Cancer Biology

Cancer Signs and Symptoms Research Literatures

Mark Herbert, PhD

World Development Institute
39 Main Street, Flushing, Queens, New York 11354, USA, ma8080@gmail.com

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

1. Introduction

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

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

Al-Darwish, A. A., et al. (2014). "Knowledge about cervical cancer early warning signs and symptoms, risk factors and vaccination among students at a medical school in Al-Ahsa, Kingdom of Saudi Arabia." Asian Pac J Cancer Prev **15**(6): 2529-2532.

BACKGROUND: Cervical cancer is the second most common cancer among females and also the most preventable. In the literature there is abundant evidence that awareness regarding cervical cancer and its prevention is low in the developing countries. Medical students are the future health professionals and can play an important role in increasing awareness among the general population. To assess the knowledge regarding symptoms, risk factors and prevention of cervical carcinoma among medical students in th Kingdom of Saudi Arabia, the present study was planned. MATERIALS AND METHODS: This cross-sectional study was conducted using a self-administered questionnaire with students at the College of Medicine, King Faisal University, Al-Ahsa, KSA, from December 2012 to May 2013. RESULTS: The responses of 188 students (males 111, females 77) in their second, third, fourth, and fifth years were recorded and used in the data analysis. The majority of the students were not aware of the early warning signs, symptoms and risk factors. On average, only 43.7% males and 56% of females were aware about the early signs and symptoms whereas 51.4% males and 57.8% females had knowledge about the risk factors of cervical cancers. Some 55% males and 46.8% females were unable to select the correct answer regarding human papilloma virus (HPV) infection as the cause of cervical cancer. Majority of the students (67%) were not aware about the availability of vaccine against HPV. CONCLUSIONS: Lack of knowledge regarding early signs and symptoms, risk factors and prevention of cervical cancer was observed in the present study.

Anzar, S., et al. (2017). "Validation of the Malayalam Version of Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale in Cancer Patients in the Regional Cancer Centre, Thiruvananthapuram, Kerala, India." Indian J Palliat Care **23**(3): 293-299.

OBJECTIVE: The Self-administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) is a 7-item self-report scale developed to identify pain which is of predominantly neuropathic origin. The aim of this study was to develop a Malayalam version of the LANSS and to test its validity and reliability in chronic pain patients. METHODOLOGY: We enrolled 101 Malayalam-speaking chronic pain patients who visited the Division of Palliative Medicine, Regional Cancer Centre, Thiruvananthapuram, Kerala, India. The translated

version of S- LANSS was constructed by standard means. Fifty-one neuropathic pain and fifty nociceptive pain patients were identified by an independent pain physician and were subjected to the new pain scale by a palliative care nurse who was blinded to the diagnosis. The "gold standard diagnosis" is what the physician makes after clinical examination. Its validation, sensitivity, specificity, and positive and negative predictive values were determined. RESULTS: Fifty-one neuropathic pain and fifty nociceptive pain patients were subjected to the Malayalam version of S-LANSS pain scale for validity testing. The agreement by Cohen's Kappa 0.743, Chi-square test P < 0.001, sensitivity 89.58, specificity 84.91, positive predictive value 84.31, negative predictive value 90.00, accuracy by 87.13, and likelihood ratio 5.94. CONCLUSION: The Malayalam version of S-LANSS pain scale is a validated screening tool for identifying neuropathic pain in chronic pain patients in Malayalam-speaking regions.

Armer, J. and M. R. Fu (2005). "Age differences in post-breast cancer lymphedema signs and symptoms." Cancer Nurs **28**(3): 200-207; quiz 208-209.

This secondary data analysis was designed to explore the age differences in lymphedema (LE) occurrence and self-reported symptoms in post-breast cancer LE. A descriptive-exploratory cross-sectional design was used with a convenience sample composed of 102 women treated and followed for breast cancer at a midwestern cancer center. Sequential circumferential arm measurement was used to estimate limb volume differences. Self-reported symptoms were assessed by the Lymphedema and Breast Cancer Questionnaire (LBCQ) designed and tested by the research team. Lymphedema occurrence was relatively higher (41.2%) in breast cancer survivors younger than 60 than in those older than 60 (30.6%). Six subjectively reported symptoms were found to occur more often (P </= .05) in the younger women with LE: numbness now and in the past year, tenderness in the past year, aching now and in the past year, increased temperature in arm now. Numbness, tenderness, and aching were the most prevalent symptoms among women in both age groups regardless of LE presence. Our findings suggest that younger breast cancer survivors may have increased LE risk and report LE-related symptoms more often. Future research should focus on age differences in LE risk, occurrence, and perceptions of LE-related symptoms in women treated for breast cancer.

Bakkevold, K. E., et al. (1992). "Carcinoma of the pancreas and papilla of Vater: presenting symptoms, signs, and diagnosis related to stage and tumour site. A prospective multicentre trial in 472 patients.

Norwegian Pancreatic Cancer Trial." Scand J Gastroenterol **27**(4): 317-325.

During the period 1984-87, 472 patients with histologically or cytologically verified carcinoma of the pancreas (n = 442) or the papilla of Vater (n = 30) were accrued. Diagnostic investigations were performed in accordance with the ordinary routines of 38 Norwegian hospitals. Jaundice at presentation, found in 47% of the patients, indicated a relatively low staging. Abdominal pain or weight loss, present in 72% and 58%, respectively, indicated higher staging. The sensitivities of the diagnostic investigations were 1) endoscopic retrograde cholangiopancreatography (ERCP), 79%, and computed tomography (CT), 75%; 2) ultrasonography (US), 57%; angiography performed in 18% to assess unresectability, sensitivity, 43%; fine-needle aspiration cytology performed in 27%, sensitivity, 86%; and percutaneous transhepatic cholangiography (PTC) performed solely on papillar and head tumours in 16%, sensitivity, 85%. In stage I, PTC and ERCP had a sensitivity of 78%; CT, 52%; and US, 40%. Patient's, physician's, and diagnostic delay averaged 1.8, 2.4, and 4.0 months, respectively. The delays were shortest in stage I and papillar carcinomas.

Barlow, W. E., et al. (2002). "Performance of diagnostic mammography for women with signs or symptoms of breast cancer." J Natl Cancer Inst **94**(15): 1151-1159.

BACKGROUND: The performance of diagnostic mammography for women with signs or symptoms of breast cancer has not been well studied. We evaluated whether age, breast density, self-reported breast lump, and previous mammography influence the performance of diagnostic mammography. METHODS: From January 1996 through March 1998, prospective diagnostic mammography data from women aged 25-89 years with no previous breast cancer were linked to cancer outcomes data in six mammography registries participating in the Breast Cancer Surveillance Consortium. We used the final mammographic assessment at the end of the imaging work-up to determine abnormal mammographic examination rate, positive predictive value (PPV), sensitivity, specificity, and area under the receiver operating characteristic (ROC) curve. We used age, breast density, prior mammogram, and self-reported breast lump jointly as predictors of performance. All statistical tests were two-sided. RESULTS: Of 41 427 diagnostic mammograms, 6279 (15.2%) were judged abnormal. The overall PPV was 21.8%, sensitivity was 85.8%, and specificity was 87.7%. Multivariate analysis showed that sensitivity and specificity generally declined as breast density increased (P =.007 and P<.001, respectively), that previous mammography decreased sensitivity (odds ratio [OR] = 0.52, 95%

confidence interval [CI] = 0.36 to 0.74; P<.001) but increased specificity (OR = 1.43, 95% CI = 1.31 to 1.57; P<.001), and that a self-reported breast lump increased sensitivity (OR = 1.64, 95% CI = 1.13 to 2.38; P =.013) but decreased specificity (OR = 0.54, 95% CI = 0.49 to 0.59; P<.001). ROC analysis showed that higher breast density and previous mammography were negatively related to accuracy (P<.001 for both). CONCLUSIONS: Diagnostic mammography in women with signs or symptoms of breast cancer shows higher sensitivity and lower specificity than screening mammography does. Higher breast density and previous mammographic examination appear to impair performance.

Beckles, M. A., et al. (2003). "Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes." Chest **123**(1 Suppl): 97S-104S.

This chapter describes the components of the initial evaluation for a patient either suspected or known to have lung cancer. The components of the initial evaluation are based on the recognized manifestations of localized lung cancer, ie, symptoms referable to the primary tumor, intrathoracic spread of lung cancer, and patterns of metastatic dissemination. Features of the history and physical signs may be useful indicators of the extent of disease. A standardized evaluation, relying on symptoms, signs, and routinely available laboratory tests, can serve as a useful screen for metastatic disease. Also described are the common features of the various paraneoplastic syndromes associated with lung cancer.

Bleyer, A. (2009). "CAUTION! Consider cancer: common symptoms and signs for early detection of cancer in young adults." Semin Oncol **36**(3): 207-212.

Because young adults frequently have longer delays in diagnosis of their cancers than younger or older persons, healthcare providers who encounter this age group should become more aware of diagnostic clues for early detection. The spectrum of cancer types and their relative frequencies is distinctly different in young adults than the array in younger and older persons, such that the symptoms and signs in aggregate are distinctly different. Of potential value in recognizing manifestations of cancer in young adults is a mnemonic-friendly list of seven symptoms each represented by a letter in CAUTION, and seven sites of signs starting with the letter B. These aids have the potential of assisting in early detection, accurate diagnosis, longer survival, and a reduced risk of premature death.

Bullough, B. (1980). "Discovery of the first signs and symptoms of breast cancer." Nurse Pract **5**(6): 31-32, 47.

A sample of 139 post-mastectomy patients was interviewed to determine how the first sign or symptom of breast cancer was identified. Eighty percent of the time the first clue was noted by the patient herself; 19 percent of the first signs were picked up by health professionals, only 1 percent of the first clues were identified by lovers. An unexpected finding was that pain was the first symptom noted by 13 percent of the women. Implications for health teaching to improved early detection are discussed.

Chen, Y. M., et al. (2004). "Impact of severe acute respiratory syndrome on the status of lung cancer chemotherapy patients and a correlation of the signs and symptoms." Lung Cancer **45**(1): 39-43.

Our aim was to describe the impact of severe acute respiratory syndrome (SARS) on the status and chemotherapy of non-small-cell lung cancer (NSCLC) patients who had entered clinical trials, and to review how to differentiate the signs and symptoms of SARS from lung cancer and its treatment-related toxicities. A prospective case series involving 79 NSCLC patients who were enrolled in clinical trials undergoing chemotherapy at Taipei Veterans General Hospital, between April 1 and July 15, 2003, was studied. Whether or not there existed a delay, omission, or refusal of scheduled chemotherapy, was recorded. Whether or not our patients had been suspected of or treated as having SARS, was recorded. The patients filled out questionnaires regarding lung cancer treatment and the risk of getting SARS from the hospital. Among these patients, five were placed in an isolation unit to rule out SARS infection during this period of time, and no patient was documented to have suffered from a SARS infection after examinations. Of 373 scheduled chemotherapy injections in 79 patients, a delay in treatment occurred only 10 times. Three patients refused further chemotherapy because of a fear of getting SARS if they visited the hospital. Fifty-eight patients responded to our questionnaires. Thirty-seven patients (63.8%) were afraid of visiting hospital during this SARS infection period. Twenty-one patients (36.2%) felt that a SARS infection was more severe and fatal than their lung cancer. In conclusion, SARS is a new disease entity that is highly contagious. Its clinical manifestations overlap with the signs and symptoms of lung cancer. Thus, a clear differentiation between the two conditions is needed, especially for those patients who are under active anti-cancer treatment.

Crane, M., et al. (2016). "Knowledge of the signs and symptoms and risk factors of lung cancer in Australia: mixed methods study." BMC Public Health **16**: 508.

BACKGROUND: Lung cancer is the leading cause of cancer death in Australia. There is potential that health promotion about the risks and warning signs of lung cancer could be used to reduce delays in symptom presentation when symptoms are first detected. This study investigated knowledge, attitudes and beliefs which might impact help-seeking behaviour and could provide insight into possible public health interventions in New South Wales (NSW). METHODS: A convergent mixed method study design was used wherein data from 16 qualitative focus groups of residents (40+ years), purposefully recruited and stratified by smoking status, age and geography (metropolitan/regional), were compared with a CATI administered population-wide telephone survey (n = 1,000) using the Cancer Research UK cancer awareness measure (LungCAM). Qualitative findings were analysed thematically using NVIVO. Logistic regression analysis was used to investigate predictors of symptom knowledge in STATA. Findings were integrated using triangulation techniques. RESULTS: Across focus groups, haemoptysis was the only symptom creating a sense of medical urgency. Life experiences evoked a 'wait and see' attitude to any health deterioration. Perceived risk was low amongst those at risk with current smokers preferring to deny their risk while former smokers were generally unaware of any ongoing risk. The quantitative sample consisted of females (62 %), 40-65 years (53 %), low SES (53 %), former (46 %) and current smokers (14 %). In quantitative findings, haemoptysis and dyspnoea were the most recognised symptoms across the sample population. Age (<65 years), sex (female) and high socio-economic status contributed to a higher recognition of symptoms. Smoking was recognised as a cause of lung cancer, yet ever-smokers were less likely to recognise the risk of lung cancer due to second-hand smoke (OR 0.7 95 % CI 0.5-0.9). CONCLUSION: While there was some recognition of risk factors and symptoms indicative of lung cancer, there was disparity across the sample population. The qualitative findings also suggest that knowledge may not lead to earlier presentation; a lack of urgency about symptoms considered trivial, and smoking-related barriers such as stigma may also contribute to time delays in presentation. Public health interventions may be required to increase awareness of risk and emphasise the importance of seeking medical attention for ongoing symptoms.

Croager, E. J., et al. (2018). "Find Cancer Early: Evaluation of a Community Education Campaign to Increase Awareness of Cancer Signs and Symptoms in People in Regional Western Australians." Front Public Health **6**: 22.

Introduction: Cancer outcomes for people living in rural and remote areas are worse than for those living in urban areas. Although access to and quality of cancer treatment are important determinants of outcomes, delayed presentation has been observed in rural patients. Methods: Formative research with people from rural Western Australia (WA) led to the Find Cancer Early campaign. Find Cancer Early was delivered in three regions of WA, with two other regions acting as controls. Staff delivered the campaign using a community engagement approach, including promotion in local media. Television communications were not used to minimize contamination in the control regions. The campaign evaluation was undertaken at 20 months via a computer-assisted telephone interview (CATI) survey comparing campaign and control regions. The primary outcome variable was knowledge of cancer signs and symptoms. Results: Recognition and recall of Find Cancer Early and symptom knowledge were higher in the campaign regions. More than a quarter of those who were aware of the campaign reported seeing the GP as a result of their exposure. Conclusion: Despite limited use of mass media, Find Cancer Early successfully improved knowledge of cancer symptoms and possibly led to changes in behavior. Social marketing campaigns using community development can raise awareness and knowledge of a health issue in the absence of television advertising.

Fijten, G. H., et al. (1995). "Predictive value of signs and symptoms for colorectal cancer in patients with rectal bleeding in general practice." Fam Pract **12**(3): 279-286.

The aim of the study is to determine the diagnostic value of (combinations of) signs, symptoms and simple laboratory test results for colorectal cancer in patients with rectal bleeding presenting in general practice. Initial complaints and findings were compared with the final diagnoses based on clinical follow-up after at least 1 year. Patients studied were those presenting overt rectal bleeding to the general practitioner (83 GPs in the South of the Netherlands). Outcome measures are sensitivity, specificity, predictive values, odds ratios and a prediction model derived from multiple logistic regression analysis. Age, change in bowel habit and blood mixed with or on stool show a statistically significant independent value in the discrimination between patients with a low and those with a high probability of colorectal cancer. Many other variables did not show predictive value. The prediction model has a sensitivitiy of 100% and a specificity of 90%. Although the number of patients with colorectal cancer is small (n = 9) it was possible to

identify three characteristics which can be helpful in the prediction of presence or absence of colorectal cancer in general practice. Application of the model presented might prevent 90% of 'unnecessary' invasive diagnostic procedures for patients with rectal bleeding who do not have colorectal cancer (true negative). Testing the performance of the model in other general practice populations is recommended.

Fonseca, M. B., et al. (2017). "Signs and symptoms of rheumatic diseases as first manifestation of pediatric cancer: diagnosis and prognosis implications." Rev Bras Reumatol Engl Ed **57**(4): 330-337.

OBJECTIVE: To assess the prevalence and describe the clinical, laboratory and radiological findings, treatment and outcome of children with cancer initially referred to a tertiary outpatient pediatric rheumatology clinic. METHODS: Retrospective analysis of medical records from patients identified in a list of 250 new patients attending the tertiary Pediatric Rheumatology Clinic, Ribeirao Preto Medical School hospital, University of Sao Paulo, from July 2013 to July 2015, whose final diagnosis was cancer. RESULTS: Of 250 patients seen during the study period, 5 (2%) had a cancer diagnosis. Among them, 80% had constitutional symptoms, especially weight loss and asthenia, and 60% had arthritis. Initially, all patients had at least one alteration in their blood count, lactate dehydrogenase was increased in 80% and a bone marrow smear was conclusive in 60% of patients. Bone and intestine biopsies were necessary for the diagnosis in 2 patients. JIA was the most common initial diagnosis. The definitive diagnosis was acute lymphoblastic leukemia (2 patients), M3 acute myeloid leukemia, lymphoma, and neuroblastoma (one case each). Of 5 patients studied, 3 (60%) are in remission and 2 (40%) died, one of them with prior use of steroids. CONCLUSION: The constitutional and musculoskeletal symptoms common to rheumatic and neoplastic diseases can delay the diagnosis and consequently worsen the prognosis of neoplasms. Initial blood count and bone marrow smear may be normal in the initial framework of neoplasms. Thus, the clinical follow-up of these cases becomes imperative and the treatment, mainly with corticosteroids, should be delayed until diagnostic definition.

Fragkandrea, I., et al. (2013). "Signs and symptoms of childhood cancer: a guide for early recognition." Am Fam Physician **88**(3): 185-192.

Although cancer in children is rare, it is the second most common cause of childhood mortality in developed countries. It often presents with nonspecific symptoms similar to those of benign conditions, leading to delays in the diagnosis and initiation of appropriate treatment. Primary care physicians should have a raised index of suspicion and explore the possibility of cancer in children who have worrisome or persisting signs and symptoms. Red flag signs for leukemia or lymphoma include unexplained and protracted pallor, malaise, fever, anorexia, weight loss, lymphadenopathy, hemorrhagic diathesis, and hepatosplenomegaly. New onset or persistent morning headaches associated with vomiting, neurologic symptoms, or back pain should raise concern for tumors of the central nervous system. Palpable masses in the abdomen or soft tissues, and persistent bone pain that awakens the child are red flags for abdominal, soft tissue, and bone tumors. Leukokoria is a red flag for retinoblastoma. Endocrine symptoms such as growth arrest, diabetes insipidus, and precocious or delayed puberty may be signs of endocranial or germ cell tumors. Paraneoplastic manifestations such as opsoclonus-myoclonus syndrome, rheumatic symptoms, or hypertension are rare and may be related to neuroblastoma, leukemia, or Wilms tumor, respectively. Increased suspicion is also warranted for conditions associated with a higher risk of childhood cancer, including immunodeficiency syndromes and previous malignancies, as well as with certain genetic conditions and familial cancer syndromes such as Down syndrome, Li-Fraumeni syndrome, hemihypertrophy, neurofibromatosis, and retinoblastoma.

Gookizadeh, A., et al. (2012). "Clinical evaluation of BIOXTRA in relieving signs and symptoms of dry mouth after head and neck radiotherapy of cancer patients at Seyed-al-Shohada Hospital, Isfahan, Iran." Adv Biomed Res **1**: 72.

BACKGROUND: Radiotherapy of head and neck cancers causes acute and chronic xerostomia and acute mucositis. Xerostomia increases risk of radiation caries and affects on oral comfort, fit of prostheses, speech, swallowing, and the growth of caries-producing organisms. Salivary flow rate can be measured by asking patients some questions. There are different types of commercial synthetic saliva such as BIOXTRA, but until now, no one can effectively relieve xerostomia. We tried to design a clinical research on BIOXTRA efficacy for treating xerostomia. MATERIALS AND METHODS: In this research, 58 patients with head and neck cancer (except salivary gland cancers) treated in Seyed-al-Shohada Hospital. The patients received at least 40-50 GY; and after 2 months of compilation treatment, they were evaluated by asking about having xerostomia. Before and after treatment with the BIOXTRA, the PH of the oral cavity, candida albicans, and lactobacillus counts measured and documented in laboratory. We used BIOXTRA for 2 weeks, 3 times daily, and then re-evaluated patients with some questions. RESULTS: The counts of candida albicans and lactobacilli statistically significant

decreased. CONCLUSION: Xerostomia for most patients improved clinically during the day and night while PH of the oral cavity increased.

Gussgard, A. M., et al. (2015). "Radiation-Induced Mucositis in Patients with Head and Neck Cancer: Should the Signs or the Symptoms Be Measured?" J Can Dent Assoc **81**: f11.

OBJECTIVE: To improve understanding of how patient-reported outcomes following radiation therapy for head and neck cancer may be influenced by factors beyond the local effects of the radiotherapy. METHODS: Initially, 50 patients with head and neck cancer who were scheduled to undergo radiation therapy consented to participate in this prospective observational study. The participants underwent an oral examination before commencement of therapy and twice weekly over the therapy period. The 33 participants who finished the therapy underwent one more examination 4 to 6 weeks after its completion. At each session, clinical signs of oral mucositis were recorded with clinician-based scoring tools, and participants completed a questionnaire based on a visual analogue scale to record the perceived degree of impairment of common oral functions caused by oral mucositis. The strength of the correlation between these signs and symptoms at various points throughout the study period was appraised using a linear mixed model with robust repeated measures. The study participants with the most extensive manifestations of oral mucositis but only minor pain and limited adverse effects on oral functions (n=6) were contrasted with those who had limited mucositis but more severe pain and adverse effects (n=7). In addition, study participants with poor to moderate correlations between signs and symptoms (n=5) were contrasted with those who had very good correlations (n=10). Simple bivariate tests were used for these comparisons. RESULTS: Correlations between various signs and symptoms at all time points varied markedly at the individual level. The characteristics of study participants in the 2 subcohorts defined by poor to moderate and very good correlations between signs and symptoms were comparable, except perhaps in terms of age ($p<0.05$, t test). Similarly, the participants in the 2 subcohorts defined by high manifestation with minor complaints and vice versa did not differ with regard to the variables recorded. CONCLUSION: Patients with head and neck cancer often report adverse effects of radiation-related oral mucositis on daily oral functions that are discordant with objective clinical findings. Patient-reported outcomes should be included in any interventional studies of oral mucositis, and trends over time should be analyzed within individuals, rather than between individuals.

Hemady, R. K., et al. (1996). "Ocular symptoms and signs associated with suramin sodium treatment for metastatic cancer of the prostate." Am J Ophthalmol **121**(3): 291-296.

PURPOSE: Therapy with suramin sodium has been associated with photophobia, iritis, optic atrophy, and vortex keratopathy. We studied the ocular findings in patients who underwent treatment with suramin sodium for metastatic cancer of the prostate. METHODS: In a prospective study, 114 patients who underwent treatment with suramin sodium for cancer of the prostate had an ophthalmologic examination with two weeks of onset of treatment and two weeks after termination of therapy. Additional examinations were performed on patients who developed ocular symptoms during suramin sodium therapy. RESULTS: Nineteen (16.6%) of 114 patients developed ocular symptoms and signs while taking suramin sodium. Thirteen of these patients developed bilateral corneal epithelial whorllike deposits. In ten patients, the corneal deposits were associated with foreign body sensation and lacrimation. Symptoms in all of these patients resolved with topical lubricants. Three patients developed asymptomatic corneal deposits. Seven patients had blurred vision and were found to have a mean hyperopic shift in refractive error of 1.13 +/- 0.45 diopters (range, 0.75 to 2.00 diopters) that persisted throughout their treatment course. None of these patients had a decrease in best-corrected visual acuity. CONCLUSIONS: In this study, ocular symptoms and signs associated with suramin sodium were common but were not considered a dose-limiting toxicity. Hyperopic shift in refractive error is a previously unreported ocular finding in association with suramin sodium therapy.

Holly, E. A., et al. (2004). "Signs and symptoms of pancreatic cancer: a population-based case-control study in the San Francisco Bay area." Clin Gastroenterol Hepatol **2**(6): 510-517.

BACKGROUND & AIMS: Pancreatic cancer usually does not cause definitive symptoms until survival is severely compromised. Prevention and early detection are urgently needed. Our aim was to collect and analyze data in a population-based study on signs and symptoms of disease reported by patients with pancreatic cancer and control participants to contribute to earlier detection and better prognosis. METHODS: A supplemental symptoms questionnaire was administered to 120 consecutive patients with pancreatic cancer who were part of a larger population-based case-control study conducted in the San Francisco Bay Area between 1994 and 2001. One hundred eighty age- and sex-matched population-based control participants also were queried about the same symptoms reported by at least 5% of patients with

pancreatic cancer. RESULTS: Most signs and symptoms occurred within 3 years before diagnosis with pancreatic cancer (cases) and interview (controls). Many signs and symptoms were more likely to have been reported by patients compared with control participants and included appetite loss (odds ratio [OR], 41; 95% confidence interval [CI], 14-120), pale stools (OR, 31; 95% CI, 7.3-134), abdominal pain (OR, 30; 95% CI, 9.1-101), jaundice (OR, 20; 95% CI, 8.0-49), unusual bloating (OR, 20; 95% CI, 5.9-67), unusual belching (OR, 17; 95% CI, 3.9-75), weight loss (OR, 12; 95% CI, 5.2-28), dark urine (OR, 10; 95% CI, 2.9-36), constipation (OR, 7.3; 95% CI, 2.0-26), diarrhea (OR, 5.6; 95% CI, 2.0-16), itching (OR, 5.0; 95% CI, 2.3-11), fatigue (OR, 3.8; 95% CI, 2.0-7.3), altered ability to sleep (OR, 2.9; 95% CI, 1.3-6.3), and unusual heartburn (OR, 2.3; 95% CI, 1.2-4.5). CONCLUSIONS: Our results show that signs and symptoms likely to be indicators of pancreatic cancer occur substantially more often among patients with pancreatic cancer than among population-based controls. The large magnitude of the risk estimates indicate that common gastrointestinal symptoms may assist clinicians in earlier diagnosis of pancreatic cancer and perhaps affect survival.

Ingeman, M. L., et al. (2015). "The Danish cancer pathway for patients with serious non-specific symptoms and signs of cancer-a cross-sectional study of patient characteristics and cancer probability." BMC Cancer **15**: 421.

BACKGROUND: A Danish cancer pathway has been implemented for patients with serious non-specific symptoms and signs of cancer (NSSC-CPP). The initiative is one of several to improve the long diagnostic interval and the poor survival of Danish cancer patients. However, little is known about the patients investigated under this pathway. We aim to describe the characteristics of patients referred from general practice to the NSSC-CPP and to estimate the cancer probability and distribution in this population. METHODS: A cross-sectional study was performed, including all patients referred to the NSSC-CPP at the hospitals in Aarhus or Silkeborg in the Central Denmark Region between March 2012 and March 2013. Data were based on a questionnaire completed by the patient's general practitioner (GP) combined with nationwide registers. Cancer probability was the percentage of new cancers per investigated patient. Associations between patient characteristics and cancer diagnosis were estimated with prevalence rate ratios (PRRs) from a generalised linear model. RESULTS: The mean age of all 1278 included patients was 65.9 years, and 47.5 % were men. In total, 16.2 % of all patients had a cancer diagnosis after six months; the most common types were lung cancer (17.9 %),

colorectal cancer (12.6 %), hematopoietic tissue cancer (10.1 %) and pancreatic cancer (9.2 %). All patients in combination had more than 80 different symptoms and 51 different clinical findings at referral. Most symptoms were non-specific and vague; weight loss and fatigue were present in more than half of all cases. The three most common clinical findings were 'affected general condition' (35.8 %), 'GP's gut feeling' (22.5 %) and 'findings from the abdomen' (13.0 %). A strong association was found between GP-estimated cancer risk at referral and probability of cancer. CONCLUSIONS: In total, 16.2 % of the patients referred through the NSSC-CPP had cancer. They constituted a heterogeneous group with many different symptoms and clinical findings. The GP's gut feeling was a common reason for referral which proved to be a strong predictor of cancer. The GP's overall estimation of the patient's risk of cancer at referral was associated with the probability of finding cancer.

Issah, F., et al. (2011). "Expressions of cervical cancer-related signs and symptoms." Eur J Oncol Nurs **15**(1): 67-72.

BACKGROUND: Cervical cancer is the second most common cancer in women worldwide. Although developing countries are the hardest hit by cervical cancer, women living in Europe are also at risk for this disease. PURPOSE OF THE STUDY: The purpose of the study was to explore how women treated for cervical cancer at an academic hospital in Tshwane, South Africa, expressed their cervical cancer-related signs and symptoms during the initial consultation with health care professionals. METHODS AND SAMPLE: A qualitative, exploratory and contextual research design was used. The sampling method was purposive and convenience. Self-reported data were gathered using semi-structured interviews. Diekelmann's hermeneutical analysis approach was used to analyze the data. The sample size totaled 12 (n = 12). RESULTS: Four themes emerged from the data-- ignorance, communication, delayed diagnosis and expectations. All participants lacked knowledge and awareness of the signs and symptoms of cervical cancer. The majority failed to communicate the real nature of their signs and symptoms and was only diagnosed after several visits to the primary health clinic. CONCLUSION: Nurses should use every opportunity to screen women for cervical cancer as the woman might not be able to express her cervical cancer-related signs and symptoms.

John, S. K., et al. (2011). "Symptoms and signs in patients with colorectal cancer." Colorectal Dis **13**(1): 17-25.

The symptoms and signs of colorectal cancer vary from the general population to primary care and in

the referred population to secondary care. This review aims to address the diverse symptoms, signs and combinations with relevance to colorectal cancer at various points in the diagnostic pathway and tries to shed light on this complex and confusing area. A move towards a lower threshold for referral and increased use of diagnostics might be a more reliable option for early diagnosis.

Jorgensen, S. F., et al. (2017). "Characteristics and outcome in patients with non-specific symptoms and signs of cancer referred to a fast track cancer patient pathway; a retrospective cohort study." BMC Cancer **17**(1): 809.

BACKGROUND: In 2012 a new cancer patient pathway for patients with non-specific symptoms and signs of cancer (NSSC-CPP) was introduced in Denmark. Limited information is available about the patients referred to the NSSC-CPP and the investigational course. The aim was to describe the population and the investigational course, estimate the prevalence of cancer and one-year mortality, and identify factors associated with a subsequent cancer diagnosis in patients referred to the NSSC-CPP. METHOD: This cohort study included patients with at least one visit at the NSSC-CPP at North Zealand Hospital in Denmark (NOH) from October 1st 2013 to September 30th 2014. Data was based on retrospective reviews of the patient files. Logistic regression identified factors associated with a subsequent cancer diagnosis. Multivariate analyses were adjusted by age, gender, smoking status and alcohol consumption. Kaplan-Meier survival plots were made at one-year follow-up. RESULTS: Eight hundred twenty-five patients were included with a median age of 67 years, 47.4% were male. Prevalence of cancer within one year was 16.7% (138/825). 70.3% (97/138) were solid cancers and 29.7% (41/138) were haematological cancers. During the investigational course 76.7% went through advanced diagnostic imaging (ultrasound, CT, FDG-PET/CT or MRI). Anaemia (OR1.63 CI1.02-2.60), leucocytosis (OR 2.06 CI 1.34-3.15), thrombocytopenia (OR 4.13 CI 2.02-8.47) and elevated LDH (OR 1.64 CI 1.07-2.52) and CRP (OR 2.56 CI 1.66-3.95) were associated with a cancer diagnosis when adjusting for possible confounders. No single non-specific symptom was significantly associated with a cancer diagnosis. One-year mortality for those diagnosed with cancer was 44.2%. CONCLUSION: The prevalence of cancer matches that of another NSSC-CPP in Denmark. Deviations in basic biochemistry were associated with a higher probability of underlying cancer and could possibly raise the level of suspicion of malignancy among physicians. High one-year mortality was seen amongst patients diagnosed with cancer.

Karesen, R., et al. (2003). "[Medical logistics: principles applied to diagnostics and therapy in women with symptoms and signs of breast cancer]." Tidsskr Nor Laegeforen **123**(12): 1687-1690.

BACKGROUND: Using breast cancer as an example, we suggest that medical logistics should be introduced as a method for continuous improvement of quality and cost-effectiveness in the health care system. MATERIALS AND METHODS: Ullevaal University Hospital has approximately 500 newly diagnosed cases of breast cancer per year. The triple diagnostic test supplemented by MRI are the diagnostic tools. We rely on fine needle aspiration cytology as the only morphological test before surgery, which is done as day surgery. 70 % of the patients return home on the same day, the others stay in a patient hotel until the drains can be removed. The sentinel node procedure is routine and has been done on 610 patients. RESULTS: Of 1502 radically operated, 2 had false positive cytology (0.12 per cent). Of 610 sentinel node cases, 91 % were found; of these, 23 % had metastasis. Among the negative cases, two have so far experienced recurrence of the disease in the axilla. The patients are well satisfied. Total yearly savings compared to the era before sentinel node and use of a patient hotel has been calculated to approximately 400 000 euro. INTERPRETATION: We find our results so far acceptable as regards the use of fine needle aspiration cytology as well as the sentinel node. Both techniques are, however, technically demanding and should only be used in centres that have continuous quality monitoring.

Khan, A. and K. Sultana (2010). "Presenting signs and symptoms of ovarian cancer at a tertiary care hospital." J Pak Med Assoc **60**(4): 260-262.

OBJECTIVE: To identify early warning signs and symptoms of ovarian cancer to create awareness for early diagnosis and management of the disease. METHODS: This study was conducted at the department of Gynaecology and Obstetrics, Liaquat National Hospital, Karachi from 2003 to 2007, having 75 patients. The information collected included age, education, and self perceived state of socio-economic class, presenting clinical signs and symptoms, basic and specific laboratory investigations. The disease was staged from I to IV upon surgical staging and the type of cancer was determined by histopathological examination. RESULTS: Mean age of the patients was 51 +/- 12.3 years. Twenty (52%) patients were uneducated, 17 (22.6%) were below and remaining 19 (25.3%) were above higher secondary level. Most of the patients belonged to the middle socioeconomic class. Abdominal pain (57.3%) was the most common presenting symptom followed by abdominal distension

(22.6%), urinary complaints (5.3%), vaginal discharge (2.6%) and postmenopausal bleeding (12%). More than half (56%) of the patients had stage III-IV disease. On histology, papillary serous cystic adenocarcinoma was the most common (54%) type followed by mucinious (22%), endometroid (10.6%), yolk sac (2.6%), dysgerminoma (4%), and adult granulose cell tumour (5.3%). CONCLUSION: There are no specific ovarian carcinoma symptoms either in early or late stages to ensure early diagnosis, but in the age group above 40 years persistent clinical symptoms should always be further investigated.

Lebech, A. M., et al. (2017). "Whole-Body (18)F-FDG PET/CT Is Superior to CT as First-Line Diagnostic Imaging in Patients Referred with Serious Nonspecific Symptoms or Signs of Cancer: A Randomized Prospective Study of 200 Patients." J Nucl Med **58**(7): 1058-1064.

A fast-track pathway has been established in Denmark to investigate patients with serious nonspecific symptoms and signs of cancer (NSSC), who are not eligible to enter an organ-specific cancer program. The prevalence of cancer in this cohort is approximately 20%. The optimal screening strategy in patients with NSSC remains unknown. The aim of the study was to investigate whether (18)F-FDG PET/CT was superior to CT as an initial imaging modality in patients with NSSC. In a randomized prospective trial, the imaging modalities were compared with regard to diagnostic performance. Methods: Two hundred patients were randomized 1:1 to whole-body (18)F-FDG PET/CT or CT of the thorax and abdomen as the imaging modality. A tentative diagnosis was established after first-line imaging. The final referral diagnosis was adjudicated by the physician, when sufficient data were available. Results: One hundred ninety-seven patients were available for analysis because 3 patients withdrew consent before scanning. Thirty-nine (20%) patients were diagnosed with cancer, 10 (5%) with an infection, 15 (8%) with an autoimmune disease, and 76 (39%) with other diseases. In the remaining 57 patients (28%), no specific disease was found. (18)F-FDG PET/CT had a higher specificity (96% vs. 85%; P = 0.028) and a higher accuracy (94% vs. 82%; P = 0.017) than CT. However, there were no statistically significant differences in sensitivity (83% vs. 70%) or negative predictive values (96% vs. 92%). No difference in days to final referral diagnosis according to randomization group could be shown (7.2 vs. 7.6 d). However, for the subgroups in which the imaging modality showed a suggestion of malignancy, there was a significant delay to final diagnosis in the CT group compared with the (18)F-FDG PET/CT group (11.6 vs. 5.7 d; P = 0.02). Conclusion: Compared with CT, we found a higher diagnostic specificity and accuracy of (18)F-FDG PET/CT for detecting cancer in patients with NSSC. (18)F-FDG PET/CT should therefore be considered as first-line imaging in this group of patients.

Lisboa, I. N., et al. (2016). "Prevalent Signs and Symptoms in Patients with Skin Cancer and Nursing Diagnoses." Asian Pac J Cancer Prev **17**(7): 3207-3211.

BACKGROUND: Skin cancer has a remarkable importance given the high incidence in the population. In Brazil, it is estimated that there were 98,420 new cases of nonmelanoma skin cancer among men and 83,710 new cases among women in 2014. OBJECTIVES: To verify signs and symptoms present in patients with skin neoplasms according to the literature and relate them to the nursing diagnoses of NANDA International. MATERIALS AND METHODS: Integrative literature review carried out from March to May 2015 in the databases: Cumulative Index to Nursing and Allied Health Literature, SCOPUS, National Library of Medicine and Nattional Institutes of Health, Latin American and Caribbean Sciences of Health and Web of Science. The descriptors used were: 'Signs and Symptoms' and 'Skin Neoplasms'. Sixteen articles were identified as the final sample. After review, the signs and symptoms of skin cancer identified in the literature were related to the defining characteristics present in NANDA International, with the aim to trace possible nursing diagnoses. RESULTS: The most prevalent signs and symptoms were: asymmetric and well circumscribed nodules with irregular borders; speckles with modified color aspect; ulcerations; blisters; pain; itching; and bleeding. The principal nursing diagnoses outlined were: risk for impaired skin integrity; impaired skin integrity; acute pain; risk of shock; and impaired comfort. CONCLUSIONS: The identification of signs and symptoms present in patients with skin cancer and the relationships of these with the nursing diagnoses of NANDA International provide a basis for qualified and systematized nursing care to this clientele.

Machida, H., et al. (2016). "Signs and Symptoms of Venous Thromboembolism and Survival Outcome of Endometrial Cancer." Int J Gynecol Cancer **26**(5): 924-932.

OBJECTIVE: This study aimed to evaluate if the presence of venous thromboembolism (VTE) diagnosed with subjective and objective measurements correlates with the survival outcome in patients with endometrial cancer. METHODS: A retrospective study was conducted on patients with endometrial cancer who developed VTE between cancer diagnosis and follow-up from 1999 to 2013. Disease-specific survival after VTE diagnosis was evaluated according to VTE symptoms and vital signs. RESULTS: Among 827

endometrial cancer cases during the study period, there were 72 (8.7%) patients with VTE identified (pulmonary embolism [PE] with or without deep vein thrombosis [DVT], n = 34; and DVT alone n = 38). In the PE group, decreased disease-specific survival after the diagnosis of VTE was associated with fatigue, systolic blood pressure (BP) less than 120 mm Hg, diastolic BP less than 70 mm Hg, and a heart rate 90 beats per minute or greater (all, $P < 0.05$) in a univariate analysis. Symptomatic PE was associated with decreased survival as compared to asymptomatic PE (2-year rate; 23.1% vs 77.8%, $P < 0.01$). In a multivariate analysis controlling for symptoms of VTE, signs, and tumor factors, a diastolic BP less than 70 mm Hg (adjusted-hazard ratio [HR], 10.0; 95% confidence interval, 2.70-37.1; $P < 0.01$) and HR greater than 90 beats per minute (adjusted-HR, 8.06; 95% confidence interval, 2.36-27.5; $P < 0.01$) remained as independent prognostic factors for decreased disease-specific survival after PE diagnosis. Patients with PE presenting with low diastolic BP and high heart rate resulted in a dismal survival outcome (diastolic BP < 70 mm Hg/heart rate >/= 90 beats per minute vs diastolic BP >/= 70 mm Hg/heart rate < 90 beats per minute; 0% vs 85.7%, $P < 0.01$). In the group of patients with DVT alone, no signs or symptoms correlated with survival outcome (all, $P > 0.05$). CONCLUSIONS: Our results suggested that both signs and symptoms of PE are important consideration in the management of patients with endometrial cancer with PE.

Moseholm, E. and B. O. Lindhardt (2017). "Patient characteristics and cancer prevalence in the Danish cancer patient pathway for patients with serious non-specific symptoms and signs of cancer-A nationwide, population-based cohort study." Cancer Epidemiol **50**(Pt A): 166-172.
        BACKGROUND: A new cancer patient pathway for patients presenting with non-specific signs and symptoms (NSSC-CPP) was implemented nationally in Denmark in 2012. This study aims to describe, on a national level, the characteristics of patients referred to the Danish NSSC-CPP, and to estimate the prevalence and distribution of cancers and other diagnosis in this population. METHODS: A population-based cohort study using the Danish national registries, including all patients who completed a diagnostic course through the NSSC-CPP between 2012 and 2015. Cancer prevalence is presented as the percentage of included patients who were diagnosed with cancer after completing a NSSC-CPP diagnostic course. Associations between patient characteristics and cancer diagnosis were estimated in a multivariate logistic regression model. RESULTS: The mean age of the 23,934 patients included in the

analysis was 64.6 years and 47% where male. In total, 11% of all patients received a cancer diagnosis after completing a diagnostic course in the NSSC-CPP; the most common types were breast cancer (18%) hematopoietic and lymphoid tissue cancer (15%), and malignant melanoma (12%). The most common non-cancer diagnosis was non-specific symptoms/observation (54%). Fifty-five patients were diagnosed with cancer within six months following a non-cancer diagnosis in the NSSC-CPP. CONCLUSIONS: The prevalence of cancer in the NSSC-CPP was 11%. The most common cancer diagnosis was breast cancer, hematopoietic and lymphoid cancer and malignant melanoma. A small proportion of patients receiving a non-cancer diagnosis in the NSSC-CPP were diagnosed with cancer in the six months following their NSSC-CPP course.

Nwosu, A. C., et al. (2016). "The Association of Hydration Status with Physical Signs, Symptoms and Survival in Advanced Cancer-The Use of Bioelectrical Impedance Vector Analysis (BIVA) Technology to Evaluate Fluid Volume in Palliative Care: An Observational Study." PLoS One **11**(9): e0163114.
        BACKGROUND: Hydration in advanced cancer is a controversial area; however, current hydration assessments methods are poorly developed. Bioelectrical impedance vector analysis (BIVA) is an accurate hydration tool; however its application in advanced cancer has not been explored. This study used BIVA to evaluate hydration status in advanced cancer to examine the association of fluid status with symptoms, physical signs, renal biochemical measures and survival. MATERIALS AND METHODS: An observational study of 90 adults with advanced cancer receiving care in a UK specialist palliative care inpatient unit was conducted. Hydration status was assessed using BIVA in addition to assessments of symptoms, physical signs, performance status, renal biochemical measures, oral fluid intake and medications. The association of clinical variables with hydration was evaluated using regression analysis. A survival analysis was conducted to examine the influence of hydration status and renal failure. RESULTS: The hydration status of participants was normal in 43 (47.8%), 'more hydrated' in 37 (41.1%) and 'less hydrated' in 10 (11.1%). Lower hydration was associated with increased symptom intensity (Beta = -0.29, p = 0.04) and higher scores for physical signs associated with dehydration (Beta = 10.94, p = 0.02). Higher hydration was associated with oedema (Beta = 2.55, p<0.001). Median survival was statistically significantly shorter in 'less hydrated' patients (44 vs. 68 days; p = 0.049) and in pre-renal failure (44 vs. 100 days; p = 0.003). CONCLUSIONS: In advanced cancer, hydration status was associated with clinical signs and

symptoms. Hydration status and pre-renal failure were independent predictors of survival. Further studies can establish the utility of BIVA as a standardised hydration assessment tool and explore its potential research application, in order to inform the clinical management of fluid balance in patients with advanced cancer.

Nylenna, M. and P. Hjortdahl (1987). "How do patients evaluate cancer related symptoms and signs? A study from general practice." Scand J Prim Health Care **5**(2): 117-122.

Descriptions of twenty different clinical situations, most of which included cancer related symptoms and signs, were assessed by 329 patients. The patients showed a satisfactory level of alertness in response to the clinical situations. Lumps and bumps and visible bleeding gave the quickest response. An inverse relationship was found between how frequent a situation was experienced among the patients and how serious it was interpreted to be. A comparison between the patients' assessment and the advice given by a random sample of 90 general practitioners revealed a quicker response rate recommended by the doctors than found among the patients for most of the symptoms and signs. The gap between doctors' and patients' understanding and interpretation of symptoms and signs is at least partly due to different levels of medical knowledge. This gap should be narrowed by public information and health education. In planning this education, knowledge of patients' evaluation of symptoms, as shown in this study, is of importance.

Olde Bekkink, M., et al. (2010). "Diagnostic accuracy systematic review of rectal bleeding in combination with other symptoms, signs and tests in relation to colorectal cancer." Br J Cancer **102**(1): 48-58.

BACKGROUND: Rectal bleeding is a recognised early symptom of colorectal cancer. This study aimed to assess the diagnostic accuracy of symptoms, signs and diagnostic tests in patients with rectal bleeding in relation to risk of colorectal cancer in primary care. METHODS: Diagnostic accuracy systematic review. Medline (1966 to May 2009), Embase (1988 to May 2009), British Nursing Index (1991 to May 2009) and PsychINFO (1970 to May 2009) were searched. We included cohort studies that assessed the diagnostic utility of rectal bleeding in combination with other symptoms, signs and diagnostic tests in primary care. An eight-point quality assessment tool was produced to assess the quality of included studies. Pooled positive likelihood ratios (PLRs), sensitivities and specificities were calculated. RESULTS: Eight studies incorporating 2323 patients were included. Average weighted prior probability of colorectal cancer was 7.0% (range: 3.3-15.4%, median:

8.1%). Age > or = 60 years (pooled PLR: 2.79, 95% confidence interval (CI) 2.00-3.90), weight loss (pooled PLR: 1.89, 95% CI: 1.03-3.07) and change in bowel habit (pooled PLR: 1.92, 95% CI: 0.54-3.57) raise the probability of colorectal cancer into the range of referral to secondary care but do not conclusively 'rule in' the diagnosis. Presence of severe anaemia has the highest diagnostic value (pooled PLR: 3.67, 95% CI: 1.30-10.35), specificity 0.95 (95% CI: 0.93-0.96), but still only generates a post-test probability of 21.6%. CONCLUSIONS: In patients with rectal bleeding who present to their general practitioner, additional 'red flag' symptoms have modest diagnostic value. These findings have implications in relation to recommendations contained in clinical practice guidelines.

Palsson, B., et al. (1997). "Tumour marker CA 50 levels compared to signs and symptoms in the diagnosis of pancreatic cancer." Eur J Surg Oncol **23**(2): 151-156.

The diagnostic merits of CA 50 and of symptoms indicating pancreatic cancer (pain, jaundice, weight loss, malabsorption) were compared prospectively in 512 consecutive patients. Among the final diagnoses were: exocrine pancreatic cancer, 175; periampullary cancer, 44; other gastrointestinal cancer, 45; and chronic pancreatitis, 64 cases. The suspected diagnoses based on symptoms and signs were correct in 80% of the patients with exocrine pancreatic cancer, in 78% with periampullary, in 76% with other gastrointestinal cancer and in 90% with chronic pancreatitis. CA 50 was pathological in 96% of the cases with exocrine pancreatic cancer, in 70% with periampullary, in 78% with other gastrointestinal malignancies and in 36% with chronic pancreatitis. The sensitivity was 96%, specificity 48%, positive prediction 49% and negative prediction 96%, depending on cut-off level. The single CA 50 value was comparable to symptoms and signs regarding sensitivity and negative prediction. In 28 of 42 cases incorrectly clinically classified, CA 50 alone indicated a benign or malignant diagnosis. If both the modalities 'signs and symptoms' and CA 50 were combined, the sensitivity was 91%, the specificity 92%, the positive prediction 86% and the negative prediction 95%. The initial CA 50 value can help to indicate in which patients a pancreatic malignancy should be suspected.

Petrovic, J., et al. (2008). "Influence of long-term radiotherapy on symptoms and signs of locally advanced primary rectal cancer of distant localisation." Acta Chir Iugosl **55**(3): 61-66.

This study is a part of a clinical trial in preoperative radiotherapy of low rectal cancer, conducted as a prospective and partly retrospective

clinical study. It was designed to estimate the influence of long-term radiotherapy on symptoms of locally advanced rectal cancer. We included 49 patients with T3/4 stage adenocarcinoma (diagnosis confirmed by clinical, pathological and CT examinations) of the lower two thirds of the rectum, who were treated with long-term radiotherapy (45 Gy in 20-25 fractions) and questioned for the presentation of symptoms before and after the treatment. The chief complaints of these patients were the presence of blood in stool, abdominal and pelvic pain, straining (tenesmus) and the alteration in bowel movement. We found a significant decrease in symptoms and signs of the illness after the radiotherapy as well as the improvement of the quality of life.

Potter, J., et al. (2003). "Identifying neuropathic pain in patients with head and neck cancer: use of the Leeds Assessment of Neuropathic Symptoms and Signs Scale." J R Soc Med **96**(8): 379-383.

The Leeds Assessment of Neuropathic Symptoms and Signs Scale (LANSS) is a simple bedside test in two parts-a patient-completed questionnaire and a brief clinical assessment. Its diagnostic capabilities have never been tested in patients with cancer pain. To determine these we conducted a prospective study in outpatients with head and neck cancer. All patients with pain completed the LANSS and underwent a medical assessment with a palliative care physician, whose findings were then reviewed by a pain specialist blinded to the LANSS scores. We assessed acceptability and understanding of the LANSS by patients and calculated the sensitivity and specificity of total LANSS scores and subscores derived from the patient-completed section. Of 130 patients approached, 125 took part. 25 (20%) of these had cancer related pain, mean score on an 11 point numerical rating scale 6.3 (median 6.0, range 3-10). Average age was 60 years (median 60, range 27-84); 56% were male. LANSS completion time was about five minutes, and the procedure was acceptable to all patients. The pain specialist diagnosed neuropathic pain in 14/25 patients, in 13 of whom the neuropathic pain was part of a mixed pain picture. The LANSS correctly identified 11 of these cases (sensitivity 79%; specificity 100%). The patient-completed section alone had a sensitivity of 86% and a specificity of 91%. The LANSS is a simple and suitable screening test for neuropathic pain in patients with head and neck cancer related pain, although some modifications might improve it.

Rasmussen, L. J. H., et al. (2017). "Inflammatory biomarkers and cancer: CRP and suPAR as markers of incident cancer in patients with serious nonspecific symptoms and signs of cancer." Int J Cancer **141**(1): 191-199.

In Denmark, patients with serious nonspecific symptoms and signs of cancer (NSSC) are referred to the diagnostic outpatient clinics (DOCs) where an accelerated cancer diagnostic program is initiated. Various immunological and inflammatory biomarkers have been associated with cancer, including soluble urokinase plasminogen activator receptor (suPAR) and the pattern recognition receptors (PRRs) pentraxin-3, mannose-binding lectin, ficolin-1, ficolin-2 and ficolin-3. We aimed to evaluate these biomarkers and compare their diagnostic ability to classical biomarkers for diagnosing cancer in patients with NSSC. Patients were included from the DOC, Department of Infectious Diseases, Copenhagen University Hospital Hvidovre. Patients were given a final diagnosis based on the combined results from scans, blood work and physical examination. Weight loss, Charlson score and previous cancer were registered on admission, and plasma concentrations of biomarkers were measured. The primary outcome was incident cancer within 1 year. Out of 197 patients included, 39 patients (19.8%) were diagnosed with cancer. Patients with cancer were significantly older and had a higher burden of comorbidities and previous cancer diagnoses compared to patients who were not diagnosed with cancer. Previous cancer, C-reactive protein (CRP) and suPAR were significantly associated with newly diagnosed cancer during follow-up in multiple logistic regression analyses adjusted for age, sex and CRP. Neither any of the PRRs investigated nor self-reported weight loss was associated with cancer. In this study, previous cancer, CRP and suPAR were significantly associated with cancer diagnosis in patients with NSSC. Ficolin-1-3, MBL and pentraxin-3 were not associated with cancer.

Rhodus, N. L. and J. Bereuter (2000). "Clinical evaluation of a commercially available oral moisturizer in relieving signs and symptoms of xerostomia in postirradiation head and neck cancer patients and patients with Sjogren's syndrome." J Otolaryngol **29**(1): 28-34.

A major complication of irradiation therapy for head and neck cancer is salivary gland dysfunction and xerostomia. The purpose of this clinical investigation was to evaluate the effects of a commercially available oral moisturizer (Optimoist) on salivary flow rate, symptoms of xerostomia, oral pH, oral microflora, and swallowing in postirradiation head and neck cancer patients (XRT) and patients with Sjogren's syndrome (SS). Subjects who were post-XRT and subjects with SS (n = 24; mean age = 54.1) discontinued their use of any salivary substitute or moisturizer for 2 weeks prior to entering the study. Baseline whole unstimulated saliva was collected for 5 minutes using a standard sialometric technique.

Candida albicans and Lactobacillus cultures were performed using kits from Orion Diagnostica, Inc., and a pH analysis was performed on the salivary sample using a Markson (model 00663) pH meter. Swallowing was assessed by clinical measures by videofluoroscopic techniques. Several subjective assessments were performed to evaluate symptoms of xerostomia. Subjects were instructed in the use of a daily diary and to use only the provided article ad libitum for a period of 2 weeks. After the 2-week period, the results indicated significant subjective and objective improvements in signs and symptoms of xerostomia. Whole unstimulated salivary flow rate improved from (mean +/- SEM) 0.1150 +/- 0.02 to 0.2373 +/- 0.09 mL/min. Salivary pH did not change. Global subjective improvement in xerostomia improved in 58% of the subjects. Candida colonization decreased in 43% of the subjects. There was no change in Lactobacilli colonization. Swallowing objectively improved in 75% of subjects. These results indicate significant improvement in both signs of hyposalivation and symptoms of xerostomia with the use of Optimoist in postirradiation head and neck cancer patients and patients with SS.

Rostad, H., et al. (1979). "Lung cancer. Symptoms, signs and diagnostic criteria." Scand J Respir Dis **60**(4): 184-190.

A consecutive hospital series of 1 053 patients treated for lung cancer during the period 1962 through 1971 has been studied. Clinical symptoms were present more often in men than in women and in 42% symptoms had been noted more than 6 months prior to the diagnosis. Peripheral tumours gave less symptoms than central ones. Although in 22% of the patients the tumour was discovered on a chest film in the absence of relevant symptoms, 12% only had been detected by regular mass X-ray screening. More than 40% of the peripherally located tumours were clinically silent. Squamous cell and anaplastic small cell cancers were predominantly centrally located (80 and 90%, respectively) against 65% and 74% for adenocarcinomas and undifferentiated large cell tumours.

Scheel, B. I. and K. Holtedahl (2015). "Symptoms, signs, and tests: The general practitioner's comprehensive approach towards a cancer diagnosis." Scand J Prim Health Care **33**(3): 170-177.

OBJECTIVE: To study the relative importance of different tools a GP can use during the diagnostic process towards cancer detection. DESIGN: Retrospective cohort study with prospective registration of cancer in general practice. SETTING AND SUBJECTS: One hundred and fifty-seven Norwegian general practitioners (GPs) reported 261 cancer patients. METHOD: During 10 consecutive days, GPs registered all patient consultations and recorded any presence of seven focal symptoms and three general symptoms, commonly considered as warning signs of cancer (WSC). Follow-up was done six to 11 months later. For each patient with new or recurrent cancer, the GP completed a questionnaire with medical-record-based information concerning the diagnostic procedure. RESULTS: In 78% of cancer cases, symptoms, signs, or tests helped diagnose cancer. In 90 cases, there were 131 consultation-recorded WSC that seemed related to the cancer. Further symptoms were reported for another 74 cases. Different clinical signs were noted in 41 patients, 16 of whom had no previous recording of symptoms. Supplementary tests added information in 59 cases; in 25 of these there were no recordings of symptoms or signs. Sensitivity of any cancer-relevant symptom or clinical finding ranged from 100% for patients with uterine body cancer to 57% for patients with renal cancer. CONCLUSION: WSC had a major role as initiator of a cancer diagnostic procedure. Low-risk-but-not-no-risk symptoms also played an important role, and in 7% of patients they were the only symptoms. Clinical findings and/or supplementary procedures were sometimes decisive for rapid referral.

Shankar, A., et al. (2015). "Level of awareness of lung cancer risk factors, signs, symptoms and safe practices among college teachers of different states in India: Do awareness programmes have an impact on adoption of safe practices?" Gulf J Oncolog **1**(19): 57-62.

UNLABELLED: Lung cancer is the one of the most common cause of cancer mortality among men in India where incidence rates are increasing although they are largely preventable diseases. In India, late presentation is generally responsible for high mortality and morbidity rates and early detection is one of the best ways to control it. The purpose of this study is to measure the level of awareness on lung cancer among women represented by a sample of college teachers in India and the impact of awareness programs in changing or adopting safer practices and the prevention and early detection of the disease. MATERIAL AND METHODS: The assessment was conducted during a Pink Chain Campaign on cancer awareness in 2011 in various women colleges in India. Pre-test related to lung cancer was followed by awareness programs. Posttest using the same questionnaire was conducted at the end of interactive session, at 1 year and 6 months. RESULTS: A total of 156 out of 182 teachers participated in the study (overall response rate was 85.7%). Mean age of the study population was 42.4 years (range- 28-59 yrs). There was a significant increase in level of knowledge regarding lung cancer at 6 months and this was

sustained at 1 year. Magazines and newspapers were the primary source for information regarding risk factors, signs and symptoms of lung cancer in more than 60% of teachers whereas more than 30% teachers were educated by doctors. At post-awareness after 1 year and 6 months, there was a significant change in alcohol and smoking habits. The main reasons for not undergoing screening tests are: ignorance (50%), lethargic attitude (44.8 %) and lack of time (34.6 %). CONCLUSION: Knowledge about lung cancer was very low among teachers. Overall awareness of risk factors, signs and symptoms, and screening modalities of lung cancer have improved after 1 year along with practices related to smoking and alcohol consumption. There was a significant improvement in people undergoing regular check-up's. Improved means of communication, access to information and effective warnings about cigarette smoking are necessary to increase public awareness. To ensure the adoption of safe practices in the lifestyle of people who smoke and consume alcohol, awareness programmes such as the pink chain campaign should be conducted regularly, frequently and more widely in various areas of India.

Smith, A., et al. (2012). "Signs of aging or the vague symptoms of ovarian cancer?" Oncol Nurs Forum **39**(2): E150-156.

PURPOSE/OBJECTIVES: To explore the feelings that occurred at the same time as the vague physical symptoms of ovarian cancer. RESEARCH APPROACH: Qualitative, descriptive methodology. SETTING: University cancer institute in southeastern United States. PARTICIPANTS: 24 women (ages 39-78) diagnosed with ovarian cancer. Most were Caucasian, were diagnosed at stage II-III, had a college-level education, and had health insurance. Eighty-three percent did not know the signs and symptoms of ovarian cancer prior to diagnosis, and 91% had no family history of the cancer. METHODOLOGIC APPROACH: SPSS (version 18.0) was used to summarize the demographic characteristics and qualitative descriptive content analysis to identify and summarize themes in the narrative data. FINDINGS: Two themes were noted in the handwritten answers provided by the women: (a) "thought symptoms were aging" and (b) "felt or knew something was not right." CONCLUSIONS: Findings demonstrate and reinforce that a need exists for education regarding signs and symptoms of ovarian cancer among the general population as well as the common providers of women's health care. INTERPRETATION: Education campaigns on signs and symptoms of ovarian cancer and normal aging are necessary so women are empowered with knowledge and healthcare providers can suspect and evaluate the symptoms.

Spiro, S. G., et al. (2007). "Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes: ACCP evidenced-based clinical practice guidelines (2nd edition)." Chest **132**(3 Suppl): 149S-160S.

BACKGROUND: This chapter of the guidelines is intended to provide an evidence-based assessment of the initial evaluation of patients recognized as having lung cancer and the recognition of paraneoplastic syndromes. METHODS: The current medical literature that is applicable to this issue was identified by a computerized search and was evaluated using standardized methods. Recommendations were framed using the approach described by the Health and Science Policy Committee of the American College of Chest Physicians. RESULTS: Patients with lung cancer usually present with multiple symptoms, both respiratory related and constitutional. There is usually a time delay between symptom recognition by the patient and the ultimate diagnosis of lung cancer by the physician. Whether this time delay impacts prognosis is unclear, but delivering timely and efficient care is an important component in its own right. Lung cancer may be accompanied by a variety of paraneoplastic syndromes. These syndromes may not necessarily preclude treatment with a curative intent. CONCLUSIONS: The initial evaluation of the patient with known or suspected lung cancer should include an assessment of symptoms, signs, and laboratory test results in a standardized manner as a screen for identifying those patients with paraneoplastic syndromes and a higher likelihood of metastatic disease.

Starling, K. A. and D. A. Shepherd (1977). "Symptoms and signs of cancer in the school-age child." J Sch Health **47**(3): 144-146.

The American Cancer Society's seven warning signs of cancer are: 1. Unusual bleeding or discharge. 2. A lump or thickening in the breast or elsewhere. 3. A sore that does not heal. 4. Change in bowel or bladder habits. 5. Hoarseness or cough. 6. Indigestion or difficulty in swallowing. 7. Change in size or color of a wart or mole. These signs apply to children as well as to adults. Cancer in children, however, is often more insidious than in adults and may well mimic many other diseases, developmental processess, or childhood psychologic problems. The knowledge that cancer kills more children than any other disease and the awareness of the presenting symptoms and signs may well save a child's life. Early detection with prompt, aggressive therapy is of paramount importance in achieving cures in childhood cancer.

Sun, T., et al. (2012). "[Effect of aconiti lateralis radix praeparata and taraxaci herba on Chinese medicine

signs and symptoms of urethane-induced lung cancer in mice]." Zhongguo Zhong Yao Za Zhi **37**(20): 3097-3101.

OBJECTIVE: To study Chinese medicine (CM) signs and symptoms of urethane-induced lung cancer in mice, and observe the effect of Aconiti Lateralis Radix Praeparata and Taraxaci Herba on symptoms in mice and tumor progress. METHOD: The mice were intraperitoneally injected with urethane twice a week for consecutively five weeks to establish a lung cancer model. The changes in their appearance, body temperature and auricle microcirculation were observed in carcinogenic process. CM signs and symptoms of urethane-induced lung cancer in mice were evaluated with energy metabolism, erythrocytic ATP emzymatic activity and hemorrheological index. During the tumor model was induced, Aconiti Lateralis Radix Praeparata and Taraxaci Herba were used to treat the mice and observe their effect on symptoms in mice and tumor progress. RESULT: During urethane was used to induce lung cancer, the mice had gradually become chill, lazy, hunched, with reduction in temperature, cyanosis in auricle and tail. Meanwhile, their energy metabolism and erythrocytic ATP enzymatic activity reduced, whereas their whole blood viscosity and erythrocytic aggregate index increased. Taraxaci Herba showed an effect on enhancing above symptoms and signs but had no effect on tumor progress. Aconiti Lateralis Radix Praeparata showed an effect on reducing above symptoms and signs and preventing tumor progress. CONCLUSION: Mice with urethane-induced lung cancer show CM signs and symptoms of congealing cold with blood stasis. The treatment with Aconiti Lateralis Radix Praeparata can alleviate symptoms and signs in mice and prevent tumor progress.

Trape, J., et al. (2015). "Clinical utility of determining tumor markers in patients with signs and symptoms of cancer." Clin Chem Lab Med **53**(3): 485-491.

BACKGROUND: Diagnosing patients with signs or symptoms suggestive of cancer is difficult. Serum tumor markers (TM) may be useful, but it is known that a range of pathologies other than cancer can increase their concentrations and so TM data must be interpreted with caution. The aim of this study is to determine the diagnostic accuracy of TMs in patients with signs or symptoms of cancer. METHODS: We prospectively studied 234 patients seen at rapid diagnostic units who presented signs or symptoms suggestive of cancer. Ninety patients had wasting syndrome, 74 had pulmonary symptoms and 70 other presentations. CYFRA21-1, CEA, CA19-9, total bilirubin and creatinine were determined. The final diagnosis was obtained after 6 months' follow-up. Patients were classified according to the absence

(group A) or presence (group B) of abnormal bilirubin or creatinine. RESULTS: Of the 234 patients studied, 103 (44.0%) had tumors diagnosed. Cut-off points for each TM were calculated for a specificity of 100%. For the total group, the values were CYFRA21-1, 15 mug/L, CEA, 43.8 mug/L and CA19-9, 7428 KU/L, with an overall sensitivity of 46.6%. For group A (n=142), the following cut-off points were established: CYFRA21-1, 7.8 mug/L, CEA, 13.8 mug/L and CA19-9, 101 KU/L, obtaining a sensitivity of 68.6%. For group B (n=92), the values were the same as for the whole group, and a sensitivity of 42.4% was achieved. CONCLUSIONS: We conclude that TMs can aid diagnosis in these patients with signs or symptoms suggestive of cancer. Their sensitivity can be improved by using different cut-off points in the presence and absence of renal and hepatic dysfunction.

van Schalkwyk, S. L., et al. (2008). "Cervical cancer: the route from signs and symptoms to treatment in South Africa." Reprod Health Matters **16**(32): 9-17.

In South Africa, in 2005-06, 100% of primary health care clinics in South Africa had health professionals trained to conduct Pap smears, yet the screening rate was only 1.3% and one in 26 women develop cervical cancer during their lifetime. Many women admitted to oncology wards are at such an advanced stage of disease that palliation is the only treatment option left. The purpose of this qualitative study in 2007, using semi-structured interviews with 15 women with advanced cervical cancer, was to understand the routes they followed from first signs and symptoms of disease to receiving treatment. The willingness of the women to be diagnosed was a positive finding of the study. The women did seek treatment, often more than once, and were not solely responsible for presenting late. The average number of months from first contact with a health care professional until diagnosis was 17.3, ranging from 11.8 months for urban participants to 28.4 months for rural participants, and three to seven months from diagnosis to referral for treatment. Lack of knowledge and awareness among health care professionals resulted in a low suspicion of cancer and misdiagnosis. A national cervical cancer strategy, including health education and re-training of health professionals, should be made a priority.

Williams, G., et al. (2004). "Assessing tumor-related signs and symptoms to support cancer drug approval." J Biopharm Stat **14**(1): 5-21.

Cancer causes premature death and significant, often devastating, symptoms. While prolongation of survival is an obvious end point for new cancer drug approval, the US Food and Drug Administration (FDA) has also utilized end points that evaluate patient

symptoms. In this article we discuss the end points, evidence, and analyses supporting cancer drug approvals based on evaluations of tumor-related signs and symptoms. With advice from the Oncologic Drug Advisory Committee (ODAC) in the late 1970s and early 1980s, FDA determined that acceptable end points for cancer drug approval were survival or an improvement in the quality of a patient's life, e.g., an improvement in tumor-related symptoms. This article summarizes 15 FDA cancer drug approvals based on patient symptom assessments and/or physical signs (thought to represent symptomatic improvement) as the primary evidence of effectiveness. These include painful bone events (three cases), cosmetic improvement in Kaposi's sarcoma and cutaneous T-cell lymphoma (six cases), the consequences (decreased transfusions, etc.) of long-duration responses in leukemias and lymphomas (two cases), relief of pulmonary or esophageal obstruction (two cases), and one case each of symptom benefit in pancreatic cancer (also associated with survival benefit) and pulmonary symptom benefit in lung cancer. An instructive example of an individual patient benefit end point is discussed, though it did not lead to a drug approval (the cisplatin-epinephrine gel application). Improved trial designs and analysis plans may allow greater reliance on morbidity assessments to support future cancer drug approvals. Drug sponsors are encouraged to include symptom assessments in cancer clinical trials and to perform further research to improve symptom-assessment methods. The FDA routinely meets with sponsors at End of Phase 2 Meetings to discuss drug development plans and the design of phase 3 trials. We encourage sponsors to request special protocol assessments (SPA) after meeting with the FDA to get written confirmation of the adequacy of plans for assessing cancer morbidity and quality of life, including protocols, end points, statistical analysis plans, and draft case report forms.

Workman, G. M., et al. (2007). "Pediatric cancer knowledge: assessment of knowledge of warning signs and symptoms for pediatric cancer among Brazilian community health workers." J Cancer Educ **22**(3): 181-185.

BACKGROUND: Field workers and lay community health educators are often children's first opportunity for correctly recognizing and responding to early signs and symptoms of pediatric cancers. Inadequate familiarity with the warning signs and symptoms of childhood cancer results in delayed referral to a physician for diagnosis and treatment. METHODS: This pilot study assessed community health workers' baseline level of knowledge about childhood cancers. Community health workers from Brazil completed a pediatric cancer knowledge

questionnaire. RESULTS: Although all respondents knew to refer a child suspected to have cancer to a physician, their knowledge of the early warning signs and symptoms of pediatric cancer was very low. CONCLUSIONS: The findings demonstrate a link between training and knowledge and confirm the need for targeted education in the warning signs and symptoms of pediatric cancer for community health workers in developing countries.

The above contents are the collected information from Internet and public resources to offer to the people for the convenient reading and information disseminating and sharing.

References
[1]. Al-Darwish, A. A., et al. (2014). "Knowledge about cervical cancer early warning signs and symptoms, risk factors and vaccination among students at a medical school in Al-Ahsa, Kingdom of Saudi Arabia." Asian Pac J Cancer Prev **15**(6): 2529-2532.
[2]. Anzar, S., et al. (2017). "Validation of the Malayalam Version of Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale in Cancer Patients in the Regional Cancer Centre, Thiruvananthapuram, Kerala, India." Indian J Palliat Care **23**(3): 293-299.
[3]. Armer, J. and M. R. Fu (2005). "Age differences in post-breast cancer lymphedema signs and symptoms." Cancer Nurs **28**(3): 200-207; quiz 208-209.
[4]. Baidu. http://www.baidu.com. 2019.
[5]. Bakkevold, K. E., et al. (1992). "Carcinoma of the pancreas and papilla of Vater: presenting symptoms, signs, and diagnosis related to stage and tumour site. A prospective multicentre trial in 472 patients. Norwegian Pancreatic Cancer Trial." Scand J Gastroenterol **27**(4): 317-325.
[6]. Barlow, W. E., et al. (2002). "Performance of diagnostic mammography for women with signs or symptoms of breast cancer." J Natl Cancer Inst **94**(15): 1151-1159.
[7]. Beckles, M. A., et al. (2003). "Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes." Chest **123**(1 Suppl): 97S-104S.
[8]. Bleyer, A. (2009). "CAUTION! Consider cancer: common symptoms and signs for early detection of cancer in young adults." Semin Oncol **36**(3): 207-212.

[9]. Bullough, B. (1980). "Discovery of the first signs and symptoms of breast cancer." Nurse Pract **5**(6): 31-32, 47.

[10]. Cancer Biology. http://www.cancerbio.net. 2019.

[11]. Chen, Y. M., et al. (2004). "Impact of severe acute respiratory syndrome on the status of lung cancer chemotherapy patients and a correlation of the signs and symptoms." Lung Cancer **45**(1): 39-43.

[12]. Crane, M., et al. (2016). "Knowledge of the signs and symptoms and risk factors of lung cancer in Australia: mixed methods study." BMC Public Health **16**: 508.

[13]. Croager, E. J., et al. (2018). "Find Cancer Early: Evaluation of a Community Education Campaign to Increase Awareness of Cancer Signs and Symptoms in People in Regional Western Australians." Front Public Health **6**: 22.

[14]. Fijten, G. H., et al. (1995). "Predictive value of signs and symptoms for colorectal cancer in patients with rectal bleeding in general practice." Fam Pract **12**(3): 279-286.

[15]. Fonseca, M. B., et al. (2017). "Signs and symptoms of rheumatic diseases as first manifestation of pediatric cancer: diagnosis and prognosis implications." Rev Bras Reumatol Engl Ed **57**(4): 330-337.

[16]. Fragkandrea, I., et al. (2013). "Signs and symptoms of childhood cancer: a guide for early recognition." Am Fam Physician **88**(3): 185-192.

[17]. Google. http://www.google.com. 2019.

[18]. Gookizadeh, A., et al. (2012). "Clinical evaluation of BIOXTRA in relieving signs and symptoms of dry mouth after head and neck radiotherapy of cancer patients at Seyed-al-Shohada Hospital, Isfahan, Iran." Adv Biomed Res **1**: 72.

[19]. Gussgard, A. M., et al. (2015). "Radiation-Induced Mucositis in Patients with Head and Neck Cancer: Should the Signs or the Symptoms Be Measured?" J Can Dent Assoc **81**: f11.

[20]. Hemady, R. K., et al. (1996). "Ocular symptoms and signs associated with suramin sodium treatment for metastatic cancer of the prostate." Am J Ophthalmol **121**(3): 291-296.

[21]. Holly, E. A., et al. (2004). "Signs and symptoms of pancreatic cancer: a population-based case-control study in the San Francisco Bay area." Clin Gastroenterol Hepatol **2**(6): 510-517.

[22]. Ingeman, M. L., et al. (2015). "The Danish cancer pathway for patients with serious non-specific symptoms and signs of cancer-a cross-sectional study of patient characteristics and cancer probability." BMC Cancer **15**: 421.

[23]. Issah, F., et al. (2011). "Expressions of cervical cancer-related signs and symptoms." Eur J Oncol Nurs **15**(1): 67-72.

[24]. John, S. K., et al. (2011). "Symptoms and signs in patients with colorectal cancer." Colorectal Dis **13**(1): 17-25.

[25]. Jorgensen, S. F., et al. (2017). "Characteristics and outcome in patients with non-specific symptoms and signs of cancer referred to a fast track cancer patient pathway; a retrospective cohort study." BMC Cancer **17**(1): 809.

[26]. Journal of American Science. http://www.jofamericanscience.org. 2019.

[27]. Karesen, R., et al. (2003). "[Medical logistics: principles applied to diagnostics and therapy in women with symptoms and signs of breast cancer]." Tidsskr Nor Laegeforen **123**(12): 1687-1690.

[28]. Khan, A. and K. Sultana (2010). "Presenting signs and symptoms of ovarian cancer at a tertiary care hospital." J Pak Med Assoc **60**(4): 260-262.

[29]. Lebech, A. M., et al. (2017). "Whole-Body (18)F-FDG PET/CT Is Superior to CT as First-Line Diagnostic Imaging in Patients Referred with Serious Nonspecific Symptoms or Signs of Cancer: A Randomized Prospective Study of 200 Patients." J Nucl Med **58**(7): 1058-1064.

[30]. Life Science Journal. http://www.lifesciencesite.com. 2019.

[31]. Lisboa, I. N., et al. (2016). "Prevalent Signs and Symptoms in Patients with Skin Cancer and Nursing Diagnoses." Asian Pac J Cancer Prev **17**(7): 3207-3211.

[32]. Ma H, Chen G. Stem cell. The Journal of American Science 2005;1(2):90-92. doi:10.7537/marsjas010205.14. http://www.jofamericanscience.org/journals/am-sci/0102/14-mahongbao.pdf.

[33]. Ma H, Cherng S. Eternal Life and Stem Cell. Nature and Science. 2007;5(1):81-96. doi:10.7537/marsnsj050107.10. http://www.sciencepub.net/nature/0501/10-0247-mahongbao-eternal-ns.pdf.

[34]. Ma H, Cherng S. Nature of Life. Life Science Journal 2005;2(1):7-15. doi:10.7537/marslsj020105.03. http://www.lifesciencesite.com/lsj/life0201/lif

e-0201-03.pdf.

[35]. Ma H, Yang Y. Turritopsis nutricula. Nature and Science 2010;8(2):15-20. doi:10.7537/marsnsj080210.03. http://www.sciencepub.net/nature/ns0802/03_1279_hongbao_turritopsis_ns0802_15_20.pdf.

[36]. Ma H. The Nature of Time and Space. Nature and science 2003;1(1):1-11. doi:10.7537/marsnsj010103.01. http://www.sciencepub.net/nature/0101/01-ma.pdf.

[37]. Machida, H., et al. (2016). "Signs and Symptoms of Venous Thromboembolism and Survival Outcome of Endometrial Cancer." Int J Gynecol Cancer **26**(5): 924-932.

[38]. Marsland Press. http://www.sciencepub.net. 2019; http://www.sciencepub.org. 2019.

[39]. Moseholm, E. and B. O. Lindhardt (2017). "Patient characteristics and cancer prevalence in the Danish cancer patient pathway for patients with serious non-specific symptoms and signs of cancer-A nationwide, population-based cohort study." Cancer Epidemiol **50**(Pt A): 166-172.

[40]. National Center for Biotechnology Information, U.S. National Library of Medicine. http://www.ncbi.nlm.nih.gov/pubmed. 2019.

[41]. Nature and Science. http://www.sciencepub.net/nature. 2019.

[42]. Nwosu, A. C., et al. (2016). "The Association of Hydration Status with Physical Signs, Symptoms and Survival in Advanced Cancer-The Use of Bioelectrical Impedance Vector Analysis (BIVA) Technology to Evaluate Fluid Volume in Palliative Care: An Observational Study." PLoS One **11**(9): e0163114.

[43]. Nylenna, M. and P. Hjortdahl (1987). "How do patients evaluate cancer related symptoms and signs? A study from general practice." Scand J Prim Health Care **5**(2): 117-122.

[44]. Olde Bekkink, M., et al. (2010). "Diagnostic accuracy systematic review of rectal bleeding in combination with other symptoms, signs and tests in relation to colorectal cancer." Br J Cancer **102**(1): 48-58.

[45]. Palsson, B., et al. (1997). "Tumour marker CA 50 levels compared to signs and symptoms in the diagnosis of pancreatic cancer." Eur J Surg Oncol **23**(2): 151-156.

[46]. Petrovic, J., et al. (2008). "Influence of long-term radiotherapy on symptoms and signs of locally advanced primary rectal cancer of distant localisation." Acta Chir Iugosl **55**(3): 61-66.

[47]. Potter, J., et al. (2003). "Identifying neuropathic pain in patients with head and neck cancer: use of the Leeds Assessment of Neuropathic Symptoms and Signs Scale." J R Soc Med **96**(8): 379-383.

[48]. Rasmussen, L. J. H., et al. (2017). "Inflammatory biomarkers and cancer: CRP and suPAR as markers of incident cancer in patients with serious nonspecific symptoms and signs of cancer." Int J Cancer **141**(1): 191-199.

[49]. Rhodus, N. L. and J. Bereuter (2000). "Clinical evaluation of a commercially available oral moisturizer in relieving signs and symptoms of xerostomia in postirradiation head and neck cancer patients and patients with Sjogren's syndrome." J Otolaryngol **29**(1): 28-34.

[50]. Rostad, H., et al. (1979). "Lung cancer. Symptoms, signs and diagnostic criteria." Scand J Respir Dis **60**(4): 184-190.

[51]. Scheel, B. I. and K. Holtedahl (2015). "Symptoms, signs, and tests: The general practitioner's comprehensive approach towards a cancer diagnosis." Scand J Prim Health Care **33**(3): 170-177.

[52]. Shankar, A., et al. (2015). "Level of awareness of lung cancer risk factors, signs, symptoms and safe practices among college teachers of different states in India: Do awareness programmes have an impact on adoption of safe practices?" Gulf J Oncolog **1**(19): 57-62.

[53]. Smith, A., et al. (2012). "Signs of aging or the vague symptoms of ovarian cancer?" Oncol Nurs Forum **39**(2): E150-156.

[54]. Spiro, S. G., et al. (2007). "Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes: ACCP evidenced-based clinical practice guidelines (2nd edition)." Chest **132**(3 Suppl): 149S-160S.

[55]. Starling, K. A. and D. A. Shepherd (1977). "Symptoms and signs of cancer in the school-age child." J Sch Health **47**(3): 144-146.

[56]. Stem Cell. http://www.sciencepub.net/stem. 2019.

[57]. Sun, T., et al. (2012). "[Effect of aconiti lateralis radix praeparata and taraxaci herba on Chinese medicine signs and symptoms of urethane-induced lung cancer in mice]." Zhongguo Zhong Yao Za Zhi **37**(20): 3097-3101.

[58]. Trape, J., et al. (2015). "Clinical utility of determining tumor markers in patients with signs and symptoms of cancer." Clin Chem Lab Med **53**(3): 485-491.

[59]. van Schalkwyk, S. L., et al. (2008). "Cervical cancer: the route from signs and symptoms to treatment in South Africa." Reprod Health Matters **16**(32): 9-17.

[60]. Wikipedia. The free encyclopedia. http://en.wikipedia.org. 2019.

[61]. Williams, G., et al. (2004). "Assessing tumor-related signs and symptoms to support cancer drug approval." J Biopharm Stat **14**(1): 5-21.

[62]. Workman, G. M., et al. (2007). "Pediatric cancer knowledge: assessment of knowledge of warning signs and symptoms for pediatric cancer among Brazilian community health workers." J Cancer Educ **22**(3): 181-185.

3/22/2022