

## มะเร็งในโรงพยาบาลศรีนครินทร์: ข้อมูลย้อนหลัง 10 ปี

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## Cancers in Srinagarind Hospital; A 10 Years Period of Hospital Records

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**หลักการและวัตถุประสงค์:** โรคมะเร็งเป็นสาเหตุการเสียชีวิตมากที่สุดทั่วโลกรวมถึงประเทศไทย เนื่องจากผลการรักษาที่ยังไม่มีประสิทธิภาพและการพยากรณ์โรคไม่ดีส่งผลให้โรคมะเร็งมีอัตราการเสียชีวิตที่สูง การศึกษาเรื่องรายงานจำนวนผู้ป่วยโรคมะเร็งรายใหม่ที่ลงทะเบียนรักษาในโรงพยาบาลศรีนครินทร์ระหว่างปี พ.ศ. 2546-2555 ซึ่งสะท้อนสถานการณ์โรคมะเร็งของภาคตะวันออกเฉียงเหนือของประเทศไทย

**วิธีการศึกษา:** ศึกษาในผู้ป่วยโรคมะเร็งรายใหม่ทุกคนที่ลงทะเบียนกับหน่วยมะเร็ง โรงพยาบาลศรีนครินทร์คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น ในช่วงเวลาปี พ.ศ. 2546-2555

**ผลการศึกษา:** จำนวนผู้ป่วยโรคมะเร็งรายใหม่เพิ่มมากขึ้นทุกปีในช่วง 10 ปีที่ทำการศึกษา โรคมะเร็งที่พบมากที่สุด 3 อันดับแรกในผู้ป่วยเพศชาย ได้แก่ มะเร็งตับและท่อน้ำดี มะเร็งปอด และมะเร็งลำไส้ใหญ่ ตามลำดับ สำหรับผู้ป่วยเพศหญิง พบมะเร็งตับและท่อน้ำดี มะเร็งเต้านม และมะเร็งต่อมไทรอยด์ มากที่สุดตามลำดับ มะเร็งตับและท่อน้ำดี เพิ่มขึ้นอย่างมากต่อเนื่อง จำนวนเพิ่มขึ้นอย่างมาก ในขณะที่มะเร็งปากมดลูกมีจำนวนลดลงโดยเฉพาะในช่วง 5 ปีหลัง นอกจากนี้พบว่ามะเร็งไทรอยด์ในเพศหญิงเพิ่มจำนวนมากขึ้นเป็นอันดับ 3

**Background and objectives:** Cancer is the most common cause of death worldwide including Thailand, where treatment outcomes and prognosis are poor and mortality rates remain high. This study reports new cancer cases and trends of all cancers registered in Srinagarind Hospital from 2003 to 2012, may provide a picture of the cancer situation in Northeast (NE) Thailand.

**Methods:** All new cases of cancer registered in the hospital-based cancer registry at Faculty of Medicine, Srinagarind hospital, Khon Kaen university during 2003-2012 were included in the study.

**Results:** The number of new cancer cases has gradually increased each year during the last 10 years. The three most common cancers at present in males are liver and bile duct cancer, lung cancer and colorectal cancer, respectively. In females, liver and bile duct cancer, breast cancer and thyroid cancer are now the most frequent cancers. Interestingly, the number of cases of liver and bile duct cancer in males noticeably increased throughout the study period. Additionally, breast cancer greatly increased in the second half of decade whilst cervix cancer dramatically dropped and

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**สรุป:** โรคมะเร็งรายใหม่เมื่อแนวโน้มเพิ่มขึ้นอย่างต่อเนื่องตลอดช่วงระยะเวลา 10 ปี ของการศึกษาทั้งสองเพศ โดยที่มะเร็งตับ และท่อน้ำดีเป็นโรคมะเร็งที่พบมากที่สุดทั้งในเพศชายและเพศหญิงตลอดช่วงระยะเวลาของการศึกษา

**คำสำคัญ:** โรงพยาบาลศรีนครินทร์, ทะเบียนมะเร็ง โรงพยาบาล

thyroid cancer in females climbed into the top three most common cancers.

**Conclusion:** The trends of all cancers continuously increased throughout 10 years of study in both genders. Liver and bile duct cancer was the most common cancer presented in both males and females during the whole decade observed.

**Key words:** Cancer, Srinagarind hospital, Hospital based

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## Introduction

Cancer is the disease, which is currently found at high frequency<sup>1</sup>, and it is the major cause of death worldwide including Thailand<sup>2</sup>. In Thailand, the incidence of all cancers and the mortality rate resulting from malignant diseases gradually increase each year. In particular, incidences of colorectal cancer and breast cancer significantly increased during 1989-2000<sup>2</sup>. Lung cancer, in both males and females, is the most common cancer in many countries<sup>3</sup>. However, in Thailand, liver cancer is the most common cancer in males and breast cancer in many parts of the country is the most common cancer in females<sup>15,16 (reported in Thai language)</sup>. The number of patients diagnosed with cancer has noticeably increased in Srinagarind hospital during the last 10 years (Annual Reports from Cancer Unit of Srinagarind hospital, 2000-2012). We therefore presented this overview of all new cancer cases recorded in Srinagarind hospital during 1993-2012, with an emphasis on changing trends in types of cancer in Northeast (NE) Thailand.

Srinagarind hospital, a tertiary health care center, provides health service for patients in the (NE) Thailand, which have population approximately 22 million, and receives referral cases from all over the region. Malignant diseases are advanced and complicated conditions, which are required the tertiary health care center for effectively appropriate treatment. Additionally, Srinagarind hospital is a health care center comprising many subspecialty physicians expertising on malignancy, hence, most cancer cases in the NE are referred to Srinagarind hospital to receive

the appropriate management. Therefore, various types of cancers have been coming to Srinagarind hospital. Therefore, the situation of cancer in Srinagarind hospital might reflect the situation of cancer in NE as a whole.

## Materials and Methods

**Case definitions:** All new cancer cases registered in Srinagarind hospital between January 1<sup>st</sup>, 2003 and December 31<sup>st</sup>, 2012 were included in this study. This study is officially approved by the Khon Kaen university Ethics Committee for Human Research based on the Declaration of Helsinki and the ICH Good Clinical Practice Guidelines with HE571238 of reference number.

**Sources of data:** Srinagarind hospital, Khon Kaen university (a thousand-bed university hospital), Khon Kaen, Thailand, is situated in the center of NE Thailand and accepts all referred cases from other health care centers in the region. Our data were obtained from the Khon Kaen Cancer Registry, which has recorded data of all cancer cases treated in this hospital since 1987. All data were verified, checked for coding duplication and entered into the CANREG software (Version 4, available from <http://www.iacr.com.fr/canreg4.htm>). The data normally collected from each cancer patient included age, sex, date of birth, date of diagnosis, method of diagnosis, primary site of cancer, extension or metastasis, histology of cancer, date of last visit, survival status at last follow-up and other necessary information. Only relevant data were presented in this study.

### Statistical methods

The data were analysed using Poisson regression to compare the trends in the first studied period (2003-2007) and the second half (2007-2012).

## Result

### Overall numbers and trends of new cancer cases, 2003-2012

The numbers of new cancer cases recorded between 2003 and 2012 in Srinagarind Hospital are shown in Figure 1. For some analyses, the data were divided into 2 intervals; the first half of decade (2003-2007) and the second half of decade (2008-2012). The overall numbers of cancer cases were stably increased in both sexes throughout the 10 years period of study. The numbers of male and female patients during the period studied were comparable, male patients being slightly more number than female in the last 4 years of study. Both genders showed an increase in the last few years, and especially after 2009.

### Overview of the most common cancers in male and female, 2003-2012

The most common cancers in patients, both male and female, registered in Srinagarind hospital for the period 2003 to 2012, are shown in Tables 1 and 2, respectively. The order of presentation in the tables is based on the case numbers of each cancer type in the final year of the study. Additionally, data on the 10 most common cancers during 2003-2012 are presented graphically in Figures 2 and 3 for male and female, respectively.

Cancer of the liver and bile ducts was the most common cancer in both males and females (Tables 1 and 2; Figures 2 and 3). In males, this made up more than half of all cancer cases (Table 1) and has shown a marked increase over the last few years. Male liver and bile duct cancer cases continuously increased from approximately 800 cases/year to nearly 1,300 cases/year through the 10 year period reviewed. The number of liver and bile duct cancer in female cases was nearly half of that in males. In females, the top three common cancers during the first half of decade were liver and

bile duct cancer, cervix cancer and breast cancer, respectively. Liver and bile duct cancer was the most common cancer presenting in female patients throughout the decade studied whilst breast cancer climbed up to the second most common ahead thyroid and cervix cancer in the later half of decade studied (Figure 3). Thyroid cancer had accelerating risen up to the third most common cancer in female in the second half of decade whereas cervix cancer dramatically dropped to the fourth place. Nevertheless, in females numbers of cases of breast cancer almost matched cervix cancer cases overall, despite very substantial reductions in numbers of cervix cancer cases during the few recent years (Table 2 and Figure 3).

The second most common cancer in males was lung cancer (Table 1) while it was the fifth most common cancer overall in females (Table 2). The number of new lung cancer cases in males was stable at approximately 300 cases/year (Figure 2), whereas the number in female fluctuated through 10 years studied and it has recently increased in the last few years (Figure 3). In 2003, the number of lung cancer cases in females was roughly 350 per year compared to 500 per year in 2012. Consequently, lung cancer climbed up into the top five most common cancer in females during the second half of 10 years observed. Breast cancer was the second most common cancer in females. Interestingly, the number of breast cancer cases was lower than that of cervix cancer during the first half of 10 years (Figure 3) then increased dramatically up to nearly 500 cases/year by the end of the second half of decade (Figure 3).

Colorectal cancer was the third and ninth most common cancer occurring in males and females, respectively (Tables 1 and 2), higher numbers of cases being reported from males (799 vs 600). The number of cases of colorectal cancer in males was stable at or below 100 cases/year during the first half of decade studied but increased slightly during the last few years observed (Figure 2). Whilst, the number of female patients with colorectal cancer has increased steadily during the last 10 years (Table 2). Interestingly, the third commonest cancer in female was thyroid cancer. In the first half of decade observed, the number of thyroid

cancer patients was less than 150 per year then such number was greatly risen up almost 2 folds at the last few years of study. Therefore, cervix cancer was surpassed by thyroid cancer to be the third most common cancer in female because the number of cervix cancer cases enormously declined in the second half of decade studied (Figure 3).

The commonest types of head and neck cancers in males and females differ: nasopharynx cancer was more common in males whereas females more commonly had oral cavity cancer (Tables 1 and 2). In males, nasopharynx cancer was the fourth most common cancer, with cases remaining stable in number during the last 10 years at less than 100 cases/year (Figure 2). Cases of mouth cancer in females were likewise relatively stable in number, at between 100 and 130 in each year (Table 2).

Non-Hodgkin lymphoma (NHL) was the fifth most common cancer in males while the fifth place in females was lung cancer. Additionally, the numbers of NHL cases were fluctuated nearly 120 cases/year during the period of study (Figure 2). Noticeably, the number of lung cancer in females was stably less than 150 cases/years in the first half of decade then such number had dramatically risen more than 150 in the recent years of study.

## Discussion

This study revealed that the trends of cancer patients studied in Srinagarind hospital during the last 10 years, accelerating increase in both genders and these results were consistent with the others worldwide including Thailand<sup>3,4</sup>. Due to the fact that human has longer life span compared to previously<sup>5</sup>. Consequently, our cells have high risk of acquiring genetic mutation leading to abnormal cells and these abnormal cells can finally transform to cancer cells. In addition, people life style has changed and acquired more Westernisation life style with consuming fast food (high fat diet and low fiber diet) without exercise<sup>6</sup>. Additionally, carcinogenic toxins in the environment from agricultural and industrial products are increased. Consequently, people are exposed to more carcinogenic agents.

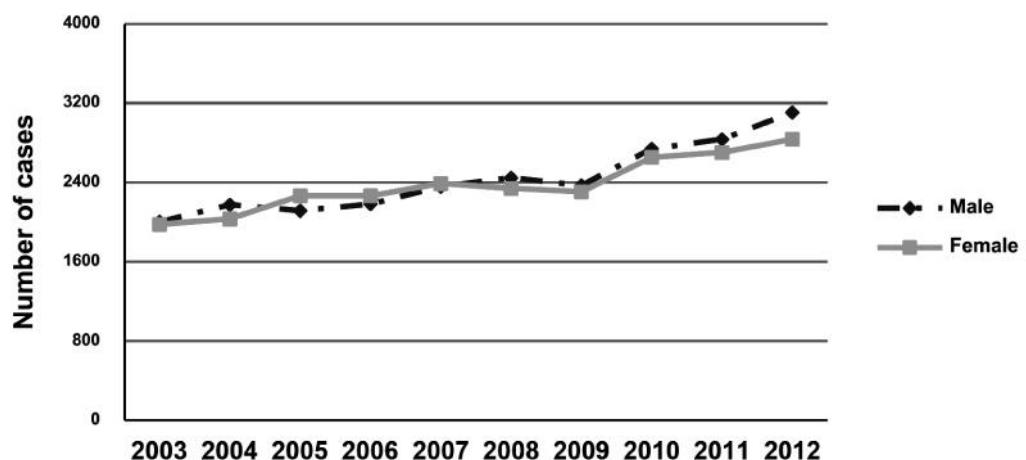
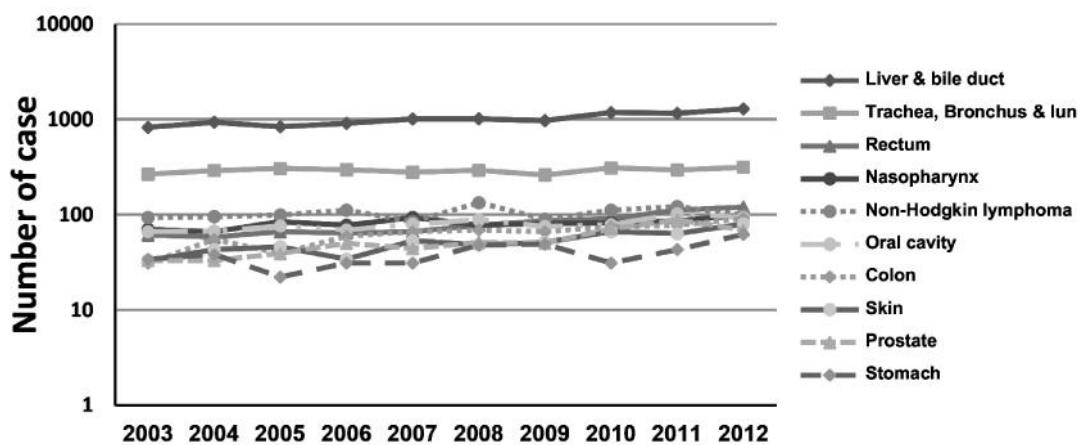
In Srinagarind hospital, liver and bile duct cancer was the most common cancer presenting in both males and females during the last decade. In Thailand, the most common cancer is lung cancer in male and breast cancer in female whilst liver and bile duct cancer is the 3<sup>rd</sup> and 5<sup>th</sup> most common cancer occurring in male and female, respectively<sup>22</sup>. A number of Cholangiocarcinoma (CCA) new cases in Srinagarind hospital was 3-5 folds higher than the number of Thailand<sup>22</sup>. CCA is a average cancer of bile duct epithelial cells. An important risk factors of CCA are consuming raw crypionoid fish

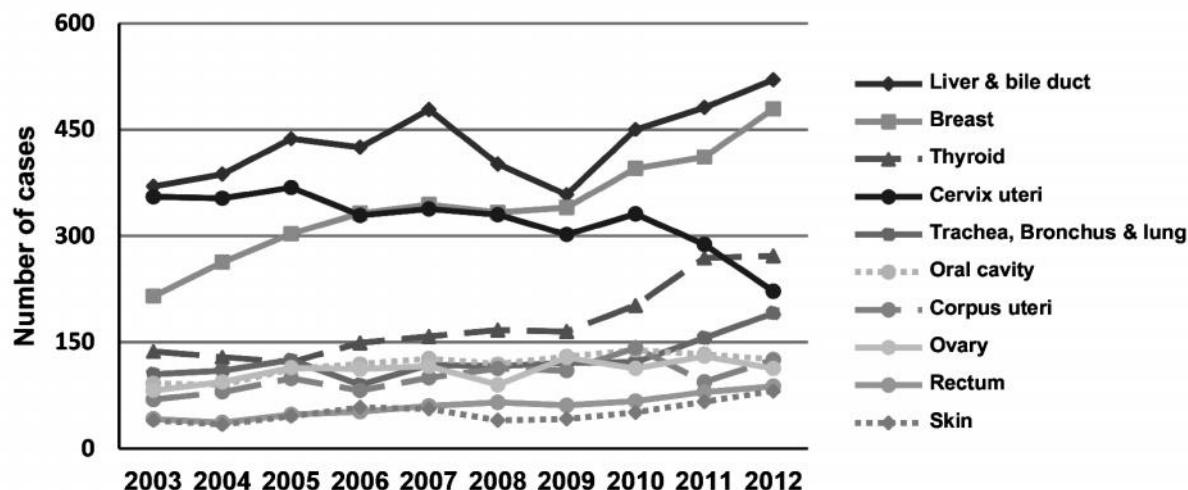
**Table 1** Numbers of cases of the most common cancers in males in Srinagarind Hospital, 2003-2012

Site	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	Total
Liver & bile duct	824	934	837	908	1,007	1,012	969	1,173	1,152	1,283	10,099
Trachea, Bronchus & lung	265	289	304	295	277	290	260	308	293	313	2894
Rectum	61	58	66	64	66	77	86	90	111	120	799
Nasopharynx	70	66	84	77	93	77	81	82	86	99	815
Non-Hodgkin lymphoma	93	95	99	111	84	133	89	111	121	99	1035
Oral cavity	66	67	76	69	79	88	75	78	102	93	793
Colon	31	55	39	59	66	69	66	74	77	91	627
Skin	33	43	46	34	53	48	51	66	63	80	517
Prostate	33	33	39	50	44	51	50	71	88	69	528
Stomach	34	38	22	31	31	48	49	31	43	62	389
<b>All sites</b>	<b>1,510</b>	<b>1,678</b>	<b>1,612</b>	<b>1,698</b>	<b>1,800</b>	<b>1,893</b>	<b>1,776</b>	<b>2,084</b>	<b>2,136</b>	<b>2,309</b>	<b>18,496</b>

**Table 2** Numbers of cases of the most common cancers in females in Srinagarind Hospital, 2003-2012

Site	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	Total
Liver & bile duct	370	387	437	425	478	401	358	450	481	520	4,307
Breast	215	263	303	332	344	333	340	395	411	479	3,415
Thyroid	137	129	122	149	158	167	165	202	269	272	1,770
Cervix uteri	355	353	368	329	338	330	302	331	288	222	3,216
Trachea, Bronchus & lung	105	110	125	90	118	116	121	122	156	191	1,254
Oral cavity	92	90	112	119	127	119	130	139	133	126	1,187
Corpus uteri	69	80	99	82	100	113	110	142	94	125	1,014
Ovary	82	94	114	112	116	90	128	113	130	113	1,092
Rectum	42	37	48	52	60	65	61	67	80	88	600
Skin	40	34	46	58	56	40	42	51	66	81	514
All sites	1,507	1,577	1,774	1,748	1,895	1,774	1,757	2,012	2,108	2,217	18,369

**Figure 1** Overall numbers of new cancer cases recorded annually during 2003-2012 in Srinagarind Hospital.**Figure 2** Numbers of cases of the five most common cancers in males, 2003-2012.



**Figure 3** Numbers of cases of the six most common cancers in females during 2003-2012

hosting for *Opisthorchis viverrinii* (OV) lava<sup>7</sup>. CCA is still persistently an unresolved problem of the Northeast Thailand and this region has the highest incidence of CCA compared to the other regions of Thailand throughout the last 10 years<sup>8,9</sup>. The trends of such incidence in this region seem to be risen every year. Due to the fact that people in NE region have a high risk of consuming behavior by eating raw crypinoïd fish, which is the intermediate host for OV lava. These parasites are an important promoting factors of CCA<sup>10</sup>. Additionally, some certain food components have a strong evidence for correlating with carcinogenesis such as N-nitrosamine (NA) and arsenic. Nitrosamine, an alkylating genotoxic agents, is generally used to preserve meat for providing the characteristics of red color, flavour and aromas in processed meat such as bacon. Particularly, volatile NA is a potent carcinogen. In *in vitro* studies, nitrosamine is a strong cancer-causing agents inducing hepatocellular neoplasms in mice, rat and rainbow trout<sup>17,18</sup>. Arsenic is commonly used as agricultural insecticides and poison in many Asian developing countries including Thailand<sup>19</sup>. It possibly contaminates in drinking water and foods. Prolonged exposure of high levels of arsenic evidently associates with increased risks of many cancers such as skin, liver, kidney and bladder cancer<sup>20,21</sup>. Thus, these carcinogens might also initiate increasing incidence of CCA.

New cases of breast cancer are increased at accelerating rate during the last 10 years especially in the second half of decade observed. There are many factors influencing on higher incidence of breast cancer such as longer average life span. This factor is very important in increasing a chance of having breast cancer in old age people. Additionally, Westernisation life style such as consuming high fat diet also enhances a chance of initiating breast cancer<sup>11</sup>. The other factors that might increase the risks of breast cancer are late child bearing, having fewer children and physical inactivity<sup>11</sup>. Presently, patients simply access medical knowledge from various sources such as internet, social network and books and the medical service is also simply accessed. Consequently, people intentionally concern about their health problems and seek for medical examinations early. In addition, self breast examination campaign is generally promoted in Thailand. Thus, amount of breast cancer new case persistently rises every year.

In the first half of decade, cervix cancer was the second commonest cancer presenting in females. Interestingly, the number of cervix cancer cases was dramatically dropped and cervix cancer was the fourth most common cancer in females in the later half of decade. Presently, cervical cancer is the second most common cancer occurring in Thailand<sup>22</sup>. Changes in

screening and early intervention methods might also have influenced the data, as is likely the case for cervical cancer. An effective campaign to promote cervical cancer scanning by Pap smear has been in place in Thailand since 2002<sup>12</sup>. In addition, HPV vaccine has been promoted during the last few years in Thailand<sup>13</sup>. These two interventions are expected to reduce the incidence of cervical cancer, and that is likely reflected in our data. Nasopharynx cancer is the fourth most common cancer presenting in males whereas it is the 7<sup>th</sup> most common cancer occurring in Thailand<sup>22</sup>. The most pivotal carcinogenic factors initiating nasopharynx cancer are cigarette smoking and chronic EBV (Epstein Bar virus) infection. Nasopharynx cancer occurring in Asian countries usually correlate to EBV infection<sup>14</sup>. Thyroid cancer is the third commonest cancer occurring in female while it is the 10<sup>th</sup> most common cancer presenting in female of Thailand<sup>22</sup>. Such new cases of thyroid cancer were high compared to the number of Thailand. Possible factor influencing on this phenomenon is that Srinagarind hospital is the centre for radiotherapy in the NE and radioactive iodine (I-131) is also available for treatment of thyroid cancer. Consequently, most of thyroid cancer cases in the NE were referred for radioactive treatment in Srinagarind Hospital.

In general, the number of new cancer cases is higher than previously. This is possibly because medical investigations for final diagnosis are enormously improved. Advanced medical high technology especially image-guide biopsy is available and all cancer patients are comfortable to undergo this investigation. Additionally, medical refer system between the hospitals are much more effective than previously. Patients are also able to access all necessary medical health information from many resources and they can easily get better health care service.

#### Limitations of study

This study provides data concerning the numbers of new cancer patients diagnosed at Srinagarind Hospital in each of the last 10 years. The record system

in the first half of decade was not fully effective and may not have captured data from all cases. Additionally, this study does not provide the mortality rate of cancer patients.

#### Conclusion

The trends of all cancers continuously increased throughout 10 years of study in both genders. Liver and bile duct cancer was the most common cancer presented in both males and females during the whole decade observed. Such high frequency of liver and bile duct cancer in NE can be declined, if people realise the danger of eating crypinoi fish, which is the important promoting factor for CCA. The number of breast cancer new cases consistently increases in females. Such high number possibly decreases when females avoid high fat diet resulting in obesity and have active physical activities.

#### References

1. Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. CA Cancer J Clin 2014; 64 (1): 9–29.
2. Sriplung H, Wiangnon S, Sontipong S, Sumitsawan Y, Martin N. Cancer incidence trends in Thailand, 1989-2000. Asian Pac J Cancer Prev 2006; 7: 239–44.
3. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012; 62: 10–29.
4. DeSantis CE, Lin CC, Mariotto AB, Siegel RL, Stein KD, Kramer JL, et al. Cancer treatment and survivorship statistics, 2014. CA Cancer J Clin 2014; 64: 252–71.
5. Rattanamongkolgul S, Sithisarankul P, Wattanasirichaigoon S. Life expectancy of Thai physicians during 1998-2002. J Med Assoc Thai 2004; 87 (suppl 4): S19–22.
6. Sangrajrang S, Chaiwerawattana A, Ploysawang P, Nooklang K, Jamsri P, Somharnwong S. Obesity, diet and physical inactivity and risk of breast cancer in Thai women. Asian Pac J Cancer Prev 2013; 14: 7023–7.
7. Sripa B, Bethony JM, Sithithaworn P, Kaewkes S, Mairiang E, Loukas A, et al. Opisthorchiasis and Opisthorchis-associated cholangiocarcinoma in Thailand and Laos. Acta Trop 2011; 120 (suppl 1): S158–68.
8. Charbel H, Al-Kawas FH. Cholangiocarcinoma: epidemiology, risk factors, pathogenesis, and diagnosis. Curr Gastroenterol Rep 2011; 13: 182–7.

9. Kamsa-ard S, Wiangnon S, Suwanrungruang K, Promthet S, Khuntikeo N, Kamsa-ard S, et al. Trends in liver cancer incidence between 1985 and 2009, Khon Kaen, Thailand: cholangiocarcinoma. *Asian Pac J Cancer Prev* 2011; 12: 2209–13.
10. Songserm N, Promthet S, Sithithaworn P, Pientong C, Ekalaksananan T, Chopjitt P, et al. Risk factors for cholangiocarcinoma in high-risk area of Thailand: role of lifestyle, diet and methylenetetrahydrofolate reductase polymorphisms. *Cancer Epidemiol* 2012; 36: e89–94.
11. Jemal A, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiol Biomarkers Prev* 2010; 19: 1893–907.
12. Kasinpila C, Promthet S, Vatanasapt P, Sasieni P, Parkin DM. Evaluation of the nationwide cervical screening programme in Thailand: a case-control study. *J Med Screen* 2011; 18: 147–53.
13. Praditsithikorn N, Teerawattananon Y, Tantivess S, Limwattananon S, Riewpaiboon A, Chichareon S, et al. Economic evaluation of policy options for prevention and control of cervical cancer in Thailand. *Pharmacoeconomics* 2011; 29: 781–806.
14. Chu EA, Wu JM, Tunkel DE, Ishman SL. Nasopharyngeal Carcinoma: The Role of the Epstein-Barr Virus. *Medscape J Med* 2008; 16; 10: 165.
15. Sriplung H, Sontipong S, Martin N, Wiangnon S, Vootiprux V, Cheirsilpa A, et al. Cancer incidence in Thailand, 1995–1997. *Asian Pac J Cancer Prev* 2005; 6: 276–81.
16. Public health Statistic. Bureau of Health Policy and Strategy Ministry of Public Health. Bangkok, Publisher: The War Veterans Organisation of Thailand, 226 pages, ISSN 08570-3093 (reported in Thai language), 2010.
17. Skibsted LH. Nitric oxide and quality and safety of muscle based foods. *Nitric Oxide*. 2011 May 31;24:176–83.
18. Metzler M. Book Review: Nitrosamines. *Toxicology and Microbiology*. (Ellis Horwood Series in Food Science and Technology). Edited by M. J. Hill. *Angewandte Chemie*-international Edition - ANGEW CHEM INT ED 1990;29:220–1.
19. Abernathy CO, Liu YP, Longfellow D, Aposhian HV, Beck B, Fowler B, et al. Arsenic: health effects, mechanisms of actions, and research issues. *Environ Health Perspect* 1999 ;107:593–7.
20. Anetor JI, Wanibuchi H, Fukushima S. Arsenic exposure and its health effects and risk of cancer in developing countries: micronutrients as host defence. *Asian Pac J Cancer Prev* 2007; 8: 13–23.
21. Bates MN, Smith AH, Hopenhayn-Rich C. Arsenic ingestion and internal cancers: a review. *Am J Epidemiol* 1992; 135: 462–76.
22. Hospital-based cancer registry, annual report Eastern Printing Public Company Limited PCL. 157. Bangkok, Publisher: National Cancer institute, Department of medical services, Ministry of Public Health, Thailand. ISSN 978-616-11-2080-1 (reported in Thai language). 2012.

