RESEARCH COMMUNICATION

Is Kelantan Joining the Global Cancer Epidemic? - Experience from Hospital Universiti Sains Malaysia; 1987-2007

Nor Hayati Othman[1], Zaini Mohd Nor[2], Biswa Mohan Biswal[3]

Abstract

Objective: To determine the trend of cancer cases in one major hospital in Kelantan over a 20 year period from 1987 to 2007 and to speculate the change in trend due to the socio-economic and other health status in the state. Methodology: All data on clinically diagnosed cancer cases in Hospital Universiti Sains Malaysia [HUSM] were retrieved from the hospital medical records. The cancers were classified according to ICD10 and scrutinized to avoid duplicate or more entries. The increment in cancer incidence was calculated based on total numbers of cancer cases per each 5-6 year period. Results: A total of 12,228 solid cancers were diagnosed during the period. There is an increment of 20.1% for 1991-1996 from 1987-1990 period, 67.4% for 1997-2001 from 1991-1996 period and 305.9% for 2002-2007 from the 1997-2001 period. The rise was steep in the last 5-6 years. After excluding referred cases from states outside Kelantan, the increments were 20.1%, 67.4% and 143.6% for the consecutive 5-6 year periods. The predominant rising trends were seen for cancers of the female organs, digestive tract and endocrine organs. Conclusion: Cancer cases in HUSM are showing a rising trend, associated with increasing prevalence of smoking, obesity and diabetes in the community served by the hospital. Since HUSM is the only hospital managing cancer in the state of Kelantan, to reduce cancer incidence in the state, life-style issues need to be addressed.

Key Words: Cancer trend - diabetes link - obesity link - smoking link - goitre link

Asian Pacific J Cancer Prev, **9**, 473-478

Introduction

Cancer is often associated with either affluence (Popkin, 2007) or low economic status (Bouchardy et al., 2006). Kelantan in the 60s through the 90s was essentially a rural state in Malaysia with per capita GDP of RM 6,134 [USD 1,918], far below the GDP for Malaysia, RM 14,582 of which 67.4% of the Kelantan state GDP is contributed by the services sector (Leete, 2004). Agriculture, fishing and forestry are the major industries in the state. In 1970, 75% of households in Kelantan were below poverty line, but the figure dropped markedly to 12% in 2002. In Kota Bharu district there are about 4% households labelled as hardcore poor [income less than RM340 per month] (Leete, 2004).

Cancer trends are showing upward trends in many developing countries (Lim, 2002; Yeole, 2008) and a mixed pattern in developed countries (Kabir and Clancy, 2006; Bouchardy et al., 2008; Lepage et al., 2008; Westlake and Cooper, 2008). Cancers which are associated with diet and life-style are seen more in developed countries while cancers which are due to infections are more in developing countries. In Malaysia, death due to cancer was ranked 3rd (10.1%) after heart disease (14.3%) and septicemia (16.5%) in 2005. According to World Health Organization (WHO) death from cancer is expected to increase to 104% worldwide by 2020. Largest impact being in developing countries in comparison to developed countries (Rastogi et al., 2004).

The most important change that would occur in the world population in the next 50 years is the change in the proportion of elderly people (more than 65 years); 7% in 2000 to 16% in 2050 (Bray and Moller, 2006). According to Department of Statistics in Malaysia, the life expectancy for males and females in Malaysia has been increasing by 0.1-0.5 year annually since 2005. Many cancers are associated with aging, although age per se is not an important determinant of cancer risk, it implies prolonged exposure to carcinogen (Franceschi and La Vecchia, 2001). By the year 2050, 27 million people are projected to have cancer. More than half of the estimated number will be residents of developing countries (Bray and Moller, 2006).

Hospital Universiti Sains Malaysia (HUSM) is located in Kubang Kerian, a small town in the state of Kelantan, at the north-eastern region of West Malaysia. It was built in 1984 to cater primarily for a rural population of about 300,000 who live around Kota Bharu and Kubang Kerian district. It is a 730-bedded hospital providing services in all clinical disciplines at tertiary level and the only cancer

*[1]Dept of Pathology, [2]Dept of Medical Records, [3]Dept of Radiotherapy, Oncology and Nuclear Medicine, Hospital Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia *For correspondence: hayati@kb.usm.my; or nor_hayati_othman@yahoo.com*

centre in the state of Kelantan. For the last 10 years or so, HUSM has been receiving referral cases from outside Kelantan, particularly from the states in the North-eastern region of peninsular Malaysia.

HUSM has also seen an increase in the number of physicians working in the hospital since it started in 1984. The Department of Nuclear Medicine, Radiotherapy and Oncology was formally established in HUSM in 1995, previously, it was just a small nuclear medicine unit under Internal Medicine Department (Lim, 2006). It is equipped with facilities and services for cancer management and palliative care catering for population in the north-eastern region of peninsular Malaysia. In HUSM cancer cases are also seen and managed in other clinical departments such as in gynaecology, general surgery, neuro-surgery, otorhinolaryngology and orthopaedics departments.

This study was performed to determine the trend of cancer cases seen in HUSM over a 20 year period from 1987 to 2007 and to speculate the change in trend in relation to the socio-economic and other health status of Kelantan.

Materials and Methods

All data on clinically diagnosed cancer cases in HUSM was retrieved from the hospital medical records. The cancers were classified according to ICD10 classifications. Data was scrutinized to avoid duplicate entries. Some patients had had more than one cancer. Malignancies of the haematopoetic systems were excluded form this study since some of the data were missing. The increment in cancer incidence was calculated based on total number of cancer cases per each 5-6 year period. Published data on life-style health issues and other diseases published from the same hospital and the state of Kelantan are used in the speculations.

Results

A total of 12,228 solid cancers were diagnosed in HUSM from 1987 to 2087. There is an increment of 20.1% for 1991-1996 from 1987-1990 period, 67.4% for 1997-2001 from 1991-1996 period and 305.9% for 2002-2007 from 1997-2001 period. The rise is steep in the last 5 years (Figure 1). From 2001-2007 periods, there were 3226 cases referred to HUSM from states outside Kelantan. The corrected increment for cancers in Kelantan for every 5-6 year period was 20.1%, 67.4% and 143.6%. The predominant rising trends are seen in cancers of the female organs, digestive tracts and endocrine organs (Figure 2).

Among cancers of the digestive organs only colorectal cancers showed a steep change in trend with a total of 1258 cancers during the period (Figure 3). Except for cancer of the vulva and vagina which is rare in our population, cancers of the breasts, cervix, ovaries and uterus show a rising trend in females (Figure 4). There were a total of 961 breast cancers, 916 cervical cancers, 753 ovarian cancers and 210 uterine cancers in this period. The trend of rising of these 4 cancers is almost similar to each other.

Thyroid carcinoma was found to supersede other endocrine carcinomas with a total of 266 cancers over the period studied (Figure 5). Like many countries in the world, prostate cancers are also particularly on the rise

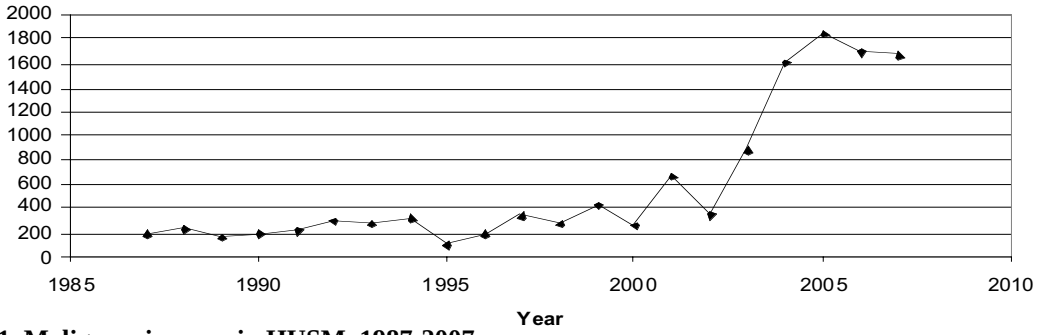

Figure 1. Malignancies seen in HUSM, 1987-2007

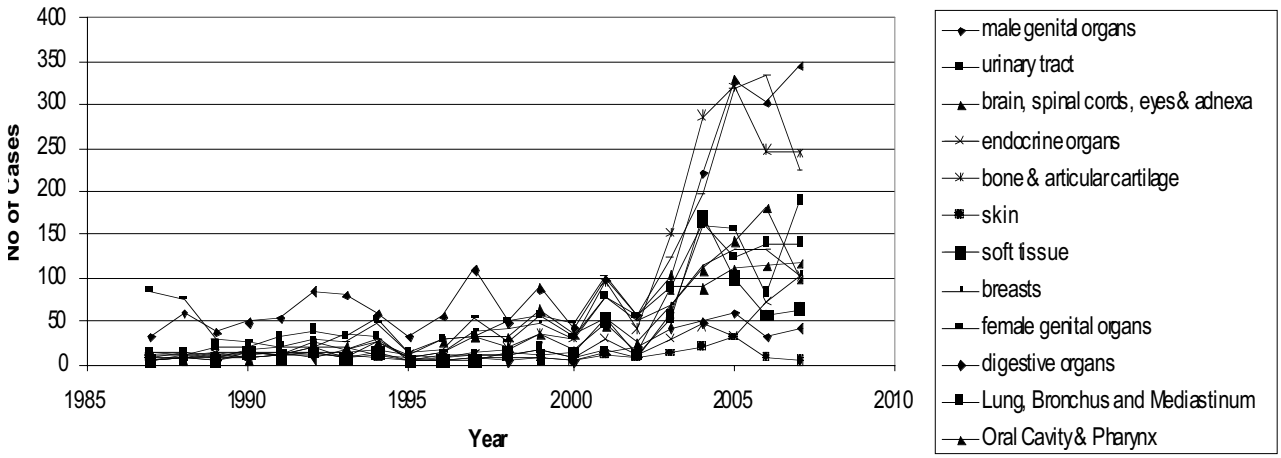

Figure 2. Malignant Cases by Systems seen in HUSM, 1987-2007

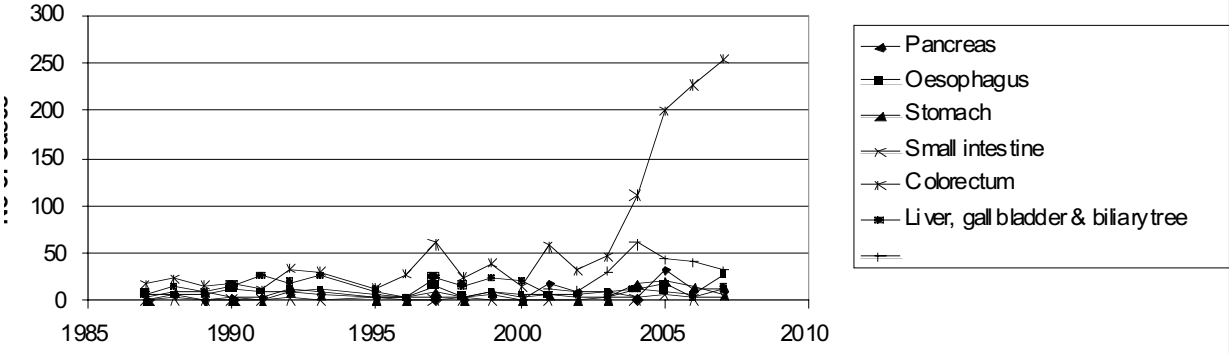

Figure 3. Malignancies of the Digestive Organs seen in HUSM, 1987-2007

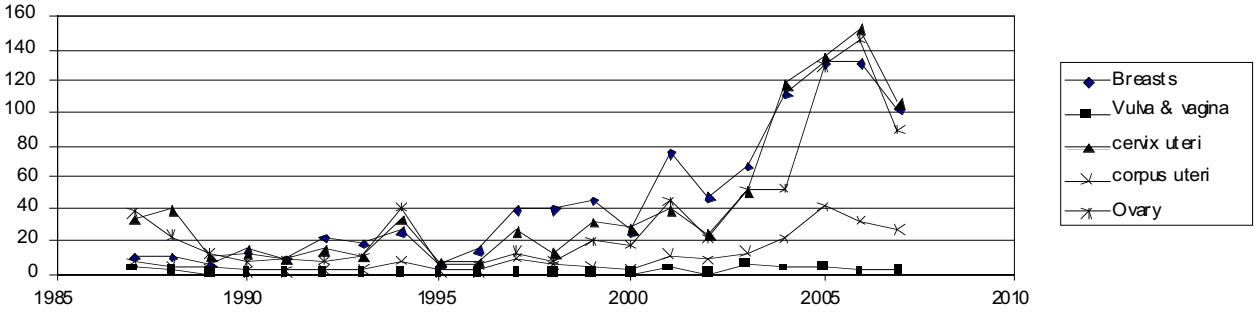

Figure 4. Malignancies of the Female Organs seen in HUSM, 1987-2007

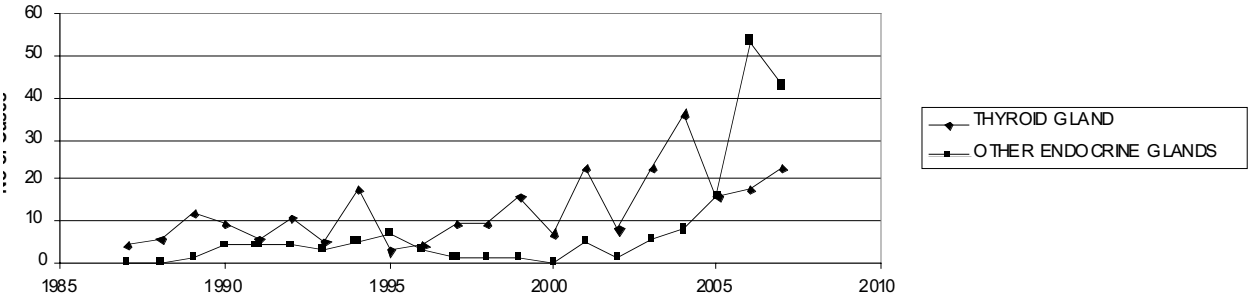

Figure 5. Malignancies of the Endocrine Organs seen in HUSM, 1987-2007

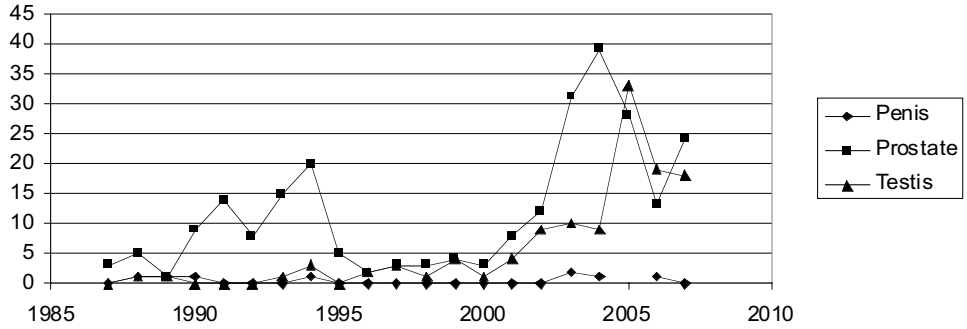

Figure 6. Malignancies of the Male Organs seen in HUSM, 1987-2007

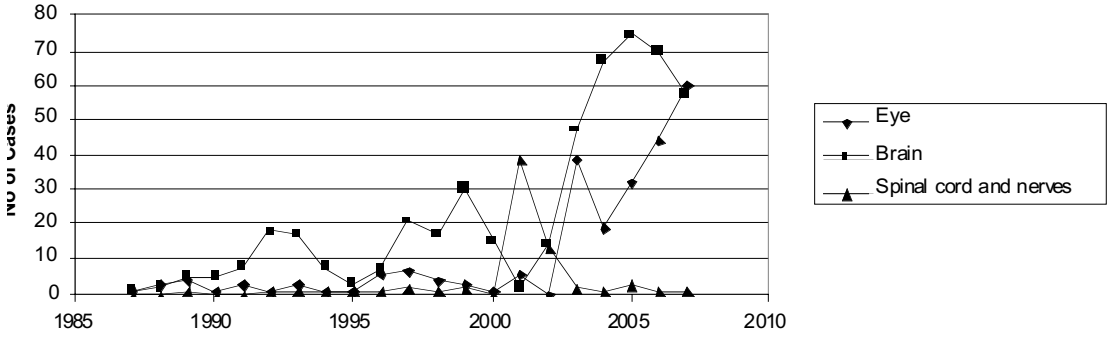

Figure 7. Malignancies of the Brain, Spinal Chord, Nerves and Eye seen in HUSM, 1987-2007

(Figure 6) as compared to other cancers of the male organs. Cancers of the brain are also showing an increasing trend (Figure 7).

Discussion

The trend of cancers seen in HUSM is showing a slow rise from 1987 to 2000 and a steep incline for the next 7 years. There was an increment of 20.1%, 67.4% and 305.9% for consecutive 5-6 years. HUSM began to see referral cancer cases from outside Kelantan towards the end of the 1990s, as it is the only centre equipped with facilities for a complete cancer management in Kelantan and the north-eastern region of peninsular Malaysia. Cases which would have been referred to Kuala Lumpur hospital were since then referred to HUSM. After correction by excluding the referred cases from other states, the increment is 20.1%, 67.4% and 143.6%. The steep jump of 143.6% from 67.4% is very significant. Some local social and other health issues may have contributed to this pattern.

A rise in cancer trend is seen in many countries globally (Belpomme et al., 2007). In Singapore, there was an average annual increase of 3.6% for breast cancers in women from 1988-1992 period (Seow et al., 1996). In Qatar, there was a 57.1% rise of cancers from 1991 – 2006 (Bener et al., 2008) and in Netherlands, there was an increase between 1.9%(females) and 3.4%(males) per year for oesophageal cancer from 1989-2003 (Crane et al., 2007).

Smoking is associated with a number of cancers notably lung, larynx, bladder, breasts, oesophagus and cervix. While in developed countries the prevalence of smoking is decreasing (Lando et al., 2005), the scenario is the opposite in developing countries. In Kelantan, the prevalence of smoking is 15.6% among primary school children (Norbanee et al., 2006), 33.2% among secondary school children (Shamsuddin and Haris, 2000) and 40.6% among secondary school teachers (Naing and Ahmad, 2001). The initiation and the influence to start smoking is similar as in many other countries (Warren et al., 2008). Malaysia has increased the price of cigarettes by increasing the import taxation from RM85/kg in 1990 to RM216/kg in 2000 (Rahmat et al., 2005), however the rate of smoking has yet to decline, supporting the idea proposed by Ragidor et al (2007) that increasing the price for cigarettes is not the answer to reduce smoking. Smoking increases the risk of colorectal carcinomas by 43% (Huxley, 2007). Ever-smokers were associated with an 8.8-fold increased risk of colorectal cancers (95% confidence interval, 1.7-44.9) when fed on well-done red meat diet if they have NAT2 and CYP1A2 rapid phenotypes (Le Marchand et al., 2001). No similar association was found in never-smokers.

Among the cancers that show a rapid increasing trend in HUSM in recent years is colorectal carcinoma. In one previous study from the same hospital, colorectal carcinoma was strongly associated with metabolic diseases such as diabetes and hypertension (own unpublished data). Other studies have shown similar findings (Yang et al., 2005; Ahmed et al., 2006; Seow et al., 2006). The prevalence of diabetes in Kelantan in 1999 was 10.5% and impaired glucose tolerance was 16.5% (Mafauzy et al., 1999). Kelantan is ranked highest in prevalence of diabetes in Malaysia in which the overall national prevalence is 8.3% (Zaini, 2000). The overall prevalence of diabetes mellitus in Kelantan in early 60s was not known, however for Malaysia was 0.65% (Mustaffa, 1990). According to a review on diabetes, WHO has estimated that by 2030, there would be 2.48 million diabetics in Malaysia, a jump of 164% from 0.94 million in 2002 (Mafauzy, 2006). With such a high prevalence of diabetes in Kelantan, a high incidence of colorectal carcinoma is not a surprise. Diabetes has also been linked with other cancers such as pancreas (Luo et al., 2007), endometrium (Friberg et al., 2007), liver and kidney (Inoue et al., 2006).

The trend of prevalence of overweight/obesity is also rising in Kelantan. Obesity and diabetes has a parallel relationship. In a study conducted in 2005 (Nazri et al., 2008) in Kota Bharu district in the state of Kelantan, the overall prevalence of overweight/obesity was 49.1%, much higher than the figure reported earlier in 1996 (Jackson et al., 1996). Obesity is not a social problem but a disease. The greatest risk is for diabetes mellitus where a body mass index above 35 kg/m^2 increases the risk by 93-fold in women and by 42-fold in men (Jung, 1997). Obesity is associated in a number of cancers (Reeves et al., 2007; Rapp et al.,2008),particularly endometrium (Bjorge et al., 2007; McCourt et al., 2007), breasts (Ahn et al., 2007; Dogan et al., 2007) and colorectal cancers (Moghaddam et al., 2007). Adipocytes have the ability to enhance the proliferation of colon cancer cells *in vitro* (Amemori et al., 2007).

Breast and cervical cancers are almost showing identical rising trends in our study. Breast cancers are often associated with developed nations and cervical cancers with developing nations. In Kelantan, as elsewhere in Malaysia, the women do have access to screening tests. Factors contributing to breast cancers in Kelantan are; nulliparity (odds ratio [OR] of 15.3), overweight (OR of 2.1), family history of breast cancer (OR of 4.3) and previous use of oral contraceptives (OR of 2.5); similar to factors seen in Western population (Norsa'adah et al., 2005). Pap smears, if done in any public clinics/hospitals in Malaysia are free and mammography is available in major hospitals is charged with nominal fee. However, the acceptance of screening is not universal. This is not unique for Kelantan alone. According to World Health organization, less than 5% of women in Malaysia age between 50-60 years had mammography screening (World Health Organization, 2008). The coverage for pap smear in Kelantan is not optimal (Othman, 2002) and in the majority is done during pre or post natal period (Nor Hayati et al., 1997). In a recently concluded study, only 5.0% of cervical cancer patients seen in HUSM had had pap smears within 3 years preceding to cancer development (Othman et al., 2008).

Thyroid cancer is also showing a rapid rise in trend. Kelantan has a high prevalence of goitre (Mafauzy et al., 1993) and the population is exposed to low iodine content in the diet. The mean urinary iodine excretion ranges from 57.1 +/- 2.1 to 56.8 +/- 2.1 (Mafauzy et al., 1995). In many

recent studies, goitres, either toxic or non-toxic (Cerci et al., 2007) have been linked as risk factors to thyroid carcinoma (Omar et al., 2004; Nagano et al., 2007). Most patients who have goitres in Kelantan, keep their goitres at an average of 50.9 months before seeking surgical removal (Omar et al., 2004). The increasing trend of thyroid cancer seen in Kelantan population is probably secondary to a rising trend of goitre prevalence in the state.

With the growing economic affluence of any nation, some health problems ensue. The improvement in the socio-economic status of the people of Kelantan has contributed to the increasing prevalence of diabetes, obesity, smoking and other life-style diseases such as coronary artery diseases and hypertension (Mafauzy et al., 2003; Raahman et al., 2007). These life-style diseases are the probable causes of the rising trend of cancer in the population.

Cancer in HUSM is on the rise. Since HUSM is the only cancer centre in the state of Kelantan, and there is no state cancer registry, the results implies that cancer in Kelantan is on the rise. The rapid rise is seen in the last 5-6 years. The predominant rising trends are seen in cancers of the female organs, digestive tracts and endocrine organs. The trend is a mixed picture of developing and a developed nation. This rising trend is associated with increasing prevalence of smoking, obesity, diabetes and goitre in the community. To reduce cancer incidence in Kelantan, these life-style disease issues need to be addressed.

References

Ahmed RL, Schmitz KH, Anderson KE, et al (2006).The metabolic syndrome and risk of incident colorectal cancer. *Cancer*, **107**, 28-36.

Ahn J, Schatzkin A, Lacey JV, Jr, et al (2007). Adiposity, adult weight change, and postmenopausal breast cancer risk. *Arch Intern Med*, **167**, 2091-102.

Amemori S, Ootani A, Aoki S, et al (2007). Adipocytes and preadipocytes promote the proliferation of colon cancer cells in vitro. *Am J Physiol Gastrointest Liver Physiol*, **292**, G923-9.

Belpomme D, Irigaray P, Sasco AJ, et al (2007). The growing incidence of cancer: role of lifestyle and screening detection. *Int J Oncol*, **30**, 1037-49.

Bener A, Ayub H, Kakil R, et al (2008). Patterns of cancer incidence among the population of Qatar: a worldwide comparative study. *Asian Pac J Cancer Prev*, **9**, 19-24.

Bjorge T, Engeland A, Tretli S, et al (2007). Body size in relation to cancer of the uterine corpus in 1 million Norwegian women. *Int J Cancer*, **120**, 378-83.

Bouchardy C, Fioretta G, Rapiti E, et al (2008). Recent trends in prostate cancer mortality show a continuous decrease in several countries. *Int J Cancer*, **123**, 421-9,

Bouchardy C, Verkooijen HM, Fioretta G (2006). Social class is an important and independent prognostic factor of breast cancer mortality. *Int J Cancer*, **119**, 1145-51.

Bray F, Moller B (2006). Predicting the future burden of cancer. *Nat Rev Cancer*, **6**, 63-74.

Cerci C, Cerci SS, Eroglu E, et al (2007). Thyroid cancer in toxic and non-toxic multinodular goiter. *J Postgrad Med*, **53**, 157-60.

Crane LM, Schaapveld M, Visser O, et al (2007) Oesophageal cancer in The Netherlands: increasing incidence and mortality but improving survival. *Eur J Cancer*, **43**, 1445-51.

Dogan S, Hu X, Zhang Y, et al (2007). Effects of high-fat diet and/or body weight on mammary tumor leptin and apoptosis signaling pathways in MMTV-TGF-alpha mice. *Breast Cancer Res*, **9**, R91.

Franceschi S, La Vecchia C (2001). Cancer epidemiology in the elderly. *Crit Rev Oncol Hematol*, **39**, 219-26.

Friberg E, Mantzoros CS, Wolk A (2007). Diabetes and risk of endometrial cancer: a population-based prospective cohort study. *Cancer Epidemiol Biomarkers Prev*, **16**, 276-80.

Huxley R (2007). The role of lifestyle risk factors on mortality from colorectal cancer in populations of the Asia-Pacific region. *Asian Pac J Cancer Prev*, **8**, 191-8.

Inoue M, Iwasaki M, Otani T, et al (2006). Diabetes mellitus and the risk of cancer: results from a large-scale population-based cohort study in Japan. *Arch Intern Med*, **166**, 1871-7.

Jackson A, Cole C, Esquiro J, et al (1996). Obesity in primary care patients in Kelantan, Malaysia: prevalence, and patients' knowledge and attitudes. *Southeast Asian J Trop Med Public Health*, **27**, 776-9.

Jung RT (1997). Obesity as a disease. *Br Med Bull*, **53**, 307-21.

Kabir Z, Clancy L (2006). Lifestyle-related cancer death rates in Ireland: decreasing or increasing? *Ir Med J*, **99**, 40-2.

Lando HA, Borrelli B, Klein LC, et al (2005). The landscape in global tobacco control research: a guide to gaining a foothold. *Am J Public Health*, **95**, 939-45.

Leete R (2004). Kelantan's Human Development Progress and Challenges, in UNDP Resident Coordinator for Malaysia SaB (ed): United Nation Development Program. Kuala Lumpur.

Le Marchand L, Hankin JH, Wilkens LR, et al (2001). Combined effects of well-done red meat, smoking, and rapid N-acetyltransferase 2 and CYP1A2 phenotypes in increasing colorectal cancer risk. *Cancer Epidemiol Biomarkers Prev*, **10**, 1259-66.

Lepage C, Remontet L, Launoy G, et al (2008). Trends in incidence of digestive cancers in France. *Eur J Cancer Prev*, **17**, 13-7.

Lim GCC (2002). Overview of cancer in Malaysia. *Jpn J Clin Oncol*, **32**, s32-s42.

Lim GCC (2006). Clinical oncology in Malaysia: 1914 to present. *Biomed Imaging Interv J*, **10**, e18.

Luo J, Iwasaki M, Inoue M, et al (2007). Body mass index, physical activity and the risk of pancreatic cancer in relation to smoking status and history of diabetes: a large-scale population-based cohort study in Japan--the JPHC study. *Cancer Causes Control*, **18**, 603-12.

Mafauzy M (2006). Diabetes mellitus in Malaysia. *Med J Malaysia*, **61**, 397-8.

Mafauzy M, Mohamad WB, Anum MY, et al (1995). Urinary iodine excretion in the northeast of Peninsular Malaysia. *Southeast Asian J Trop Med Public Health*, **26**, 138-42.

Mafauzy M, Mokhtar N, Mohamad WB, et al (1999). Diabetes mellitus and associated cardiovascular risk factors in north-east Malaysia. *Asia Pac J Public Health*, **11**, 16-9.

Mafauzy M, Mokhtar N, Wan Mohamad WB (2003). Hypertension and associated cardiovascular risk factors in Kelantan. *Med J Malaysia*, **58**, 556-64.

Mafauzy M, Wan Mohamad WB, Yasmin Anum MY, et al (1993). The prevalence of endemic goitre in Kelantan, Malaysia. *Med J Malaysia*, **48**, 64-70.

McCourt CK, Mutch DG, Gibb RK, et al (2007). Body mass index: relationship to clinical, pathologic and features of microsatellite instability in endometrial cancer. *Gynecol Oncol*, **104**, 535-9.

Mustaffa BE (1990). Diabetes in Malaysia: problems and challenges. *Med J Malaysia*, **45**, 1-7.

Moghaddam AA, Woodward M, Huxley R (2007). Obesity and risk of colorectal cancer: a meta-analysis of 31 studies with 70,000 events. *Cancer Epidemiol Biomarkers Prev*, **16**, 2533-47.

Nagano J, Mabuchi K, Yoshimoto Y, et al (2007). A case-control study in Hiroshima and Nagasaki examining non-radiation risk factors for thyroid cancer. *J Epidemiol*, **17**, 76-85.

Naing NN, Ahmad Z (2001). Factors related to smoking habits of male secondary school teachers. *Southeast Asian J Trop Med Public Health*, **32**, 434-9.

Nazri SM, Imran MK, Ismail IM, et al (2008). Prevalence of overweight and self-reported chronic diseases among residents in Pulau Kundur, Kelantan, Malaysia. *Southeast Asian J Trop Med Public Health*, **39**, 162-7.

Norbanee TH, Norhayati MN, Norsa'adah B, et al (2006). Prevalence and factors influencing smoking amongst Malay primary school children in Tumpat, Kelantan. *Southeast Asian J Trop Med Public Health*, **37**, 230-5.

Nor Hayati O, Mukarramah C, Wok Aimi A, et al (1997). Pap smears - is it an effective screening method for cervical neoplasia? - an experience with 2289 cases. *Malay J Med Sci*, **4**, 45-50.

Norsa'adah B, Rusli BN, Imran AK, et al (2005). Risk factors of breast cancer in women in Kelantan, Malaysia. *Singapore Med J*, **46**, 698-705.

Omar E, Madhavan M, Othman NH (2004). Immuno-histochemical localisation of RET and p53 mutant protein of thyroid lesions in a North-Eastern Malaysian population and its prognostic implications. *Pathology*, **36**, 152-9.

Othman NH (2002). Cancer of the cervix- from bleak past to bright future; a review, with an emphasis on cancer of the cervix in Malaysia. *Malay J Med Sci*, **9**, 4-17.

Othman NH, Ravindran J, Devi BCR, et al (2008). Effectiveness of cervical cancer screening: Patients' understanding of screening for cervical cancer in major hospitals in Malaysia. *Med J Malaysia*, (in press).

Popkin BM (2007). Understanding global nutrition dynamics as a step towards controlling cancer incidence. *Nat Rev Cancer*, **7**, 61-7.

Raahman S, Raahman T, Ismail AA, et al (2007). Diabetes-associated macrovasculopathy: pathophysiology and pathogenesis. *Diabetes Obes Metab*, **9**, 767-80.

Rahmat A, Ismail R, Nordin I, et al (2005). Policy on Tobacco Industry in Malaysia.

Rapp K, Klenk J, Ulmer H, et al (2008). Weight change and cancer risk in a cohort of more than 65,000 adults in Austria. *Ann Oncol*, **19**, 641-8.

Rastogi T, Hildesheim A, Sinha R (2004). Opportunities for cancer epidemiology in developing countries. *Nat Rev Cancer*, **4**, 909-17.

Reeves GK, Pirie K, Beral V, et al: Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. Bmj 335:1134, 2007

Regidor E, Pascual C, Gutierrez-Fisac JL (2007). Increasing the price of tobacco: economically regressive today and probably ineffective tomorrow. *Eur J Cancer Prev*, **16**, 380-4.

Seow A, Duffy SW, McGee MA, et al (1996). Breast cancer in Singapore: trends in incidence 1968-1992. *Int J Epidemiol*, **25**, 40-5.

Seow A, Yuan JM, Koh WP, et al (2006). Diabetes mellitus and risk of colorectal cancer in the Singapore Chinese Health Study. *J Natl Cancer Inst*, **98**, 135-8.

Shamsuddin K, Haris MA (2000). Family influence on current smoking habits among secondary school children in Kota Bharu, Kelantan. *Singapore Med J*, **41**, 167-71.

Warren CW, Jones NR, Peruga A, et al (2008). Global youth tobacco surveillance, 2000-2007. *MMWR Surveill Summ*, **57**, 1-28.

Westlake S, Cooper N (2008). Cancer incidence and mortality: trends in the United Kingdom and constituent countries, 1993 to 2004. *Health Stat Q*, **??**, 33-46.

World Health Organization (2008). World Health Statstics 2008.

Yeole BB (2008).Trends in cancer incidence in female breast, cervix uteri, corpus uteri, and ovary in India. *Asian Pac J Cancer Prev*, **9**, 119-22,

Yang YX, Hennessy S, Lewis JD (2005). Type 2 diabetes mellitus and the risk of colorectal cancer. *Clin Gastroenterol Hepatol*, **3**, 587-94.

Zaini A (2000). Where is Malaysia in the midst of the Asian epidemic of diabetes mellitus? *Diabetes Res Clin Pract*, **50 Suppl 2**, S23-8.

Zehbe I, Voglino G, Wilander E, Genta F, Tommasino M (1999). Codon 72 polymorphism of p53 and its association with cervical cancer. *Lancet*, **354**, 218-9.

Zhong S, Wyllie AH, Barnes D, Wolf CR, Spurr NK (1993). Relationship between the GSTM1 genetic polymorphism and susceptibility to bladder, breast and colon cancer. *Carcinogenesis*, **14**, 821-4.