RESEARCH ARTICLE

Breast Cancer in Surat Thani, a Province in Southern Thailand: Analysis of 2004-2012 Incidence and Future Trends

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Abstract

Background: With the recent epidemiologic transition in Thailand, featuring decreasing incidences of infectious diseases along with increasing rates of chronic conditions, cancer is becoming a serious problem for the country. Breast cancer has the highest incidence rates among females, not only in the southern regions, but throughout Thailand. Surat Thani is a province in the upper part of Southern Thailand. A study was needed to identify the current burden, and the future trends of breast cancer. Materials and Methods: Here we used cancer incidence data from the Surat Thani Cancer Registry to characterize the incidences of breast cancer. Joinpoint analysis was used to investigate the incidences in the province from 2004 to 2012 and to project future trends from 2013 to 2030. Results: Age-standardized incidence rates (world) of breast cancer in the upper parts of Southern Thailand increased from 35.1 to 59.2 cases per 100,000 female population, which is equivalent to an annual percentage change of 4.5-4.8%. Linear drift effects played a role in shaping the increase of incidence. Joinpoint projection suggested that incidence rates would continue to increase in the future with incidence for women aged 50 and above, at a higher rate than for women below the age of 50. Conclusions: The current early detection measures increase detection rates of early disease. Preparation of a budget for treatment facilities and human resources, both in surgical and medical oncology, is essential.

Keywords: Breast cancer - cancer incidence - joinpoint - Surat Thani - Thailand

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Introduction

Decreasing rates of mortality due to infectious diseases along with increasing rates of chronic and metabolic conditions, including cancer are observed as a consequence of an epidemiologic transition in Thailand.

New cancer cases and deaths, in less developed countries are estimated to contribute for 57% and 65% of the world cancer burden, whilst new cancer cases are expected to rise to 63% in less developed countries (Globocan 2012 - Home, n.d.). Breast cancer poses a particular problem over the coming decades as less developed countries are increasingly adopting the characteristics of a Western lifestyle.

There is a strong association between Western lifestyle factors, such as diet and parity, and the incidences of breast cancer (Layde et al., 1989; Althuis, 2005; Cui et al., 2007; Kruk, 2007). Mammographic screening is limited to women who can financially access it in their country, and those who have an indication to undergo screening. The method of breast self examination is affordable, and is promoted through the country-wide health care network by the Ministry of Public Health. Thus, to target resources for breast cancer prevention and control, accurate incidence predictions are crucial.

Breast cancer incidence rates are increasing throughout Thailand (Sriplung et al., 2006; Khuhaprema et al., 2013). The estimated age-standardized incidence rate (ASR) of breast cancer in Thailand increased from 13.5 to 30.7 cases per a 100,000 female population in 1990 and 2008 (Vatanasapt et al., 1995; Khuhaprema et al., 2013). The regions of Thailand dramatically vary in terms of population characteristics, and risk factor exposures i.e. ethnic composition and diet, and incidence rates (Khuhaprema et al., 2012).

Southern Thailand's population consists of a unique ethnic and cultural make-up. The Thai National Statistics Office estimates that Muslims make up approximately 30% of Southern Thailand's population (National Statistical Office, 2005). Since Surat Thani is a province in the upper part of Southern Thailand, and Muslims comprise only 2% of the province's population (National Statistical Office, 2011) while, the percentage of Muslims is as high as 85% in the three south, easternmost provinces closest to the Thailand-Malaysia border.

Surat Thani province (Surat Thani Province -

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Figure 1. Map of Thailand. The province of Surat Thani has been highlighted

Wikipedia, n.d.) occupies an area of 12,891.5 sq.km (Figure 1) and the population of the 2010 census was almost 1 million. The province is subdivided into 19 districts. The main income of the province is from tourism, the seafood industry as well as agricultural products.

Surat Thani Cancer Center was established in 1993 to cover cancer control activities and for the treatment of cancer patients in the upper parts of Southern Thailand. A population-based cancer registry of Surat Thani was set up by the Cancer Center in 2001 to provide cancer statistics for the upper region of Southern Thailand, (Health Care Service Region 11) particularly in Surat Thani province, where the Cancer Center is located. It was established long after the registry of Songkhla province which serves the lower regions of Southern Thailand (Health Care Service Region 12).

The goal of this study was to characterize the breast cancer incidence trends in Surat Thani province by the calendar year, birth-cohort and age of diagnosis and to project future female breast cancer rates in the upper parts of Southern Thailand through till 2030. The investigation in this study included incidence rates of female breast cancer data from the Surat Thani registry from the years of 2004 to 2012 using joinpoint regression and age-period-cohort models.

Materials and Methods

Cancer registry and cancer case recruitment

The Surat Thani cancer registry covers nineteen districts in the upper part of Southern Thailand. The

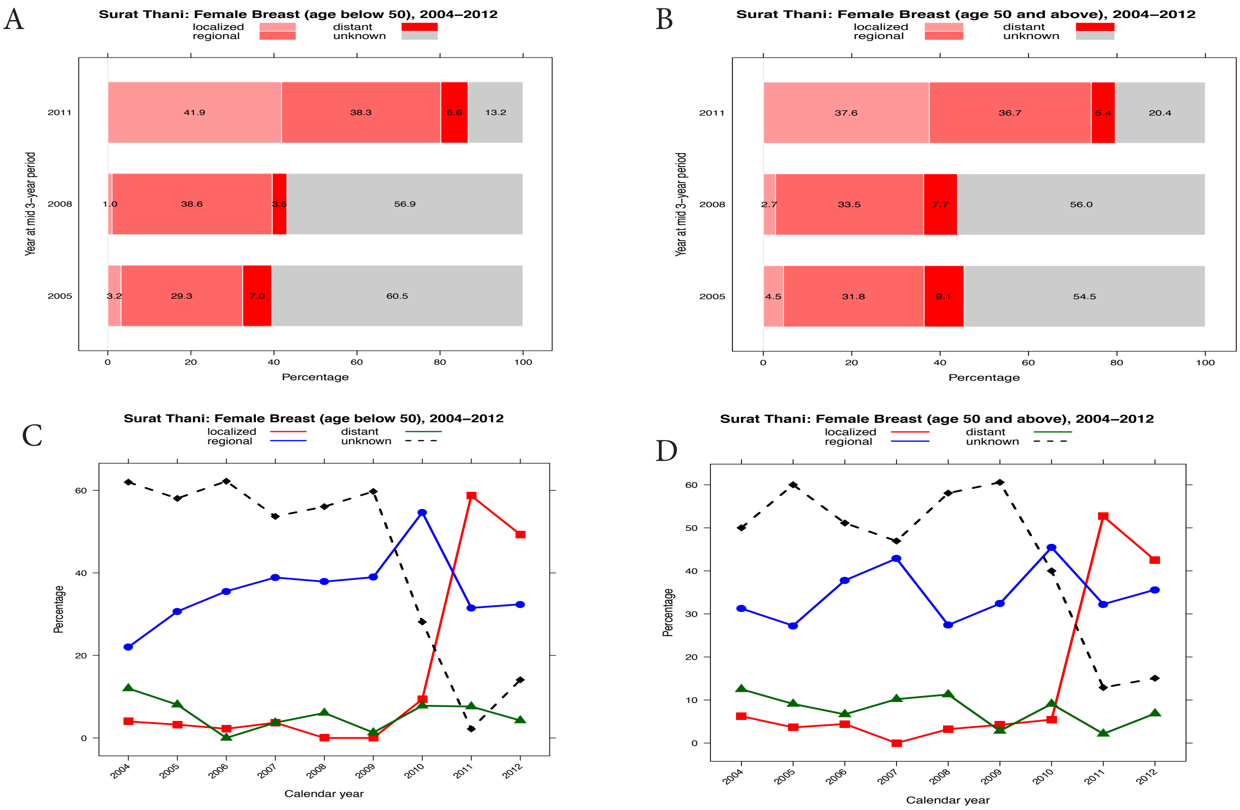

Figure 2. Stage distribution across 3-year periods for; a) women below the age of 50 and b) women at, or above the age of 50. Percentage of stage for each year for; c) women below the age of 50 and d) women at or above the age of 50

population in Surat Thani province from the 2010 census was 0.95 million people of which 0.51 million were females (National Statistical Office, 2011). The registry actively ascertains cancer cases from various sources including, but not limited to community hospitals, private hospitals, and the Bureau of Policy and Strategies along with, the Ministry of Public Health.

The number of undetected cases is difficult to estimate due to remote villages with limited access to health facilities, but it is expected to be low. Female breast cancer cases were extracted from the registry database from 2004 through till 2012 using ICD-10 codes C50.X. Information included age and date of diagnosis.

Population denominators

Population denominators, to calculate incidence rates, were estimated from the three population censuses surveyed by the National Statistical Office in 2000 and 2010 (National Statistical Office, 2011, 2002). The population denominators by both sexes for all districts were readily present in the censuses. Intercensus populations were estimated using a log-linear function between two consecutive censuses. The populations beyond 2010 were estimated, and reported by the Office of the National Economic and Social Development Board (2013).

Statistical analysis

ASRs standardized to the world population proposed by Segi (1960), and later modified by Doll (1976), were computed for each particular year then plotted to visually illustrate the trends. Person-years used as the denominators in the computation were calculated from census data (National Statistical Office, 2011). Age-specific incidence rates were calculated for eighteen age groups ranging from 0-4 through to 80-84, and 85 years and older and nine calendar periods from 2004 to 2012 (At 1-year intervals).

We evaluated trends in incidence using the Joinpoint-Regression Program version 4.0.4 (National Cancer Institute, 2013). Joinpoint regression identifies statistically significant trend change points (joinpoints) and the rate of change (annual percent change) in each trend segment using a Monte Carlo permutation method (Kim et al., 2000). Analyses were conducted for all females, and then for females younger than the age of 50, and females 50 years of age, or older to determine the differences in incidence trends above, and below the mean age of menopause (Thomas et al., 2001; Henderson et al., 2008).

Age-period-cohort (APC) regression models were used to investigate the effects of age, the calendar year and birth-cohort on the incidence of breast cancer. Since the time period is only 9 years, age-specific incidence rates were calculated for 1-year rather than 5-year age groups. Although, the use of 1-year intervals had the limitation of high fluctuating rates, and caused wide confidence intervals, it allowed us to use the dataset within a short time period to visualize the trend, as well as being able to project the future incidence rates. We used the classical method which, fits a log-linear model with a Poisson distribution to the observed data to estimate age, period and cohort effects in a multiplicative APC model as follows:

$$log[R(a,p)]= f(a) + g(p) + h(c)$$

Where the expected log-incidence rates $R(a,p)$ is assumed to be equal to a linear combination of effects that adjusts for age a, period p and birth-cohort c, where $c=p-a$. To address the non-identifiability problem of the APC models, two-effects models (age-period and age-cohort) were first chosen, and the remaining effect (cohort or period) was then identified to the respective model's residuals using natural splines to reduce random variation (Carstensen, 2012). These are referred to as the AP-C and AC-P models. The analysis of APC models was performed using the Epi package (Carstensen et al., 2013) for R statistical software version 3.1.2 (R Core Team, 2014).

We used the two independent methods to project the incidence rates of breast cancer in Surat Thani province joinpoint and age-period-cohort model projections. Joinpoint: Each best-fit joinpoint model was separated into its linear and residual components. The residuals described the curvature while, the linear component illustrated the secular drift of the trend. APC: The linear drift (D) of period and cohort parameter was identified. With both methods, the incidence rates were extrapolated out to 2030. We also followed the cut trend system mentioned by Olsen et al. (2008) in projection by attenuation of the linear drift obtained by the APC model by 0/4 D, 1/4 D, 2/4 D, and 3/4 D respectively, for the four future 5-year projection periods.

We also applied the cut trend concept to the projection with the joinpoint method with a reduction of the trend in the first future 5 years by 0% and after that by 5% per year, so as to get 1/4 D by the year 2020 and up to 3/4 D by the year 2030 at the end of the forth 5-year period.

Results

A total of 1,118 female breast cancer cases were diagnosed in Surat Thani Province during the years of 2004 through to 2012. Of these, 583 occurred in females

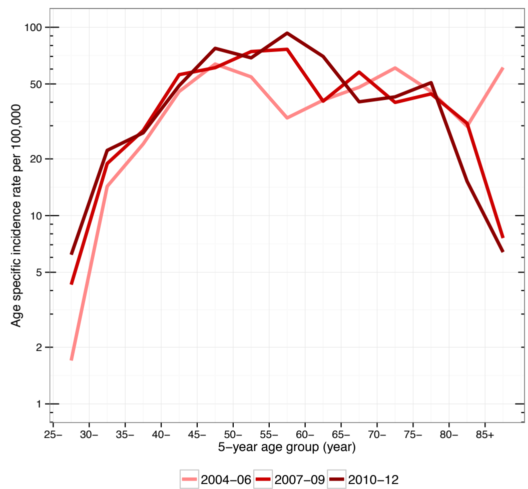

Figure 3. Age-specific incidence curves of breast cancer in Surat Thani in three 3-year periods from; 2004-2006, 2007-2009, and 2010-2012

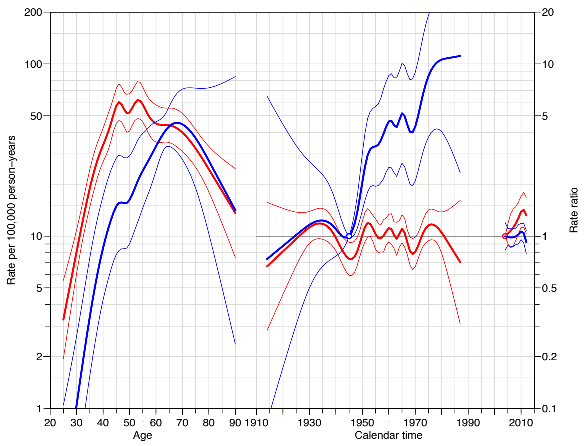

Figure 4APC trend analysis. AC-P (blue) and AP-C (red) models for all females. Incidence rates are plotted in the log scale (left y-axis)

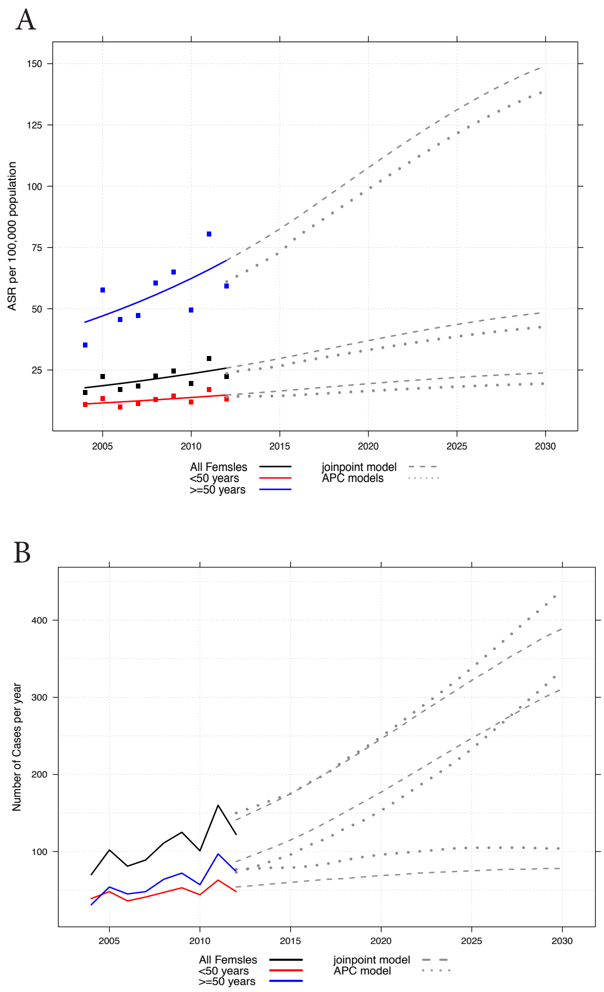

Figure 5. Trend Projection of Breast Cancer Incidence and Number of Cases to 2030. a) Rate projections using Joinpoint (dashed lines) and age-period-cohort (dotted lines) models both for females 50 years of age and older are much higher than those of women aged less than 50. b) Number of cases projected for all females are greater influenced by; women aged 50 years and older than those less than 50 years of age

under the age of 50 and 535 of the cases were females over the age of 50. Stage distribution was shown by each age group, as shown in Figure 2. The underlying trends in stage classification, for both age groups, shows a dramatic increase in the percentage of cases in the last 3-year period for localized cancers and a decrease in unknown cancers. Because the huge decrease in unknown cases, across time, would create bias in trend analysis, stage was not used as a parameter in our analyses of female breast cancer rates.

At the year 2010 and after, the unknown stage showed the largest decrease in percentage among women in both age groups while the localized stage obviously increased at the same time among women below the age of 50, and one year after, among women at 50 and above 50 years of age as shown in Figure 2.

The age group at peak incidence was around 45-49 and seemed to be shifting towards the older age group over the time periods (Figure 3). The second rise in age-specific incidence rates was observed around the age groups of 65 to 74 and dropped again in the oldest age group.

Age-period-cohort analyses and joinpoint analysis

The AP-C and AC-P models of age-period-cohort trend analysis (Figure 4) show rough linear trends in cohort and period across the calendar years. Thus, the overall increase in incidence was explained by the age-drift model with the drift parameter (coefficient) of 0.044 and 95%CI of 0.021- 0.067.

Breast cancer incidence rates increased from an ASR of 35.1 in 2004 to 59.2 cases per 100,000 people-years in 2012 (Figure 5). Zero join point model was the best fit for all ages and the two subgroups women below 50 years of age, and age 50 and above. Overall, the incidence rate of female breast cancer increased at an annual percentage change (APC) of 4.8% (95%CI:-0.4%, 10.3%) and 4.9% (95%CI: 2.4%, 7.6%) by joinpoint and APC models, respectively. In comparing the two models, joinpoint gave a slightly higher estimate along with a wider confidence interval than the APC models.

The projection showed that the incidence rates would be continuously increasing in the future through till 2030 and beyond, especially among those aged over 50. By 2030, the projected ASR would reach 48.5 per 100,000 of a female population by joinpoint, and slightly lower at 42.7 by the APC models. Among those aged over 50, the ASR would reach 149.2, and 138.9 per 100,000 of a female population by the joinpoint and APC models, respectively.

As the proportion of elderly in the province also increase in the future, the number of patients would reach 389, and 440 cases per year by the joinpoint and APC models while, the number of females over the age of 50 would reach 311 and 336 (around 80% of all cases) by the two methods, respectively.

Discussion

In this paper we show that breast cancer incidence in Surat Thani has increased significantly since the year 2004. This is likely due to a combination of changes in demographics, the risk profile of the population as well as, increases in surveillance and breast cancer awareness.

Projections from the joinpoint regression model shows that the burden of breast cancer in the province will continue to rise in the near future, potentially reaching an ASR of 43 cases per 100,000 people-years for all females in 2030. The ASR estimated from APC model was lower than that estimated from joinpoint model through 2030, in contrast, the number of patients estimated from APC model rose more rapidly than that estimated from joinpoint model (Figure 5). The higher number of cases estimated from APC than from joinpoint model was from the fact that APC model gives 5-year age-specific incidence rates. While the proportion of the old age groups is estimated to be high in the future, the projected annual number of patients increases more rapidly over the future years. The 5-year age-specific incidence rates are not known in joinpoint model, the projected annual number of patients can be roughly estimated by multiplying the incidence rates for females under and over the age of 50 with the estimates of the number of females in the same age group in the province in the future years.

The increase could be partly affected by future healthcare planning and other cancer burden control measures which, increase the early cancer detection rate by screening measures such as the use of self breast examination techniques and mammography. Increased awareness of breast cancer in the population could be playing a role and the decrease in stage of the disease would reflect the effect of both awareness and such screening measures.

Surat Thani cancer registry has only recently been established, and the clearance of unknown stage in the registry has only been in effect for the last few years. Hence, the estimation of the effect by stage shifting is not possible at the time of this study (Figure 2).

In Thailand, the Ministry of Public Health has advised all health promotion hospitals (formerly known as health centers) to teach women aged from 25 and over how to do a breast self-examination. Younger women in Southern Thailand tend to be more aware of early detection measures, such as breast self-examination which, could explain this significant increase. Though breast self-examination cannot reduce breast cancer mortality(Lauby-Secretan et al., 2015), increasing, and sustaining women awareness for clinical breast checkups and mammography can be expected in the setting of Thailand, as a middle income country.

After an exponential increase in young ages, age-specific-incidence rates of breast cancer plateaus at an age range around 10 years, or more and is followed by a drop in older ages, however, it can be bimodal.

In some Asian countries, there are two peaks where, the first peak is usually observed around the age of 40-60 and the second peak is at 85 plus years, while bimodal curve is not present in western countries it usually peaks at the age of 70 and over (CI5I-X, n.d.).

The age effect estimates of the AC-P model exhibit the well-known 'Clemmensen's hook' where incidence rates increase exponentially until around the age of 50, then dip slightly before rising again at a lower rate. This phenomenon has been observed for breast cancer incidence and mortality across countries and is thought to be due to the overlap of rates between pre- and post-menopausal women (Waard et al., 1964; Anderson, 1974).

Compared to a high income country, such as the United States, where the ASR of breast cancer in CIV volume X was over 100 cases per 100,000 of the population (CI5I-X, n.d.). The ASR of breast cancer in Surat Thani is also relatively low in comparison to other low- and middle-income countries (LMICs). The ASRs from 1998 to 2002 in Korea, Taiwan, Hong Kong and Singapore were 37.2, 59.7, 69.1 and 90.1 cases per 100,000 of the population, respectively (Shin et al., 2010). Thailand is undergoing an epidemiologic transition in lifespan and lifestyle characteristics, thus, the increasing burden of breast cancer is observed in our analysis.

The risk profile and breast cancer screening of women in southern Thailand was discussed elsewhere (Virani et al., 2014). In brief, the percentage of Southern Thai women who were overweight, having diabetes, or hypertension was found to be increasing by the two consecutive health examination surveys in 2004 and 2009. Considering parity, the total fertility rate in the Thai population has been gradually decreasing from 6 in 1970 to 3 in 1985, 2 in 1998 and 1.6 in 2010. This shift in risk profiles of Southern Thai women makes it necessary to focus on the early detection and more awareness of breast cancer.

The change in the proportion of patients over the age of 50 from 65% in 2014 to almost 80% in 2030 is an important phenomenon which implies that postmenopausal patients are going to make up a higher proportion among breast cancer patients. This phenomenon is also true in Songkhla where the shift over time towards regional and localized stages was striking, and the proportion of distant metastatic cancers was gradually decreasing (Virani et al., 2014). It implies that the proportion of operable cases, and patients who need hormonal and chemotherapy treatment, is increasing as well. Therefore the need for surgical and medical oncologists for breast cancer patients, and in fact, for other adenocarcinoma cancers will not only be a big constrain for health and medical care in Southern Thailand, but for the country as a whole.

The major limitation in this study was the fact that prevalence cases are usually registered as incidence cases in a newly established registry. It usually happens when a registry ascertain of new cancer cases, from the hospital information system, (HIS) fails to trace back, to find the correct date of diagnosis which, may be years before the date appears in the computerized HIS.

The shift in peak age of incidence towards older age groups in Figure 4, which is the same phenomenon appears in other registries in Thailand (Deerassamee et al., 1999; Sriplung et al., 2003; Vatanasapt et al., 1995; Khuhaprema et al., 2007, 2010, 2012, 2013) and China (Fan et al., 2009).

In conclusion, breast cancer in the upper Southern part of Thailand has been, and will, be increasing continuously. The majority of the patients in the future are going to be among women aged 50 years and older. Primary prevention measures depend on the effectiveness of the control measures of metabolic disorder conditions, which is the general trend towards a western lifestyle.

Screening measures, and increased detection rates of early disease alone cannot reduce the increasing trend of the disease. And for these reasons the budget for treatment facilities, such as tertiary hospitals, with surgical facilities, and personnel in both surgical and medical oncology is going to be essential in the future.

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