CHAPTER 1

Introduction & Objectives

Globally, the burden of new cancer cases in the year 2000 was estimated to be 10.1 million representing a 20% incidence over the previous decade with 53% occurring in the developing world (Parkin et al., 2005). Cancer incidence and mortality rates in a defined population for a specified time period serve as a measure of the disease severity. Estimating probability of developing cancer is useful for planning, risk estimation, and measuring the population burden of cancer. They also form a useful baseline measure of comparison for more detailed risk models that take into account individual behaviors and risk factors. Several approaches are available for estimating the probability of a disease. Statistical models are used to compute the probability of developing and dying of cancer from birth or conditional on a certain age.
The problem of cancer is likely to become more acute than it is today in the future. With the control of infectious and communicable diseases and increased life expectancy more of the population in India particularly in the state of Kerala is being exposed to develop cancer. Examination of how cancer incidence and mortality have been changing over time is of interest for usual questions such as why the cancer risk has been changing, and what is likely to happen in the future?

The question of why a given cancer has been increasing or declining in frequency, often with temporal patterns by age and gender between various populations, requires a more complete understanding of the causes of cancer, and of how human exposure to these causes has been changing over time. Analysis of trends in cancer incidence or mortality may provide support for the plausibility of a hypothesis based on other types of evidence. The information on trends or change in cancer incidence and mortality rates forms the scientific basis for planning and organization of prevention, diagnosis and treatment of cancer in a community. Further, trend analysis represents a summary curve of changes that have occurred within different groups of people living under different conditions. Additionally trend analyses make the best use of a very long time-series of cancer incidence and mortality data.

The vast majority of cancer data over time are captured through cancer registration. Cancer registration is the process of continuing, systematic collection of data on cancer, with the purpose of assessment and controls the impact of malignancies on the community. Cancer registry has been defined as an organization for collection, storage, analysis and interpretation of data on persons with cancer. Although the means of recording cases may to a large extent be identical, a distinction must be made between the population based and hospital based cancer registries. The population-based cancer registry (PBCR) records all newly diagnosed cases of cancer occurring in a population of well-defined composition and size. The hospital-based cancer registry (HBCR) records all cases in a given hospital without knowledge of the background population and the emphasis is on clinical care and hospital administration. The HBCR form the nucleus for a PBCR.
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As PBCR continuously produce statistics on incidence and mortality rates of all types of cancers by age, gender and calendar period, the long time-series of cancer data can be used for trend analyses. Model fitting can yield useful summaries of data in terms of parameters in the model. Different regression models such as log-linear model, Poisson regression model, Joint-point regression model etc. have been used for estimating the overall effect (annual percent change) on cancer data.

The next question of what is likely to happen in the future is implicit in any attempt to analyze cancer trends, since the methods generally incorporate an assumption that the relationship between cancer risk by time has a particular form, the nature of which is not likely to change suddenly. A more useful answer to the question about future trends in cancer risk requires projections of cancer incidence or mortality rates, or of the number of cases or deaths likely to arise each year in a given population, or of the rate of change in risk over time. The choice of measure will depend on whether the information is to be used for planning the provision of health care facilities, or for evaluating the priorities for cancer prevention, screening or research. The extra uncertainties in making projections of cancer risk into the future, and the constraints on interpretation imposed by the underlying assumptions, such as the accuracy of population projections, will also vary accordingly.

Morbidity and mortality rates are routinely used to quantify the burden of cancer in cancer registries, but these are often used separately. The Disability-Adjusted Life Years (DALY) is a summary measure that can reflect the burden of both morbidity and mortality in a single indicator. Using PBCR data, burden of cancer [The concept of burden of disease was developed in the 1990s by the Harvard School of Public Health, the World Bank and the World Health Organization to describe death and loss of health due to diseases, injuries and risk factors] is estimated by adding the number of years of life a person loses as a consequence of dying early because of the disease (called YLL, or Years of Life Lost); and the number of years of life a person lives with disability caused by the disease (called YLD, or Years of Life lived with Disability). Adding together the Years of Life Lost and Years of Life lived with Disability gives a single-figure estimate of disease burden, called the Disability
Adjusted Life Year (or DALY). The DALY is based on years of life lost from premature death and years of life lived in less than full health. One DALY represents the loss of one year of life lived in full health (Murray and Lopez 1996 a,b).

In Kerala, statewide cancer statistics is not available as the cancer registration is made through an active method of data collection from hospital records, supplemented by data from vital statistics division. Population-based cancer registration is made possible in the Regional Cancer Centre, Thiruvananthapuram since 1991 covering the city (urban population) and three neighboring community development blocks (rural population) in Thiruvananthapuram district.

Based on the above cancer registry data, it is observed that breast and reproductive tract (cervix uteri, ovary and corpus uteri) cancers of the have a high incidence amongst women in Thiruvananthapuram. Approximately 50-60% of all cancers among women in Thiruvananthapuram pertain to mainly these four organs (PBCR 2011). More than 50% of breast and ovarian cancer women are reported with less than 50 years of age and with high potential years of life lost due to these cancers. These cancers exercise adverse influence on the productive role of women in the society.

With the above scenario, the present thesis mainly aim to assess the distribution of female breast and reproductive tract cancer, to estimate the probability of developing these cancers, to summarize the time-trend estimates in incidence rates of these cancers using the past 20 years Thiruvananthapuram cancer registry data and further to estimate the burden and projection of these cancers in the entire state of Kerala.

**Specific objectives**

1) To compare various methods for estimating incidence and mortality rates of breast, and reproductive tract (cervix uteri, ovary and corpus uteri) cancers in Thiruvananthapuram Taluk.
ii) To compare various methods for estimating probability of developing cancers on breast cervix uteri, ovary and corpus uteri cancers in Thiruvananthapuram Taluk.

iii) To estimate the burden of breast cervix uteri, ovary and corpus uteri cancers in terms of Disability Adjusted Life Years (or DALY) in Thiruvananthapuram Taluk and to compare DALY according to various social value choices.

iv) To compare various analytic approaches for estimating trends in breast, cervix uteri, ovary and corpus uteri cancers in Thiruvananthapuram Taluk for the period 1991 to 2010.

v) To estimate the future burden of breast cervix uteri, ovary and corpus uteri cancers in Thiruvananthapuram Taluk and the state of Kerala till 2026).

The thesis is organized into 7 chapters. Chapter 1 gives introduction of the work with specific objectives. In chapter 2, methods to estimate cancer incidence or mortality rates (Section 2.1), analytical approaches used for estimating time trends in incidence or mortality rates of cancer (Section 2.2), methods such as age-conditional probability and cumulative risk to estimate probability of developing or dying due to cancer, either over a lifetime or over a specified number of years (Section 2.3) and methods for estimating the burden of cancer in terms of disability-adjusted life years (Section 2.4) are provided.

In chapter 3, the data sources used for illustrating the various above methods are provided. The data sources mainly include Thiruvananthapuram Population-Based Cancer Registry (Section 3.1). In Section 3.2, incidence and mortality rates of breast, cervix uteri, ovary and corpus uteri cancers in Thiruvananthapuram are provided. In Section 3.3, the above results are compared with worldwide and Indian data. Section 3.4 provides the various established risk factors associated with the above four cancers.

In chapter 4, various analytical approaches employed in the present thesis to estimate trends in incidence rates of cancer are provided. Breast, cervix uteri, ovary and corpus uteri cancer cases reported in Thiruvananthapuram cancer registry for the period 1991-2010 are used for the trend analysis (Section 4.1). Section 4.2 to 4.4
provide estimates for percent change, estimated annual percent change, and average annual percent change via joinpoint regression model respectively of the above four cancers in Thiruvananthapuram. In Section 4.5, the advantages and limitations of the data are discussed and in Section 4.6, trends in incidence and mortality rates of the above four cancers published worldwide are provided.

In chapter 5, the methods such as age-conditional probability and cumulative risk to estimate the probability of developing or dying from cancer over a lifetime are provided. Section 5.2 and 5.3 provide the probabilities estimated using age-conditional probability and cumulative risk methods for developing and dying due to breast, cervix uteri, ovary and corpus uteri cancers in Thiruvananthapuram are provided. The advantages and limitations of each method are discussed in section 5.4. Probabilities of cancers estimated using the above two methods published in the literature are provided in Section 5.6.

In chapter 6, the methods for estimating burden of breast, cervix uteri, ovary, corpus uteri cancers in Thiruvananthapuram using disability-adjusted life year (DALY) method are provided (Section 6.1). Burden of the above cancers estimated using Thiruvananthapuram Cancer Registry data are compared according to different social value choices (Section 6.2). Different approaches such as i) without considering social value choices such as discount rate and age-weighting (i.e. zero discounting rate and uniform age-weighting) ii) only considering non-uniform discounting (at a rate of 3%) and uniform age-weights and iii) considering both non-zero discounting (at a rate of 3%) and non-uniform age-weights are used for estimating years of life lost (YLL) due to female breast, cervix, ovary and corpus uteri cancers. Further, years lived with disability (YLD) and DALY for the above four cancers in Thiruvananthapuram are estimated with and without considering competing risk and based on different social value choices

Section 6.3 provides burden of breast, cervix uteri, ovary and corpus uteri cancers in Thiruvananthapuram estimated for the years 2011, 2016, 2021 and 2026 and section 6.4 provides the corresponding burden of the above cancers in Kerala. For estimating the future burden of the above four cancers, non-zero age-weighting and
non-zero discounting values are chosen (Gold et al., 1996; Murray and Acharya 1997). The advantages and limitations of DALY method are discussed in section 6.5. Burden of the above cancers estimated using DALY published worldwide are provided in Section 6.6.

Overall, the thesis deals with a number of findings such as estimation of incidence and mortality rates of breast, cervix uteri, ovary and corpus uteri cancers in Thiruvananthappuram, probability of developing and dying due to these cancers, time trends in incidence rates of these cancers in Thiruvananthappuram and projection of burden of these cancers (DALY) in Kerala till 2026. The results of this thesis are published in 16 research papers in international journals which are listed in the publications. The results are summarized and concluded in Chapter 7.

References