI = 0.55 to 0.96). Compared with luminal A cases, triple-negative cases tended to be younger at diagnosis (P < or = 0.0001) and African American (OR = 3.14, 95% CI = 2.12 to 4.16), were more likely to have not breastfed if they had parity greater than or equal to three (OR = 1.68, 95% CI = 1.00 to 2.81), and were more likely to be overweight (OR = 1.82, 95% CI = 1.03 to 3.24) or obese (OR = 1.97, 95% CI = 1.03 to 3.77) if premenopausal. Her2-overexpressing cases were more likely to be younger at diagnosis (P = 0.03) and Hispanic (OR = 2.19, 95% CI = 1.16 to 4.13) or Asian (OR = 2.02, 95% CI = 1.05 to 3.88), and less likely to use HRT (OR = 0.45, 95% CI = 0.26 to 0.79). CONCLUSIONS: These observations suggest that investigators should consider tumor heterogeneity in associations with traditional breast cancer risk factors. Important modifiable lifestyle factors that may be related to the development of a specific tumor subtype, but not all subtypes, include obesity, breastfeeding, and alcohol consumption. Future work that will further categorize triple-negative

cases into basal and non-basal tumors may help to elucidate these associations further.

La Vecchia, C. (2001). "Epidemiology of ovarian cancer: a summary review." Eur J Cancer Prev **10**(2): 125-9.

Ovarian cancer is among the five leading sites for cancer incidence and mortality in women from developed countries. Its incidence and mortality rates have, however, been declining over the last few decades following the introduction of oral contraceptives, which - together with parity - are the best recognized protective factor for the disease. Late menopause and irregular menstrual cycles may also reduce the risk, while the role of hormone replacement therapy in menopause and fertility treatments is still unclear. Cosmetic talc use and some aspect of diet (i.e. saturated fats, refined carbohydrates) have been associated with increased risk, in some--though not all--studies), while vegetable consumption appears to be inversely related to risk. These issues remain open to debate. Women with a family history of ovarian and breast cancer in first-degree relatives are also at increased risk, but family history accounts for only 4-5% of cases. Most ovarian cancers are therefore environmental in origin and consequently, at least in principle, avoidable.

La Vecchia, C., L. Chatenoud, et al. (2001). "Nutrition and health: epidemiology of diet, cancer and cardiovascular disease in Italy." Nutr Metab Cardiovasc Dis **11**(4 Suppl): 10-5.

Most epidemiological data suggest a protective role for fruits and vegetables in the prevention of several common epithelial cancers, including digestive and major non-digestive neoplasms. The relation between frequency of consumption of vegetables and fruit and cancer and myocardial infarction risk was analysed using data from a series of case-control studies conducted in Italy. For digestive tract cancer, population attributable risks for low intake of vegetables and fruit ranged between 15 and 40%. A selected number of antioxidants showed a significant inverse relation with breast and colorectal cancer risk, although the main components responsible for the favourable effect of a diet rich in vegetables and fruit remain undefined. Fish tends to be another favourable indicator of reduced cancer risk. In contrast, subjects reporting frequent red meat intake showed a relative risk consistently above unity for several common neoplasms. Whole grain food intake was consistently related to reduced risk of several types of cancer, particularly of the upper digestive tract neoplasms. Epidemiological evidence of the relation between fiber and colorectal cancer indicated a possible protections. In contrast, refined grain intake was associated to increased risk of different types of cancer, pointing to a potential role of insulin-like growth factor 1 (IGF-1). A low risk diet for cardiovascular disease includes high consumption of fish, vegetables and fruit, and hence rich in ascorbic acid and other antioxidants, thus sharing several aspects with a favourable diet for cancer.

La Vecchia, C., F. Levi, et al. (1992). "Descriptive epidemiology of ovarian cancer in Europe." Gynecol Oncol **46**(2): 208-15.

Trends in ovarian cancer mortality over the period 1955-1989 were analyzed for 25 European countries (excluding the Soviet Union and a few small countries) on the basis of the official death certification data from the World Health Organization database. The overall variation in age-standardized ovarian cancer mortality at all ages declined appreciably, from over 17-fold during the period 1955-1959 (i.e., between 10.5/100,000 in Denmark and 0.6/100,000 in Spain, world standard) to 3.4-fold (i.e., between 9.9/100,000 in Denmark and 2.9/100,000 in Spain) in the late 1980s. When a comparison was made between the late 1950s and the 1980s, ovarian cancer mortality increased in most European countries, except Denmark, Sweden, and Switzerland, where certified mortality was already elevated in the late 1950s, although also in these countries the peak rate around or over 10/100,000 was reached during the 1960s. However, when the changes over the last decade were considered, ovarian cancer mortality trends were downward in all Nordic countries, Germany, Switzerland, Austria, and Czechoslovakia. Mortality was rising somewhat, though to a smaller extent, in Ireland, Britain, and Southern Europe. Trends were more favorable in middle-aged women (35 to 64 years), and, to an even greater extent, in young women (aged 20 to 44), among whom substantial declines, particularly over the last decade, were observed in most European countries, approaching 50% in Britain and Scandinavia. These trends are discussed in terms of changes in risk factor exposure (i.e., trends in average parity and oral contraceptive use), diagnostic and therapeutic improvements, ovariectomy, and changes in case ascertainment and certification.

Lawes, C. M., C. F. Tukuitonga, et al. (1999). "The epidemiology of breast cancer in Pacific women in New Zealand." N Z Med J **112**(1096): 354-7.

AIM: To describe the epidemiology of breast cancer in Pacific women in New Zealand and determine whether ethnic disparities exist. METHODS: Analysis of data obtained from the New Zealand Cancer Registry for breast cancer

notifications from 1987-94 inclusive. Statistical analysis compared the age-specific incidence, tumour stage at presentation and pathological tumour type of Pacific, Maori and Other women. RESULTS: Notification data were analysed for 12,914 breast cancer cases including 688 Maori and 227 Pacific women. The age-standardised incidence rate per 100,000 person years for Pacific women (104.5) was statistically significantly ($p<0.05$) lower than that for Other (139.1) and Maori (148.6) women. Pacific and Maori women presented with significantly less localised tumours (31.4% and 41.3% respectively) than Other women (47.2%). CONCLUSION: Ethnic disparities in breast cancer epidemiology exist in New Zealand. Pacific women may have decreased incidence rates of breast cancer but they and Maori women present with a more advanced stage of breast cancer than Other women. The latter is a modifiable factor which could be targeted by improved participation in screening programmes.

Lee, Y. C., P. Boffetta, et al. (2008). "Involuntary smoking and head and neck cancer risk: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium." Cancer Epidemiol Biomarkers Prev **17**(8): 1974-81.

Although active tobacco smoking has been identified as a major risk factor for head and neck cancer, involuntary smoking has not been adequately evaluated because of the relatively low statistical power in previous studies. We took advantage of data pooled in the International Head and Neck Cancer Epidemiology Consortium to evaluate the role of involuntary smoking in head and neck carcinogenesis. Involuntary smoking exposure data were pooled across six case-control studies in Central Europe, Latin America, and the United States. Adjusted odds ratios (OR) and 95% confidence interval (95% CI) were estimated for 542 cases and 2,197 controls who reported never using tobacco, and the heterogeneity among the study-specific ORs was assessed. In addition, stratified analyses were done by subsite. No effect of ever involuntary smoking exposure either at home or at work was observed for head and neck cancer overall. However, long duration of involuntary smoking exposure at home and at work was associated with an increased risk (OR for >15 years at home, 1.60; 95% CI, 1.12-2.28; P(trend) < 0.01; OR for >15 years at work, 1.55; 95% CI, 1.04-2.30; P(trend) = 0.13). The effect of duration of involuntary smoking exposure at home was stronger for pharyngeal and laryngeal cancers than for other subsites. An association between involuntary smoking exposure and the risk of head and neck cancer, particularly pharyngeal and laryngeal cancers, was observed for long duration of exposure. These results are consistent with those for active smoking and suggest that elimination of involuntary smoking exposure might reduce head and neck cancer risk among never smokers.

Leiter, U. and C. Garbe (2008). "Epidemiology of melanoma and nonmelanoma skin cancer--the role of sunlight." Adv Exp Med Biol **624**: 89-103.

Melanoma and nonmelanoma skin cancer (NMSC) are now the most common types of cancer in white populations. Both tumor entities show an increasing incidence rate worldwide but a stable or decreasing mortality rate. The rising incidence rates of NMSC are probably caused by a combination of increased sun exposure or exposure to ultraviolet (UV) light, increased outdoor activities, changes in clothing style, increased longevity, ozone depletion, genetics and in some cases, immune suppression. A dose-dependent increase in the risk of squamous cell carcinoma (SCC) of the skin was found associated with exposure to Psoralen and UVA irradiation. An intensive UV exposure in childhood and adolescence was causative for the development of basal cell carcinoma (BCC) whereas for the aetiology of SCC a chronic UV exposure in the earlier decades was accused. Cutaneous malignant melanoma is the most rapidly increasing cancer in white populations. The frequency of its occurrence is closely associated with the constitutive colour of the skin and depends on the geographical zone. The highest incidence rates have been reported from Queensland, Australia with 56 new cases per year per 100,000 for men and 43 for women. Mortality rates of melanoma show a stabilisation in the USA, Australia and also in European countries. The tumor thickness is the most important prognostic factor in primary melanoma. There is an ongoing trend towards thin melanoma since the last two decades. Epidemiological studies have confirmed the hypothesis that the majority of all melanoma cases are caused, at least in part, by excessive exposure to sunlight. In contrast to squamous cell carcinoma, melanoma risk seems not to be associated with cumulative, but intermittent exposure to sunlight. Therefore campaigns for prevention and early detection are necessary.

Levine, P. H. and C. Veneroso (2008). "The epidemiology of inflammatory breast cancer." Semin Oncol **35**(1): 11-6.

The epidemiology of inflammatory breast cancer (IBC) has been of great interest to a number of investigators, but epidemiological research has been hampered by the lack of an agreed upon case definition and the relatively small number of patients available to any single investigator or institution. Several features of IBC have become apparent

through population-based studies, which, although varying somewhat in case definition, generally agree on some key features of the disease. These include the incidence of the disease, apparently less than 3% of breast cancer cases in the United States, the younger age of onset compared to non-inflammatory breast cancer, the much higher incidence in Black women compared to White, the generally poor outcome of this disease compared to non-inflammatory breast cancer, and the continued increase in reported incidence, particularly as compared with non-inflammatory breast cancer in general and locally advanced breast cancer (LABC) in particular. There is an apparent striking geographic pattern, with a higher percentage of cases reported from North Africa, best documented in Tunisia. The risk factors for developing IBC are suggested by smaller studies with concordant conclusions, and some appear to be different than the risk factors for developing breast cancer in general. For example, obesity appears to be a risk factor for premenopausal IBC but is not for premenopausal non-inflammatory breast cancer. In addition, there is evidence that a young age at first birth predisposes to IBC but is protective against developing non-inflammatory breast cancer. In some malignancies, the use of molecular markers is helpful in defining subgroups that could assist in improving case definition as well as predicting prognosis. The increasing combination of improved epidemiologic and laboratory methods will hopefully accelerate our understanding of this challenging disease.

Link, B. G., M. E. Northridge, et al. (1998). "Social epidemiology and the fundamental cause concept: on the structuring of effective cancer screens by socioeconomic status." Milbank Q **76**(3): 375-402, 304-5.

Since the early 1800s, studies have consistently demonstrated that people higher in the socioeconomic hierarchy live longer than people of lower rank. One hypothesis for the persistence of this association is that people who are relatively better off are more able to avoid risks by adopting currently available protective strategies. In a partial test of this idea, the social distributions of two cancer screening tests--Pap smears and mammography--were examined. A review of the literature and an analysis of Behavioral Risk Factor Surveillance System (BRFSS) data showed a consistent association between indicators of socioeconomic status and recent screening. These findings support the theory that societies create and shape patterns of disease. Innovations beneficial to health are carried out within the context of inequalities that shape the distribution of the health benefit, thereby affecting patterns of morality.

Lissowska, J., A. Pilarska, et al. (2003). "Smoking, alcohol, diet, dentition and sexual practices in the epidemiology of oral cancer in Poland." Eur J Cancer Prev **12**(1): 25-33.

The effect of smoking, drinking, diet, dental care and sexual habits on the risk of oral and pharyngeal cancer was investigated in a case-control study conducted in Warsaw, Poland. The study comprised 122 patients (including 44 females) aged 23-80 years with histologically confirmed cancer of oral cavity and pharynx. Controls were 124 subjects (including 52 females) admitted to the hospital for different non-neoplastic conditions unrelated to tobacco and alcohol consumption, with frequency matched to cases by age and sex. Smoking and drinking were strongly associated with an increased risk of oral cancer. Among consumers of both products, risks of oral cancer tended to combine in a multiplicative fashion and were increased more than 14-fold among those who consumed more than 15 cigarettes and seven or more drinks per day. Cessation of smoking was associated with reduced risk of this cancer. The risks varied by type of cigarettes smoked, being lower among those consuming filtered cigarettes only (OR = 1.6) than nonfilter (OR = 6.5) or mixed (OR = 4.2) cigarettes. High fruit intake was associated with significantly decreased risk (OR = 0.4) with the strongest significant inverse association found for fruit juices and citrus fruits (< 0.01). After adjustment for tobacco smoking and alcohol drinking, poor dentition as evidenced by missing teeth, frequency of dental check-ups and frequency of teeth brushing emerged as a strong risk factor. Number of missing teeth and frequency of dental check-ups and frequency of tooth brushing showed increased ORs of 9.8, 11.9 and 3.2, respectively. Denture wearing did not affect oral cancer risk. No differences were detected in sexual practices (including oral sex and intercourse with prostitutes). In terms of attributable risk, smoking accounted for 57% of oral cancer cases in Poland, alcohol for 31% and low fruit intake for 12%. Attributable risks for low frequency of tooth brushing and dental check-ups were 56% and 47%, respectively. In conclusion, smoking and drinking cessation and increase of fresh fruit intake are likely to be effective preventive measures against oral cancer. These findings indicate also that poor oral hygiene may be an independent risk factor.

Liu, G., W. Zhou, et al. (2005). "Molecular epidemiology of non-small cell lung cancer." Semin Respir Crit Care Med **26**(3): 265-72.

Although smoking is the primary risk factor for most lung cancers, genetic predisposition may play an important role. Familial aggregation studies

suggest a greater genetic component in the risk for younger individuals developing lung cancer, for lifetime nonsmokers, and possibly for women. Low-penetrance, high-prevalence polymorphic genes may explain part of this genetic predisposition. Functional polymorphisms of xenobiotic metabolism may alter the total exposure of tobacco carcinogens in the host. Subtle alterations in the DNA repair, inflammatory, and cell cycle pathways may also alter lung cancer susceptibility. The role of individual polymorphisms has been evaluated for several genes including the CYP and glutathione s-transferase superfamilies, and the NAT genes; DNA repair genes such as XPD (nucleotide excision pathway), XRCC1 (base excision pathway), and MGMT; and tumor suppressor or cell cycle genes such as p53. Molecular epidemiological studies are now focused on building larger databases from existing smaller studies and developing strategies to simultaneously evaluate multiple polymorphisms and genes within the same pathway.

Lowenfels, A. B. and P. Maisonneuve (2004). "Epidemiology and prevention of pancreatic cancer." Jpn J Clin Oncol **34**(5): 238-44.

Pancreatic cancer is an uncommon tumor, but because the mortality rate approaches 100%, this form of cancer has now become a common cause of cancer mortality. In the United States it is the fourth most frequent cause of cancer mortality; in Japan it ranks as the fifth commonest cause of death from cancer. Smoking is the major known risk factor for pancreatic cancer, accounting for approximately 25-30% of all cases. Some of the time-dependent changes in the frequency of pancreatic cancer can be explained by smoking trends. Aggressive public health measures to control smoking would substantially reduce the burden of pancreatic cancer. Dietary factors are less important for pancreatic cancer than for other digestive tract tumors, but consumption of a diet with adequate quantities of fruits and vegetables, plus control of calories either by dietary measures or by exercise will help to prevent this lethal tumor. There are more than a dozen inherited germline mutations that increase the risk of pancreatic cancer. Of these, hereditary pancreatitis confers the greatest risk, while BRCA2 mutations are the commonest inherited disorder. In addition to germline defects, there are several common polymorphisms in genes that control detoxification of environmental carcinogens that may alter the risk of pancreatic cancer. More research will be needed in this area, to explain and to clarify the interaction between genes and environmental factors.

Lowenfels, A. B., P. Maisonneuve, et al. (1999). "Epidemiology of gallbladder cancer." Hepatogastroenterology **46**(27): 1529-32.

Gallbladder cancer, although rare in most Caucasian populations, is among the most frequently observed cancers in native populations of North and South America, and in the Maori population of New Zealand. In all populations, there is a strong correlation between gallstones and gallbladder cancer: the risk of gallbladder cancer is approximately 4-5 times higher in patients with gallstones, than in patients without gallstones. In those populations where the onset of gallstone disease occurs in the first few decades, the risk is much higher. Obesity, which is also a risk factor for gallstones, increases the risk of gallbladder cancer, as does the consumption of diets high in fats and calories. Other risk factors, such as increased parity, also increase the frequency of gallbladder cancer, most probably explained by the association between gallstones and parity. Prophylactic cholecystectomy for asymptomatic gallstones cannot be justified for the control of gallbladder cancer, but the increasing frequency of this procedure in many countries, secondary to the widespread use of laparoscopic surgical techniques, will clearly lower the incidence and mortality rates for this lethal disease.

Lukanova, A. and R. Kaaks (2005). "Endogenous hormones and ovarian cancer: epidemiology and current hypotheses." Cancer Epidemiol Biomarkers Prev **14**(1): 98-107.

The effect of major epidemiologic risk factors for ovarian cancer has been reviewed in the light of several hormonal hypotheses, including the gonadotropin, androgens, progesterone, estrogens, insulin-like growth factor-I, and insulin hypotheses. The role of inclusion cyst formation and Mullerian epithelium differentiation in the pathology of the disease are also briefly outlined. Although based on limited data, the observed tendency in current evidence suggests possible etiologic roles for elevated androgens and estrogens and decreased progesterone in the pathogenesis of ovarian cancer. A direct effect of gonadotropins cannot be entirely ruled out, but it is plausible that their effect on ovarian cancer risk is mediated by stimulation of ovarian steroidogenesis. Insulin-like growth factor-I also emerges as a hormone that may be directly involved in the pathogenesis of the disease, but thus far only one prospective study has examined this association. Hyperinsulinemia is an unlikely risk factor for ovarian cancer. The observed tendency for an increased risk with androgens from ovarian origin (in premenopausal women), the lack of association with adrenal androgens, and the relatively weak associations observed with obesity, hormonal replacement therapy use, and endogenous hormones after menopause suggest that ovarian synthesis of sex steroids rather

than their circulating levels may be etiologically important. More data from prospective studies will be crucial to improve our understanding of the etiologic role of endogenous hormones in the pathogenesis of ovarian cancer. Such data will ultimately provide opportunities for research targeted; at early detection and preventive interventions.

MacFarlane, E., D. Glass, et al. (2009). "Is farm-related job title an adequate surrogate for pesticide exposure in occupational cancer epidemiology?" Occup Environ Med **66**(8): 497-501.

OBJECTIVES: Accurate assessment of exposure is a key factor in occupational epidemiology but can be problematic, particularly where exposures of interest may be many decades removed from relevant health outcomes. Studies have traditionally relied on crude surrogates of exposure based on job title only, for instance farm-related job title as a surrogate for pesticide exposure. METHODS: This analysis was based on data collected in Western Australia in 2000-2001. Using a multivariate regression model, we compared expert-assessed likelihood of pesticide exposure based on detailed, individual-specific questionnaire and job specific module interview information with reported farm-related job titles as a surrogate for pesticide exposure. RESULTS: Most (68.8%) jobs with likely pesticide exposure were farm jobs, but 78.3% of farm jobs were assessed as having no likelihood of pesticide exposure. Likely pesticide exposure was more frequent among jobs on crop farms than on livestock farms. Likely pesticide exposure was also more frequent among jobs commenced in more recent decades and jobs of longer duration. Our results suggest that very little misclassification would have resulted from the inverse assumption that all non-farming jobs are not pesticide exposed since only a very small fraction of non-agricultural jobs were likely to have had pesticide exposure. CONCLUSIONS: Classification of all farm jobs as pesticide exposed is likely to substantially over-estimate the number of individuals exposed. Our results also suggest that researchers should pay special attention to farm type, length of service and historical period of employment when assessing the likelihood of pesticide exposure in farming jobs.

Malekzadeh, R., M. H. Derakhshan, et al. (2009). "Gastric cancer in Iran: epidemiology and risk factors." Arch Iran Med **12**(6): 576-83.

Although the global incidence of gastric cancer has been decreased dramatically in recent decades, it is the most common cancer in north and northwest Iran. The wide variation in incidence across different geographical areas and higher proportion of cardia cancer are two main characteristics of gastric cancer in Iran. Current investigations indicate that a high prevalence of H.pylori infection, high dietary intake of salt and smoking are the main environmental factors of gastric cancer in Iran. Gastroesophageal reflux disease is another contributing factor in populations with a higher incidence of gastric cardia cancer. While interventions on modifiable environmental risk factors should be considered as the main modality to reduce gastric cancer development, surveillance programmes for early detection of cancer in highly selected groups may increase overall survival rates in potential patients in this country.

Marur, S. and A. A. Forastiere (2008). "Head and neck cancer: changing epidemiology, diagnosis, and treatment." Mayo Clin Proc **83**(4): 489-501.

Head and neck cancers account for less than 5% of all cancers and for less than 3% of all cancer deaths in the United States. The populations at risk for head and neck cancers are those who have a long-standing history of smoking and alcohol use. More recently, the incidence of oropharyngeal cancer in younger populations has been increasing and is associated with exposure to the human papillomavirus. This subset of patients appears to have a better overall prognosis and to respond better to treatment. This review is limited to head and neck cancers of squamous cell histology, which constitute more than 90% of head and neck cancers. Because treatment of head and neck cancers is complex and involves multiple modalities, a multidisciplinary approach is needed. This review focuses on the goal of organ preservation and postoperative treatment of high-risk patients with the concurrent use of chemotherapy and radiation therapy. This review also highlights recent advances in treatment using molecularly targeted therapies, specifically the role of inhibitors of the epidermal growth factor receptor in locally advanced and recurrent/metastatic squamous cell cancer of the head and neck. Studies in the English language were identified by searching the MEDLINE, EMBASE database (1980-2007) using the search terms head and neck, squamous cell, carcinoma, chemotherapy, radiation, human papillomavirus, epidermal growth factor receptor, and targeted therapy.

Matsuba, T., D. Qiu, et al. (2005). "Overview of epidemiology of bile duct and gallbladder cancer focusing on the JACC Study." J Epidemiol **15 Suppl 2**: S150-6.

BACKGROUND: This review discusses the epidemiologic features of bile duct and gallbladder cancer in Japan, mainly focusing on results of Japan Collaborative Cohort Study (JACC Study) for

Evaluation of Cancer Risk Sponsored by the Ministry of Education, Science, Sports and Culture of Japan (Monbusho) in comparison with results of other studies. METHODS: The theses and papers derived from JACC Study on bile duct and gallbladder cancer were all collected for this review. Hirayama's cohort study, which is a representative epidemiologic study, and a large scale case-control study on bile duct and gallbladder cancer in Japan by Kato et al. were also taken into consideration. Small scale cross-sectional studies or ecological studies and the studies conducted outside Japan were collected by the literature reference services on the web net such as Pub Med or Japan Centra Revuo Medicina (Igaku- Chuo- Zasshi) limited to the published after 1980 and use key words bile duct cancer, gallbladder cancer and epidemiology. RESULTS: In the JACC Study, high intake of fried food was regarded as a factor that significantly elevated the risk of the diseases (hazard ratio [HR]=2.58, 95% confidence interval [CI]: 1.08-6.16 in males; HR=2.98, 95% CI: 1.28-6.86 in females). The JACC Study indicated that a high intake of boiled beans had a significant preventive relation to the diseases in females (relative risk [RR]=0.50, 95% CI: 0.26-0.98). High consumption of fish also had a significant preventive relationship to bile duct cancer in males (RR=0.53, 95% CI: 0.26-0.98) and gallbladder cancer in females (RR=0.43, 95% CI: 0.24- 0.79). A history of blood transfusion also had a significant relationship (HR=2.27, 95% CI: 1.29-3.98) as which elevated the risk. The JACC Study determined bowel movement as a risk factor. The group with bowel movements less than once per six days had a significantly elevated hazard ratio (HR=5.21, 95% CI: 1.25-21.68). CONCLUSION: As to recent epidemiologic features of bile duct and gallbladder cancer revealed by the JACC Study, its outline became obvious in comparison with the results of other studies. Evidence for the contribution of the JACC Study is strong because it provides some important findings on the epidemiology of bile duct and gallbladder cancer.

Meirow, D. and J. G. Schenker (1996). "The link between female infertility and cancer: epidemiology and possible aetiologies." Hum Reprod Update **2**(1): 63-75.

Infertility has been suggested as a risk factor for various gynaecological cancers. Data analyses show that among infertile women, those with anovulation or polycystic ovarian syndrome (PCOS) have an increased risk of cancer. Clinical and laboratory data such as anthropometric measurements, endogenous hormones and growth factors may explain mechanisms which link tumorogenesis or tumour promotion to infertility. The possible association between ovulation induction and cancer is discussed both on theoretical grounds and based on epidemiological data. We conclude that according to epidemiological studies, laboratory data and on theoretical grounds, infertile patients have an increased lifetime risk of gynaecological cancer. The risk of cancer should be evaluated further for each subpopulation of infertile patients. Thus, more adequate means of monitoring these patients will become available. These data are necessary for a further evaluation of the possible cancer risks of infertility treatments.

Memik, F., M. Gulten, et al. (1996). "The epidemiology of gastrointestinal cancer in Turkey: a review of our accumulated experience." J Environ Pathol Toxicol Oncol **15**(2-4): 209-13.

Among all organ cancers, gastrointestinal tract cancers present an interesting pattern in distribution over the world. There are several hundred differences between some incidences of cancer. Probably due to different geographical and climatic differences between western and eastern regions of Turkey, we found varying incidences in esophageal, gastric, and colonic carcinomas. The type of diet, and an excess or lack of some essential nutrients and vitamins are probably the main causes in determining what kind of gastrointestinal tumor might occur. Besides diet, living areas, socioeconomic status, salinity of soil, drinking water and many other factors may play a role. Contrary to the findings of some authors, excessive tea and alcohol consumption has not been found to be a risk factor in our study.

Mettlin, C. (1994). "The relationship of breast cancer epidemiology to screening recommendations." Cancer **74**(1 Suppl): 228-30.

The epidemiology of breast cancer involves several factors that may be useful in deciding to recommend breast cancer screening. Paramount among these factors is age. A family history of breast cancer may be a basis for modifying screening recommendations, but this may be appropriate only for a subset of women with breast cancer in a relative. Although there are several known risk factors for breast cancer, no single factor accounts for a large proportion of disease, and many patients with breast cancer have none of the recognized risk factors. A decision to forgo screening based on the absence of any single factor other than age may not be justified by current epidemiologic knowledge.

Michaud, D. S. (2004). "Epidemiology of pancreatic cancer." Minerva Chir **59**(2): 99-111.

Worldwide, over 200000 people die annually of pancreatic cancer. The highest incidence and

mortality rates of pancreatic cancer are found in developed countries. In the United States, pancreatic cancer is the 4(th) leading cause of cancer death, and in Europe it is the 6th. Because of high fatality rates, pancreatic cancer incidence rates are almost equal to mortality rates. Pancreatic cancer is diagnosed late in the natural history of the disease, given the few early indicators of illness, and the lack of screening tests for this disease. Treatment has not improved substantially over the past few decades and has little effect on prolonging survival time. Therefore, prevention could play an important role in reducing pancreatic cancer mortality. International variations in rates and time trends suggest that environmental factors are likely to play a role in the etiology of pancreatic cancer. Variations in rates are substantial and occur even within industrialized nations. While rates have been stabilizing over the past 2 decades in many countries where they are already high, they continue to increase in countries where rates were relatively low 4 decades ago, such as Japan. In the US, the highest rates of pancreatic cancer incidence and mortality are observed among blacks, who have some of the highest rates in the world. A known cause of pancreatic cancer is tobacco smoking. This risk factor is likely to explain some of the international variations and gender differences. A number of studies observed a reduction in pancreatic cancer risk within a decade after smoking cessation, when compared to current smokers. With tobacco smoking as an exception, risk factors for pancreatic cancer are not well-established. Over the past 2 decades, epidemiological studies on pancreatic cancer have been plagued with methodological issues associated with studying a highly fatal disease, and inconsistent findings have hindered our understanding of the etiology of pancreatic cancer. Although familial pancreatic cancer is well-documented, the genes responsible for this condition have not been identified and are unlikely to explain more than 5-10% of all pancreatic cancer cases. Chronic pancreatitis and diabetes mellitus are medical conditions that have been consistently related to pancreatic cancer. Data from numerous studies suggest that these conditions are likely to be causally related to pancreatic cancer, rather than being consequences of the cancer. Recent cohort studies, which are less prone to biases than case-control studies, suggest that obesity increases the risk of pancreatic cancer. Other studies support the hypothesis that glucose intolerance and hyperinsulinemia are important in the development of pancreatic cancer. Other potential risk factors include physical inactivity, aspirin use, occupational exposure to certain pesticides, and dietary factors such as carbohydrate or sugar intake.

Millikan, R. C., B. Newman, et al. (2008). "Epidemiology of basal-like breast cancer." Breast Cancer Res Treat **109**(1): 123-39.

Risk factors for the newly identified "intrinsic" breast cancer subtypes (luminal A, luminal B, basal-like and human epidermal growth factor receptor 2-positive/estrogen receptor-negative) were determined in the Carolina Breast Cancer Study, a population-based, case-control study of African-American and white women. Immunohistochemical markers were used to subtype 1,424 cases of invasive and in situ breast cancer, and case subtypes were compared to 2,022 controls. Luminal A, the most common subtype, exhibited risk factors typically reported for breast cancer in previous studies, including inverse associations for increased parity and younger age at first full-term pregnancy. Basal-like cases exhibited several associations that were opposite to those observed for luminal A, including increased risk for parity and younger age at first term full-term pregnancy. Longer duration breastfeeding, increasing number of children breastfed, and increasing number of months breastfeeding per child were each associated with reduced risk of basal-like breast cancer, but not luminal A. Women with multiple live births who did not breastfeed and women who used medications to suppress lactation were at increased risk of basal-like, but not luminal A, breast cancer. Elevated waist-hip ratio was associated with increased risk of luminal A in postmenopausal women, and increased risk of basal-like breast cancer in pre- and postmenopausal women. The prevalence of basal-like breast cancer was highest among premenopausal African-American women, who also showed the highest prevalence of basal-like risk factors. Among younger African-American women, we estimate that up to 68% of basal-like breast cancer could be prevented by promoting breastfeeding and reducing abdominal adiposity.

Molina, J. R., P. Yang, et al. (2008). "Non-small cell lung cancer: epidemiology, risk factors, treatment, and survivorship." Mayo Clin Proc **83**(5): 584-94.

Lung cancer is the leading cause of cancer-related mortality not only in the United States but also around the world. In North America, lung cancer has become more predominant among former than current smokers. Yet in some countries, such as China, which has experienced a dramatic increase in the cigarette smoking rate during the past 2 decades, a peak in lung cancer incidence is still expected. Approximately two-thirds of adult Chinese men are smokers, representing one-third of all smokers worldwide. Non-small cell lung cancer accounts for 85% of all lung cancer cases in the United States. After the initial diagnosis, accurate staging of non-small cell lung cancer using

computed tomography or positron emission tomography is crucial for determining appropriate therapy. When feasible, surgical resection remains the single most consistent and successful option for cure. However, close to 70% of patients with lung cancer present with locally advanced or metastatic disease at the time of diagnosis. Chemotherapy is beneficial for patients with metastatic disease, and the administration of concurrent chemotherapy and radiation is indicated for stage III lung cancer. The introduction of angiogenesis, epidermal growth factor receptor inhibitors, and other new anti-cancer agents is changing the present and future of this disease and will certainly increase the number of lung cancer survivors. We identified studies for this review by searching the MEDLINE and PubMed databases for English-language articles published from January 1, 1980, through January 31, 2008. Key terms used for this search included non-small cell lung cancer, adenocarcinoma, squamous cell carcinoma, bronchioalveolar cell carcinoma, large cell carcinoma, lung cancer epidemiology, genetics, survivorship, surgery, radiation therapy, chemotherapy, targeted therapy, bevacizumab, erlotinib, and epidermal growth factor receptor.

Moore, M. A. and K. Tajima (2004). "Cervical cancer in the asian pacific-epidemiology, screening and treatment." Asian Pac J Cancer Prev **5**(4): 349-61.

Squamous cell carcinoma (SCC) of the cervix continues to be a major problem in many areas of the Asian-Pacific, particularly in the Indian subcontinent and Papua New Guinea, and to a lesser extent in South-East Asia, Korea and Mongolia. In contrast, levels in the developed countries of the region are low, as is also the case for the Muslim countries of Western Asia, and mainland China. Incidence generally mirrora associated mortality, although with some exceptions reflecting facilities and infrastructure for early detection. Over the last 25 years there has been a marked decrease in incidence rates across most of the Asian Pacific, although less pronounced in India than elsewhere, and there are exceptions where the incidence is on the increase. The predominant risk factor is well established to be persistent infection with a high risk 'oncogenic' type of human papilloma virus (HPV), along with multiple partners, other sexually transmitted diseases and smoking. Consumption of vegetables, in contrast, appears to be protective. Hormonal factors may also play some role. Modifying factors may either impact on neoplasia by directly influencing the processes underlying carcinogenesis, or indirectly by affecting persistence of viral infections. For primary prevention, avoidance of repeated infections and smoking, as well as a high antioxidant intake may be beneficial. Vaccines against HPV also have promise for the future, but a better understanding of the mechanisms underlying spontaneous clearance of both infection and cervical intraepithelial neoplasia (CIN) of different grades is also essential for optimal intervention. For screening, the choice of whether the PAP smear, HPV testing or some form of visual inspection are utilized depends on the resources which are available, all approaches having their own advantages and disadvantages, but with similar sensitivity and specificity. One complication is the increase in adenocarcinoma of the cervix which has been reported in some countries, for which risk factors and most effective screening may differ from the SCC case. A focus on high risk groups like sex workers might be warranted where financial and technical support are limited. If cervical intraepithelial neoplasias are detected then cryotherapy or the loop electrosurgical excision procedure (LEEP) are effective for their removal. Control of cancer of the cervix, however, demands that a comprehensive approach to screening and management is adopted, necessitating major training of personnel and provision of appropriate resources.

Moran, E. M. (1996). "Environment, cancer, and molecular epidemiology: air pollution." J Environ Pathol Toxicol Oncol **15**(2-4): 97-104.

Most cancers result from human interaction with the environment. As may be expected, air pollution is the most frequent factor responsible for environmental carcinogenesis due to natural exposures (such as air contamination, background radiation, and asbestos) or man-made pollution (e.g., smoking). A challenging problem in clinical epidemiology has been the nonuniform distribution of cancer among populations equally exposed to carcinogenic circumstances. Recent findings made available through the development of molecular biology techniques have provided new insights into cancer susceptibility. The wide variations in the uptake and ability to activate xenobiotics are key phenomena in environmental carcinogenesis. The intracellular DNA repair systems are probably responsible for the end result of neoplastic transformation or normalcy in the presence of carcinogenic encounters.

Morgensztern, D., S. Waqar, et al. (2009). "Improving survival for stage IV non-small cell lung cancer: a surveillance, epidemiology, and end results survey from 1990 to 2005." J Thorac Oncol **4**(12): 1524-9.

BACKGROUND: Although there has been a significant survival improvement for patients with metastatic NSCLC enrolled in randomized trials, it is not clear whether a similar benefit is seen in an unselected group of patients. Therefore, we conducted

a study to evaluate for survival changes in a large national cancer registry database. PATIENTS AND METHODS: The Surveillance, Epidemiology, and End Results (SEER) registry was queried for patients with NSCLC stage IV, aged 21 years or older, and diagnosed between 1990 and 2005. We analyzed four equally divided time periods between 1990 and 2005 (1990 to 1993 or period 1, 1994 to 1997 or period 2, 1998 to 2001 or period 3, and 2002 to 2005 or period 4) to determine changes in overall survival for all patients and according to histology. RESULTS: We identified 129,337 patients meeting eligibility criteria. There was a significant improvement in overall survival since period 1. One-year and 2-year overall survival increased from 13.2 and 4.5%, respectively, in period 1 to 19.4% and 7.8%, respectively, in period 4. On multivariate analysis, survival for adenocarcinoma was increased compared with squamous cell carcinoma only in period 4 ($p = 0.02$). CONCLUSIONS: There has been a modest but statistically significant improvement in overall survival for stage IV NSCLC over the past 16 years. The recent differences in outcomes based on histology observed in period 4 may reflect the increased activity of epidermal growth factor receptor tyrosine kinase inhibitors in adenocarcinoma compared with squamous cell carcinoma.

Murta-Nascimento, C., B. J. Schmitz-Drager, et al. (2007). "Epidemiology of urinary bladder cancer: from tumor development to patient's death." World J Urol **25**(3): 285-95.

Urinary bladder cancer (UBC) ranks ninth in worldwide cancer incidence. It is more frequent in men than in women. We review the main established/proposed factors, both environmental and genetic, associated with bladder cancer etiology and prognosis. Data were extracted from previous reviews and original articles identified from PubMed searches, reference lists, and book chapters dealing with the reviewed topics. Evaluation and consensus of both the contribution of each factor in bladder cancer burden and the appropriateness of the available evidences was done during an ad hoc meeting held during the 18th Congress of the European Society for Urological Research. Cigarette smoking and specific occupational exposures are the main known causes of UBC. Phenacetin, chlornaphazine and cyclophosphamide also increase the risk of bladder cancer. Chronic infection by Schistosoma haematobium is a cause of squamous cell carcinoma of the bladder. NAT2 slow acetylator and GSTM1 null genotypes are associated with an increased risk of this cancer. Vegetables and fresh fruits protect against this tumor. Regarding prognosis, there is little knowledge on the predictive role of environmental exposures and genetic polymorphisms on tumor recurrence and progression and patient's death. Although active tobacco smoking is the most commonly studied factor, no definitive conclusion can be drawn from the literature. More research is needed regarding the effect of complex etiological factors in bladder carcinogenesis. Subgroup analysis according to stage, grade, and molecular features may help in identifying specific etiological and prognostic factors involved in different bladder cancer progression pathways.

Nagataki, S. and E. Nystrom (2002). "Epidemiology and primary prevention of thyroid cancer." Thyroid **12**(10): 889-96.

The purpose of this review is to provide an account of our present knowledge about the epidemiology of nonmedullary thyroid carcinoma, to discuss the effects of environment, lifestyle and radiation on the risk of developing thyroid cancer, and to discuss aspects on primary prevention of the disease. In areas not associated with nuclear fallout, the annual incidence of thyroid cancer ranges between 2.0-3.8 cases per 100,000 in women and 1.2-2.6 per 100,000 in men, women of childbearing age being at highest risk. Low figures are found in some European countries (Denmark, Holland, Slovakia) and high figures are found in Iceland and Hawaii. Differences in iodine intake may be one factor explaining the geographic variation, high iodine intake being associated with a slightly increased risk of developing thyroid cancer. In general, lifestyle factors have only a small effect on the risk of thyroid cancer, a possible protective effect of tobacco smoking has been recently reported. Because of the (small) increase in risk of thyroid cancer associated with iodination programs, these should be supervised, so that the population does not receive excess iodine. The thyroid gland is highly sensitive to radiation-induced oncogenesis. This is verified by numerous reports from survivors after Hiroshima and Nagasaki, the Nevada, Novaja Semlja and Marshal Island atmospheric tests, and the Chernobyl plant accident, as well as by investigations of earlier medical use of radiation for benign diseases in childhood. These reports are summarized in the review. There appears to be a dose-response relation for the risk of developing cancer after exposure to radioactive radioiodine. The thyroid gland of children is especially vulnerable to the carcinogenic action of ionizing radiation. Thus, the incidence of thyroid cancer in children in the Belarus area was less than 1 case per million per year before the Chernobyl accident, increasing to a peak exceeding 100 per million per year in certain areas after the accident. It is a social obligation of scientists to inform the public and politicians of these risks. All nuclear power plants should have a program in operation for stockpiling

potassium iodide for distribution within 1-2 days after an accident.

Narod, S. (1999). "Genetic epidemiology of prostate cancer." Biochim Biophys Acta **1423**(1): F1-13.

A family history of prostate cancer is a consistent risk factor for prostate cancer, and can also be used to predict the presence of prostate cancer among asymptomatic men who undergo PSA screening. Approximately 5% of cases of prostate cancer have a familial component. The genetic epidemiology of prostate cancer is complex, and genes on chromosome 1 and X chromosome contribute to familial aggregation. Neither of these prostate cancer susceptibility genes have been identified, but are the subject of an active search. Hereditary prostate cancer resembles non-hereditary cancer in terms of age of onset, pathologic appearance and grade.

Neugut, A. I., M. Hayek, et al. (1996). "Epidemiology of gastric cancer." Semin Oncol **23**(3): 281-91.

The incidence of gastric cancer varies widely by country and population, with higher rates among the lower socioeconomic groups. Although the most common cause of cancer death in the United States in 1930, its incidence has decreased dramatically during the past 60 years. Most populations show a 2-1 ratio for male to female gastric cancer cases, and a higher incidence rate among United States blacks than whites. Although rates have generally decreased, there has been a dramatic increase in the incidence of gastric cancer in the cardia. Diet has been the most studied risk factor for gastric cancer. Of particular interest have been N-nitroso compounds derived from the consumption of preserved, smoked, and cured foods. An inverse association with the consumption of fruits and vegetables has also been consistently demonstrated, though the specific nutrient(s) that this represents has been unclear, although ascorbate and beta-carotene have been intensively studied. Among nondietary factors, substantial evidence has accumulated for an increased risk with Helicobacter pylori infection. Other exposures which have been fairly consistently associated with gastric cancer include cigarette smoking, partial gastrectomy, radiation exposure, family history, pernicious anemia, blood group A, certain occupational exposures, and Epstein-Barr virus.

Oliveria, S. A. and P. J. Christos (1997). "The epidemiology of physical activity and cancer." Ann N Y Acad Sci **833**: 79-90.

Experimental studies in animals and epidemiological studies in human populations support an inverse association between exercise and the development of cancer. Physical activity has been shown to be protective against the development of breast and colon cancer and may also be important for other kinds of cancer such as that of the prostate. The proposed biological mechanisms for the physical activity--cancer association include exercise's effect on immune function, transit time of digestion, hormones, and body fat. There has been little research on physical activity and the effect on progression of cancer, although there are studies to suggest that it may slow the clinical course of the disease. Furthermore, exercise may be beneficial in the treatment of cancer through mood elevation, decreased loss of lean tissue, and increased quality of life. Much is still to be learned about the effect of exercise on cancer. The intensity, duration, frequency, and type of exercise that is relevant need to be clarified. As well, the time period during life when exercise is important has not been determined. It seems reasonable to conclude that exercise, a modifiable risk factor, is beneficial in preventing certain forms of cancer. Public health interventions may hold promise for cancer prevention.

Oliveria, S. A., P. J. Christos, et al. (1997). "The role of epidemiology in cancer prevention." Proc Soc Exp Biol Med **216**(2): 142-50.

Cancer is a major cause of morbidity and mortality throughout the world. As the population lives to an older age, cancer incidence and mortality are expected to increase because of the strong relationship between cancer and advancing age. Epidemiology plays a key role in cancer prevention and control by describing the distribution of cancer and discovering risk factors for cancer. Epidemiologic study designs include descriptive, ecologic, cross-sectional, and analytic (cohort, case-control, and intervention) studies. In the past 50 years, epidemiologic research has helped to elucidate many risk factors for cancer. Lifestyle factors such as smoking, diet, alcohol consumption, reproduction (pregnancy, lactation, age at menarche, and menopause), obesity, and inactivity have been suggested as the major contributors to the development of cancer. Epidemiologists have demonstrated that cancer is largely an avoidable disease and estimated that more than two-thirds of cancer might be prevented through lifestyle modification. Epidemiologic research is crucial to public health and cancer prevention. Individuals or communities at increased risk of cancer can be targeted for risk factor modification, as well as for secondary prevention and chemoprevention strategies.

Palli, D. (1996). "Epidemiology of gastric cancer." Ann Ist Super Sanita **32**(1): 85-99.

Despite a dramatic reduction in incidence and mortality rates, gastric cancer (GC) was still recently the second most common neoplastic cause of death worldwide. GC treatment has not been substantially improved and screening programmes have not proven feasible outside Japan. On the other hand, primary prevention of GC is hampered by the lack of a single specific causal factor, even if diet has been shown to play a relevant role in its etiology. A large number of studies have indicated that salted/smoked and pickled/preserved foods (rich in salt, nitrites and preformed nitrosocompounds) are associated with an increased risk of GC. In contrast, a high consumption of fresh fruit and raw vegetables and a high intake of antioxidants have been shown to reduce the risk of GC. Domestic refrigeration and a reduced use of salt contribute to explain the decreasing temporal trend and the geographical patterns of GC. Results of human chemoprevention trials are encouraging but have not been confirmed. Evidence of an association between Helicobacter pylori infection and GC has been recently provided, even if several aspects of GC epidemiology do not fit in this hypothesis. Studies on H. pylori eradication and its effects on GC risk represent a priority for future research in view of the potential preventive applications.

Pashos, C. L., M. F. Botteman, et al. (2002). "Bladder cancer: epidemiology, diagnosis, and management." Cancer Pract **10**(6): 311-22.

PURPOSE: The purpose of this article is to present an overview of the epidemiology diagnosis, and management of bladder cancer, with a focus on the early stage of this disease. OVERVIEW: English-language articles published between 1990 and 2000, as well as selected abstracts published in non-English languages before 1990, were reviewed. Epidemiologic data clearly indicate that bladder cancer is much more common in men, White persons, and the elderly. Cigarette smoking appears to be the most significant environmental risk factor. Screening for the disease is currently not standard in the United States or Canada. Potential tests include urine cytology, hematuria dipstick, and the urinary biomarkers. Diagnosis is made most often on the basis of the findings of cystoscopy, tumor biopsy, and urine cytology. Transurethral resection (TUR) of the tumor is generally the first-line treatment for superficial disease. Cystectomy is the "gold standard" treatment for invasive disease in many countries, although trimodality therapy (TUR, radiation, systemic chemotherapy) has shown promise as a bladder-preserving strategy. Intravesical therapy is effective for preventing disease recurrence, although its role in slowing disease progression is uncertain. Chemotherapy and radiation also can be used with cystectomy to treat or prevent pelvic recurrence of invasive disease or to prolong life in patients with metastatic disease. CLINICAL IMPLICATIONS: Bladder cancer is a commonly occurring disease. Prevention efforts must focus on the avoidance or cessation of cigarette smoking and on public education relating to known environmental risk factors. Patient and disease factors must be considered in making treatment decisions and determining prognosis. Careful follow-up after treatment is essential. It is hoped that ongoing research on potential tumor markers and tumor-specific therapies ultimately will result in improved clinical outcomes for patients with this malignancy.

Pera, M. (2000). "Epidemiology of esophageal cancer, especially adenocarcinoma of the esophagus and esophagogastric junction." Recent Results Cancer Res **155**: 1-14.

The incidence of adenocarcinoma of the esophagus and esophagogastric junction (EGJ) has been increasing over the past 15 years in western countries. Surgical series and population-based studies show that, by 1994, adenocarcinomas of the esophagus accounted for half of all esophageal cancer among white men. The causes of this increase in incidence remain to be elucidated. Esophageal adenocarcinomas and a portion of EGJ adenocarcinomas arise from long and short segments of specialized intestinal metaplasia (Barrett's esophagus). The prevalence of long segments of Barrett's esophagus (> 3 cm) in patients having endoscopy for reflux symptoms is 3%, and 1% in those undergoing endoscopy for any clinical indication. However, a silent majority of patients with Barrett's esophagus remain unrecognized in the general population and may not be diagnosed unless adenocarcinoma develops. Recent studies document a rise in the diagnosis of specialized intestinal metaplasia of the cardia. Nearly all these patients have associated carditis, and Helicobacter pylori infection has been linked to this condition. The possible origin of EGJ adenocarcinomas in the sequence carditis--specialized intestinal metaplasia needs to be clarified. Smoking and obesity are additional risk factors for adenocarcinoma of the esophagus and EGJ. Current data does not confirm H. pylori as a risk factor for cancer of the EGJ.

Petersen, G. M. (1994). "Epidemiology, screening, and prevention of lung cancer." Curr Opin Oncol **6**(2): 156-61.

With an estimated 170,000 new cases and 149,000 deaths in the United States during 1993, lung cancer is now the leading cause of cancer deaths in both men and women. Tobacco smoking is an

important risk factor, and a large fraction of the risk can be attributed to it. Other risk factors have been implicated, including environmental tobacco smoke, occupational exposures to carcinogens, and genetic susceptibility. Prevention of lung cancer through early detection and identification of individuals at risk is the goal of many recent studies. This review summarizes the current status of epidemiologic and biomarker research in understanding both the etiology and prognostic utility of environmental and host factors.

Pilz, S., A. Tomaschitz, et al. (2009). "Epidemiology of vitamin D insufficiency and cancer mortality." Anticancer Res **29**(9): 3699-704.

There is growing evidence that vitamin D exerts anticarcinogenic effects. Ultraviolet-B (UV-B) radiation, which is required for vitamin D production in the skin, was found to be inversely associated with cancer incidence and mortality. Recent studies have largely but not consistently shown that low 25-hydroxyvitamin D (25(OH)D) levels, which are considered to be the best indicator of vitamin D status, are a significant risk factor for cancer mortality. Circulating 25(OH)D levels were also associated with improved survival in colorectal and lung cancer patients and vitamin D insufficiency was observed in various other diseases such as autoimmune, infectious, musculoskeletal, neurological and cardiovascular diseases. In conclusion, we still need further studies to evaluate the association of vitamin D insufficiency and cancer incidence and mortality, but the multiple health benefits of vitamin D and the easy, safe and inexpensive way by which vitamin D can be supplemented should already guide current public health strategies to achieve 25(OH)D levels of at least 75 nmol/l (30 ng/ml) in the general population.

Powell, I. J. (2007). "Epidemiology and pathophysiology of prostate cancer in African-American men." J Urol **177**(2): 444-9.

PURPOSE: Along with increasing age and a positive family history subSaharan African ancestry has long been recognized as an important risk factor for prostate cancer. In the United States the incidence of prostate cancer is approximately 60% higher in African-American than in European-American men and the mortality rate from the disease is more than twice as high. The purpose of this review article is to examine specific reports highlighting racial disparity and its possible causes. MATERIALS AND METHODS: The reports chosen for review of this epidemiology and pathophysiology study were included to demonstrate conditions in which racial differences as well as similarities exist in African-American and European-American men. Reports also include autopsy, biological and clinical studies, and early and late stage prostate cancer. RESULTS: From the 1970s to the current statistical analysis of the National Cancer Institute Surveillance, Epidemiology, and End Results program African-American men have continued to have a significant higher incidence and mortality rate than European-American men. Autopsy studies show a similar prevalence of early small subclinical prostate cancers but a higher prevalence of high grade prostatic intraepithelial neoplasia. Clinical studies show a similarity in prostate cancer outcome when pathological stage is organ confined but a worse outcome when disease is locally advanced and metastatic in African-American vs European-American men. There is increasing genetic evidence that suggest that prostate cancer in African-American vs European-American men may be more aggressive, especially in young men. CONCLUSIONS: Improving the outcome in African-American men with prostate cancer requires awareness of the epidemiological patterns of the disease and willingness on the part of physicians to implement targeted study initiatives with end points designed to detect the disease early in this population and begin appropriate management. It is proposed that a multi-institutional study should be done to demonstrate the ability to decrease racial outcome disparity by education, aggressive testing and treatment.

Raghu, G., F. Nyberg, et al. (2004). "The epidemiology of interstitial lung disease and its association with lung cancer." Br J Cancer **91 Suppl 2**: S3-10.

The criteria and terminology for diagnosing interstitial lung disease (ILD), a diverse range of pulmonary fibrotic disorders that affect the alveoli of the lungs, have been variable and confusing; however, there have been recent major improvements to an internationally agreed classification. Evidence from recent analyses of populations suggests that the incidence and prevalence rates of ILD are on the increase, particularly when the broad definition of ILD is used. In most patients with ILD a cause is not identified; nevertheless, among the established causes are a number of drug therapies and infections. Occupational causes are lessening in importance, while cigarette smoking is now an established risk factor. Radiation therapy for cancer is a well-established cause of ILD that usually, but not always, localises within the radiation portal and may occur later after completion of therapy. Similarly, exposure to drugs long after radiation therapy may be an aetiological factor for the development of ILD later in life, although the magnitude of this risk requires further epidemiological investigation. The possibility that ILD and lung cancer are associated has been recognised for >50 years, but it remains unclear

whether ILD precedes lung cancer or vice versa. In this review, we examine the epidemiology of ILD and the basis for its association with lung cancer.

Rahu, M. and T. Hakulinen (1994). "Descriptive epidemiology of cancer around the Baltic Sea." Acta Oncol **33**(8): 849-58.

Baltic Sea countries--Denmark, Estonia, Finland, Germany, Latvia, Lithuania, Poland, the Russian Federation and Sweden--have expressed deep interest in developing collaborative research projects chiefly in descriptive epidemiology of cancer. In order to assess potentials for joint studies, an attempt was undertaken to characterize cancer registration, cancer incidence patterns, temporal trends in cancer mortality and research productivity between these countries. Standards of cancer registration are highest in the Nordic countries (Denmark, Finland, Sweden). These countries and Germany are also doing more productive research. Great differences in incidence and in mortality trends around the Baltic Sea offer promising opportunities for epidemiologic studies. Scarcity of well-trained professional epidemiologists and other resources in Latvia, Lithuania, Estonia and the Russian Federation is the main factor limiting the planning of joint large-scale epidemiologic studies of cancer.

Raimondi, S., P. Maisonneuve, et al. (2009). "Epidemiology of pancreatic cancer: an overview." Nat Rev Gastroenterol Hepatol **6**(12): 699-708.

Pancreatic cancer, although infrequent, has an exceptionally high mortality rate, making it one of the four or five most common causes of cancer mortality in developed countries. The incidence of pancreatic cancer varies greatly across regions, which suggests roles for lifestyle factors, such as diet, or environmental factors, such as vitamin D exposure. Smoking is the most common known risk factor, and is the cause of 20-25% of all pancreatic tumors. Alcohol does not seem to be a risk factor, unless it leads to chronic pancreatitis, which is a probable risk factor. Long-standing diabetes increases the risk of pancreatic cancer, but can also be an early manifestation of pancreatic tumors. 5-10% of patients with pancreatic cancer have an underlying germline disorder, while the remaining percentage of cancer cases is thought to be caused by somatic mutations. Some individual studies suggest that mutations in various polymorphic genes can lead to small increases in the risk of pancreatic cancer, but these findings need to be replicated. Rising prevalence of smoking in developing countries, improved diagnosis and increasing population longevity are all likely to increase the global burden of pancreatic cancer in the coming decades.

Renehan, A. G., J. O'Connell, et al. (2003). "Acromegaly and colorectal cancer: a comprehensive review of epidemiology, biological mechanisms, and clinical implications." Horm Metab Res **35**(11-12): 712-25.

Acromegaly is an endocrine disorder characterised by sustained hypersecretion of growth hormone (GH) with concomitant elevation of insulin-like growth factor (IGF)-I, and is associated with malignancy and premature mortality from cardiovascular and respiratory diseases. In particular, there may be an increased risk of colorectal neoplasia, but the exact extent of this is contentious. Colonoscopy-based studies of adenoma prevalence rates in acromegalic patients are misleading, but population-based studies on colorectal cancer risk are more consistent - a meta-analysis estimated a pooled risk ratio of 2.04 (95 % CI: 1.32, 3.14). Possible mechanisms underlying this increased risk include direct actions as a consequence of elevated levels of circulating GH and IGF-I and/or other perturbations within the IGF system. Other possible mechanisms include altered bile acid secretion, altered cellular immunity, hyperinsulinaemia, shared genetic susceptibility and increased bowel length. However, most explanations only offer indirect evidence, and the expectation of acromegaly as a natural model of colorectal carcinogenesis has not materialised. From a clinical perspective, it seems reasonable to consider a once-only colonoscopic screening at approximately age 55 years, but potential risks and benefits should be balanced.

Rivera, M. P. (2009). "Lung cancer in women: the differences in epidemiology, biology and treatment outcomes." Expert Rev Respir Med **3**(6): 627-34.

Although the prevalence of lung cancer in men has been decreasing, it has been increasing in women. Without a doubt, lung cancer is a major health problem for women in the USA, not only owing to its high incidence rate but, more alarming, the high mortality rate. Lung cancer kills more women each year than breast, ovarian and uterine cancers combined. One of the most important risk factors for the development of lung cancer in both men and women is cigarette smoking. Unfortunately, the prevalence of smoking among women has increased significantly since 1980, which is a major concern as epidemiologic data suggest that women may be more susceptible to developing lung cancer than men. Many will argue, however, that after adjusting for tobacco exposure, some studies have failed to show that women are at a higher risk for developing lung cancer. Indeed, the increased risk of lung cancer in women remains controversial. There is, however, little

controversy to the fact that the biology of lung cancer differs between the sexes. This paper summarizes the explanations for the sex differences in lung cancer, including differences in molecular abnormalities, growth factor receptors, hormonal influences, differences in cytochrome P-450 enzymes and DNA repair capacity, as well as variations in treatment outcomes.

Samet, J. M. (1993). "The epidemiology of lung cancer." Chest **103**(1 Suppl): 20S-29S.

Lung cancer rates and mortality have risen in epidemic proportions in the United States and other industrialized nations during the 20th century. Case-control and cohort studies performed in the 1950s and 1960s firmly established cigarette smoking as the single greatest risk factor for lung cancer. In the United States, overall lung cancer mortality rates in men and women rose progressively from the 1950s. Fortunately, lung cancer incidence and mortality are now declining in middle-aged men. Smoking has significantly increased lung cancer rates among women and is on the rise in developing countries. Environmental agents found in the home and workplace, including radon and asbestos, have also been shown to increase lung cancer risk in both smokers and nonsmokers. Government regulations have helped curtail quantities of these and other atmospheric carcinogens. Efforts to reduce lung cancer risk must be continued and their scope expanded in order to have a global impact on the incidence and mortality of this fatal malignancy.

Sellers, C. (1997). "Discovering environmental cancer: Wilhelm Hueper, post-World War II epidemiology, and the vanishing clinician's eye." Am J Public Health **87**(11): 1824-35.

Today, our understanding of and approach to the exogenous causes of cancer are dominated by epidemiological practices that came into widespread use after World War II. This paper examines the forces, considerations, and controversies that shaped postwar risk factor epidemiology in the United States. It is argued that, for all of the new capabilities it brought, this risk factor epidemiology has left us with less of a clinical eye for unrecognized cancer hazards, especially from limited and localized exposures in the work-place. The focus here is on Wilhelm Hueper, author of the first textbook on occupational cancer (1942). Hueper became the foremost spokesman for earlier identification practices centering on occupational exposures. The new epidemiological methods and associated institutions that arose in the 1940s and 1950s bore an unsettled relation to earlier claims and methods that some, Hueper among them, interpreted as a challenge. Hueper's critique of the new epidemiology identified some of its limitations and potentially debilitating consequences that remain with us today.

Shi, J. F., Y. L. Qiao, et al. (2008). "Epidemiology and prevention of human papillomavirus and cervical cancer in China and Mongolia." Vaccine **26 Suppl 12**: M53-9.

To develop a comprehensive intervention policy for future management of cervical cancer in China and Mongolia, it is essential to review the prevalence of human papillomavirus (HPV) infection, cervical cancer incidence and mortality, status of cervical screening and issues related to prophylactic HPV vaccines. Invasive cervical cancer (ICC) remains an important health problem among women in both China and Mongolia. However, a significant proportion of the burden is observed in rural settings. In areas of China and Mongolia where data are available, HPV prevalence is relatively high, with sexual activity being the most important risk factor. Nationwide programs for cervical cancer screening do not exist, and the majority of women have never been screened. However, government and non-governmental organizations have been collaborating to establish demonstration centers in both high- and low-resource settings to provide screening and obtain geographic specific data. To date, the prophylactic HPV vaccines are not licensed in China or Mongolia, although with wide coverage, the HPV vaccine could potentially prevent as much as three quarters of ICC cases among Chinese and Mongolian women. Ultimately, the introduction of HPV vaccination will present specific challenges, as well as opportunities, for developing advocacy, information and communication strategies that will involve policymakers and the general public.

Silverman, D. T., P. Hartge, et al. (1992). "Epidemiology of bladder cancer." Hematol Oncol Clin North Am **6**(1): 1-30.

Approximately 49,000 persons in the United States develop bladder cancer each year, and about 9700 die of it. White men face a lifetime risk of almost 3%; white women and black men face a risk of about 1%, and black women, about 0.5%. Cigarette smoking is accepted widely as a cause of bladder cancer. Smoking accounts for about half of bladder cancer diagnosed among men and about one third of that among women. Moderate to heavy smokers typically show a two to five fold risk of bladder cancer, compared with persons who never smoked. When cigarette smokers quit smoking, their bladder cancer risk falls measurably within 2 to 4 years, but probably does not continue to decline with increasing years since quitting and does not appear to return to

the baseline level of nonsmokers. Occupational exposure to certain aromatic amines causes human bladder cancer. Clear evidence of bladder cancer risk also is apparent for a small number of occupational groups: dye workers, rubber workers, leather workers, painters, truck drivers, and aluminum workers. Many other occupational groups have been reported to have increased bladder cancer risk, but evidence for these is not as strong. Coffee drinking has been studied extensively as a potential risk factor, but the inconsistency of the observed associations suggests that the relationship is either quite weak, noncausal, or dependent in a complex way on unmeasured factors. Artificial sweeteners confer little or no excess bladder cancer risk. Alcohol consumption apparently does not affect risk either. Consumption of fruits, vegetables, and foods high in vitamin A have been suggested as possible protective factors; consumption of high-fat foods, pork, and beef have been suggested as possible risk factors. Further epidemiologic research is needed to elucidate the role of diet in human bladder carcinogenesis. Less common risk factors for bladder cancer include ionizing radiation, cyclophosphamide use, and abuse of phenacetin-containing analgesics. Schistosomiasis infection may contribute substantially to the bladder cancer burden in Egypt and elsewhere, though not in the United States.(ABSTRACT TRUNCATED AT 400 WORDS)

Spanik, S., J. Trupl, et al. (1996). "Bloodstream infections due to anaerobic bacteria in cancer patients: epidemiology, etiology, risk factors, clinical presentation and outcome of anaerobic bacteremia." Neoplasma **43**(4): 235-8.

Thirty one bacteremic episodes (BE) in 31 patients due to anaerobic bacteremia (AB) in 979 BE among 9986 admissions at a 360 beds National Cancer Institute within last 6 years were analyzed for time distribution, risk factors, clinical presentation and outcome. Overall incidence of AB was 3.6%, but the proportion to other groups of microorganisms is decreasing. 73% were Bacteroides fragilis, 10.8% Peptostreptococci and Propionibacteria and 5.4% Clostridia. The most common risk factor for AB was prior surgery, solid tumor as underlying disease, prophylaxis with quinolones and previous therapy with third generation cephalosporines. 48.4% of AB were polymicrobial. Infected wound was the most common source of infection in 38.7% of our cancer patients. Six patients (19.4%) presented septic shock, and 45.2% died, but only in 22.6% death was related to bacteremia. Comparing the groups of AB due to B. fragilis (BF) to non-Bacteroides spp. (NB)AB, infection-associated mortality was higher in BFAB in comparison to NBAB. Other risk factors such as hematologic malignancies, previous prophylaxis with quinolones, prior surgery and prior therapy with broad spectrum antimicrobials, were more frequently associated with BFAB.

Swaen, G. G., O. Teggeler, et al. (2001). "False positive outcomes and design characteristics in occupational cancer epidemiology studies." Int J Epidemiol **30**(5): 948-54.

BACKGROUND: Recently there has been considerable debate about possible false positive study outcomes. Several well-known epidemiologists have expressed their concern and the possibility that epidemiological research may loose credibility with policy makers as well as the general public. METHODS: We have identified 75 false positive studies and 150 true positive studies, all published reports and all epidemiological studies reporting results on substances or work processes generally recognized as being carcinogenic to humans. All studies were scored on a number of design characteristics and factors relating to the specificity of the research objective. These factors included type of study design, use of cancer registry data, adjustment for smoking and other factors, availability of exposure data, dose- and duration-effect relationship, magnitude of the reported relative risk, whether the study was considered a 'fishing expedition', affiliation and country of the first author. RESULTS: The strongest factor associated with the false positive or true positive study outcome was if the study had a specific a priori hypothesis. Fishing expeditions had an over threefold odds ratio of being false positive. Factors that decreased the odds ratio of a false positive outcome included observing a dose-effect relationship, adjusting for smoking and not using cancer registry data. CONCLUSION: The results of the analysis reported here clearly indicate that a study with a specific a priori study objective should be valued more highly in establishing a causal link between exposure and effect than a mere fishing expedition.

Taioli, E., J. Barone, et al. (1995). "A case-control study on breast cancer and body mass. The American Health Foundation--Division of Epidemiology." Eur J Cancer **31A**(5): 723-8.

A hospital-based case-control study was carried out to examine the effect of body weight/fat and physical activity on risk of breast cancer on 617 newly diagnosed breast cancer cases and 531 controls matched to the cases by age (+/- 5 years), race, year of interview (+/- 1 year) and hospital of admission. Breast cancer was not found to be associated with height, while being overweight appeared to be protective in premenopausal women [odds ratio, OR = 0.4 (0.2-0.7) for cases who weighted > or = 72.7 kg versus controls]. Increased body mass index (BMI)

was protective in premenopausal women [OR = 0.4 (0.2-0.6) in breast cancer cases with BMI > or = 27 versus controls], but not in postmenopausal women, for whom it was a risk factor [OR = 1.5 (1.0-2.3)]. Few women reported any strenuous physical activity from ages 15 to 22 years (22% of premenopausal, 13% of postmenopausal women), and no significant effect on breast cancer risk was observed.

Takkouche, B. and J. J. Gestal-Otero (1996). "The epidemiology of lung cancer: review of risk factors and Spanish data." Eur J Epidemiol **12**(4): 341-9.

Lung cancer is the main form of cancer among men both in Spain and in the rest of europe. However, Spanish incidence rates are among the lowest of the European registries, especially for women. In this country, lung cancer mortality increased much more rapidly for men than for women between the fifties and the eighties. This increase was larger for lung cancer than for any other site. The trend of incidence, in Spain as well as in the greatest part of the world, is entirely explained by tobacco consumption, which remains the major risk factor for lung cancer. Occupational radon and asbestos exposures are other important but less extended determinants of lung cancer. Genetic factors could also play a role in the occurrence of the disease. On the other side, a high consumption of fruit and vegetables is protective, but, so far, no single dietary component has been found to be preventive. In this article, we review the major risk factors of lung cancer with an emphasis on Spanish and European data.

Tominaga, S. and T. Kuroishi (1999). "Epidemiology and Prevention of Breast Cancer in the 21st Century." Breast Cancer **6**(4): 283-288.

The incidence and mortality of breast cancer are high in Western industrialized and relatively low Japan and other Asian countries. In Japan the incidence and mortality of breast cancer have gradually been increasing. Marrying later, having fewer children, a larger intake of fat, dairy products and meats and a larger body mass index in menopausal women may be related to the increased incidence of breast cancer in Japan. A review of risk factors identified from recent epidemio-logical studies in Japan indicates that obesity after 50 years of age is an important risk factor for post-menopausal breast cancer. Future estimations of cancer mortality and incidence predict that breast cancer will further increase to become a leading cancer in Japan in the 21st century.

Trivers, K. F., M. J. Lund, et al. (2009). "The epidemiology of triple-negative breast cancer, including race." Cancer Causes Control **20**(7): 1071-82.

OBJECTIVE: Predictors of intrinsic breast cancer subtypes, including the triple-negative (TN) subtype, are largely unknown. We evaluated whether anthropometrics, demographics, and reproductive history were associated with distinct breast cancer subtypes. METHODS: Invasive breast tumors from a population-based case-control study of 476 (116 black and 360 white) Atlanta women aged 20-54, diagnosed between 1990 and 1992, were centrally reviewed and immunohistochemically analyzed for estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2); then grouped [TN (ER-PR-HER2-); ER-PR-HER2+; ER/PR+HER2+; ER/PR+HER2- (case-only reference group)]. Data were from interviews and anthropometric measurements; adjusted odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression, including both case-only and case-control comparisons. RESULTS: From the case-only analyses and compared with the ER/PR+HER2- subtype, women with TN tumors were more likely to be obese than normal/underweight [OR = 1.89 (95% CI = 1.22, 2.92)]. Regardless of HER2 status, ER-PR- tumors were associated with black race, young age at first birth, having a recent birth, and being overweight. CONCLUSIONS: Distinct breast cancer subtypes have unique sociodemographic, anthropometric and reproductive characteristics and possibly different pathways for development.

Ugolini, D., R. Puntoni, et al. (2007). "A bibliometric analysis of scientific production in cancer molecular epidemiology." Carcinogenesis **28**(8): 1774-9.

OBJECTIVES: The main purpose of this research was to compare the scientific production in the field of cancer molecular epidemiology among countries and to evaluate the publication trend between 1995 and 2004. METHODS: A bibliometric study was carried out searching the PubMed database with a combined search strategy based on the keywords listed in the medical subject headings and a free text search. Only articles from a representative subset of 92 journals--accounting for 80% of papers identified--were selected for the analysis, and the resulting 13,240 abstracts were manually checked according to a list of basic inclusion criteria. The study evaluated the number of publications and the impact factor (mean and sum), absolute and normalized by country population and gross domestic product. RESULTS: A total of 3,842 citations were finally selected for the analysis. Thirty-seven percent came from the European Union (UK, Germany, Italy, France and Sweden ranking at the top), 31.6% from USA and 9.7% from Japan. The highest mean impact

factor was reported for Canada (6.3), USA (5.9), Finland (5.8) and UK (5.2). Finland, Sweden and Israel had the best ratio between scientific production and available resources. 'Genetic polymorphism, glutathione transferase, breast neoplasm, risk factors, case-control studies and polymerase chain reaction' were the most used keywords in each of the subgroups evaluated, although inclusion criteria may have privileged studies dealing with exogenous carcinogens. CONCLUSION: Cancer molecular epidemiology is an expanding area attracting an increasing interest. The identification of an operative definition is a necessary condition to give to this discipline a unique scientific identity.

Veys, C. A. (1993). "Towards causal inference in occupational cancer epidemiology--II. Getting the count right." Ann Occup Hyg **37**(2): 181-9.

This second paper in the series assessing causal inference in occupational cancer epidemiology highlights the importance of using the right data sources when examining the association between exposure and tumour incidence in groups of workers. Using the wrong ones can lead to omissions which become insidious and cumulative during a long-term follow-up study, often extending over several decades. The main cause is the changing survival pattern of some cancers and it is a new and important factor to be taken into account. This was illustrated during an in-depth study of an excess of bladder cancer at a large tire factory, where the workforce was exposed to beta-naphthylamine-contaminated antioxidants used in processing. At first the study was confined to a mortality analysis using death certificates to identify those whose underlying cause of death was bladder cancer [International Classification of Diseases (8th Rev.), No. 188]. It soon became apparent, however, that several cases had outlived the study end-date, or had died of an unrelated cause, often with bladder cancer not being mentioned anywhere on the death certificate. The study was then changed also to include morbidity (incidence) data using cancer registration. Between 1946 and 1949 some 2090 men were exposed to two antioxidants contaminated with about 0.2% of beta-naphthylamine. Altogether there were 45 bladder tumours relevant to this 'at risk' group, whereas only 24.8 were expected at the national incidence rates ($P < 0.001$), which clearly reflects the group's exposure to a recognized bladder carcinogen.(ABSTRACT TRUNCATED AT 250 WORDS)

Vizcaino, A. P., D. M. Parkin, et al. (1994). "Bladder cancer: epidemiology and risk factors in Bulawayo, Zimbabwe." Cancer Causes Control **5**(6): 517-22.

The incidence of bladder cancer, and the importance of some selected risk factors in its etiology, were estimated from the data collected in the cancer registry of Bulawayo, Zimbabwe, during the period 1963-77. Cancer cases were interviewed with a standard questionnaire, and more than 70 percent of these were complete. Incidence rates in the urban population of Bulawayo in the first 10-year period were relatively high, with age standardized rates of 17.9 per 100,000 in men and 9.5 in women. Risk-factor distribution was compared in 680 bladder cancer cases (494 males, 186 females) and a control group comprising other cases with non-tobacco-related cancers (8,201). Seventy-one percent of bladder cancer cases were squamous cell carcinomas. The presence of schistosomiasis, evaluated from past history of bilharzia or hematuria, was associated with a significantly increased risk of bladder cancer in both genders (odds ratio [OR] = 3.9 for men, 5.7 for women), a result reflected in the differing risk by province of residence, which correlated with the prevalence of infection among cancer cases. The proportion of bladder cancer attributable to schistosomiasis was estimated to be 28 percent. Social status, as reflected by education level, also influenced risk (ORs for literate cf illiterate males = 0.6), but tobacco smoking in men had no effect on the risk of squamous cell tumors. For transitional cell carcinomas or adenocarcinomas, there was a nonsignificant increased risk of 2.0 in the highest smoking categories (15 g of tobacco per day), compared with non smokers.

Vogel, V. G. (2008). "Epidemiology, genetics, and risk evaluation of postmenopausal women at risk of breast cancer." Menopause **15**(4 Suppl): 782-9.

Breast cancer risk factors have been studied for the past three decades, and the single most important risk factor is age. Hormonally linked adult reproductive and anthropometric risk factors contribute to the etiology of postmenopausal breast cancer. The risk of breast cancer increases among women older than 50 years of age who have benign breast disease, especially those with atypical ductal or lobular hyperplasia. Lobular carcinoma in situ increases risk significantly, as do a family history of breast cancer in first-degree relatives and the presence of BRCA1 or BRCA2 mutations. Diet, exercise, and environmental factors play a very small role in overall risk. Mammographic breast density increases relative risk fivefold among women with the highest density, and breast cancer risk is two to three times greater in women with elevated serum levels of estradiol or testosterone. Multivariate risk models allow determination of composite relative risks and cumulative lifetime risk, although improved models

for African American women are required. For postmenopausal women, newer risk models are being developed and validated that include age, breast density, race, ethnicity, family history of breast cancer, a previous breast biopsy, body mass index, age at onset of natural menopause, hormone therapy, and previous false-positive mammography. A simpler model that includes only age, breast cancer in first-degree relatives, and previous breast biopsy performs well for estrogen receptor-positive breast cancer in postmenopausal women. As many as 10 million women in the United States are at increased risk, and clinicians are obligated to identify these women and manage their risk appropriately.

Webb, P. M., K. J. Hengels, et al. (1994). "The epidemiology of low serum pepsinogen A levels and an international association with gastric cancer rates. EUROGAST Study Group." Gastroenterology **107**(5): 1335-44.

BACKGROUND/AIMS: Low serum levels of pepsinogen A are indicative of chronic atrophy, a risk factor for gastric cancer. This study investigated the relationships between low pepsinogen A levels, Helicobacter pylori seropositivity, and gastric cancer rates in 17 populations worldwide. METHODS: In each center, about 200 randomly selected subjects (50 male and 50 female, aged 25-34 and 55-64 years) provided serum samples for pepsinogen analysis and H. pylori serology. RESULTS: Cumulative gastric cancer rates were associated with the prevalence of low pepsinogen A levels in men (coefficient, 0.15 [P = 0.06] for mortality; coefficient, 0.36 [P = 0.01] for incidence) but not women. The prevalence of low pepsinogen A levels was also correlated with H. pylori seropositivity in the older age group (r = 0.55; P = 0.02). Low pepsinogen A levels were significantly more common in the older group (7.5% vs. 2.1% in the younger group; P < 0.001), among women (5.5% vs. 4.1% in men; P = 0.04), and among nonsmokers (5.8% vs. 2.9% in current smokers; P = 0.001). CONCLUSIONS: Low pepsinogen A levels are more common in areas with a high seroprevalence of H. pylori and in men in areas with high rates of gastric cancer. The prevalence of low pepsinogen A levels increases with age, but the excess in women and nonsmokers could reflect factors other than gastric pathology.

Wynder, E. L., Y. Fujita, et al. (1991). "Comparative epidemiology of cancer between the United States and Japan. A second look." Cancer **67**(3): 746-63.

Vital statistics were examined for the years 1955 through 1985 for Japanese natives and United States whites to elucidate changes in cancer mortality and related antecedent patterns of life-style in these two populations. Results show that lung cancer rates are rapidly accelerating among Japanese males as a consequence of their prior history of heavy cigarette smoking. Oropharyngeal cancer rates are also rising in Japan paralleling increases in alcohol and tobacco utilization. As the Japanese life-style and diet continue to become more "westernized," the rates of malignancies of the breast, ovary, corpus uteri, prostate, pancreas, and colon also continue to rise. Nevertheless, the mortality patterns of certain malignancies, viz., laryngeal, esophageal, and urinary bladder cancer, are discrepant with their established risk factor associations, suggesting the existence of other differences in risk factor exposure between the two countries. Epidemiologists and health educators need to develop innovative international programs of investigation and health promotion with preventive impact on common malignancies associated with risk factors of life-style.

Wynder, E. L. and J. E. Muscat (1995). "The changing epidemiology of smoking and lung cancer histology." Environ Health Perspect **103 Suppl 8**: 143-8.

In 1950, the first large-scale epidemiological studies demonstrated that lung cancer is causatively associated with cigarette smoking, a finding subsequently confirmed by the Royal College of Physicians in London, the U.S. Surgeon General, and the World Health Organization. Although cigarette consumption has gradually decreased in the United States from a high of about 3800 cigarettes per adult per year in 1965 to about 2800 cigarettes in 1993, death from lung cancer has reached a high among males at the rate of 74.9/100,000/year and among females at the rate of 28.5. However, in the younger cohorts, the lung cancer death rate is decreasing in both men and women. In this overview we discuss the steeper increase during recent decades of lung adenocarcinoma incidence compared with squamous cell carcinoma of the lung. In 1950, the ratio of these two major types of lung cancer in males was about 1:18; today it is about 1:1.2-1.4. This overview discusses two concepts that are regarded as contributors to this change in the histological types of lung cancer. One factor is the decrease in average nicotine and tar delivery of cigarettes from about 2.7 and 38 mg in 1955 to 1.0 and 13.5 mg in 1993, respectively. Other major factors for the reduced emission of smoke relate to changes in the composition of the cigarette tobacco blend and general acceptance of cigarettes with filter tips; the latter constitute 97% of all cigarettes currently sold. However, smokers of low-yield cigarettes compensate for the low delivery of nicotine by inhaling the smoke more deeply and by smoking more intensely; such smokers may be taking up to 5 puffs/min with puff

volumes up to 55 ml. Under these conditions, the peripheral lung is exposed to increased amounts of smoke carcinogens that are suspected to lead to lung adenocarcinoma. Among the important changes in the composition of the tobacco blend of the U.S. cigarette is a significant increase in nitrate content (0.5% to 1.2-1.5%), which raises the yields of nitrogen oxides and N-nitrosamines in the smoke. Furthermore, the more intense smoking by the consumers of low-yield cigarettes increases N-nitrosamines in the smoke 2- to 3-fold. Among the N-nitrosamines is 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), a powerful lung carcinogen in animals that is exclusively formed from nicotine. This organ-specific tobacco-specific nitrosamine (TSNA) induces adenocarcinoma of the lung. All of these factors, the more intense smoking, the deeper inhalation of the smoke, and the increased yields of N-nitrosamines in the smoke of low-yield cigarettes, are considered major contributors to the drastic increase in lung adenocarcinoma among cigarette smokers in recent years. This overview also discusses the differences in the major lung cancer types in female compared with male smokers as well as the likely underlying factors for increased lung cancer risk among African Americans compared with that among white Americans. Although the only sure way to prevent smoking-related diseases is giving up the tobacco habit, there must be a measure of protection for those who cannot accomplish this. Therefore, setting upper permissible limits of tar levels for the smoke of U.S. cigarettes, similar to strategies already taken in Western Europe, should be considered.

Zembower, T. (1998). "Epidemiology of infectious complications in cancer patients." Cancer Treat Res **96**: 33-75.

Patients with underlying malignancies are at risk for a wide array of infectious diseases that cause significant morbidity and mortality. To develop a clear etiologic understanding of the infectious agents involved first requires a knowledge of the factors that predispose to infection. Neutropenia is clearly the single most important risk factor for infection in the cancer patient. However, a variety of both host and treatment-associated factors act together to predispose these patients to opportunistic infections. Approaching the individual malignancies with a knowledge of the underlying risk factors helps logically guide diagnosis and therapy. The astute clinician must also be aware of new and emerging infections in this patient population. As new pathogens are discovered and established pathogens become increasingly drug resistant, they will continue to present challenges for physicians caring for these patients in the years ahead.

References

1. Akslen, L. (1994). "Thyroid-cancer - some aspects of epidemiology and etiologic factors, pathological features and tumor biology." Int J Oncol **4**(4): 931-42.
2. Alberg, A. J., A. P. Lam, et al. (1999). "Epidemiology, prevention, and early detection of breast cancer." Curr Opin Oncol **11**(6): 435-41.
3. Alberg, A. J., K. Visvanathan, et al. (1998). "Epidemiology, prevention, and early detection of breast cancer." Curr Opin Oncol **10**(6): 492-7.
4. Ali, O., P. Cohen, et al. (2003). "Epidemiology and biology of insulin-like growth factor binding protein-3 (IGFBP-3) as an anti-cancer molecule." Horm Metab Res **35**(11-12): 726-33.
5. Al-Zahrani, A. S. and K. Ravichandran (2007). "Epidemiology of thyroid cancer: a review with special reference to Gulf Cooperation Council (GCC) states." Gulf J Oncolog(2): 17-28.
6. Anderson, W. F., N. Chatterjee, et al. (2002). "Estrogen receptor breast cancer phenotypes in the Surveillance, Epidemiology, and End Results database." Breast Cancer Res Treat **76**(1): 27-36.
7. Arab, L. and D. Il'yasova (2003). "The epidemiology of tea consumption and colorectal cancer incidence." J Nutr **133**(10): 3310S-3318S.
8. Badar, F., N. Anwar, et al. (2005). "Geographical variation in the epidemiology of esophageal cancer in Pakistan." Asian Pac J Cancer Prev **6**(2): 139-42.
9. Bedwani, R., F. el-Khwsky, et al. (1997). "Epidemiology of bladder cancer in Alexandria, Egypt: tobacco smoking." Int J Cancer **73**(1): 64-7.
10. Bernstein, L. (2002). "Epidemiology of endocrine-related risk factors for breast cancer." J Mammary Gland Biol Neoplasia **7**(1): 3-15.
11. Blot, W. J. and J. K. McLaughlin (1999). "The changing epidemiology of esophageal cancer." Semin Oncol **26**(5 Suppl 15): 2-8.
12. Brenner, H., D. Rothenbacher, et al. (2009). "Epidemiology of stomach cancer." Methods Mol Biol **472**: 467-77.
13. Broeders, M. J. and A. L. Verbeek (1997). "Breast cancer epidemiology and risk factors." Q J Nucl Med **41**(3): 179-88.
14. Bucsky, P. and T. Parlowsky (1997). "Epidemiology and therapy of thyroid cancer in childhood and adolescence." Exp Clin Endocrinol Diabetes **105 Suppl 4**: 70-3.
15. Caporaso, N. E. and M. T. Landi (1994). "Molecular epidemiology: a new perspective for the study of toxic exposures in man. A consideration of the influence of genetic susceptibility factors on risk in different lung cancer histologies." Med Lav **85**(1): 68-77.
16. Ceschi, M., F. Gutzwiller, et al. (2007). "Epidemiology and pathophysiology of obesity as cause of cancer." Swiss Med Wkly **137**(3-4): 50-6.
17. Chan, J. M., M. J. Stampfer, et al. (1998). "What causes prostate cancer? A brief summary of the epidemiology." Semin Cancer Biol **8**(4): 263-73.
18. Chen, W. Y. and G. A. Colditz (2007). "Risk factors and hormone-receptor status: epidemiology, risk-prediction models and treatment implications for breast cancer." Nat Clin Pract Oncol **4**(7): 415-23.
19. Chen, Y. C. and D. J. Hunter (2005). "Molecular epidemiology of cancer." CA Cancer J Clin **55**(1): 45-54; quiz 57.
20. Chhabra, S. K., V. L. Souliotis, et al. (1996). "Nitrosamines, alcohol, and gastrointestinal tract cancer: recent epidemiology and experimentation." In Vivo **10**(3): 265-84.
21. Christiani, D. C. (2000). "Smoking and the molecular epidemiology of lung cancer." Clin Chest Med **21**(1): 87-93, viii.
22. Chuang, S. C., C. La Vecchia, et al. (2009). "Liver cancer: descriptive epidemiology and risk factors other than HBV and HCV infection." Cancer Lett **286**(1): 9-14.
23. Cohen, S. M. and S. L. Johansson (1992). "Epidemiology and etiology of bladder cancer." Urol Clin North Am **19**(3): 421-8.
24. Cote, T. R., A. Manns, et al. (1996). "Epidemiology of brain lymphoma among people with or without acquired immunodeficiency syndrome. AIDS/Cancer Study Group." J Natl Cancer Inst **88**(10): 675-9.
25. Cresanta, J. L. (1992). "Epidemiology of cancer in the United States." Prim Care **19**(3): 419-41.

26. Crucitti, F., L. Sofo, et al. (1995). "Colorectal cancer. Epidemiology, etiology, pathogenesis and prevention." Rays **20**(2): 121-31.
27. Curado, M. P. and M. Hashibe (2009). "Recent changes in the epidemiology of head and neck cancer." Curr Opin Oncol **21**(3): 194-200.
28. Damber, J. E. (1998). "Prostate cancer: epidemiology and risk factors." Curr Opin Urol **8**(5): 375-80.
29. Dijkman, G. A. and F. M. Debruyne (1996). "Epidemiology of prostate cancer." Eur Urol **30**(3): 281-95.
30. dos Santos Silva, I. and A. J. Swerdlow (1993). "Thyroid cancer epidemiology in England and Wales: time trends and geographical distribution." Br J Cancer **67**(2): 330-40.
31. Fincham, S. M., A. M. Ugnat, et al. (2000). "Is occupation a risk factor for thyroid cancer? Canadian Cancer Registries Epidemiology Research Group." J Occup Environ Med **42**(3): 318-22.
32. Friedberg, J. S. and L. R. Kaiser (1997). "Epidemiology of lung cancer." Semin Thorac Cardiovasc Surg **9**(1): 56-9.
33. Fu, J. B., T. Y. Kau, et al. (2005). "Lung cancer in women: analysis of the national Surveillance, Epidemiology, and End Results database." Chest **127**(3): 768-77.
34. Garte, S., C. Zocchetti, et al. (1997). "Gene--environment interactions in the application of biomarkers of cancer susceptibility in epidemiology." IARC Sci Publ(142): 251-64.
35. Gilbert, S. M. and J. M. McKiernan (2005). "Epidemiology of male osteoporosis and prostate cancer." Curr Opin Urol **15**(1): 23-7.
36. Glaser, S. L., C. A. Clarke, et al. (2005). "Cancer surveillance research: a vital subdiscipline of cancer epidemiology." Cancer Causes Control **16**(9): 1009-19.
37. Greenwald, P. and B. K. Dunn (2009). "Landmarks in the history of cancer epidemiology." Cancer Res **69**(6): 2151-62.
38. Gunter, M. J. and M. F. Leitzmann (2006). "Obesity and colorectal cancer: epidemiology, mechanisms and candidate genes." J Nutr Biochem **17**(3): 145-56.
39. Gupta, P. C., P. R. Murti, et al. (1996). "Epidemiology of cancer by tobacco products and the significance of TSNA." Crit Rev Toxicol **26**(2): 183-98.
40. Hall, J., M. Artuso, et al. (1996). "Molecular epidemiology of skin cancers: DNA repair and non-melanocytic skin cancer." Ann Ist Super Sanita **32**(1): 43-51.
41. Hashibe, M., P. Brennan, et al. (2007). "Alcohol drinking in never users of tobacco, cigarette smoking in never drinkers, and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium." J Natl Cancer Inst **99**(10): 777-89.
42. Hawk, E. T., P. J. Limburg, et al. (2002). "Epidemiology and prevention of colorectal cancer." Surg Clin North Am **82**(5): 905-41.
43. Holschneider, C. H. and J. S. Berek (2000). "Ovarian cancer: epidemiology, biology, and prognostic factors." Semin Surg Oncol **19**(1): 3-10.
44. Hortobagyi, G. N., J. de la Garza Salazar, et al. (2005). "The global breast cancer burden: variations in epidemiology and survival." Clin Breast Cancer **6**(5): 391-401.
45. Igisinov, S., E. Soodonbekov, et al. (2002). "Epidemiology of Esophagus, Lung and Breast Cancer in Mountainous Regions of Kyrgyz Republic." Asian Pac J Cancer Prev **3**(1): 73-76.
46. Jaga, K. and C. Dharmani (2005). "The epidemiology of pesticide exposure and cancer: A review." Rev Environ Health **20**(1): 15-38.
47. Jani, A. B., V. A. Master, et al. (2007). "Grade migration in prostate cancer: an analysis using the Surveillance, Epidemiology, and End Results registry." Prostate Cancer Prostatic Dis **10**(4): 347-51.
48. Jarup, L., N. Best, et al. (2002). "Geographical epidemiology of prostate cancer in Great Britain." Int J Cancer **97**(5): 695-9.
49. Johansson, S. L. and S. M. Cohen (1997). "Epidemiology and etiology of bladder cancer." Semin Surg Oncol **13**(5): 291-8.
50. Kabat, G. C. (1996). "Aspects of the epidemiology of lung cancer in smokers and nonsmokers in the United States." Lung Cancer **15**(1): 1-20.
51. Kikuchi, S. (2002). "Epidemiology of Helicobacter pylori and gastric cancer." Gastric Cancer **5**(1): 6-15.
52. Knight, J. A., L. Bernstein, et al. (2009). "Alcohol intake and cigarette smoking and risk of a contralateral breast cancer: The Women's Environmental Cancer and Radiation Epidemiology Study." Am J Epidemiol **169**(8): 962-8.
53. Koc, M. and P. Polat (2001). "Epidemiology and aetiological factors of male breast cancer: a ten years retrospective study in eastern Turkey." Eur J Cancer Prev **10**(6): 531-4.
54. Kuijken, I. and J. N. Bavinck (2000). "Skin cancer risk associated with immunosuppressive therapy in organ transplant recipients: epidemiology and proposed mechanisms." BioDrugs **14**(5): 319-29.
55. Kwan, M. L., L. H. Kushi, et al. (2009). "Epidemiology of breast cancer subtypes in two prospective cohort studies of breast cancer survivors." Breast Cancer Res **11**(3): R31.
56. La Vecchia, C. (2001). "Epidemiology of ovarian cancer: a summary review." Eur J Cancer Prev **10**(2): 125-9.
57. La Vecchia, C., F. Levi, et al. (1992). "Descriptive epidemiology of ovarian cancer in Europe." Gynecol Oncol **46**(2): 208-15.
58. La Vecchia, C., L. Chatenoud, et al. (2001). "Nutrition and health: epidemiology of diet, cancer and cardiovascular disease in Italy." Nutr Metab Cardiovasc Dis **11**(4 Suppl): 10-5.
59. Lawes, C. M., C. F. Tukuitonga, et al. (1999). "The epidemiology of breast cancer in Pacific women in New Zealand." N Z Med J **112**(1096): 354-7.
60. Lee, Y. C., P. Boffetta, et al. (2008). "Involuntary smoking and head and neck cancer risk: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium." Cancer Epidemiol Biomarkers Prev **17**(8): 1974-81.
61. Leiter, U. and C. Garbe (2008). "Epidemiology of melanoma and nonmelanoma skin cancer--the role of sunlight." Adv Exp Med Biol **624**: 89-103.
62. Levine, P. H. and C. Veneroso (2008). "The epidemiology of inflammatory breast cancer." Semin Oncol **35**(1): 11-6.
63. Link, B. G., M. E. Northridge, et al. (1998). "Social epidemiology and the fundamental cause concept: on the structuring of effective cancer screens by socioeconomic status." Milbank Q **76**(3): 375-402, 304-5.
64. Lissowska, J., A. Pilarska, et al. (2003). "Smoking, alcohol, diet, dentition and sexual practices in the epidemiology of oral cancer in Poland." Eur J Cancer Prev **12**(1): 25-33.
65. Liu, G., W. Zhou, et al. (2005). "Molecular epidemiology of non-small cell lung cancer." Semin Respir Crit Care Med **26**(3): 265-72.
66. Lowenfels, A. B. and P. Maisonneuve (2004). "Epidemiology and prevention of pancreatic cancer." Jpn J Clin Oncol **34**(5): 238-44.
67. Lowenfels, A. B., P. Maisonneuve, et al. (1999). "Epidemiology of gallbladder cancer." Hepatogastroenterology **46**(27): 1529-32.
68. Lukanova, A. and R. Kaaks (2005). "Endogenous hormones and ovarian cancer: epidemiology and current hypotheses." Cancer Epidemiol Biomarkers Prev **14**(1): 98-107.
69. MacFarlane, E., D. Glass, et al. (2009). "Is farm-related job title an adequate surrogate for pesticide exposure in occupational cancer epidemiology?" Occup Environ Med **66**(8): 497-501.
70. Malekzadeh, R., M. H. Derakhshan, et al. (2009). "Gastric cancer in Iran: epidemiology and risk factors." Arch Iran Med **12**(6): 576-83.
71. Marur, S. and A. A. Forastiere (2008). "Head and neck cancer: changing epidemiology, diagnosis, and treatment." Mayo Clin Proc **83**(4): 489-501.
72. Matsuba, T., D. Qiu, et al. (2005). "Overview of epidemiology of bile duct and gallbladder cancer focusing on the JACC Study." J Epidemiol **15 Suppl 2**: S150-6.
73. Meirow, D. and J. G. Schenker (1996). "The link between female infertility and cancer: epidemiology and possible aetiologies." Hum Reprod Update **2**(1): 63-75.
74. Memik, F., M. Gulten, et al. (1996). "The epidemiology of gastrointestinal cancer in Turkey: a review of our accumulated experience." J Environ Pathol Toxicol Oncol **15**(2-4): 209-13.
75. Mettlin, C. (1994). "The relationship of breast cancer epidemiology to screening recommendations." Cancer **74**(1 Suppl): 228-30.
76. Michaud, D. S. (2004). "Epidemiology of pancreatic cancer." Minerva Chir **59**(2): 99-111.

77. Millikan, R. C., B. Newman, et al. (2008). "Epidemiology of basal-like breast cancer." Breast Cancer Res Treat **109**(1): 123-39.
78. Molina, J. R., P. Yang, et al. (2008). "Non-small cell lung cancer: epidemiology, risk factors, treatment, and survivorship." Mayo Clin Proc **83**(5): 584-94.
79. Moore, M. A. and K. Tajima (2004). "Cervical cancer in the asian pacific-epidemiology, screening and treatment." Asian Pac J Cancer Prev **5**(4): 349-61.
80. Moran, E. M. (1996). "Environment, cancer, and molecular epidemiology: air pollution." J Environ Pathol Toxicol Oncol **15**(2-4): 97-104.
81. Morgensztern, D., S. Waqar, et al. (2009). "Improving survival for stage IV non-small cell lung cancer: a surveillance, epidemiology, and end results survey from 1990 to 2005." J Thorac Oncol **4**(12): 1524-9.
82. Murta-Nascimento, C., B. J. Schmitz-Drager, et al. (2007). "Epidemiology of urinary bladder cancer: from tumor development to patient's death." World J Urol **25**(3): 285-95.
83. Nagataki, S. and E. Nystrom (2002). "Epidemiology and primary prevention of thyroid cancer." Thyroid **12**(10): 889-96.
84. Narod, S. (1999). "Genetic epidemiology of prostate cancer." Biochim Biophys Acta **1423**(1): F1-13.
85. Neugut, A. I., M. Hayek, et al. (1996). "Epidemiology of gastric cancer." Semin Oncol **23**(3): 281-91.
86. Oliveria, S. A. and P. J. Christos (1997). "The epidemiology of physical activity and cancer." Ann N Y Acad Sci **833**: 79-90.
87. Oliveria, S. A., P. J. Christos, et al. (1997). "The role of epidemiology in cancer prevention." Proc Soc Exp Biol Med **216**(2): 142-50.
88. Palli, D. (1996). "Epidemiology of gastric cancer." Ann Ist Super Sanita **32**(1): 85-99.
89. Pashos, C. L., M. F. Botteman, et al. (2002). "Bladder cancer: epidemiology, diagnosis, and management." Cancer Pract **10**(6): 311-22.
90. Pera, M. (2000). "Epidemiology of esophageal cancer, especially adenocarcinoma of the esophagus and esophagogastric junction." Recent Results Cancer Res **155**: 1-14.
91. Petersen, G. M. (1994). "Epidemiology, screening, and prevention of lung cancer." Curr Opin Oncol **6**(2): 156-61.
92. Pilz, S., A. Tomaschitz, et al. (2009). "Epidemiology of vitamin D insufficiency and cancer mortality." Anticancer Res **29**(9): 3699-704.
93. Powell, I. J. (2007). "Epidemiology and pathophysiology of prostate cancer in African-American men." J Urol **177**(2): 444-9.
94. Raghu, G., F. Nyberg, et al. (2004). "The epidemiology of interstitial lung disease and its association with lung cancer." Br J Cancer **91 Suppl 2**: S3-10.
95. Rahu, M. and T. Hakulinen (1994). "Descriptive epidemiology of cancer around the Baltic Sea." Acta Oncol **33**(8): 849-58.
96. Raimondi, S., P. Maisonneuve, et al. (2009). "Epidemiology of pancreatic cancer: an overview." Nat Rev Gastroenterol Hepatol **6**(12): 699-708.
97. Renehan, A. G., J. O'Connell, et al. (2003). "Acromegaly and colorectal cancer: a comprehensive review of epidemiology, biological mechanisms, and clinical implications." Horm Metab Res **35**(11-12): 712-25.
98. Rivera, M. P. (2009). "Lung cancer in women: the differences in epidemiology, biology and treatment outcomes." Expert Rev Respir Med **3**(6): 627-34.
99. Samet, J. M. (1993). "The epidemiology of lung cancer." Chest **103**(1 Suppl): 20S-29S.
100. Sellers, C. (1997). "Discovering environmental cancer: Wilhelm Hueper, post-World War II epidemiology, and the vanishing clinician's eye." Am J Public Health **87**(11): 1824-35.
101. Shi, J. F., Y. L. Qiao, et al. (2008). "Epidemiology and prevention of human papillomavirus and cervical cancer in China and Mongolia." Vaccine **26 Suppl 12**: M53-9.
102. Silverman, D. T., P. Hartge, et al. (1992). "Epidemiology of bladder cancer." Hematol Oncol Clin North Am **6**(1): 1-30.
103. Swaen, G. G., O. Teggeler, et al. (2001). "False positive outcomes and design characteristics in occupational cancer epidemiology studies." Int J Epidemiol **30**(5): 948-54.
104. Taioli, E., J. Barone, et al. (1995). "A case-control study on breast cancer and body mass. The American Health Foundation--Division of Epidemiology." Eur J Cancer **31A**(5): 723-8.
105. Takkouche, B. and J. J. Gestal-Otero (1996). "The epidemiology of lung cancer: review of risk factors and Spanish data." Eur J Epidemiol **12**(4): 341-9.
106. Tominaga, S. and T. Kuroishi (1999). "Epidemiology and Prevention of Breast Cancer in the 21st Century." Breast Cancer **6**(4): 283-288.
107. Trivers, K. F., M. J. Lund, et al. (2009). "The epidemiology of triple-negative breast cancer, including race." Cancer Causes Control **20**(7): 1071-82.
108. Ugolini, D., R. Puntoni, et al. (2007). "A bibliometric analysis of scientific production in cancer molecular epidemiology." Carcinogenesis **28**(8): 1774-9.
109. Veys, C. A. (1993). "Towards causal inference in occupational cancer epidemiology--II. Getting the count right." Ann Occup Hyg **37**(2): 181-9.
110. Vizcaino, A. P., D. M. Parkin, et al. (1994). "Bladder cancer: epidemiology and risk factors in Bulawayo, Zimbabwe." Cancer Causes Control **5**(6): 517-22.
111. Vogel, V. G. (2008). "Epidemiology, genetics, and risk evaluation of postmenopausal women at risk of breast cancer." Menopause **15**(4 Suppl): 782-9.
112. Webb, P. M., K. J. Hengels, et al. (1994). "The epidemiology of low serum pepsinogen A levels and an international association with gastric cancer rates. EUROGAST Study Group." Gastroenterology **107**(5): 1335-44.
113. Wynder, E. L. and J. E. Muscat (1995). "The changing epidemiology of smoking and lung cancer histology." Environ Health Perspect **103 Suppl 8**: 143-8.
114. Wynder, E. L., Y. Fujita, et al. (1991). "Comparative epidemiology of cancer between the United States and Japan. A second look." Cancer **67**(3): 746-63.
115. Zembower, T. (1998). "Epidemiology of infectious complications in cancer patients." Cancer Treat Res **96**: 33-75.
116. PubMed (2012). http://www.ncbi.nlm.nih.gov/pubmed.
117. Cancer. Wikipedia. (2012) http://en.wikipedia.org/wiki/Cancer.

8/21/2011