EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 6
Issue: 4
232-236
Year: 2019

POTENTIAL YEARS OF LIFE LOST DUE TO CANCERS AMONG WOMEN IN SOUTH KERALA: KULLBACK-LEIBLER SURVIVAL DIVERGENCE APPROACH

***Jagathnath Krishna K. M., Preethi Sara George and Aleyamma Mathew**

Division of Cancer Epidemiology & Biostatistics, Regional Cancer Centre, Thiruvananthapuram - 685011, Kerala.

***Corresponding Author: Dr. Jagathnath Krishna K. M.**
Division of Cancer Epidemiology & Biostatistics, Regional Cancer Centre, Thiruvananthapuram - 685011, Kerala.

Article Received on 23/01/2019 **Article Revised on 14/02/2019** **Article Accepted on 05/03/2019**

ABSTRACT
Incidence with five-year follow-up and mortality data of Trivandrum Cancer Registry for the year 2012 showed that the burden due to cancer among women is increasing substantially. The total female cancer deaths in Trivandrum accounts for 784 (42.2%), of the total breast, cervix-uteri, ovary, corpus-uteri and lung together accounted for 48% of female cancer deaths in 2012. Hence potential years of life lost (PYLL) due to cancers among females and burden due to cancers among women in Thiruvananthapuram were assessed. Measures like PYLL, Kullback-Leibler Survival (KLS) divergence measure (relative entropy), Mortality Incidence Ratio (MIR) were used to estimate the burden. The present study observed that PYLL due to cancer in women are substantial as majority of our cancer load is due to breast, lung, cervix uteri and ovary. PYLL and KLS analysis together would help to assess the life-years lost from premature death due to cancer.

KEYWORDS: Burden estimation, Cancer, Kullback-Leibler Survival Divergence measure, Kaplan-Meier method, Mortality Incidence Ratio, Potential years of life lost.

INTRODUCTION
Cancer is a leading cause of premature death among both genders in India after cardiovascular disease.[1] Patients with cancer generally have a poorer prognosis in low-income and middle-income countries, including India, because of relatively low cancer awareness, late diagnosis, and the lack of or inequitable access to affordable curative services compared with patients in high-income countries.[2,3] Death records are an important data source for assessing mortality rates and health disparities because they cover the whole population and include the information regarding age, sex, place of residence and of death, and underlying causes of death. But in most of the developing countries, the cause of death may not be correctly registered especially for cancer cases. Usually, cause-specific mortality is typically reported using traditional epidemiologic measures, especially counts and rates (including age adjusted rates), that are heavily influenced by deaths among older residents. For most causes, these measures are not very sensitive to deaths occurring at younger ages, which are more likely to be premature, preventable deaths if it has been detected in early stages.

Deaths due to cancer accounted for 1594 deaths in Thiruvananthapuram district during 2012.[4] Many of these deaths may be postponed or avoided entirely through the use of appropriate interventions such as primary prevention, screening/early detection, and increased application of state-of-the-art treatment.[5] A death which occurs before the end of average life expectancy is, by definition, a premature death. The age-adjusted and age-specific cancer mortality rates do not fully address the issue of premature mortality and therefore other measures are needed. Cancer death is an important public health concern, and a major cause of premature deaths worldwide.[6,7] The number of deaths alone does not reflect the complete burden put on the society, as some cancers harm younger people more than others. The number of potential years of life lost (PYLL) therefore depends on the age at death and the number of deaths at each age, and may resolve some of the mismatch of disease impact derived from death numbers alone. PYLL data may be more useful in resource allocation and design of prevention programs.[8,9,10,11,12] The different cancer subtype contribution to cancer-caused PYLL varies substantially, and hence comprehensive and updated data on a population level are warranted.

A total of 2480 females reported in Trivandrum district in 2012.[13] Of the total 1594 cancer deaths, in 2012, female cancer deaths accounts for 784 (42.2%) (Breast: 175, Cervix: 43, Ovary: 32, Corpus Uteri: 13, Lung: 56 together accounts for 50.9% of all female cancer deaths)[4]. The leading cancers among females in Thiruvananthapuram are breast (28.8%), cervix-uteri (6.7%), ovary (6%), corpus-uteri (4.5%) and lung (4.1%)

(excluded thyroid 10.7%). Many of these cancers are diagnosed in younger age group[8]. The number of potential years of life lost (PYLL) depends on the age at death and the number of deaths at each age. The specific objectives of the study are to estimate PYLL due to all cancers among females in Thiruvananthapuram district and to assess the burden of life lost due to cancers among women in Thiruvananthapuram.

METHODS

Demographic and death-specific data for 2012 were obtained from the population based cancer registry data base[4], with five years of follow-up. Tabulated life expectancies for each age level per sex are available from Census of India: Life tables (www.censusindia.gov.in - 2010-2014).[14] The mortality-to-incidence ratio (MIR) is generally used as a high-level comparative measure to identify inequities in cancer outcomes. It is calculated by dividing the mortality count by the incidence count in a given year.[15] The deaths and population estimates were aggregated into four age intervals (<40, 40-49, 50-59 and >60 years). The 4-level age intervals were used for calculating expected PYLL for women. The calculation of PYLL was done with the following formula for each type of cancer[16]:

$$PYLL = \sum_{i=1}^{n} D_i * EL_i \quad (1)$$

D_i = No. of deaths at age *i*

EL_i= expected remaining life years at age *i*.

The Kullback–Leibler survival (KLS) divergence[17] is a measure of how one probability density function (f_n) diverges from a second (g_n), the expected probability density. It is also called the relative entropy of f_n with respect to g_n in information theory. The KLS divergence between the survival functions, F_n and G_n is given by[18]

$$KLS(F_n||G_n) = \sum_x \left\{ F_n(x)\ ln\left(\frac{F_n(x)}{G_n(x)}\right) - \left(F_n(x) - G_n(x)\right)\right\} \quad (2)$$

A KLS value close to zero indicates no difference between the two survival function (larger the value, the higher the information loss). Here in the present study, F_n is the survival probability corresponding to the observed life years gained after disease (OLYGAD) and G_n is survival probability corresponding to the expected remaining life years (ERLY). The F_n and G_n is estimated using Kaplan-Meier[19] method. Hence KLS measures the information loss (potential loss of life years) due to premature death. The estimation was done using Microsoft Excel and SPSS version 11.0.

RESULTS

The life expectancy from birth was 74.9 years for males and 77.8 years for females in 2012.[14] The mortality to incidence ratio (MIR) was, 55.4, 34.7, 24.5, 23.5 and 14.3 respectively for lung, cervix-uteri, breast, ovary and corpus-uteri (Table 1). Based on the total number of deaths at each age level, the total of 14337 PYLL over a period of 5 years was observed. Cancer caused PYLL of total PYLL in five-year follow-up period were 3451.1 (24.1%), 1034.5 (7.2%), 971.7 (6.8%), 74.5 (5.2%), 251.3 (1.8%) respectively for breast, lung, cervix uteri, ovary & corpus uteri. In all age group, the major contributor to YLL are due to breast cancer [< 40 years (14.7%), 40-49 (28.2%), 50-59 (31.3%) & >60 (17.7%)] (Figure 1). For age group <40 years, followed by breast cancer, the leading sites based on PYLL are lung (8.2%), ovary (7.1%) and cervix uteri (2.6%) (Figure 1). For all other age groups, the PYLL is of the order cervix (7.4%, 7.5%, 9.1% respectively for 40-49, 50-59 & > 60), lung (7.1%, 5.7%, 8.6%), Ovary (5.8%, 4.3%, 3.8%) and corpus uteri (4%, 1.3%, 2.5%) (Figure 1). The expected PYLL, the difference in OLYGAD and ERLY survival probabilities was obtained and are given in Figure 2. The KLS divergence shows that the deviation from the average expected survival is higher for lung cancer followed by cervix, breast, ovary and corpus uteri (Table 2).

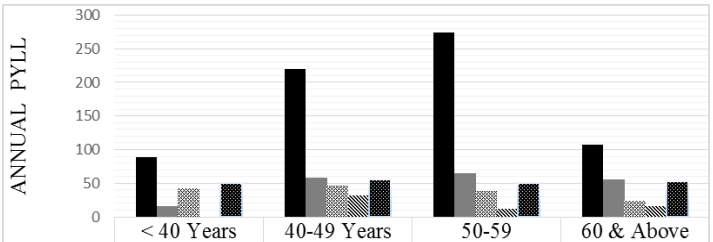
Table 1: Incidence & mortality rates of leading cancers among women (2012).

Sites	CIR	CMR	MIR
Breast	41.5	9.8	24.5
Cervix Uteri	9.6	3.3	34.7
Ovary	8.6	1.9	23.5
Corpus Uteri	6.5	0.9	14.3
Lung	5.8	2.6	55.4
All Cancers	**114.3**	**35.6**	**31.7**

CIR: Crude Incidence Rate, CMR: Crude Mortality Rate, MIR: Mortality Incidence Ratio

Table. 2: Kullback-Leibler divergence measure for various cancers among women.

Sites	Breast	Cervix Uteri	Ovary	Corpus Uteri	Lung	All Cancers
$KLS(F_n\|\|G_n)$	16.49	17.02	13.46	11.88	17.61	9.81



	< 40 Years	40-49 Years	50-59	60 & Above
Breast	88.62	219.88	274.18	107.54
Cervix	15.76	57.78	65.54	55.24
Ovary	42.52	45.42	37.56	23.2
Corpus	0	31.24	11.06	15.1
Lung	49.3	55.72	49.74	52.12

Figure. 1: Comparison of PYLL due to cancers among women.

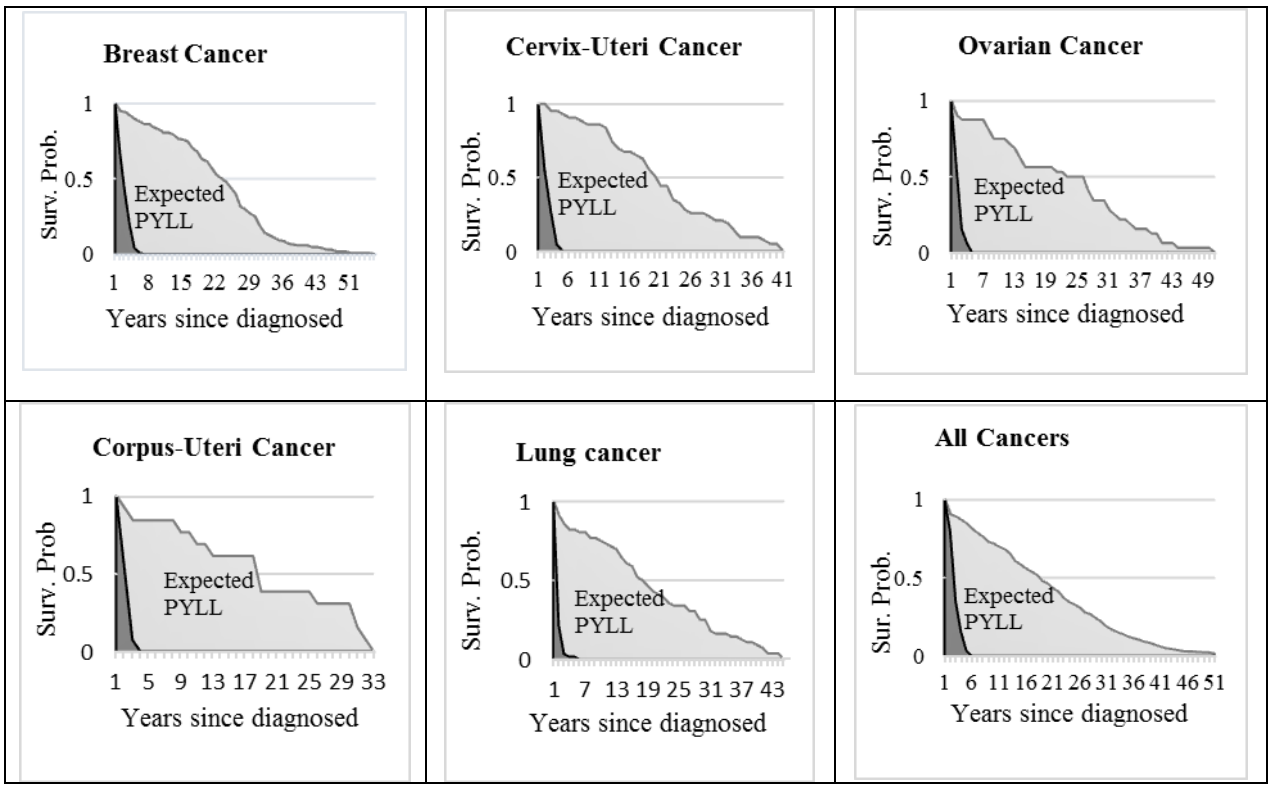


Figure. 2: Expected survival probabilities for potential years of life lost due to cancer among women.

DISCUSSION

The PYLL estimates obtained for female cancers gives a clear indication of the cancer specific burden in Thiruvananthapuram among women over a period of 5 years. The knowledge about the burden was cross verified using the KLS measure (relative entropy) and it was observed that the information loss on the survival probability is high for lung cancer among women followed by cervix uteri and breast cancer and the difference in KLS value for all these three sites are marginal. The results obtained using KLS divergence measure also moving in line with the MIR ratio, whereas the PYLL is highest for breast and it is mainly due to the larger mortality. Brustugun et al.[20] has studied the YLL as a measure of cancer burden in Norway and showed the relative contribution to premature death due to number of cancers can be expressed using PYLL. The present study also agrees with the findings by Brustugun et al.[20] that cancer risk is inherently linked to higher age, but a number of cancers harm relatively young people (eg. breast, lung, ovary). The cancer burden estimate made by Dhillon et al.[1] showed that there was a heterogeneity in site wise burden between the states in India and supports our findings of increase in cancer burden among women.

The study by Yabroff et al.[21] estimated the value of life lost due to cancer death in the United States, showed the cancer burden among female was higher for lung followed by breast, colorectal, ovary and pancreas, whereas for the present study higher PYLL were for breast followed by cervix-uteri, ovary, corpus-uteri and lung. This shows the trend for cancer burden in Indian is different from United States. Yabroff et al.[21] also

pointed out that life lost due to cancer is substantial and was projected to increase dramatically even if mortality rates remain constant because of expected changes in population size, age composition, and life expectancy. Small decreases in mortality rates may lead to large reductions in the value of life lost.

The age group wise PYLL shows that the mortality due to breast cancer is high in all age group, whereas PYLL for ovary is comparatively high for younger age group. The difference in survival probability between the OLYGAD and ERLY using the area under curve (Expected PYLL), also gives clear picture about the potential years of life lost and the KLS shows the corresponding magnitude of loss in life years. The PYLL shows higher for breast, whereas KLS is higher for lung; this is because PYLL take into account only the difference between The CIR, CMR and MIR are useful measures to identify trends in incidence and mortality in a specific population. But to assess the burden of a particular disease, these measures alone is not sufficient, hence these measures along with PYLL and KLS gives meaningful information and inference. The estimated PYLL and KLS is substantial and expected to increase even if mortality rates remain the same, as the life expectancy is showing an increasing trend for the last four decades.

In conclusion, the present study observed that PYLL and Kullback-Leibler divergence measure, which gives the magnitude of information loss, can be used as a useful measure to resolve the mismatch of disease impact derived from premature death alone to estimate the burden of cancer.

CONFLICT OF INTEREST: NIL

REFERENCES

1. Dhillon PK, Mathur P, Nandakumar A et al. The burden of cancers and their variations across the states of India: the Global Burden of Disease Study 1990–2016. Lancet Oncol, 2018; 19: 1289-306.
2. Chalkidou K, Marquez P, Dhillon PK, et al. Evidence-informed frameworks for cost-effective cancer care and prevention in low, middle, and high-income countries. Lancet Oncol, 2014; 15: e119–31.
3. Sivaram S, Majumdar G, Perin D, et al. Population-based cancer screening programmes in low-income and middle-income countries: regional consultation of the International Cancer Screening Network in India. Lancet Oncol, 2018; 19: e113–22.
4. PBCR Thiruvananthapuram. Cancer Incidence & Mortality in Thiruvananthapuram- Report (2012-2014), Regional Cancer Centre, Thiruvananthapuram; 2017.
5. Horm JW and Sondik EJ. Person-Years of Life Lost Due to Cancer in the United States, 1970 and 1984. AJPH, 1989; 79(11): 1490 – 1493.
6. Burnet NG, Jefferies SJ, Benson RJ, Hunt DP, Treasure FP. Years of life lost (YLL) from cancer is an important measure of population burden–and should be considered when allocating research funds. Br J Cancer, 2005; 92(2): 241–245.
7. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer, 2010; 127(12): 2893–2917.
8. Mariotti S, D'Errigo P, Mastroeni S, Freeman K. Years of life lost due to premature mortality in Italy. Eur J Epidemiol, 2003; 18(6): 513–521.
9. Aragón TJ, Lichtensztajn DY, Katcher BS, Reiter R and Katz MH. Calculating expected years of life lost for assessing local ethnic disparities in causes of premature death. BMC Pub Health, 2008; 8: 116.
10. Liu PH, Wang JD, Keating NL (2013). Expected years of life lost for six potentially preventable cancers in the United States. Preventive Medicine, 56(5): 309–313.
11. Kamel MH, Moore PC, Bissada NK and Heshmat SM. Potential years of life lost due to urogenital cancer in the United States: Trends from 1972 to 2006 based on data from the SEER database. The Journal of Urology, 2012; 187: 868-871.
12. Dubey M, Mohanty SK. Age and sex patterns of premature mortality in India. BMJ Open 2014; 4:e005386. doi:10.1136/bmjopen-2014- 005386
13. International Agency for Research on Cancer, World Health Organization. GLOBOCAN 2012—estimated cancer incidence, mortality and prevalence worldwide in 2012. http://globocan.iarc.fr/Default.aspx (accessed April 1, 2018).
14. Census. Census of India 2011. New Delhi: Registrar General & Census Commissioner, 2011.
15. Hébert JR, Daguise VG, Hurley DM, Wilkerson RC, Mosley CM, Adams SA, et al. Mapping cancer mortality-to-incidence ratios to illustrate racial and sex disparities in a high-risk population. Cancer. 2009; 115: 2539–2552.
16. Gardner JW, Sanborn JS. Years of potential life lost (YPLL)--what does it measure? Epidemiol (Cambridge, Mass) 1990; 1: 322–9.
17. Kullback S and Leibler RA. On information and sufficiency. Annals of Mathematical Statistics. 1951; 22(1): 79-86.
18. Yari G, Mirhabibi A and Saghafi A. Estimation of the Weibull parameters by Kullback-Leibler divergence of Survival functions. Applied Mathematics & Information Sciences. 2013; 7(1): 187-192.
19. Kaplan EL and Meier P (1958). Nonparametric estimation from incomplete observations. Journal of American Statistical Association. 1958; 53(282): 457–481.
20. Brustugun OT, Moller B, Helland A. Years of life lost as a measure of cancer burden on a national level. British Journal of Cancer 2014; 111: 1014-1020.
21. Yabroff KR, Bradley CJ, Mariotto AB, Brown ML, Feuer EJ. Estimates and Projections of Value of Life

Lost From Cancer Deaths in the United States. J Natl Cancer Inst. 2008; 100(24): 1755 – 1762.