Are breast cancer incidence statistics internationally comparable? The effect of cancer registration practices on the data.

By
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A Thesis
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A Thesis/Practicum submitted to the Faculty of Graduate Studies of The University of Manitoba in partial fulfillment of the requirement of the degree

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Abstract

Background: Incidence rates of breast cancer vary widely around the world. These large geographical variations can be due to two major factors: efficacy of the cancer registry system and differences in distribution of key risk factors.

Purpose: The purpose of this study was to investigate the role of the differences in cancer registry practices on the large variation in breast cancer incidence rates between Canada and Iran as areas of high and low incidence respectively.

Methods: Review of publications and two questionnaires to be filled in by key informants in the two registries were the main sources of data collection.

Results: Structural and process requirements as well as outcome measures were compared between the two registries. Part of the variation in breast cancer incidence statistics was explained by differences in cancer registration practices but after removing the effect of such differences, the incidence rates were still significantly different.

Conclusion: Genuine international differences in incidence statistics are likely to exist and comparison of risk factors of breast cancer in high and low incidence areas is recommended. We also developed recommendations to improve data quality in developing registries.

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This thesis is dedicated to the Cancer Registry Unit of CancerCare Manitoba, the Tehran Population-based Cancer Registry of Cancer Institute of Iran, and all cancer registries who might benefit from this work.

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Chapter 1: Introduction

1.1 Background

Cancer registration is the process of continuous and systematic collection of data about characteristics and incidence of certain neoplasms [1]. A **Cancer registry** is an information system designed for data collection, storage, analysis, and interpretation of cancer cases [1]; cancer registries are considered the most valid source of information about cancer in a defined population [2].

The first attempts of systematic collection of data on cancer incidence can be traced back to the 1930s. The longest established centers are from North America and Europe [3]. The first countries to establish population-based cancer registries within their jurisdictions are Germany (in 1929), US (in 1940), and Canada (in 1944) and Denmark established the first national cancer registry in 1942 [4].

Cancer registration has an essential role in cancer control programs, epidemiologic research about cancer determinants, and planning and evaluating health services for prevention, diagnosis and treatment of cancer [5]. The quality of data from a cancer registry determines the value of the information derived from it and the efficiency of the services planned based on it [6].

In order to make the best use of data from different cancer registries, the data should be comparable among different centers and internationally [7]. International comparisons

assume that these data are of high and similar quality [8-10]; thus, there is a need to set standardized structure and definitions for all cancer registries [7].

In 1959, recommendations for establishing cancer registries worldwide were developed by the World Health Organization (WHO), where development of cancer registries in as many different countries as possible, with a central registry in each nation, and setting common standards for making data comparable were suggested [4]. WHO also established the International Agency for Research on Cancer (IARC) in 1965 which was followed by the foundation of the International Association of Cancer Registries (IACR) in 1966 [3]. IARC and IACR collaborate on providing cancer registries with "guidelines on all aspects of cancer registration" [2]; they also collect and analyze data from different registries and publish jointly "Cancer Incidence in Five Continents".

1.2 Research Problem

Breast cancer is the most frequently diagnosed cancer and the second cause of cancer death in women worldwide [11]. One in 9 Canadian women is expected to develop breast cancer during her lifetime [12]. Moreover, the incidence rate of breast cancer has been steadily on the rise worldwide. For instance, in Canada, during the past 25 years, incidence rates have increased by 28% [13]. Also, in recent years, steep increases in breast cancer incidence rates have been reported in many Asian, central European and some South American countries [14].

However, breast cancer incidence rates vary widely around the world. For many years, these rates have been the highest in North America and northern Europe, intermediate in

southern Europe and Latin America, and the lowest in Asia and Africa [15]. The differences in incidence statistics can be as large as 25 fold between the highest and the lowest incidence countries [16]. Theoretically these large geographical variations can be due to two major factors: effectiveness of the cancer registry system and differences in distribution of risk factors including genetic, life style, and environmental factors.

International comparisons between high and low incidence areas that are performed to identify the key risk factors of breast cancer are based on the assumption that data from these registries are of high and similar quality and are thus comparable [8-10]. However, differences in cancer registration practices in different countries may also explain these large variations in statistics totally or in part. Therefore, it is essential to assess the role of cancer registration effectiveness before performing any studies on the role of differences in key risk factors on incidence variations.

The importance of the quality of data reported by cancer registries has made quality control an essential part of the performance for all cancer registries [17]. Many studies have indicated the importance of data quality for comparability of statistics reported from different registries [e.g. 6, 18]. International agencies, such as IARC which report cancer statistics, are responsible for assessing the quality of the data reported by different cancer registries in the world [19]. In their publications, these agencies have discussed the problems of cancer registration in developing registries [20] which can lead to under-registration and make international comparisons invalid.

1.3 Importance of this Study

The most well-established registry centers are located in North America and Europe [2] and the highest incidence rates are also reported from these locations [16]. On the other hand, the lowest incidence rates of breast cancer are reported from developing countries with newly established registration centers [16]. Thus it is important to study the role of the effectiveness of a developing registry on these large observed variations in statistics. Since the differences in reported statistics might be mainly due to differences in cancer registry practices, this study is a major and essential step before studying the role of breast cancer risk factors on such geographical variations. In fact, it is pivotal to establish the real existence of any significant international differences in incidence statistics before any further studies are performed and any conclusions are made. Also the incidence rate of breast cancer is reported to be increasing in many developing countries and since without quality control it would be impossible to differentiate changes in data quality from changes in incidence rates, quality control is a basic requirement for making unbiased conclusions about the trends of incidence rates.

Although in publications such as "Cancer Incidence in Five Continents" data quality has been assessed for many cancer registries, this measure is absent for many newly established and developing registries [20]. Also the importance of differences in cancer registry effectiveness has been neglected by many previous studies which have focused on risk factors of breast cancer [e.g. 21]; such studies would be invalid if these rates are not comparable due to differences in registry practices. There are few studies available in the literature on quality of data reported from cancer registries in developing countries

where cancer registries are newly established and these studies have admitted deficiencies in their cancer registration practices [22, 4]. Despite a few studies which have addressed the impact of data quality on variations in statistics reported by registries in different developed countries with better established registries [6, 18], no comparison has been performed between a developed and a developing registry where generally the largest differences in incidence rates lie.

1.4 Rationale

In GLOBOCAN 2002 Iran had one of the lowest reported incidence rates of breast cancer in the world while in the same year Canada had one of the highest rates; the estimated age-standardized (to the world population) incidence rate of breast cancer for the year 2002 is 84/100 000 women for Canada and 17/100 000 women for Iran [16].

Iran has recently developed a few population-based cancer registries [23], while Canada was one of the first countries to develop population-based cancer registries [2]. Despite the scattered efforts for cancer registration in Iran dating back to 1968, it was only in 1994 that the Cancer Institute of Iran started a cancer registry initiative program with a grant from Ministry of Health and Medical Education to help in establishing regional population-based cancer registries [23]. This campaign resulted in a series of activities in different regions including the establishment of the Tehran Population-based Cancer Registry in collaboration with IARC in 1999 [23]. This is the first population-based cancer registry in Iran to publish its data in Cancer in Five Continents, which is evidence of being the most reliable source of cancer data from Iran.

Manitoba boasts one of the oldest cancer registries in Canada, with cases dating back to the 1930s and a population-based approach beginning in the 1950s [2]. Its quality is demonstrated by its consistent certification by the North American Association of Central Cancer Registries (NAACCR) [24].

Based on the above background, we decided to compare Iran and Canada as areas of high and low incidence of breast cancer in the world and we selected Tehran and Manitoba as representative samples for these populations.

1.5 Purpose of the Study

The purpose of this study is to investigate the role of the differences in cancer registry practices in the large variation in breast cancer incidence rates between Canada and Iran, as areas of high and low incidence respectively. This objective will be achieved by describing the approaches to cancer registration and by comparing the measures of data quality and existence of quality assurance procedures in two cancer registries. The problems of a developing cancer registry in the early stages of its performance are suspected to be key issues in the quality of data reported by these centers.

Therefore, an important purpose of this study is to describe the problems encountered by a developing registry which can cause deficiencies in the effectiveness of the cancer registry and affect the quality of data reported by them. Such deficiencies may result in under-reporting of cases and thus underestimation of the incidence of breast cancer by these registries, which in turn can explain part of the geographical variation in incidence rates.

Chapter 2: Literature Review

2.1 Introduction

The aim of the literature review section is to provide evidence of the importance of an efficient cancer registry besides looking at the literature on quality assurance issues in cancer registries. Purposes of cancer registration and different types of cancer registries are discussed to give background information about the performance of cancer registries.

Also by reviewing data sources and data items in a cancer registry this chapter attempts to provide the reader with the necessary knowledge for understanding data quality assurance procedures. Data quality and measures of quality control are then reviewed in detail.

Confidentiality issues are also discussed since they can certainly affect the quality of data collected by and reported from a cancer registry. Then previous studies which have attempted to measure the quality of data in different registries will be discussed and the chapter is concluded with a discussion of two major sets of quality control standards.

2.2 Purposes of cancer registration

The main purpose of cancer registration is to control cancer in populations [25]. This purpose is achieved through using registry data for research into causes of cancer and

planning health care services [5]. The following are the potential areas for utilization of cancer registry data.

2.2.1 Epidemiologic research

The data from cancer registries can be used for both descriptive and analytical epidemiologic studies, which are complementary. Since cancer registries collect data from the whole population, the problem of bias present in clinical series is removed [25].

Descriptive studies: The main focus of cancer registries is to provide a picture of the occurrence and distribution of cancer in a population [25]. Hence, the most common and primary use of cancer registry data is to measure mortality and incidence rates which is present in the reports of all cancer registries [e.g. 26-28]. Prevalence can also be measured using incidence and survival data or can be derived from cancer registry data if it has been long enough in operation [25].

Comparison of descriptive measures (cancer incidence and mortality) in different populations will give rise to etiologic hypotheses to be tested through analytical studies and highlight important areas for planning preventive measures. Therefore, geographical, international, social, and racial comparisons of cancer incidence can be very rewarding [e.g. 29-31]. The linkage of cancer registry records with other databases can provide additional valuable information on cancer cases and generate etiologic hypotheses [e.g. 32-34].

Another important objective of the cancer registry is monitoring incidence and mortality trends over time [32]. Trends of incidence rates over time are important in evaluating

primary prevention programs; trends of mortality rates indicate the success of secondary and tertiary prevention programs; they can also show the influence of risk factors in specific populations and can be used for planning health care services [25].

Analytic studies: Descriptive studies rarely imply causality but they can indicate probable associations to be tested through more in-depth analytic studies [35].

The longer the data have been gathered and the larger the area from which they have been collected, the better they are for cohort studies [25].

Cancer registry data can be used in retrospective studies and prospective clinical trials but they are not usually useful for prospective studies since reporting and processing take time. However, some centers have developed a new system of "Rapid Case Ascertainment" to support prospective studies by identifying potential cases early through regular surveys of hospitals and laboratories and providing timely information to investigators [36]. Cancer registry data can also be used to test completeness and representativeness of recruited cases in prospective studies. In retrospective studies this database can well serve the purposes of these studies [25].

These studies use cancer registry data to study exposures and identify risk factors of cancer; however, data linkage is often essential for this purpose [e.g. 37].

2.2.2 Health-care planning and monitoring

If cancer registry data are population-based, they can well reflect the present and future burden of different cancer types in different populations [25]. This information can be

used by healthcare planners to make decisions on "resource allocation, such as the placement of radiotherapy facilities, proper staffing of cancer control programs, and "market share" reports for existing facilities" [38]. The types of planning and monitoring activities that use cancer registry data include prevention, screening, patient care, and outcome studies (especially where the outcome is survival).

Prevention: As noted previously, registry data are essential for risk factor identification through performing descriptive and analytic epidemiologic studies. They are also critical for planning and monitoring the success of the programs focused on risk-related behaviours or environmental risk factors of cancer (e.g. tobacco use or chemical exposures) [39].

Screening: Early detection is becoming increasingly important in cancer control, especially for cancers of the breast and cervix. The success of these programs in controlling cancer can best be monitored by comparison of populations where these programs are well established with other populations where no such programs exist [25] and also by following the trends in the incidence of higher stage cancers [39]. The data from the cancer registry provide information about high-risk populations and are, therefore, essential for identifying when and where cancer screening efforts should be implemented [39].

Patient care: Cancer registries have both an indirect role in patient care, e.g. in describing referral pathways and helping the physicians to follow up their patients, and a more direct role in cancer care programs for specific cancer types, e.g. to make sure that all patients receive the best available referral, diagnosis, treatment, classification, staging,

and follow-up for that cancer; additionally the survival of patients can be monitored [25]. Data from cancer registries are also important for monitoring the effectiveness of the treatment provided to cancer patients [39].

Survival: One of the functions of cancer registries is to follow all incident cases of cancer and record the date and reason for their death to calculate survival rates [40]. Monitoring of such survival rates will help in planning health care services; for example, comparing survival rates in different subpopulations and over time can guide health care planners to target services to populations with lower survival rates [25]. These rates can also provide information about treatment success and case follow-up in clinical trials [e.g. 41].

2.3 Types of cancer registries

There are two main types of cancer registries [1]:

1. **A hospital-based cancer registry** registers all cases treated in a specific hospital with a focus on clinical care and usually without information about the background population.

2. **A population-based cancer registry** registers all the new cases diagnosed in a defined (usually geographical) population with a focus on epidemiology and public health.

2.3.1 The hospital-based cancer registry

Hospital-based cancer registries collect data about all cancer patients diagnosed and/or

treated in a particular hospital for the following purposes [42-44]:

- Administrative information
- Clinical research
- Patient follow-up
- Improvement of patient care
- Professional education

Hospital-based cancer registries are usually the first registry centers to develop in populations and have valuable application in evaluating cancer treatment strategies; additionally they can act as the nucleus for population-based cancer registries [1]. Although hospital-based cancer registries are relatively easier to develop and data collection is more straightforward, the trade off is a biased picture because the results from such registries that are not generalizable to the reference population; also registries based on histopathological diagnoses, despite having a very high quality data, are biased because the demographic data about patients are not usually complete and accessible tumours are over-represented [20].

Therefore, the ultimate goal for all cancer registries is population-based registration to have maximum usefulness for public health and epidemiologic studies and for planning the most effective cancer control programs [20].

2.3.2 The population-based cancer registry

Population-based cancer registries collect data about cancer cases in a community from various sources and are not limited to hospital medical records [45].

The goals of population-based registries are [20, 43, 46]:

- Identifying cancer patterns in various populations
- Determining cancer rates and trends over time
- Determining patterns of care and outcomes
- Planning for cancer prevention and early detection
- Helping to set priorities for allocation of health resources
- Providing data for research especially about cancer aetiology
- Evaluating cancer control efforts

It is ideal to establish population-based registries for their advantages over hospital-based registries, including:

- Multiple data sources will ensure the capture of all cases and the completeness of data items collected for each person under a single file [45].

- Various rates reported by these registries are more accurate, realistic, and reliable and reflect the reality in reference communities [20].

- The data collected by these registries serve a wider range of purposes, such as cancer control programs, epidemiologic studies, and resource allocation for health services [38], specifically:

    1. Data from population-based registries can be used for monitoring the distribution of cases of cancer among certain occupations, communities, ethnicities, ages, and other demographic groups [38] and thus identifying high-risk groups [46].
    2. Population-based data can also be used to monitor the distribution of late-

diagnosed cases of cancer in different communities, ethnicities, age and other demographic groups especially for cancer types for which early diagnosis is the strategy for control [38].

3. Data from these registries help public health administrators to discover suspected clusters of cancer within communities, which is not possible based on data from hospital registries [38].
4. Finally, cancer control purposes including prevention, screening, and treatment of cancer are best served through data from a population-based registry. It is also the best source of information for healthcare planners to allocate resources within communities [39].

Data linkage becomes increasingly important in a population-based registry to avoid multiple registrations [45]. Such linkage services will additionally provide a cost-effective source of information for clinical programs, e.g. follow-up of the results of a mammography program, stage of diagnosis data which is necessary to manage health care organizations, and monitoring of treatment guidelines [38].

2.4 Data sources for population-based registries

Population-based registries will be facilitated in the presence of hospital registries but still other sources will improve the quality of the registry [45]. The following section describes all suggested data sources for a population-based cancer registry according to IARC and IACR joint publication [45]; these suggested data sources have been summarized in Figure 2-1.

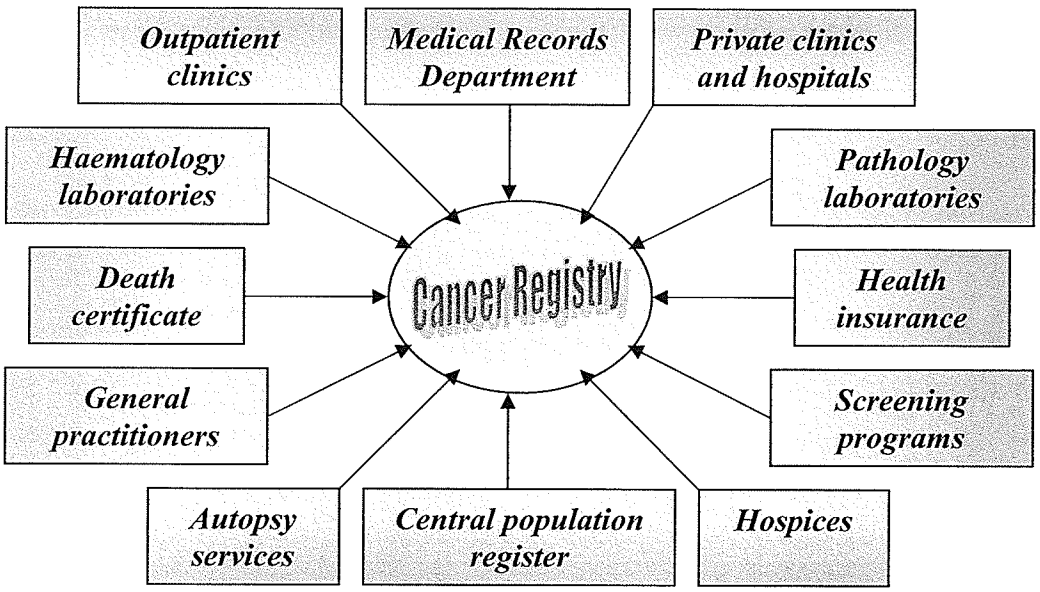


Figure 2-1: Sources of data for a population-based cancer Registry

Medical Records Department: The health records department is the main source of data from hospital records of cancer patients who have been admitted, diagnosed, or treated in that hospital [47]. At every stage there is the possibility of losing cases, for example, medical records might systematically miss special records of clinicians' interest that are kept by them and thus escape being screened by the medical records staff; therefore, in each registry one person should be responsible for each hospital in order to notice any variation in quality and quantity of the data from that hospital [45].

Pathology laboratories: It is desirable that all cases of definite or possible malignancy in pathology reports be reported to the registry from all laboratories of the region and it is optimal that they are reported directly to the population-based registry [e.g. 48]. It is important that all kinds of pathology reports be screened including bone marrow biopsy, autopsy, and cytology from all different pathology labs in private settings and specialist labs; the disadvantage is that specialist labs are more likely to attract patients from

outside the registry area [45].

Haematology laboratories: Haematology laboratories generally have separate reporting systems from other pathology labs and should ensure that their reports are also sent to registries [45]. There might be more borderline diagnoses which might cause difficulty in accurate registration [49]; thus the included cases should be well defined [45]. Also since rheumatologic malignancies have long term treatment, the lab reports might not appear in the medical records department until the patient has deceased; haematology labs can play an important role in capturing these cases [45].

General practitioners: Physicians in the community are often the first contacts of cancer patients. This source is frequently used as a follow-back method for death certificate only cases because some patients, especially elderly and end stage patients, might not receive any treatment; they may also avoid contact with health services for fear of painful procedures knowing that treatment will not likely result in cure [45]. Some registries, however, have designed forms or methods to be used by general practitioners when they come into contact with a patient with cancer [e.g. 50, 51].

Health insurance: Where available, health insurance agencies' databases are especially accurate for personal identifiers; however, medical information might not be sufficient [45]. Confidentiality issues which may lead to difficulty accessing data and the inclusion of the dependents in one's insurance record might make the use of this source limited [45].

Screening programs: Acquiring information from these sources is usually easy. However, coding in situ and invasive carcinomas must be done carefully [45]. If a screening program does not have specially trained coders, the resulting inclusion of in situ cases in the cancer registry might increase incidence rates; the reason is that shortly after initiation of a screening program some cases are identified earlier than usual and some might have never been clinically diagnosed because they may not progress to invasive cancer [45]. Therefore, it is important to calculate incidence rates with and without screening detected cases [36].

Private clinics and hospitals: It is important that cases treated in these settings be included; pathology reports and records of clinician notes in these settings can help to a high degree in ensuring cancer data capture [45].

Outpatient clinics: Outpatient referrals are not usually captured by many sources of data. Gynaecologic and skin cancer cases are examples of cancers which might only contact outpatient clinics and receive laser or radiotherapy as an outpatient [45]. The capture of these cases is very difficult since they comprise a small part of outpatient cases; however, it is important that they be included to avoid bias and incompleteness of a cancer registry [e.g. 52, 53].

Autopsy services: Where available, autopsy reports are a good source of data with high accuracy [54]. The autopsy rate might well vary in different cultures and countries [54]. This can influence incidence rates; therefore, there should be a specific code for cases diagnosed incidentally through autopsy because they reflect the intensity of investigations and the impact of autopsies on incidence rates [45].

Hospices: Homes for terminally ill people are becoming increasingly important in the care of cancer patients. Some of these patients might have never been admitted to a hospital and can be registered in the cancer registry when sufficient information is available from the care home [45].

Death certificate: Records of death are an important source for case finding. In vital statistics the cause of death is generally coded according to an International Classification of Diseases (ICD) system [55]. However, if the cancer patient dies because of other causes, malignancy might not be mentioned in vital statistics documents; thus it is important to examine death certificates directly instead of looking at the list provided by vital statistics staff [45]. The advantage of this source is the accuracy of identification items; they are also very important for identifying endpoints for survival analysis [45].

Central population register: The central repository enumerating population is an important source of information for following patients who move from one registration area to another [56]. The comparison of statistics reported from different regional registries to a central registry will also highlight high-risk populations [45].

The choice of data sources used by different registries is important in understanding the probable source of under- or over-reporting in cancer registries; for example, under-reporting of leukemia is expected where the access to haematology laboratories is limited [57]. Also, when interpreting the trends of incidence statistics over time, it is important to consider any changes in data sources; for instance, incidence rates increased in Nova Scotia, Canada, when death certificates were added as a source of data for cancer registration in 1986 [57].

2.5 Data items

According to IARC and IACR, the data items collected by cancer registries are divided into basic and optional items. Basic items are recommended for all registries but optional items are to be collected based on the objectives of the registry, the method of the information collection, and the available resources of the registry data; the emphasis must be on quality of data rather than quantity of data [58].

2.5.1 Basic items

These items might be the only items collected by registries in developing countries. These items include:

- ***Person items:***

  -**Personal identifiers:** name, sex, and date of birth

  -**Demographic variables:** age, address, and ethnic group

- ***Tumour items:*** incidence date, most valid basis of diagnosis, topography (site) of primary tumour, morphology (histology), behaviour, source of information.

2.5.2 Optional items

Each additional item increases the cost and thus its collection should be justifiable. These optional items include:

- ***Person items:***

  -**Personal identifiers:** index number, personal identification number

  -**Demographic variables:** place of birth, marital status, nationality, religion, occupation and industry, year of immigration, country of birth of father and/or mother

- ***Tumour items:*** certainty of diagnosis, method of first detection, clinical extent of the disease before treatment, surgical-cum-pathological extent of disease before treatment, TNM staging system, sites of distant metastases, multiple primaries, laterality

- ***Treatment items:*** initial treatment, response to treatment (usually not collected)

- ***Outcome items:*** date of last contact, status at last contact, date of death, cause of death, place of death (especially for registries which measure survival rates)

- ***Information Source:*** type of source (physician, laboratory, etc.), actual source (name of the source), dates

For special ad hoc studies there might be a need for collecting specific extra information for a limited period of time, such as studies on quality of life of cancer patients.

2.6 Data Quality

Data quality is influenced by the method of data collection and the way it has been presented [59]. The quality of information reported from cancer registries is presented using three major attributes of completeness, accuracy, and timeliness.

2.6.1 Completeness

This attribute includes completeness of case-finding and completeness of items:

Completeness of case finding (cover): Complete case finding means registration of all incident cases of cancer in a defined population and should ideally be 100% [7]. It is equally important that duplicates be avoided [59]. This makes the international comparison of incidence rates reliable since they reflect the reality in different populations instead of differences in data completeness [60].

Completeness of data items (details): It is important that all necessary items be filled for each case. Some of these items are essential such as sex and primary site of the tumour, and the completeness of these essential items is routinely used for quality control purposes [59]. The errors of completeness of data items include "omission" (missing of the information) or "commission" (presence of the information where it should not be) [59].

2.6.2 Accuracy (validity and reliability)

Validity is defined as the conformity of data with truth and reliability is the stability of the results with repeated trials [49].

Accuracy of data items or details (validity): The items that are present for each case might be incorrect; the proportion of correctly registered characteristics for each case is measured through special studies such as re-abstraction (see quality control section) [19]. Registry related errors can happen during abstraction, transcription, coding, or data entry [59].

Accuracy of reporting (reliability): In this context, reliability means the extent to which the registry cases will yield the same results when abstracted by different abstractors [61]. When the staff who register cases or design data entry systems do not have enough knowledge of the data, reporting errors might arise and may not be detected before causing unexpected results [59].

Accuracy of interpreting: Appropriate interpretation is only possible when we have knowledge about the accuracy of data, the data sources, and how the information was collected and processed; this knowledge will be gained only through experience and involvement in the activities of the registry [59].

2.6.3 Timeliness

Timeliness reflects the time lag between diagnosis of a patient and registration of the case in a cancer registry. It is an important requirement for assuring high quality of data

reported by registries since data should be reported in a timely manner in order to be useful [17]. Generally registration cannot be completed immediately after diagnosis because of the time required for reporting from facilities, completion of treatments, and finally completion of the death clearance process [62].

2.7 Quality control

The main applications of cancer registry data are based on the assumption of reliable data [63, 64]. Therefore, quality control is essential for successful performance of a registry and must be incorporated into all systems from the initiation of their operation; for example, without quality control it would be impossible to differentiate changes in data quality from changes in incidence rates and thus, quality control is a basic requirement for making unbiased conclusions about the trends of incidence rates [61]. Quality control will help to demonstrate the degree and area(s) of weakness in the quality of the data collected and presented by each registry and tries to assist in improving them; for example, if the error or missing rate for an item is too high, investing more resources should be prompted; alternatively, depending on the importance of that variable, removing that data item may be considered [59].

There are four principles of quality control in a cancer registry [17]:

1. Quality control must be part of the system from the beginning of its operation: For this purpose reliable sources for case-finding, appropriate abstraction forms, and training of the personnel should be considered before the registry starts its operation [61].

2. Standards must be set for this purpose: This principle requires setting minimum levels for quality measures "below which the data are unacceptable" [17].

3. All registry personnel must be involved in the process as quality control inspectors: This principle ensures detection of errors which might happen in every stage of the operation of a cancer registry. These stages include: 1) entering information from medical records; 2) abstraction; 3) data entry or key punching; 4) programming; 5) computer failures; and 6) management decisions [61].

4. Finally the loop of quality-control procedure must be closed: This means that errors are fed back into the system which ensures eliminating such deficiencies from the system [61].

Quality control can be performed through continuous or ad hoc evaluation of data quality as a standard procedure; critical use of the data from a registry can also serve as a very useful but informal way of quality control [58]. Statistical quality control procedures are designed to ensure the previously stated measures of data quality [19]. These procedures are summarized below.

2.7.1 Assessing completeness of case-finding

This assessment is recommended to be a continuous procedure rather than an occasional monitor [59]. Four methods are generally used: the death certificate method, independent case ascertainment, the historic data method, and the mortality-to-incidence ratio [19,

65].

The ***death certificate method*** is based on matching death certificates with cases registered by the registry through other data sources [66]. For cases found for the first time through death certificates, it is important to follow-back and get information from the hospital or pathologist; if the patient has not been hospitalized, physicians can be contacted [20]. When no other source is found the cases are recognized as death certificate only [67] and the number of these cases is used to calculate the "Death Certificate Only" (DCO) percent [66]. High percentage of these cases might reflect insufficient reporting of cases or avoidance of medical services by specific ethnic or religious groups [20].

For rapidly fatal diseases, DCO percent is expected to be higher than slowly progressive diseases [59]. Since cancer incidence rates generally change slowly, any marked change must be followed seriously [59]. This monitoring is best done through site-specific rates, because for rare cancer sites the change might not be reflected in the overall rates [59]. The importance of continuous follow up is to detect any significant change in DCO proportion which can be a sign of change in completeness of case notification and requires rapid intervention to correct the problems [67].

This process is inexpensive and is routinely performed as part of quality control procedures by all registry centers and is, thus, a good measure for completeness especially for detecting clearly incomplete registries; however, this measure should be interpreted carefully for newly established registries because of the absence of data for previous years [62]. It is also insensitive for the diseases that have low case-fatality [61].

This measure has also been frequently used as a measure of accuracy and item completeness since DCOs are indications of low accuracy in diagnosis and high rates of missing items such as diagnosis date [49].

Independent case ascertainment means assessing registry completeness by comparing the cancer registry database with another independent study in the population or independent case search by drawing a random sample from facilities that support the registry [e.g. 68, 69]. It is also possible to ascertain cases from two or more independent sources and use the degree of overlap to estimate the total number of cases; this is called the capture-recapture method [e.g. 49, 70].

This is very useful especially for slow progressive cancers or those diagnosed early through screening [1]. This method is more sensitive than other methods of assessing completeness of case-finding but it is time-consuming and more expensive [31].

The ***historic data method*** includes examining observed-to-expected ratios, comparing incidence rates in different populations, analyzing age-specific incidence curves, and comparing childhood cancer rates [19]. These measures estimate the completeness of registration based on the *history* of the registry performance [62]. For example, a higher number of expected cases compared to the observed numbers suggests incomplete case registration [61]; conversely, lower than expected rates for several sites in a defined population compared to a similar population suggests under-registration [19]. The comparison of childhood cancers among different populations can reveal under-/over-registration of these cancers, since childhood cancers are generally constant across registries and large variations from the observed rates in other population may indicate

over- or under- registration of cases [19]. This method is fast but since it is based on previous performance of the registry, it is relatively crude [61].

The ***Mortality/Incidence Ratio (M/I ratio)*** is routinely used by IARC (International Agency for Research on Cancer) for quality checking of reported data from registries around the world [19]. Higher numbers of cancer deaths compared to incident cases suggests incomplete case registration [67]. For example, higher M/I ratios in Canadian registries between 1969 and 1973 are indications of under-reporting in those registries in earlier years [71].

This measure should be interpreted cautiously for a newly established registry and with enough consideration of case-fatality of the cancer under study [49]. Both the survival rate and the quality of mortality statistics are dependent on facilities and data sources which are normally less accurate in developing countries and thus require careful consideration when this measure is being interpreted [19].

2.7.2 Assessing completeness of data items

Two methods are available for assessment of data item completeness: Shewhart control charts and percent of unknown for important data items.

Shewhart control chart: in this method a fixed number of samples are drawn for which the missing proportion of specific variables are measured, then lower and upper acceptable values are calculated and a graph is drawn for each sample [61]. These points should not exceed control limits and should also be distributed randomly with time and should not follow any specific pattern [72].

Percent of unknown variables: Important data items are used to calculate the percent unknown for a specific variable such as age, sex, place of residence, and primary site [62]. For example, NAACCR (North American Association of Central Cancer Registries) recommends all North American registries to monitor their data for an unknown primary site rate of less than 5% and missing rates of sex, age, and county variables of less than 3% [62].

2.7.3 Assessing accuracy

This assessment can be performed using three methods: diagnostic criteria, re-abstracted records, and internal consistency.

Diagnostic criteria: For cases registered in a cancer registry the most important diagnostic criterion is histological confirmation [73]; therefore, the percent of cases with histologic confirmation is a measure of validity of diagnosis [e.g. 74]. This method is limited to diagnosis and does not assess validity of other important variables such as age and sex; however, since presence of histologic confirmation should be routinely recorded by all registries this is an easy and inexpensive way of assessing data validity [61].

This method has also been used by IARC as a measure of completeness since higher than expected proportions of such cases suggests over-reliance on pathology as the case-finding method and implies failure to capture cases through other means of case-finding [60].

Re-abstracted records: Re-abstraction is performed on a random sample of records (usually 10% of the total) [75]. The re-abstracted records are considered as correct (gold

standard) and are compared against the original registry abstracts [e.g. 76, 77]. Such quality assessment is usually weighted against the more common tumours in order to avoid re-abstracting a large number of similar cases but at the same time considering the role of more common tumours in overall error rates [59]. This method is the most objective method and very exact but it is expensive and labour-intensive [61].

Internal consistency: Assessing internal consistency involves a computer assisted check of the registry database to prevent entering meaningless codes [78]. This is performed through range, format, and consistency checks [59]. Incoming codes are checked and invalid codes are rejected or reported; for example, the type of tumour can be checked against sex to ensure ovarian cancer is not recorded for men, and the sequence of dates for different items can be checked [59]. Some of these consistency checks might produce warning messages for unusual cases to be double checked, such as diagnosis of breast cancer in a man [59]. This method is inexpensive but it is only able to detect highly deviant cases and cannot detect a logical but incorrect code [61].

2.7.4 Assessing reliability

The main method of assessing reliability is the agreement between data abstractors.

Agreement between data abstractors: The level of agreement in data simultaneously entered by different abstractors from the same source can be measured by kappa statistics [61]. Since agreement can always occur by chance alone, kappa statistics is used as a measure of agreement providing a reference for deciding whether the observed agreement is likely to be due to mere chance [35]. Kappa can range between 1 and -1, with the

amount of 0 showing complete accidental agreement; researchers usually consider an absolute kappa value above 0.6 as good and above 0.8 as excellent agreement [35].

2.7.5 Assessing timeliness

Timeliness studies include the accrual method and the median diagnosis to registration interval.

Accrual method: In this method the actual number of cases present in the registry in a specific period is compared against the expected numbers, with an accepted time lag allowed when calculating the expected numbers [17]. Accepted time lag for registration differs by standard setting agency; for example, NAACCR requires 95% of the expected cases to be reported within 23 months of a diagnosis year [62].

Median diagnosis to registration interval: This measure of timeliness is performed through measuring the median time between diagnosis of cases and the time that the case has been registered; i.e. the later the cases are registered, the longer this interval would be [e.g. 68]. This method is easier and more straight-forward than the previous method and can be easily calculated but it depends on the time of reporting [49]. Different registries report their data from three months after year end to two years after it [71]. This time lag can affect this measure, i.e. the later it is calculated, the larger it would be because it is influenced by the cases that are registered later (the late registered cases will increase this interval) [49].

2.7.6 Continuous versus ad hoc quality control

Critical items should be checked continuously for duplicates and coding errors; this is an example of continuous monitoring of data quality, which makes it possible to correct any errors quickly and also promotes staff motivation for maintaining high quality [59]. However, this method is expensive and as a result ad hoc method has become the method of choice for many registries. The quality check through re-abstracting and recoding are examples of ad hoc quality control methods and should be part of all registry systems [59].

2.7.7 Pre-requisites for quality control

Rules and documentation: There must be well-defined rules for each data item and these rules must be documented to improve data accuracy [62]. Some cases might be decided on an individual basis after consulting senior members; these cases should also be documented for future guidelines [59].

Good coding systems: A good coding system allows only appropriate terms to be entered as a code; for example "not stated" and "unknown" codes must be well defined to inform appropriate use [59]. Changes in coding systems must also be well documented to prevent misinterpretations in future studies [62].

Standards: There must be standards for tolerable errors for each operating registry; for example, in a specific registry, a 5% error at the three-digit level of ICD-O [59] or a 2% error for sex might be acceptable [62]. When the rates exceed these limits, immediate actions to rectify the situation must be taken [59].

2.8 Active versus passive registration

Cancer registries may collect data through two main methods: active and passive data collection.

If the facilities (i.e. hospitals, laboratories, clinics, etc.) are required by law to report all cases of cancer that are diagnosed within or by them [79], they support a passive case-finding method for cancer registries. For example, in Ontario cancer registration is mainly passive which means the Ontario Cancer Registry relies "almost completely on records collected for other purposes" [80, 81], i.e. within the four different sources of data (hospital discharge summaries, pathology reports, records of patients referred to Cancer Care Ontario's eight Regional Cancer Centers or the Princess Margaret Hospital, and death certificates) all records that contain a cancer diagnosis are sent to cancer registry [82].

On the other hand, if the facilities or physicians are directly contacted to obtain information and collect data [62], the registration is active.

Although many registries rely mainly on passive case-finding, active case-finding is recommended to all registries in order to ensure that all cases are reported and registered [79]. For example, although Cancer Registry Division (CRD) of the Texas Department of Health is a passive registry, some staff are responsible for case-finding checks at reporting sources to ensure accurate and complete registration [83].

2.9 Confidentiality and the cancer registry

Completeness and accuracy of cancer registration cannot be achieved without assuring the public and healthcare professionals about the confidentiality of the data [84]. Confidentiality regulations ensure: "1) the preservation of anonymity for individuals reported to the registry", "2) that cancer registry data are of the best quality possible, and 3) that the best possible usage of cancer registry data is made for the benefit of cancer patients" [84].

The data that cancer registries deal with are highly confidential and it is essential for all cancer registries to safeguard patients' confidential information even after the patients have died [85]. The American Health Insurance Portability and Accountability Act (HIPAA) is an example of protective laws against release of any "individually identifiable information" referring to a patient [86]. Besides patient-related information that is always considered as confidential, in the case of cancer registries, any kind of data related to health care professionals and institutes must also be regarded as confidential [85].

Guidelines and recommendations are provided by national and international agencies such as IACR and NAACCR for confidentiality assurance in all cancer registries. Highlights of these guidelines are summarized below:

- There should be clearly stated regulations for confidentiality in each cancer registry [86, 87].

- As part of employment contracts, all registry staff should sign a confidentiality pledge declaring that they will not release confidential information to unauthorized persons [62]. They should also be trained for maintaining confidential data before they start work [86].

- Operational, physical, and technical security is required to ensure information security [86]. For this purpose, the director of the registry should maintain a list of people who are authorized to enter the registry [87]. It should be well defined which personnel may have access to registry materials and lockable cabinets for paper files and password protection for computers should be considered [84].

- Since release of cancer registry data is necessary for research and health care planning, which are the main purposes of developing a cancer registry, the registry should design procedures to ensure the maintenance of confidentiality after its release [85].

- Registry regulations should specify conditions for transferring identifiable data [87]. Although transfer of identifiable data to other registries for complete and accurate cancer registration should be permitted [87], such data should not be transmitted without "explicit authority from administration" [84]. Transmission by telephone should be avoided and the use of registered post or courier services should be considered [84].

2.10 Results from previous studies

Different studies have used previously discussed measures of quality control for evaluating data quality from cancer registries. These studies are from both developed registries, which comprise the largest body of the literature, and developing registries.

There are several studies from European and American countries which have attempted to assess the quality of data from well-established centers in more developed countries. Although many studies indicate high data quality and complete and accurate registration in these countries [e.g. 77, 88-92], there is still some evidence of under-registration and inaccuracy even in the long established centers [e.g. 74, 93-95]. These differences in data quality might make international comparisons biased. For example, a British study has revealed that the differences in survival rates reported from European countries are not because of major differences in patient care but the main reason is the differences in cancer registration practices in these countries [18].

There are only a few studies about the quality of data reported from newly established cancer registries in developing countries, e.g. those in Indonesia, Gambia, and Saudi Arabia [22, 61, 96]. These studies demonstrate the numerous problems encountered frequently by developing registries especially in developing countries. Some of the problems are: determination of place of residence (e.g. because of high rate of migration), estimation of age, unavailability of current census on the population which is required for calculating different rates, scarcity of post-mortem autopsy because of cultural and religious issues, absence of high quality diagnostic facilities including pathology laboratories, the remoteness of health care facilities for many residents of the area, weak

health care infrastructure, unawareness of cancer symptoms, unavailability of in-country advanced treatment facilities for cancer, absence of belief in "western" medicine, and inadequate number of trained registry staff [96-98]. Such problems are suspected to exist in developing registries that are established in similar situations in other developing countries. For example, cultural and religious issues and scarce resources are known to be also present in Iran [99].

These problems will unavoidably cause the quality of data reported from these developing registries to be low. Improved data quality and intensive quality control is thus an important requirement and a priority for these registries [22, 61].

What is currently lacking in the literature and remains to be explored is a comparison between the old and newly established cancer registry centers. One effective way of doing such comparison is to use a validated set of standards for quality assurance procedures to examine the conformity of different registries to such standards and relative to each other. Such sets of standards are routinely used by organizations such as IARC (International Agency for Research on Cancer)/IACR (International Association of Cancer Registries) and NAACCR (North American Association of Central Cancer Registries).

2.11 Standards of data quality

IARC routinely uses some of the previously mentioned data quality measures for quality checking of the information reported by different cancer registries. Among these, the three most important and routinely utilized measures are: the proportion of DCOs, the

proportion of histologically confirmed cases, and the mortality-to-incidence ratio [19]. However, these measures exclusively are not very useful for a study involving developing registries. For example, as stated above, the proportion of DCOs and the mortality-to-incidence ratio are not good measures for assessing newly established registries like that in Tehran. These measures will underestimate data quality since they are relative to the previous performance of the registry. IARC has also admitted that there are many considerations required when interpreting such measures [19]. A more comprehensive set of standards is used by NAACCR [62]. The NAACCR certification program examines all member registries for their ability to produce complete, accurate, and timely data [100]. NAACCR was formed to establish standards for completeness, timeliness, and quality of cancer registry data and document requirements of cancer registries with different interests (population or hospital-based registries) under a single reference. Its objectives are: "1) to improve state-to-state comparability; 2) to enhance the representativeness of data; 3) to increase the data accuracy; 4) to make information more rapidly available; 5) to reduce or eliminate conflicts in the data requirements and standards among the standard-setting organizations." [101]

An important advantage of NAACCR standard is that it has also defined the procedures as required (M=must) and highly recommended (S=should) for quality assurance. These criteria are defined in detail under three major topics: structural requirements (such as legal aspects of establishing a new registry, documentation of their methods and procedures, staffing requirements, and software requirements), process standards (standards for quality control including data codes and edits, and quality control activities), and outcome measures (such as re-abstracting and recoding audits, and

unknown values).

Another advantage of this standard is that it has been designed to be used for quality assurance in both established and developing registries in the North America. A superior aspect of this standard is setting Gold and Silver error tolerance which makes it more suitable for comparing registries at different stages of development (Table 2-1 [62]).

Table 2-1: NAACCR Criteria and Standards for Gold/Silver Certification

Criterion	Gold Standard	Gold Error Tolerance	Silver standard	Silver Error tolerance
1. Completeness	≥ 95%	-1.0	≥ 90%	-1.0
2. Passing Edits	100%	0	≥ 97%	-0.4
3. DCOs	≤ 3%	0.4	≤ 5%	0.4
4.Timeliness	Within 23 months		Within 23 months	
5. Duplicate Records	≤ 1/1,000	0.4	≤ 2/1,000	0.4
6. Missing Data Fields: Sex, Age, County	≤ 2%	0.4	≤ 3%	0.4
7. Race	≤ 3%	0.4	≤ 5%	0.4

Chapter 3: Methods

3.1 Introduction

This study was performed to compare the function of two cancer registries in two countries with very different reported breast cancer incidence. To make this comparison, we used two sets of international guidelines for quality assurance in cancer registries. Our ultimate goal was to remove the effect of differences in cancer registration practices from the incidence statistics to facilitate the drawing of unbiased conclusions about differences in breast cancer incidence.

Therefore, we designed two questionnaires based on two cancer registry guidelines (NAACCR and IARC/IACR) to compare structural requirements, process standards and outcome measures in two samples (Manitoba and Tehran) of the two countries (Canada and Iran).

In addition to asking the key informants in the two registries to fill in the questionnaires, we also reviewed the publications from the two registries to better understand and confirm the answers of the registry staff and to resolve discrepancies in their answers to the questions in the questionnaires.

The design of this study was based on Donabedian's model of quality assessment which considers three separate components for assessing healthcare services: structure, process,

and outcome [102]. This model will be described in detail in methodology section.

3.2 Terminology

Cancer includes all cancers excluding non-melanoma skin cancers.

Breast cancer includes all cases of invasive breast cancer.

3.3 Sampling

The results of this study are intended to be generalized to Iran and Canada as reference populations. However, we selected Manitoba's and Tehran's cancer registries as our study samples.

The main reasons for selecting the Tehran Cancer Registry to represent Iran were:

1. It is the first population-based registry established in Iran, and hence, the data from this center will present a better picture of the population compared to hospital-based registries.

2. It will be the first Iranian registry to publish its data in "Cancer Incidence in Five Continents". This confirms that data from this center are currently the most reliable data available from Iran.

3. About 10% of Iran's population lives in the Tehran Metropolitan Area and the statistics from this center have a large influence on reported incidence rates for the whole country.

4. Tehran represents all different ethnicities in the country.

The main reasons for selecting Manitoba to represent Canada were:

1. The breast cancer incidence rates in Manitoba are around the Canadian average.

2. It boasts one of the oldest and most efficient cancer registries in Canada. Its high data quality is demonstrated by being consistently certified by NAACCR.

3. It was the most accessible registry in Canada for the student researcher of this study.

3.4 Data collection

Review of the publications from the two registries and two questionnaires specifically designed for this study were the main two sources of data collection.

3.4.1 Questionnaires

Two questionnaires were designed to collect information about structural requirements, process standards, and outcome measures from the two registries. The questions in these questionnaires were mainly designed to:

1. compare the incidence of breast cancer in two the populations (Questionnaire I, Section 1);

2. describe the history of developing the cancer registries and the basic procedures performed in the two registries (Questionnaire I, Section 2);

3. assess comparability of data collected about cancer incidence in the two populations (Questionnaire I, Sections 4);

4. identify the structural requirements and the process standards necessary for quality assurance in cancer registries (Questionnaire II); and

5. assess the success of each center in controlling data quality based on the measures of data quality available from the two centers (Questionnaire I, Section 3).

Questionnaire I (Appendix 1) consists of four parts:

The first part (Section 1) asks about the year with the most recent cancer statistics in Tehran and Manitoba, and breast cancer incidence rates for the most recent year that statistics are available from both registries. It also asks about world population standardized rates in order to make these rates comparable.

The second part (Section 2) collects information about the history of development of the two cancer registries and the basic procedures performed in these registries. The questions in this section aimed to identify:

1. the year in which the center started working (long established centers are more experienced and might have developed more comprehensive quality control procedures)

2. the type of registry (population-based registries report a better picture of cancer incidence in the community) and when it became population-based (with the same rationale as the first question)

3. the definition and description of the area of coverage (it is important that a population-based registry includes all residents of the area of coverage)

4. the sources of data collection (employing more sources for data collection is expected to improve completeness of case-finding)

5. the general method of data collection (active data collection is desired for complete and accurate registration)

6. the range of collected data items (it is important that data items necessary for precise calculation of incidence rate and quality measures are collected; for example, date of incidence and date of registration that are used to calculate the timeliness)

7. the system of coding used for primary tumours (this is important for comparability of data; each method has advantages and disadvantages)

8. the methods of data abstraction and storage (computerized methods are expected to be more exact and have the option of computer edits)

The third part (Section 3) asks about data quality measures that are available from these centers. These measures have been discussed in detail in the literature review.

Finally, the fourth part (Section 4) asks about the definitions and the data sources used to define incidence in order to assess comparability of incidence rates reported by different centers.

Questionnaire II (Appendix 2) asks about structural requirements and the process standards necessary for quality assurance in cancer registries. These include: legal aspects of the cancer registry, documentation, confidentiality, reporting, data collection, quality control, staffing, and training of the staff.

The questions were derived from NAACCR standards for quality assurance designed to be used by developed and developing cancer registries in North America; NAACCR has one of the most comprehensive available guidelines (see literature review). The advantage of NAACCR guidelines over IARC/IACR guidelines are: a) an objectivity which is not clear from IARC/IACR publications; b) NAACCR has assigned a degree of importance to all structural and process criteria to be met by cancer registries. This importance is recognized by wording them as MUST or SHOULD. "MUST" implies the necessity of that criterion for an efficient cancer registry and "SHOULD" implies that it is highly recommended to ensure high quality of data. These aspects of registry performance have also been described in the guidelines provided by IARC/IACR in their publication for cancer registries. However, there are no objective measures similar to NAACCR guidelines. The president of the IACR was asked about any objective measures but he confirmed that the decision for acceptable data quality in order to enter data from a registry in their publication "Cancer Incidence in Five Continents" is very subjective although they have their own strict criteria [103].

3.4.2 Review of the publications

All publications from the two centers in addition to the registry manuals and/or reports were reviewed in order to find the answers to the questions in the two questionnaires. Where there were no statements about a particular aspect in publications, staff answers were used.

3.5 Methodology

We first approached the heads of the two registries in each of the two centers and explained the study design and purposes based on a pre-designed consent form (Appendix 3). They were provided with a copy of the consent form and two copies of the two questionnaires to read through them. The consent forms did not ask for the participants' signature but stated that by filling in the questionnaires they expressed their consent. The heads of the registries had the opportunity to review the consent form and questionnaires to decide if they and their center agreed to participate in this study.

After receiving the consent of both registries to participate in the study, the heads of the registries were asked to fill in the first and second questionnaires and also to introduce us the most informed staff in their center.

An orientation session was arranged for the proposed staff in both registries. For the Tehran Registry this orientation session was through teleconference but in Manitoba, we met the staff in person. In this session, the study's design and purposes, along with other contents of consent form, were presented to the staff. Four staff from Manitoba and four

staff from Tehran were introduced and all of them agreed to participate in this study. They were provided with copies of the consent form and the second questionnaire, which they were asked to complete and return to the study investigators.

After receiving back the questionnaires, the answers were reviewed. We needed to follow back to the staff for three reasons:

1. Although the second questionnaire required an explanation for all "yes" or "no" answers, some questions missed such explanations.

2. There were some discrepancies in the answers of the staff of the same registry.

3. We needed to confirm our understanding of their answers to the questions.

This follow back was performed based on individual interviews with the registry staff in Manitoba and telephone conversations with the registry staff in Tehran.

When there were discrepancies in answers or the staff did not have any definite answer for a question, the answer from the head of the registries was considered as the most reliable answer.

At the end, the available manuals, reports, and publications were reviewed to confirm the questionnaire answers and to determine the right answer in contradictory cases.

The answers of the staff were summarized in tables, including a brief description of the questions with their answers. These were then fed back to the registry staff to confirm their answers.

After all discrepancies in the answers were cross-checked with participants and we

certified the participants' explanations, and after confirming this information with publications, one final report in the form of a summary table based on the most documented answers to the questions was prepared for each center. Then the two tables from the two registries were combined to produce a table in which the staff view points and the information from each registry were summarized.

We used Donabedian's structure-process-outcome model to organize all data. Avedis Donabedian designed the structure/process/outcome (SPO) model for assessing quality of healthcare services [102]. This model defines structural measures as "the professional and organizational resources associated with the provision of care, such as staff credentials and facility operating capacities" [104], process measures as "the things done to and for the patient by practitioners in the course of treatment [104], and outcome measures as "the desired states resulting from care processes" [104]. However, these definitions were modified to serve our purpose which was assessing quality of cancer registries as healthcare organizations, which are not directly in contact with patients.

This model assumes that these quality measures are interdependent and form an underlying framework: "Good structure should promote good process and good process in turn should promote good outcome" [105].

In this study, we used this model to organize our data, i.e. the tables were rearranged in a format summarizing structural requirements, process standards, and outcome measures in three separate tables. Then the data from the two centers were compared in these three frameworks.

3.6 Data Analysis

Data analysis consisted of both qualitative and quantitative methods of analysis; although it was performed in three separate frameworks: structural requirements, process standards, and outcome measures.

3.6.1 Structural requirements

Structural characteristics of each center were summarized based on the documented answers of the registry staff. When a structural requirement was present in a center, it was described and when it was absent, the staff were asked about the problems their center encountered in meeting this criterion.

After preparing the descriptive tables, the structural characteristics were compared between the two registries with regard to their important differences and the advantages and disadvantages of them in each registry. The problems encountered by a registry in meeting such criteria were discussed.

At the end, the structural differences were examined to highlight differences in necessary versus highly recommended criteria based on NAACCR guidelines.

3.6.2 Process standards

Similar steps as in the structural requirements assessment were taken to compare the processes performed in the two registries.

The processes were scrutinized in order to find the advantages and disadvantages in each center and also to highlight the differences in the two registries. These differences were later used to adjust incidence statistics. Also, the problems of a registry were described in terms of not being able to perform a standard procedure which might affect data quality and comparability.

Finally, the process differences were examined to highlight differences in necessary versus highly recommended criteria based on NAACCR guidelines.

3.6.3 Outcome measures

After reviewing the structural and process characteristics of Manitoba's and Tehran's cancer registries, the outcome measures which reflected the effect of those characteristics were studied. Outcome measures were studied at two levels: intermediate outcome, i.e. the data quality measures and ultimate outcome, i.e. breast cancer incidence rates.

This part of analysis was more quantitative in methodology.

3.6.3.1 Measures of data quality

These measures were obtained from the third section in the first questionnaire. Where the actual numbers were present for both registries a Chi-squared test was performed to compare them, since they were mostly proportions and percentages. All percentages and proportions were used to calculate the actual numbers in the populations as well as expected features. Microsoft Excel 2002 [106] and the function CHITEST was used to compare observed and expected numbers; p-value was the result of this function and was regarded as significant using the level of $p<0.05$. Chi-squared value was also calculated.

3.6.3.2 Breast cancer incidence

First the most recent breast cancer incidence rates available for the two jurisdictions were age-standardized using the world standard population. Then the crude and standardized rates were compared between the two jurisdictions using a Chi-squared test in the same method as described for data quality measures.

3.6.4 Inter-relation of the three parts of this framework

Using Donabedian's model, we discussed how the described differences in structural characteristics can influence the processes performed in each registry, and subsequently the outcome measures reported from that registry.

Following the discussion of structural issues, the role of differences in process standards was discussed in relation to their effect on outcome measures.

Where it was possible, the effects of the structural and process differences as well as differences in data quality measures were quantified and the incidence rates were adjusted accordingly in the two jurisdictions. This was done to remove, as much as possible, the effect of differences in registration practices from the reported incidence statistics. The adjustments included:

- Age-standardizing the rates to the world standard population using the direct method;
- Adjusting for the effect of different coding rules in the two countries regarding multiple primaries (Manitoba uses rules that might tend to count multiple breast cancers as individual cases, whereas Tehran uses rules that are more conservative and

tend to assign several breast tumours as one breast cancer "case");

- Adjusting for additional sources of information available in Manitoba (screening, autopsy) which might systematically increase the observed breast cancer rates;
- Adjusting for cases that were missed due to non-participating hospitals; and
- Accounting for "missed" cases, based on independent completeness studies.

Chapter 4: Results

4.1 Introduction

The results are presented in three sections: structure, process, and outcome (see methods). In the first section, the structures of the two registries and their differences are discussed. The second section describes the process of cancer registration in each center and their differences. In the last section, the outcome measures (breast cancer incidence and data quality) are described and the differences between the two centers are statistically tested, where possible.

The results in each section have been summarized in a table. These tables provide a summary of the results from the Tehran and Manitoba Cancer Registries. The last column of the first two tables demonstrates the level of emphasis for that criterion by two widely used cancer registry guidelines, NAACCR and IARC/IACR. NAACCR has clearly classified its recommendations based on their necessity for a cancer registry. "MUST" indicates required and "SHOULD" indicates highly recommended. In contrast, IARC/IACR does not have such distinct classification; however, it has also provided the registries around the world with comprehensive guidelines (see methods). In these guidelines some areas have been more emphasized. In the tables below, those aspects of a cancer registry that are more emphasized by IARC/IACR are indicated by "E".

4.2 Structural aspects

The structures of the two registries are described based on the answers of the staff of the two registries to the questions in the first and second questionnaires (see Appendices 1 and 2), which were then confirmed by reviewing the manuals, reports and/or publications of the two centers. Table 4-1, summarizes the structural characteristics of the two registries.

Table 4-1: Structural aspects of the Tehran and Manitoba Cancer Registries

Registry Center / Questions	Manitoba	Tehran	Level of emphasis in registry guidelines:	
			NAACCR	IARC/IACR
Basic structure				
1.2. Started working in	1930	1995	N/A	N/A
1.2. If population-based, when became population-based	1956	1998	N/A	N/A
1.2. Defined population	Residents of province of Manitoba	Residents of 22 areas of Tehran Metropolitan Area	N/A	N/A
1.2. Method of data collection	Active	Active	N/A	N/A
1.2. Data sources	Medical records, some outpatient clinics, pathology labs, haematology labs, death certificate, general practitioners, screening programs, autopsy services, central registry	Medical records, outpatient clinics, pathology labs, haematology labs, death certificate, private clinics and hospitals	N/A	N/A
1.2. Collected data items	Name, sex, date of birth or age, address, incidence date, most valid basis of diagnosis, topography, morphology, behaviour, personal identification number, place of birth if given, data source, date of registration, actual source, marital status,	Name, sex, date of birth or age, address, incidence date, most valid basis of diagnosis, topography, morphology, behaviour, personal identification number, place of birth, data source, date of registration	N/A	N/A

Registry Center / Questions	Manitoba	Tehran	Level of emphasis in registry guidelines:	
			NAACCR	IARC/IACR
	religion if given, occupation if given, certainty of diagnosis, multiple primaries, laterality, initial treatment, date of last contact (partial), date of death, cause of death, place of death			
Structural requirements				
2.1. Regulations/legislation? If yes, are there any statements about the following six questions in these regulations/ legislation:	Yes	Yes	M	N/E
2. 1.1 Reporting requirements	Yes, reporting requirements outlined by CCR and NAACCR data dictionary	Yes, cancer registry proposal which is based on IARC guidelines	M	E
2. 1.2 Granting registry access to patients' records by facilities	Yes, PHIA gives the right to facilities including cancer registry to have such access	No, the registry coordinator takes a letter to the manger of hospitals but still 1-2% do not grant access	S	N/E
2.1.3 Penalties for failure to report cases or grant access	No, because it has never been a major problem	No, because failure to report cases is not easy to find	S	N/E
2.1.4 Standards for data quality	Yes, CCR and NAACCR data standards are followed	No, since it is a new system, quality control projects have just started	M	N/E
2.1.5 Confidentiality standards	Yes, cancer registry complies with PHIA	No, no confidentiality standards are stated in the regulations but IARC confidentiality rules are used to train the staff	M	N/E
2. 1.6 Source of funding	Yes, government funded	No, small amounts from different sources	S	N/E
2.3. Number of staff based on caseload	Yes, for registration purposes there are 8 registrars / No, for performing many projects and quality control studies more staff are needed	No, the number of staff is not enough because of budgetary problems, in abstraction phase on average 8 abstractors work but only about 30% of the reviewed records belong to the registry area	S	E

Registry Center / Questions	Manitoba	Tehran	Level of emphasis in registry guidelines:	
			NAACCR	IARC/IACR
2.22. Quality control programs are part of registry activities	Yes, through regular procedures for quality assurance and ad hoc studies	Yes, studies of completeness and recoding and re-abstracting are performed	M	E
2.23. Adequate funding for quality control	No, about 12% of the total budget + grants	No, about 30% of the budget	M	N/E
2.24. Staff determined for quality control	Yes, there is currently one quality control technician	Yes, 1-4 health information technologists perform quality control studies	S	N/E
2.25. Manual which documents current and historic practices	Yes	Yes	M	E
2.25.1 If the answer to the previous question is yes: This manual includes definitions and methods	Yes, all included in the registry coding and procedural manual	Yes, there is a report which describes all used methods and definitions	M	E

M: Must, S: Should, E: Emphasized, N/E: Not Emphasized, N/A: Not Applicable
The first number beside each question demonstrates the number of the questionnaire (first or second) and the second number determines the number of question or the number of section in that questionnaire

In the first part of this table (Table 4-1), the basic structure of the two registries is defined with a historical perspective.

The Manitoba Cancer Registry is among the longest established registries in Canada and worldwide. It was established in 1930 and became population-based in 1956. The Tehran Registry, on the other hand, is quite a new registry. It started operation in 1995 and became population-based only in 1998. This indicates a significant difference in the experience of the two registries.

Both the Tehran and Manitoba Cancer Registries have clear definitions of the population they cover. The Manitoba Cancer Registry collects cancer data about the population of the province of Manitoba (rural and urban areas). However, since the Tehran Registry covers only an urban area (22 areas of the Tehran Metropolitan Area), population mobility is more problematic for this center.

Although the two registries perceive their center as an active surveillance system, they are in two different parts of a spectrum. The Tehran Cancer Registry has a complete active data collection process while the Manitoba Cancer Registry has a more passive system with a component of active follow-up to get more information on a case once it becomes known to the registry.

Both registries collect their data from medical records, pathology labs, haematology labs, outpatient clinics, and death certificates. The Tehran Cancer Registry also uses private hospitals and clinics as other data sources. Manitoba, on the other hand, also uses a central registry (the Canadian Cancer Registry which supports a process of interprovincial exchange of information), autopsy services, general practitioners, and screening programs for data collection. Part of this difference in data sources is explained by differences in health care systems. For example, health care system is not privatized in Manitoba and thus private hospitals do not exist in this province. In Tehran, for cultural reasons, autopsy is not very routine and general practitioners are known not to keep good record of their patients and to be less cooperative with cancer registries (see Questionnaire II, Question 8); hence, these sources are not very efficient for that center.

Basic data items are collected by the two registries. However, the Manitoba Cancer Registry collects many other optional items. Tehran, as a newly developed registry, focuses mainly on basic data items.

After a brief introduction to the basic structure of the two systems, the structural requirements of the two registries are explored.

The operation of the two registries is based on well-defined regulations and/or legislation.

The Manitoba Cancer Registry is mandated by the "CancerCare Manitoba Act" and the reporting of cancer is mandated by the "Public Health Act". Additionally, the Manitoba Cancer Registry follows its detailed registry manuals. The Tehran Cancer Registry, on the other hand, operates as a temporary project and is run based on the proposal of this project. Although the compulsory reporting of cancer was passed from the National House of Representatives in 1984 [23], it is not generally being reported by healthcare providers. However, the manual of the Manitoba's registry and the proposal of the Tehran's registry both include statements about reportable tumours to the registries.

In Manitoba according to the "Personal Health Information Act" (PHIA), any health care organization including the Manitoba Cancer Registry has access to patients' records. Also, through agreements with city hospitals, cancer registrars have regular visits to such facilities to collect the necessary information. In contrast, in Tehran, there are no regulations granting access to patients' records by cancer registries. The result is that 1-2% of hospitals (most military and some private) do not permit registry staff to access their medical records.

Neither of the centers have any statements in their regulations about penalties for failure of facilities to report cases or grant access to cancer registry staff. Manitoba staff have never been prevented from accessing patient records nor has any facility been known to fail to report a case. Tehran staff believe that the active system of data collection eliminates the need for dependence on facility reports. However, as regards granting access to the cancer registry staff, it is currently a problem without any penalties in place.

The Manitoba Cancer Registry follows data quality standards stated in its manual, which

are based on the Canadian Cancer Registry's guidelines (a detailed set of standards for all aspects of data quality) and NAACCR guidelines. These standards do not exist for the Tehran Cancer Registry because they are still in the early stages of development and do not believe it would be practical to meet high levels of international standards at this point.

Confidentiality rules are very important for all cancer registries based on IARC/IACR and NAACCR guidelines. Manitoba follows PHIA confidentiality rules in protecting release of patient information; Tehran does not state such rules in its regulations. However, the staff are trained using IARC/IACR guidelines of confidentiality for maintaining the confidentiality of the collected data and the information produced by the registry.

The main source of funding for the Manitoba Cancer Registry is the Government of Manitoba. The Tehran Cancer Registry, on the other hand, receives its funding from different sources including the Cancer Institute of Iran research funding, IARC, the Digestive Research Center, and Tehran University of Medical Sciences. All these sources provide small amounts of the project budget and there is no responsible funding source clearly stated in their regulations.

For registration purposes, the Manitoba Cancer Registry has eight registrars and believes that they have adequate number of staff for their caseload; however they also believe that they require more staff for various projects and special quality control studies that they perform. The Tehran Cancer Registry, on the other hand, does not have a fixed number of staff because of budgetary problems. The number of staff changes based on the workload.

Overall, in abstraction phase they have on average eight registrars who collect data; however, they have to review the medical records of all diagnosed cancer patients in Tehran although only 30% of them belong to the population covered by the registry.

Quality control programs are performed by both the Tehran and Manitoba Cancer Registries. However, the kind of quality control activities differs in that the Manitoba Cancer Registry performs both continuous and ad hoc quality control while the Tehran Registry basically performs ad hoc studies of completeness and accuracy.

Both registries believe their funding for quality control programs is not adequate. In Manitoba the proportion of funding devoted to this purpose is differs from one year to the other. Since 1999, 10% of the total budget is paid for one full-time quality control technician (who performed the quality control for the 1998 data submitted to NAACCR). There are also many ad hoc studies based on the available annual grant budgets. In a "new development" stage, when there many quality control studies, the budget spent on quality control activities can account for up to 27% of the total budget. In Tehran approximately 30% of the total budget is devoted to all quality control activities which are mostly ad hoc studies.

The number of staff designated for quality control purposes is one full time technician in Manitoba as well as 2-3 staff performing different ad hoc studies. In contrast in Tehran, because of the difference in the nature of quality control programs which are ad hoc rather than continuous, there are not any staff employed merely for this purpose; however, 1-4 people perform different quality control studies.

Both of the studied cancer registries document their processes and standards; however,

this documentation differs in type. The Manitoba Cancer Registry is equipped with a comprehensive manual where all activities and processes are documented. This manual can be used to obtain information both about current and past activities. The Tehran Registry, in contrast, records all its activities at the year end in a report along with the results from analyses.

In summary, the Manitoba and Tehran Cancer Registries do not agree in five structural characteristics. Four of these differences rise from regulations governing the two registries. The Manitoba Cancer Registry has developed more concrete regulations which have legitimized registry access to patient records, defined the funding source of the registry, and set data quality and confidentiality standards. Such regulations are not present in Tehran. In addition, the number of staff in the Tehran Registry is relatively low.

In next section, we proceed to examine how the two registries with these structural characteristics differ in the process of cancer registration.

4.3 Process standards

The process of cancer registration is described in the two centers based on the answers of the staff of the two registries to the questions in the first and second questionnaires (Appendices 1 and 2), which were then confirmed by reviewing the manuals, reports and/or publications of the two registries. Table 4-2 summarizes the process questions and the answers provided by each registry.

Table 4-2: Process of registration in the Tehran and Manitoba Cancer Registries

Registry Center / Questions	Manitoba	Tehran	Level of emphasis in registry guidelines: NAACCR	IARC/IACR
Basic procedures				
1.2. System of coding Topography Morphology Behaviour	 ICD-O-3 ICD-O-3 ICD-O-3	 ICD-O-2 ICD-O-2 ICD-O-2	N/A	N/A
1.2. Data abstraction	Manual	Manual	N/A	N/A
1.2. Data storage	computerized	computerized	N/A	N/A
1.4 Comparability issues: definition of multiple primary Screening used for case-finding Autopsy used for case-finding	 CCR definition Yes Yes	 IARC definition No No	N/A	N/A
Advanced procedures				
2.2. Precise definition of reportable tumour	Yes, according to CCR, NAACCR, and coding manuals	Yes, based on IARC standards	M	E
2.15. Training for case reportability	Yes, part of the original staff orientation and training according to registry manuals	Yes, included in training sessions based on IARC guidelines	S	N/E
2.16. Training for multiple primary determination rules	Yes, covered in registry coding manuals and CCR data dictionary also in SEER* training ...	Yes, according to IARC rules	S	N/E
2.4. Staff trained for their duty	Yes, they are Health Information technologists with 2 years college course + 18 months on-the-job training	Yes, they are Health Information technologists who receive ongoing training by an expert who has taken the IARC summer school on cancer registry	M	E
2.5. Continuing education	Yes, CCR, NAACCR, and NCRA workshops	Yes, training classes and review and exercise sessions held regularly, discussion about problems every 1-2 months especially on coding difficulties	S	N/E
2.6. Access of the registry to 100% of hospitals	Yes, 100% access to urban hospitals + contact with rural facilities via mail, phone, or fax	No, 1-2% of hospitals do not cooperate because of the absence of support by Iran Ministry of Health	S	N/E
2.7. Data about cases diagnosed and treated out of hospital	Yes, mostly. The most concerned area is physicians' private offices	No, but since most cases are visited in hospital at some point, it should not affect the registry	M	N/E

Registry Center / Questions	Manitoba	Tehran	Level of emphasis in registry guidelines:	
			NAACCR	IARC/IACR
2.8. Follow-back to physician office	Yes, letters, "report of malignant neoplasm forms", phone calls, faxes	No, physician cooperation is generally poor and is not worth the time and expense	S	N/E
2.9. Notify the reporting facilities about reporting requirements	Yes, every few years by sending a letter	Yes, stated in a letter that the registry coordinator takes to the hospital manager	S	N/E
2.10. Capture tumours of all at risk population	Yes, the cancer registry reports all cancer cases diagnosed and/or treated in Manitoba	No, for the same reasons that there is not access to all hospitals	M	N/E
2.11. Confidentiality in data collection and maintenance	Yes, databases are protected by firewall and passwords. Reports are stored in a locked office	Yes, all records are kept in a locked office and the computers are password protected	M	E
2.12. Staff sign confidential pledge	Yes, when first employed	No	M	E
2.13. DCOs followed-back	Yes, nursing homes and hospital chart reviews are done when the place of death is received from vital statistics or on obituary	No, because of the problem with physician follow-back and the fact that the registry is very new and data for previous years are not available	M	E
2.14. Record linkage between complete data file of vital statistics & registry	Yes, registry has linkage with provincial and national vital statistics file	No, only deaths with the cause of cancer will reach the registry	M	E
2.17. Regular audits of completeness	Yes, ad hoc when there is time and need/ also quarterly to complete all registered cases	Yes, as separate studies/ no, not regularly as part of the routine activities of registry	S	E
2.18. Regular recoding audits	Yes, during the training period 100% of the records and after that random samples are recoded	Yes, recoding is performed by a general practitioner and then confirmed by a pathologist on a regular basis	S	E
2.19. Regular re-abstracting audits	Yes, visual editing is done prior to data submission	Yes , some random re-abstractions are performed for finding staff difficulties	S	E
2.20. Compare expected & observed cases in a year	Yes, once a year at the year end	No, expected is not clear because the registry has just started performance	S	E
2.21. Monitor if incidence is higher than mortality	Yes, as part of editing prior to publication of the annual report	No, this is possible based on the available data but it is not done as a routine	S	E
2.26. Edits used for data entry	Yes, online and system built-in edits + NAACCR check	Yes, after data entry IARC check program is run	S	E

Registry Center / Questions	Manitoba	Tehran	Level of emphasis in registry guidelines:	
			NAACCR	IARC/IACR
2.27. Process controls (stability over time and regions)	Yes, time trend are performed at provincial level + CCR checks both region and time trends for all provinces	No, regional comparison was done for only childhood and pancreatic cancers and time trend check is not applicable since there is data for only one year	S	E
2.28. Errors fed back to staff	Yes, fed back to registrars for correction	Yes, all errors are fed back to the staff in training sessions	S	N/E

M: must, S: Should, E: Emphasized, N/A: Not Applicable, N/E: Not Emphasized
The first number beside each question demonstrates the number of the questionnaire (first or second) and the second number determines the number of question or the number of section in that questionnaire
* Surveillance, Epidemiology, and End Results

In this section, the basic procedures that are performed in the two centers are described. They are then followed by a description of more advanced processes of cancer registration.

For coding purposes, these two registries use the ICD-O (International Coding of Diseases-Oncology) system. Manitoba uses the most recent version (ICD-O version 3) along with previous versions while Tehran uses ICD-O version 2. However, this does not affect breast cancer coding.

Data abstraction and data storage methods are similar in the two centers, i.e. both registries abstract data manually and store it in a computerized system.

For comparability purposes, the definition of multiple primary tumours and the utilization of screening and autopsy as a means of data collection were contrasted. One important difference between the Tehran and Manitoba Cancer Registries relates to the guidelines that they follow. Specifically, in the case of multiple primary tumours determination, the definition is mainly different based on IARC/IACR for Tehran and CCR guidelines for

Manitoba. IARC/IACR multiple primary rules are more conservative, in which several tumours of the same site are more likely to be considered as a single case. Also the Manitoba Cancer Registry uses screening and autopsy as means of case-finding while Tehran does not. These differences can result in relative increases in incidence rates in Manitoba (see chapter 5).

Structural and process aspects of a cancer registry are closely related. For example, in the previous section, we mentioned that the reportability of tumours is stated in the regulations of both registries. In practice, both registries use definitions to recognize if a tumour is eligible to be included in the cancer registry. For example, words indicating malignancy are well defined in registry guidelines ["probable", "suspect", "suspicious", "compatible with", or "consistent with"]; in practice, staff are trained to recognize key terms and follow coding rules carefully. However, even though training for case reportability and multiple primary determination exists in both cancer registries, the guidelines they use for training and coding is different, i.e. IARC/IACR in Tehran and NAACCR and CCR (the Canadian Cancer Registry) in Manitoba.

The concept of staff training and continuing education also differed in the two registries. Manitoba and Tehran registrars are health information technologists with two years of college education. In Manitoba, there is an on-the-job training of about 18 months. In Tehran, this training is a one-day orientation session followed by on going training by an expert who has taken the one-month IARC summer school on cancer registration. However, the concept of continuing education differed in the two centers; what Tehran Cancer Registry staff perceived as continuing education was on going training sessions every 1 to 2 months to practice the problematic areas with the staff. This is called on-the-

job training by Manitoba staff. But the workshops and international conferences that Manitoba Cancer Registry staff perceived as continuing education is not available to Tehran Cancer Registry staff due to limited resources.

As reviewed in the structure of the two registries, granting access to patients' records by cancer registrars is mandated by law in Manitoba, while Tehran does not have this essential regulation. The consequence is that Manitoba effectively has access to 100% of the hospitals in the coverage area while Tehran does not have access to 1-2% of the hospitals in the Tehran Metropolitan Area.

Manitoba has the opportunity to follow back with most urban clinics and community cancer clinics. The area of most concern, in their opinion, is physicians' private offices. The Tehran Cancer Registry does not have access to many outpatient clinics and any physician offices. Physicians do not keep good record of their patients and do not generally cooperate with the Tehran Cancer Registry; therefore, it is not a cost-effective activity for them. The Manitoba Registry, however, uses phone calls, letters, and faxes, beside a "Malignant Neoplasm Report" form through which it requests physicians to provide them with information about patients. Both centers consider outpatient data as a minor concern since they believe most cancer patients visit a hospital at some point of their disease and, hence, will be captured through medical records.

It is recommended that cancer registries notify all reporting facilities about reporting requirements. This is performed by both registries. For example, the Manitoba Cancer Registry sends letters to pathology laboratories to inform them of reporting requirements. The Tehran Cancer Registry does this through a letter submitted to the hospital head by

the staff who visit hospitals for collecting data.

It is required by NAACCR that cancer registries capture tumours of all the at-risk population of the registration area. The Manitoba Cancer Registry captures tumours diagnosed and/or treated in Manitoba population. The Tehran Cancer Registry, in contrast, does not cover all the at-risk population because 1-2% of hospitals, which serve 1.5% of Tehran population, do not provide access to registrars for the collection of information about the tumours diagnosed in that part of the population.

All data that are collected and stored in the two registries are maintained confidentially. These include password protected computers and locked offices for storing the abstracts.

The Manitoba Cancer Registry staff sign a confidentiality pledge when they are first employed. Even though the Tehran Cancer Registry complies with IARC/IACR confidentiality rules, it lacks this aspect of confidentiality identified in IARC/IACR guidelines.

Based on both IARC/IACR and NAACCR guidelines, it is very essential to follow-back the death certificate only (DCO) cases before reporting them as DCOs. In fact, the cases first diagnosed through death certificate are known as "Death Certificate Notified" (DCN) cases before being followed back. DCN follow-back, however, might not be very successful for newly established registries who lack data from previous years. Manitoba follows all DCN cases before registering them as DCOs. This includes reviewing the charts and medical records from the hospitals near the place of residence, following back to physician offices, and visiting nursing homes. In Tehran, in contrast, all cases reported through death certificate for the first time are regarded as DCO.

Record linkage between the cancer registry database and vital statistics files is necessary for finding DCO cases. It is also required for survival studies. Manitoba has the advantage of having such linkage with both provincial and national vital statistics databases. However, Tehran only receives reports of deaths with the cause of cancer. These cases are then checked against the registry database to find out the newly diagnosed cases.

Completeness studies are performed by the two registries. As mentioned before, Manitoba performs continuous completeness audits for completeness of data items and ad hoc studies for completeness of case-finding. The Tehran Cancer Registry performs ad hoc studies for completeness of data items as well as case-finding.

Both registries perform audits of re-coding and re-abstracting continuously for training purposes. These studies are recommended by NAACCR and IARC/IACR guidelines and help to improve the accuracy of data in a cancer registry.

It is important for all cancer registries to compare the observed number of cases with the number expected. This is performed at the year end in Manitoba. The Tehran Cancer Registry, as a newly developed cancer registry, does not have precise estimates of the expected number of cases, and therefore, this comparison is not pragmatic for them.

It is also important to check if incidence rates are greater than mortality rates for each cancer site. If cancer occurrence is not decreasing dramatically in the community, incidence rates should be greater than mortality rates. This association is checked before the Manitoba Cancer Registry publishes its data at the end of each year. Even though IARC/IACR requires that such comparison be made before data submission, the Tehran

Cancer Registry staff assumed this had not yet been performed, as their first submission to IARC/IACR is still pending.

Edits are performed in both registries, but different methods are used. The Manitoba Cancer Registry uses online edits that are built-in to the software so that errors are not allowed to be entered into the system. Staff also run NAACCR edits after data entry is completed. The Tehran Cancer Registry uses IARC checks after complete data entry and does not have simultaneous edits.

It is important to check the stability of rates over time and across regions. Manitoba performs these at provincial and national level. The Tehran Cancer Registry, on the other hand, cannot perform time trend analysis since currently there is only a single year data available for this center. The stability over regions has been checked for only two cancers in Tehran, pancreatic and childhood cancers.

Both registries satisfactorily feed back the errors detected in the process of quality control to their staff.

In summary, there are many similarities but also many meaningful differences in the processes used by the two cancer registries under study. Both process and structure differences in the cancer registries can result in differences in outcome measures; thus in next section, we will examine how the outcome measures differ in these two registries.

4.4 Outcome measures

Outcome measures can be studied at two levels: the intermediate outcome (data quality measures which reflect the registry performance) and the ultimate outcome (breast cancer incidence rates). Incidence rate, the final outcome, indicates the frequency of breast cancer occurrence in a population; however, it also reflects the performance of the cancer registries in regard to capturing incident cases. Therefore, data quality measures act as "intermediate outcome" because they show the success of the registries in performing their role. We can then adjust the incidence rates for data quality, allowing an understanding of the actual cancer incidence.

Table 4-3 summarizes the outcome measures from the two centers based on the answer of the head of the two registries to the questions in the first questionnaire and review of their reports.

Table 4-3: Outcome measures from the Tehran and Manitoba Cancer Registries

Questions \ Registry Center	Manitoba	Tehran	Statistical assessment (chi-squared)
1. The year of the most recent available statistics	2002	1998	N/A
All data are derived from 1998 statistics in both centers			
3. Measures of case-finding completeness:			
DCO	1.6%	9%	441.5*
Independent case ascertainment	98.7-99.95%	79.8%	1511.8*
Observed/expected ratio	94%	N/A	N/A
Mortality/Incidence rate ratio	0.28#	0.39#	11.1*
3. Measures of item completeness:			
Unknown percent for age,	0.0%	2%	172.4*
sex,	0.0%	0.02%	1.7(NS)
address.	0.8%	15-20%	1152.1*
Percent with unknown origin	2.83%	20%	1180.3*
3. Measures of accuracy & reliability:			
Histologically confirmed percent	85%	N/A	N/A
Re-abstracting audit	N/A	73%	N/A

Questions \ Registry Center	Manitoba	Tehran	Statistical assessment (chi-squared)
Percent passed final edit Inter-abstractor agreement	100% N/A	50-90% N/A	893.1* N/A
3. Measures of timeliness: Accrual method Diagnosis to registration interval	98% of cases are registered within 14 months of closing a diagnosis year 6-8 months	N/A	N/A
1. Numerator of the incidence rate (number of cases of invasive breast cancer)	729	778	N/A
1. Denominator of the incidence rate (female population of registry area)	579,031	3,476,394	N/A
1. Crude incidence rate	125.9	22.4	4242.3*
1. Direct world population standardized rate	83.8	27.5	3266.4*
1. Numerator of incidence rate	All invasive malignant tumours of the breast diagnosed in that year	All tumours of the breast with a behaviour code of 3, diagnosed in a specific year	N/A
1. Denominator of incidence rate	Updated population count for that year, received from Manitoba Health	Tehran population obtained from Bureau of Statistics and age and sex distribution based on 1995 census	N/A

N/A: Not Available or Not Applicable
#: Not available from registries and was calculated by the author
*: significant at the level of $p<0.001$
NS: Not Significant $p=0.19$
The number beside each question demonstrates the number of the section where the reference question comes from in the first questionnaire

The latest available incidence rate from Manitoba was from the year 2002. However since Tehran did not have any incidence rates available more recent than 1998, we inspected all the available statistics and measures using 1998 statistics from both centers.

4.4.1 Intermediate Outcome Measures: Data Quality

All these measures were obtained from the two registries for the year 1998. Since all data quality measures in two registries were not available for "breast cancer" specifically, the available measures for "all cancer sites" were contrasted. For example, the proportion of DCO cases indicates the proportion of "all cancer cases" that are registered through "death certificate only". Only for the mortality-to-incidence rate ratio were "breast cancer" specific measures compared.

For assessing the completeness of case-finding in the two registries, four measures were explored: the DCO rate, independent case ascertainment studies, the observed-to-expected ratio, and the mortality-to-incidence rate ratio.

DCO rates were available from both registries. Of the total 8548 cancers diagnosed in 1998 in Manitoba, 1.6% were based only on death certificate while 9% of the total 6412 cancers diagnosed in 1998 in Tehran were DCOs and the difference is highly significant (Table 4-3).

Two different methods of case ascertainment were used for assessing completeness of case-finding in these two centers. Manitoba has used independent data sets to evaluate the completeness of cancer registry. Tehran used re-screening of cases for this purpose. Both of these methods are sensitive and their results are comparable. The Manitoba Cancer Registry had a completeness of a range of 98.7% to 99.95 depending on various assumptions. In contrast, the Tehran Cancer Registry demonstrated a completeness of 79.8%. Using the worse case scenario in Manitoba (98.7%), the difference in completeness of case-finding was still highly significant (Table 4-3).

One way to examine the completeness of a cancer registry involves comparing the observed number of cases to an expected number. NAACCR uses this approach in certification, comparing a registry's observed rate to that expected in gold standard registries, in this case SEER (Surveillance, Epidemiology, and End Results) incidence and US mortality statistics. Manitoba undergoes this analysis annually. Tehran's data could be checked against data from all Middle Eastern countries in a similar way if we assumed two things: firstly, the cancer incidence rate is similar in these countries (given that breast cancer risk factors are distributed similarly in these populations) and secondly, completeness of cancer registration in other Middle Eastern countries. The first assumption meets to some extent because of similar cultural background which results in similar life style in those countries as well as similar or close ethnic background. However, most cancer registries in this region are newly established and might not be a suitable gold standard. Therefore the second assumption was not met and this comparison was not performed.

Mortality-to-incidence rate ratios were not available directly from either of the two registries, but it could be calculated using the data provided. These ratios were 0.39 and 0.28 for the Tehran and the Manitoba Cancer Registries, respectively and the difference was highly significant (Table 4-3). M/I ratio should not exceed 1; however, it is important to note that this ratio not only reflects the effectiveness of cancer registration practices, but also the success of health care system in prolonging cancer patient survival as well as the accuracy of mortality data. Hence, it should be interpreted very carefully [7].

In the next step, measures of item completeness were compared between the two registries. These measures included percent of unknown age, sex, address, and primary

site (the essential data items). The missing percentage of these items for all cancers in the Manitoba Cancer Registry database for the year 1998 was 0.0%, 0.0%, 0.8%, and 2.83% for age, sex, address, and primary site, respectively. In Tehran Registry, missing percentages were 2%, 0.02%, 15-20%, and 20% for age, sex, address, and primary site, respectively. The differences for missing percent of age, address, and primary site were highly significant; the proportion of cases with missing sex, however, was not significantly different (Table 4-3).

Four measures of accuracy and reliability were investigated, including percent of histologically confirmed cases, results from re-abstracting audits, percent passing final data submission edits, and inter-abstractor agreement rate.

Percent of "histologically confirmed cases" in the Tehran Registry includes only pathology reports but in Manitoba it also includes haematology and cytology reports. However, this rate was not reported by both registries and thus could not be compared.

Among these four measures only the percent of cases which passed final edits when data were submitted were available for comparison between the two centers. All Manitoba cases (100%) passed NAACCR's checks while in Tehran the percent of the cases that passed IARC's checks ranged from 50% to 90% depending on the items being crosschecked. Most of the checked data items had an agreement of over 90% (e.g. for sex and site) except for the date of birth and incidence date where the agreement was only 50%; the reason was that for a high percentage of cases the date of birth was missing in the database. Using the best case scenario in Tehran (i.e. 90% agreement) the difference between the two centers was still significant (Table 4-3).

Finally, information about timeliness was requested from the two registries. For Manitoba, 98% of cases are captured within 14 months of the end of a diagnosis year and the median diagnosis to registration time is 6 to 8 months. No measure of timeliness is available from Tehran; however, the fact that at the time of this study [2005] the latest reported data belonged to 1998 is an indication that the data from this registry are less timely.

4.4.2 Ultimate Outcome Measures: Cancer Incidence Rates

The ultimate outcome was the reported breast cancer incidence rate. Both registries counted the number of invasive (excluding in situ) tumours of the breast as the numerator of the incidence rate (778 versus 729 for Tehran and Manitoba, respectively). The denominator of the incidence rate was defined as the population of the area covered by the registries. Manitoba receives this information through Manitoba Health (based on the population covered by Manitoba Health Insurance Plan). Tehran receives this information from the Bureau of Statistics based on the latest census in 1995 (3,476,394 versus 579,031 for Tehran and Manitoba, respectively).

The crude incidence rate of breast cancer is 22.4/100 000 women for Tehran and 125.9/100 000 women for Manitoba. There is a significant difference in these crude rates, i.e. a diagnosis of invasive breast cancer is approximately 5.5 times more frequent in Manitoba compared to Tehran. Age-standardization is used to make the rates that are reported from populations with different structures comparable. Figure 4-1 compares the structure of the female population in Tehran (1995) and Manitoba (1996).

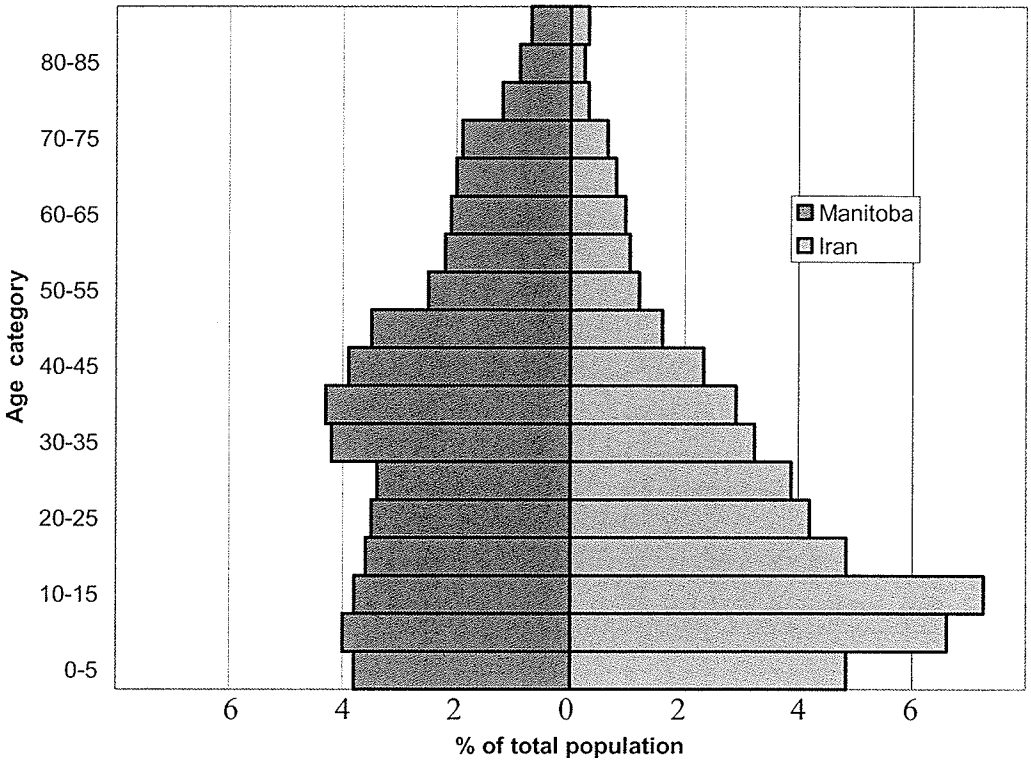


Figure 4-1: Female population pyramid of Iran and Manitoba

This figure is produced based on the data from the Iran Cancer Institute for Iran's female population [23] and the Atlas of Natural Resources of Canada (based on the data from Statistics Canada) for Manitoba's female population [107].

Since the population structure is dramatically different in Tehran/Iran and Manitoba, with a delay of about 40 years in the "baby boom" in Tehran/Iran, we decided to standardize incidence rates (see Figure 4-1).

The world standard population was used to standardize the breast cancer incidence rate in both jurisdictions. Since Tehran population is relatively young, the standardization increased the incidence of breast cancer from 22.4 to 27.5/100 000 women, while Manitoba's incidence rate decreased after standardization from 125.9 to 83.8/100 000

women, due to its relatively old population. However, after standardizing the incidence rates, there is still a large difference in incidence of breast cancer between the two jurisdictions which is statistically significant.

In summary, examining the structure of the Tehran and Manitoba Cancer Registries and the process of cancer registration in the two centers revealed some differences that could affect observed cancer incidence. Thus it was not surprising that examination of the outcome measures showed substantial differences. The following chapter will make an attempt to discuss and explain how differences in the structure and processes of the two registries might have caused such differences in the outcome measures.

Chapter 5: Discussion

5.1 Introduction

The aim of this chapter is to discuss how the previously described differences in the structure of cancer registries and the process of cancer registration can affect the outcome measures (data quality and incidence rates) in Manitoba's and Tehran's cancer registries. Additionally, the effect of variations in data quality measures and the methods used to define numerators and denominators of incidence rates will be outlined.

We will also make an attempt to quantify these effects, where possible, in order to determine if all the variation in reported incidence statistics between the two jurisdictions is likely to be explained solely in terms of the differences in registration practices.

Note: all incidence rates calculated by the author in this chapter are age-standardized using the world standard population, unless otherwise stated.

5.2 Effect of structural differences

The first noticeable contrast is the large difference in the experience of the two registries (see Table 4-1). Although a greater experience does not necessarily imply any superior performance, it has been frequently reported that the performance of registries around the world has improved over time, especially in their first few years of operation [108-110].

The German Population-based Cancer Registry has shown improvements in its completeness over time [108]. The data quality of Hong Kong's cancer registry has improved significantly between 1983 and 2002, e.g. the percent of microscopically verified cases (an indicator of accuracy) has improved from 55% in 1983 to 86% in 2002 and the DCO percent (an indicator of accuracy and completeness) improved from 13.3% in 1983 to 1.3% in 2002 [109]. Similar patterns for DCNs and DCOs have also been shown for the Tarragona Cancer Registry in Spain between 1980 and 1990, i.e. these rates have dropped dramatically during this period [7]. As another example, Australia's Queensland Cancer Registry reported that data quality has improved constantly since 1982, when this registry started its performance [110]. Therefore, if completeness is expected to increase over time, an increase in incidence rates is also anticipated. Consequently, it can be predicted that reported incidence rates in the first few years of operation of a registry are underestimates of the true cancer occurrence in that community. Thus, the data from a cancer registry will be ready for international comparisons and for time trend analyses only when its completeness reaches a plateau, i.e. its changes are slight and negligible, which will take time as the registry becomes more established and the staff become more experienced. A good example of this phenomenon has been reported from a neighboring country of Iran; results from Karachi Cacncer Registry in Pakistan, which started operation in 1995, have demonstrated an increase in incidence rates over the following 4 years of operation [111].

As explained in Chapter 2 (page 32), cancer registries can be active or passive. However it is a spectrum in which some registries are more or less passive with or without an active follow-up component or they act as a completely active surveillance system.

Because of the pressure on health care staff in developing countries to perform the administrative duties more related to patient care and because serving functions in the field of public health and research is not generally of their interest, a completely active data collection is usually necessary for a registry in a developing country [20]. On one hand, a completely active registry might not be able to cover all data sources because of limited resources. On the other hand, a completely passive system may miss some cases who have escaped being captured by reporting facilities. Ontario's cancer registry is as an example of a completely passive registry [82]. A passive registry with an active follow-up is, therefore, the most successful registry [79]. In the case of the two studied registries, Tehran collects its data in a completely active manner while in Manitoba there is a passive data collection with an active follow-up. Therefore, conceptually higher completeness of registration is anticipated for the Manitoba Cancer Registry.

On a related structural topic, data sources are slightly different in the two registries. However, such slight differences can cause major issues in the process of registration, consequently affecting the outcome measures. These effects will be discussed in detail in the section under effects of process differences.

The number of data items collected by a registry does not affect incidence statistics, although it will make calculation of other statistics, e.g. survival rates, possible. Therefore, the larger number of data items collected by the Manitoba Cancer Registry is another indication of relatively more resources and the complexity of this registry [58]. For a developing registry, like the one in Tehran, the quality of collected data items is more important than the number of them [58].

As regards the quality of data reported from different registries, IARC has recommended some basic levels of data quality for registries based on their specific needs and purposes but has not clearly emphasized any definite standards for them [7]. On the other hand, NAACCR uses well defined data quality standards to certificate the North American cancer registries (Table 2-1) [62]. Although meeting the standard levels of data quality that are set for developed registries is difficult and sometimes impossible for a developing registry, it has been recommended that all cancer registries set such standards from the beginning of their operations [17]. This will help those registries to define their goals in terms of meeting those standards. By developing procedures which will result in improving the quality of data, registries are able to produce more reliable statistics.

Documenting activities, including definitions and methods used by registries, is emphasized by both NAACCR and IARC/IACR guidelines (see Table 4-1). Although this documentation exists in both registries, the report from the Tehran Cancer Registry lacks utility as a manual for registry staff. The reason is the nature of this registry which is a project-based registration. However, developing a manual can increase accuracy and reliability of data by ensuring consistency among staff and providing them with a detailed guide.

As regards regulatory aspects of registration, both centers have well-defined regulations and/or legislation. Clear statements about reporting requirements are essential for cancer registries based on both guidelines [62, 45]. Not surprisingly, this requirement is met by both registries.

However, the regulations in the Tehran Cancer Registry do not include all necessary or recommended statements that are suggested by NAACCR basically because Tehran follows IARC/IACR guidelines. IARC/IARC does not emphasize legal authority for cancer registration because it believes that many registries with a voluntary basis of operation are more efficient than their obligatory counterparts [84]. On the other hand, NAACCR requires all its members to develop legislation and/or regulations which include certain statements; NAACCR perceives the inclusion of those statements as necessary or highly recommended criteria [62]. This is the main area of structural differences between the two registries under study, explained by the differences in the guidelines that they follow.

Another statement in regulations that is highly recommended by NAACCR is granting the cancer registries access to patients' records by health care facilities. The Manitoba Cancer Registry is granted such access through PHIA. Tehran, in contrast, lacks such regulations which will result in inaccessibility of data about cancers diagnosed in a certain part of the population. Other cancer registries, which have experienced similar problems for accessing patient records [112], have developed policies to enhance this essential requirement for cancer registration [113]; since inability to access patient records will reduce the completeness of data [62] and consequently will result in underestimating the incidence rates. The magnitude of this effect in this study is quantified in next section (see effects of process differences).

Although IARC/IACR does not emphasize the need for a statement of confidentiality rules in registry legislation, it has acknowledged that these rules can ensure accuracy and completeness of data in a cancer registry through assurances to healthcare and public

health staff about the protection of data provided to a registry [84]. Absence of such statements in regulations might result in failure to report and consequently incompleteness and underestimation of statistics. An example of this is the sudden drop in cancer incidence statistics for Hamburg in 1985 because healthcare professionals were afraid of the consequences of reporting data to the Hamburg Cancer Registry [84].

One statement that is missing from the regulations in both centers is penalties for failure to report cases or grant access to patient records. Incorporating such penalties into legislation is highly recommended by NAACCR. While this could improve accessibility to data by registrars and completeness of data, IARC/IACR sees it as impractical and undesirable to take action against healthcare staff for their failure to cooperate with cancer registries in developing countries [20].

Finally, the statement of the source of funding in registry regulations ensures a secure funding for a registry and thus ensures continuation of its performance. The absence of such a statement in the regulations of the Tehran Cancer Registry could inhibit the longevity of this registry.

As a general rule, very few institutions believe their funding is adequate. Therefore, not surprisingly, both of the studied registries believe that they require more funding for quality control programs. Thus, to judge objectively, the proportion of total funding which is spent on quality control was compared. In Manitoba, this proportion ranged from 10% to 27% depending on the amount of grant funds available to support ad hoc studies. In the Tehran Cancer Registry, there is no budget devoted to continuous programs but 30% of the total budget is spent for ad hoc quality control studies. There is

not any standard for the amount or proportion of the funding devoted to quality assurance programs in a cancer registry. As a rule of thumb, the quality control costs can range from 10 - 35% of the total cost of a project [114]. Perhaps part of the ad hoc quality control budget could be used to support continuous activities in the Tehran Cancer Registry.

Relative restrictions on financial resources lead to restrictions in terms of human resources. The two human resource issues are the number of staff and the education of staff.

To provide a basis for an objective comparison of the sufficiency of the number of registry staff in the two centers, we considered the number of staff in relation to the number of diagnosed cases. The Manitoba Cancer Registry has eight full time registrars and the Tehran Cancer Registry has, on average, eight abstractors who work full time in the abstracting phase. However, Tehran does not have a fixed number of staff because of budgetary problems and the number of staff increases only when there is a higher workload, e.g. in the abstracting phase. On the other hand, the staff in the Tehran Cancer Registry are responsible for reviewing cases diagnosed and treated in Tehran, 70% of who are not residents of the Tehran Metropolitan Area. Therefore, although a total number of 6,412 cases of cancer are reported to be diagnosed in Tehran population, these abstractors need to review about 21,373 medical records or pathology reports. A survey of 61 cancer registries found that approximately one staff person is required for each 1,000 new cases occurring in the population [115]. Considering the total number of new cancer cases reviewed by the two cancer registries in 1998 (21,373 in Tehran and 8,548 in Manitoba) and based on the results from the previous survey by IARC/IACR [1], the

number of staff is adequate for the Manitoba Cancer Registry (one staff per 1,068 cases) but this number is inadequate for the Tehran Cancer Registry (one staff per 2,672 cases).

Budgets also affect the integration of quality control into registration practices. The results of this study revealed that Tehran and Manitoba use different approaches. The Tehran Cancer Registry performs continuous re-abstracting and re-coding checks but completeness checks are mostly ad hoc. However, increased budget could allow continuous quality control, which has been shown to improve actual data quality and staff awareness of the quality of data they produce [59]. In turn, more complete data can improve the estimates of cancer occurrence in the population.

NAACCR perceives enough funding as essential and enough staff as highly recommended for quality control activities in cancer registries [62]. The Manitoba Cancer Registry, which follows NAACCR guidelines, has assigned one full time technician for quality control purposes but Tehran only employs staff for ad hoc studies but not for continuous quality control programs. The reason is that although IARC/IACR acknowledges the importance of continuous quality control activities [59], it does not emphasize providing staff and funding specifically for this purpose.

In summary, the main reason for variations in structural requirements of the two registries is the difference in the guidelines that they follow, i.e. the Tehran Cancer Registry does not meet some of the criteria outlined by NAACCR because IARC/IACR guidelines do not emphasize those aspects. IARC/IACR guidelines for cancer registries emphasize more of the process aspects of a registry rather than its structure; even though structural issues have been discussed in IARC/IACR guidelines, they are not emphasized as a

determinant for accepting data from a registry.

Another reason is that, since these are mainly regulatory differences and regulations generally evolve over time by acquiring more political support based on the years of experience and a realization of the need for developing such regulations, they are expected to improve over time in the Tehran Cancer Registry. A larger and more immediate issue is the inadequate and unsecured funding available to the Tehran Cancer Registry, which potentially affects the number of registry staff and the range of tasks (such as continuous data quality control) they are able to complete.

5.3 Effects of process differences

As regards basic processes, the two cancer registries are similar in their coding, abstracting and data storage systems. Although the coding system that they use is different in version (ICD-O-3 by Manitoba and ICD-O-2 by Tehran), these two systems have very minor differences in the coding of invasive breast cancer which would not affect incidence estimates [116]. But there are major issues in basic processes as regards comparability of rates. One of these issues involves guidelines for determining multiple primary tumours. Tehran uses IARC/IACR guidelines which is more conservative in making a second primary tumour diagnosis compared to the CCR rules used by the Manitoba Cancer Registry. It has been shown that breast cancer is the most likely site to be affected by varying definitions of multiple primaries; when SEER and IARC/IACR rules are compared crude incidence rates of breast cancer may be overestimated under SEER rules by up to 5.8% [19].

To remove this effect, the number and the age of the cases of second primary tumours of the breast diagnosed in the year 1998 were derived from Manitoba Cancer Registry database (the first primary could occur in any previous year or in the same year). Overall, 122 cases of second primary tumours of the breast were diagnosed in Manitoba women in 1998. The number of cases in each age category was then subtracted from the numerator of the age-specific incidence rates and the rate was then standardized using the world standard population. After removing the effect of differences in the definition of multiple primary tumours, the age-standardized incidence rate of breast cancer in Manitoba changed from 83.8 to 71.5. This reduction of nearly 15% in incidence estimates is notable and highlights the importance of differences in definitions when comparing data from two registries.

Also, as mentioned in the discussion of structural characteristics, the Manitoba Cancer Registry uses screening and autopsy as sources of data while Tehran does not. Cases diagnosed through these two sources, when they have not been clinically suspected, are known as "incidentally" diagnosed cases and can increase incidence estimates somewhat artificially [7]. In the early years of introduction of a screening program, the cases detected earlier through these programs, who would have otherwise been detected later, result in an increase in incidence rates known as "lead time bias" [7]. Also some of these cases might have never been diagnosed in the subjects' life time which results in another bias called "over-diagnosis bias" [7]. These effects have been shown by many previous studies [e.g. 117-120]. In the present study, Manitoba has introduced screening programs, in 1995 and Tehran does not count for such cases. Therefore, the previously discussed biases are likely to be present in this study and it is important to remove those cases when

making a comparison between the two registries. Similarly, more frequent and thorough autopsies and inclusion of cases diagnosed incidentally through them can cause overestimation of incidence [7]. In Sweden, where the autopsy rates are very high, it has been shown that in some registries up to 22.1% of cases are diagnosed through autopsy [121]. Additionally, it has been demonstrated that regional differences in the practice of autopsy introduced a large difference in area-specific incidence rates of prostate cancer, as large as nearly two times between areas of high autopsy rate (47%) versus Sweden as a whole (7%) [122].

To remove these effects, the number and the age of the cases diagnosed incidentally through autopsy were derived from Manitoba Cancer Registry database. No cases were detected through autopsy in 1998. The number of cases diagnosed through screening was available for the period of 1995 to 2003 through Manitoba Breast Screening Program (MBSP) [123]. Only women between 50 and 69 years of age without any clinical symptoms and those between 40 and 49 or above 70 years with a physician recommendation are eligible to enter this program [124]. Therefore, we are confident that these are cases "incidentally" diagnosed through screening and not symptomatic patients who used mammography as a means of diagnosis. The total number for the period of 1995 to 2003 was divided by the number of years, assuming even distribution of cases or constant changes in detection rate, since the year 1998 is nearly the median year in this period. Then we estimated the number of screening detected cases in each age group based on the proportion of total cases diagnosed through screening in each age group in this period. These numbers were subtracted from the numerator of the last adjusted age-specific incidence rates and age-standardized breast cancer incidence rate was

recalculated. After removing the effect of differences in data sources, the Manitoba's age-standardized rate changed from 71.5 to 69.4/ 100 000 women.

It is an essential requirement for all cancer registries to have precise definition for reportable tumours. These definitions should determine cases to be included and cases to be excluded. For example, according to IARC/IACR guidelines: "probable", "suspect", "suspicious", "compatible with", or "consistent with" should be interpreted as being a case and "questionable", "possible", "suggests", "equivocal", "approaching", or "very close" should be interpreted as not being a case [44]. These words are specified in the regulations of both centers, and along with multiple primary determination rules, are introduced during training of the staff in the two centers.

As regards training and continuing education processes, the only difference appears to be unavailability of international educational resources for the Tehran Cancer Registry. IARC/IACR has admitted that staff training is a major problem for establishing a cancer registry in a developing country [20]. This problem has been related to the differences in the healthcare environment of developing countries, such as differences in healthcare systems or having fewer staff to serve a larger population, relative to other countries [20]. The Tehran Cancer Registry has adopted a system which works well and suits their needs and circumstances. However, the lower data quality measures compared to the Manitoba Cancer Registry may partly be explained by relative experience and also to the relative opportunities for training in Manitoba. Therefore, keeping their knowledge about other developed registries up-to-date by participating in international meetings is a possible option for gradually improving the registry system in Tehran. In this regard, international organizations can contribute significantly to this effort which has benefits for

international health.

Tehran's cancer registry could also benefit from additional supporting regulations [e.g. 113] to allow the registry access to 100% of the hospitals in Tehran. A small proportion of the hospitals do not grant access to the Tehran Cancer Registry mainly because of lack of support by legislation and the department of health. The concern is that without these structural supports, there will be systematic loss of information about the population covered by those hospitals, which will give rise to incompleteness of case-finding. The magnitude of this incompleteness is discussed later on in this section.

Cancer cases that are diagnosed and treated completely out of a hospital setting may not be captured by cancer registries if they rely solely on hospital medical records. Gynaecologic and skin cancers are the most likely cancer sites that might only contact outpatient clinics and receive laser or radiotherapy as an outpatient [45], but this is not a major concern for breast cancer. Another group of patients who might never become hospitalized or receive any treatment are the elderly and the end stage patients who may also avoid painful procedures knowing that treatment is not likely to result in cure [45]. Therefore, the only contact they might have with the healthcare system is with their general practitioners. For these reasons, missing these two data sources (outpatient clinics and in this case more importantly physician offices) may result in biased and incomplete registration. This is one of the areas that the Tehran Cancer Registry may need to consider particular strategies for encouraging cancer reporting. The sudden drop in incidence of breast cancer in the oldest age groups in Tehran (see Figure 4-1) raises the possibility of biased, incomplete registration for the older age groups. The effect of this possible bias on the incidence rates would be described later in this section.

Both registries have a method of notification for reporting facilities, but since the registries collect the information from medical records actively, they do not completely rely on reports from hospitals. Therefore, this is not an area of concern in relation to outcome measures of interest in this study. However, access to other sources varies. Access to information from physician offices is also very important for the cases that are first notified through death certificate. Some registries, like the Tehran Cancer Registry, record all the cases notified first through death certificate as DCO cases and do not follow them back. However, it is important to contact certifying physicians to obtain more information about these cases before registering them as DCO [7]. This will improve completeness and accuracy of data in the cancer registry [7].

As mentioned earlier in this section, the Tehran Cancer Registry does not capture tumours diagnosed in all at risk population of the Tehran Metropolitan Area. According to the Tehran Cancer Registry staff, the hospitals that are excluded from the cancer registry database serve approximately 1.5% of Tehran's population. Assuming equal risk and characteristics for this population in regard to developing breast cancer, in the worst case scenario an additional 1.5% of incompleteness might be assumed for the registry. Adding this number to the numerator of breast cancer incidence rate in Tehran should increase the age-standardized rate from 27.5 to 27.9/100 000 world female population. However, given that breast cancer cases have several hospitalizations in Tehran, it is unlikely that these cases are completely missed.

When describing the structural differences, we mentioned that although IARC/IACR does not emphasize the regulatory aspects of confidentiality, it discusses in detail the need for following confidentiality rules [84]. Both registries follow confidentiality rules

in maintaining their data; however, the Tehran Cancer Registry's staff do not sign a confidentiality pledge as part of their employment process. This aspect of confidentiality should also be encouraged in the Tehran Cancer Registry.

As discussed before, it is desirable that registries follow back all cases notified first through death certificate (DCN) before registering them as DCO cases. There is some evidence in the literature showing that as cancer registries become experienced, they improve their methods of follow-back and the DCO proportion decreases resulting in improved estimates of completeness and accuracy of data [7]. One of the reasons for the large DCO proportion in the Tehran Cancer Registry is that DCN cases are not currently followed back due to resource limitations and the newness of the cancer registry. When follow-back is implemented, the Tehran Cancer Registry may benefit not only from improved DCO rates, but also in terms of continuous data quality assessment. The reasons for improved data quality after implementing follow back procedures include [7]:

1. reasons that DCO cases have escaped being captured by the system will be identified, and

2. non-cancer cases that would have been recorded as DCO if they had not been followed back will be excluded.

Ideally a registry should be able to match the complete death file from vital statistics with its database (as is in the case of the Manitoba Cancer Registry). The Tehran Cancer Registry's ability to perform analysis using death dates, such as survival analysis, would be improved if it were able to link the cancer registry and death information. But also as regards the incidence statistics, incomplete record linkage with vital statistics and

examining only death files with the cause of cancer can result in missing cases for which cancer was not mentioned as first or second cause of death [7]. This will increase the incompleteness of data to an unpredictable extent. However, this problem has apparently resolved for the data collected after 1998.

Quality assurance and quality control procedures are performed in both registries. But still some procedures outlined by IARC/IACR are not yet performed by the Tehran Cancer Registry; these include measuring observed-to-expected ratios and mortality-to-incidence rate ratios as well as process controls to show stability of registration over time and among regions. The continuous performance of these quality control activities can improve the quality of data by detecting possible errors contemporaneously and giving the registry an opportunity to rectify them while medical records are still available [7]. However, we are not able to quantify the magnitude of the effect that the presence or absence of such procedures may have on cancer incidence estimates in Tehran and Manitoba.

In summary, there are some notable differences in terms of the processes of registration in the two cancer registries. Manitoba's cancer registry meets all process criteria based on the two guidelines. However, it appears that many of the issues of the younger registry, the Tehran Cancer Registry, which are expected to manifest in terms of data quality estimates, arise from process aspects. This is the area where experience plays an important role and is expected to improve over time for the Tehran Cancer Registry.

5.4 Effect of differences in data quality measures

The structure and process characteristics of a cancer registry can affect the quality of data from that registry and ultimately affect the cancer incidence statistics reported from the registry.

In this section the influence of data quality measures on incidence rates will be discussed and breast cancer incidence rates will be further adjusted using these measures in order to remove the effect of differences in registry practices as much as possible.

The first studied category of data quality measures was completeness of case-finding. All available measures of completeness were significantly different between the two registries (see Chapter 4); these are discussed below.

The first measure in this category is the DCO proportion. The study results revealed that there is a highly significant difference in the proportion of cancer cases in the two registries whose diagnosis is solely based on death certificate. The following structure and process differences that have been detected so far may have caused this difference:

1. *Difference in experience:* the more the experience of a cancer registry, the lower the DCN and DCO percents [7]. It is also important to note that in the first few years of a cancer registry's operation the DCO cases are more a measure of prevalence than incidence [e.g. 111] because the registry database does not include the cases diagnosed in previous years [62]. It is known that the DCO percentage steadily decreases after the first few years of operation of a registry because of the exclusion of prevalent cases as well as improved data collection

and case finding processes [7].

2. *Difference in follow-back processes:* since the Tehran Cancer Registry does not follow back the DCN cases, the DCO percent equals the DCN percent. Effective and meticulous follow-back processes have been shown to reduce the DCO percent significantly [125].

3. *Difference in completeness of case-finding:* the primary use of DCO statistics is to indicate one aspect of incompleteness. For this purpose DCN% is more frequently used because it is an indication of the cases that the registry has failed to capture before their death [49].

Since the DCN% for breast cancer was not available from the Tehran Cancer Registry, it could not be used here to estimate the true incidence rate of breast cancer in two jurisdictions.

A second approach to data quality assessment uses results from the independent case ascertainment studies. This study found significant differences in the estimates of completeness for the Tehran and Manitoba Cancer Registries. Notably, the Manitoba Cancer Registry used independent datasets to estimate the completeness of its case-finding, a design feasible only when there is relatively complete source of data that has not been utilized by the cancer registry as a data source [7]. In Manitoba, when compared with hospital discharge data from the provincial health care insurance plan, the registry was found to capture at least 98.7% of the diagnosed cases in 1998 [126]. The Tehran Cancer Registry used re-screening of cases to evaluate the case-finding completeness. Re-examining all records from four hospitals and pathology laboratories revealed an

overall completeness of 79.8% [127]. These rates can be used to correct the incidence estimates in these two populations. The adjusted rates that we have already calculated in this chapter were used for this purpose. For the Manitoba Cancer Registry a maximum of 1.3% should be added to incidence estimates, while for the Tehran Cancer Registry, 20.2% should be added to previous rates to account for incompleteness of registry database. Applying these corrections, breast cancer incidence rates in 1998 increased from 69.4 to 70.3/100 000 women for Manitoba and from 27.9 to 33.5/100 000 women for Tehran.

Mortality-to-incidence rate ratios (M/I ratios), despite being readily measurable were not reported by either of the two registries. The Manitoba Cancer Registry uses a different measure called incidence-to-mortality rate ratio which is calculated by NAACCR using a complicated method [62]; this ratio is actually an observed-to-expected ratio and is explained in more details in the discussion of observed-to-expected ratio. The M/I ratio, however, is a necessary part of IARC/IACR quality control before publishing data from cancer registries. This ratio reflects the performance of three different components: the healthcare system, the vital statistics reporting system, and the cancer registry.

The better the performance of the healthcare system, the longer the survival of cancer patients. Aspects of better performance include access to healthcare services, earlier diagnosis, and more effective treatment. When the accuracy of vital statistics file and completeness of the cancer registry are 100% and the incidence and survival rates are not changing rapidly, the M/I ratio is:

M/I ratio= 1- Probability (survival) [7].

Therefore the M/I ratio for breast cancer, because of its relatively long survival, especially when diagnosed in early stages, is quite small. For example, according to Cancer Incidence in Five Continents (Volume VII), this ratio for female breast cancer was 0.32 for Canada and about 0.25 for the US [128]. However, M/I ratio has been shown to be much higher for some developing countries like India (see Figure 5-1) [129]. In the present study this ratio was 0.28 for Manitoba (close to the Canadian estimate for 1997) and 0.39 for Iran (close to the Indian estimate for 1997).

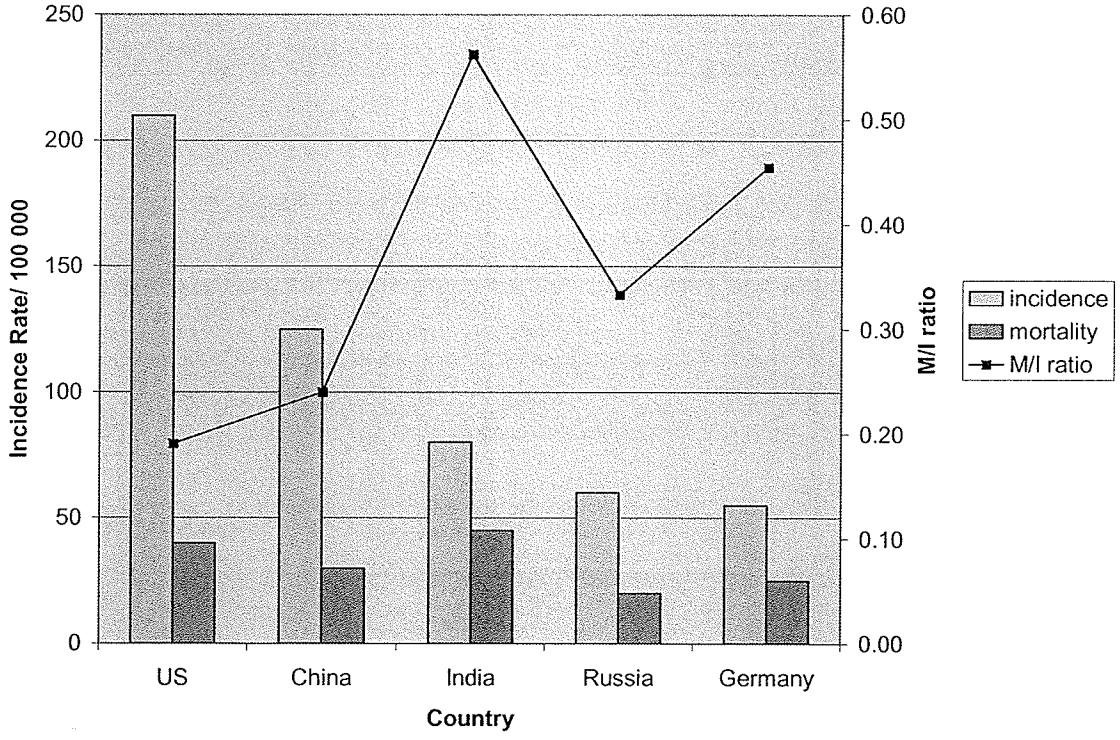


Figure 5-1: Mortality-to-Incidence ratio of breast cancer, estimates for 2003

The M/I ratio cannot be used as an estimate of survival when any incompleteness in the capture of either incidence or mortality features interferes with the basic assumptions; for example, in the present study we observed that the Tehran Cancer Registry is estimated to be about 79% complete.

On the other hand, another application of this ratio (and the main reason that it was calculated here) is to compare the effectiveness of cancer registration. When this ratio exceeds 1, it is usually an indication of under-registration when incidence and mortality rates are not changing rapidly [7]. But this benchmark is generally useful for fatal cancers and has limited application for breast cancer [49]. Further, in comparing Manitoba to Tehran, there is also the assumption of similarity in survival rates and vital statistics, and the problem of incomparability arises once again. Previous studies have shown that breast cancer cases in Iran are usually diagnosed in later stages [99] and therefore lower survival is expected in comparison to Manitoba where intensive screening programs are in place for the early detection of breast cancer [124]. IARC/IACR has also indicated inaccuracy of vital statistics as a problem that cancer registries encounter in developing countries [20]. Therefore M/I ratio reflects differences in registry practices along with differences in survival rates and accuracy of vital statistics. These effects are so largely entangled that it is beyond the scope of this study to measure the influence of each effect.

One of the measures of completeness which was desirable to be compared between the two registries is the observed-to-expected incidence ratio. This ratio was available for Manitoba using NAACCR method, which compares the observed rate in Manitoba to that expected using the experience of SEER registries as a gold standard. It was not possible to calculate this rate for Tehran, but there are some indications that Iran's rate is consistent with the reported incidence rates from Middle Eastern countries [128], suggesting that Tehran's observed rate is similar to that expected. However, this is not conclusive because it is not possible to remove the effect of unknown data quality of these registries in order to make objective comparisons.

The next category of data quality measures investigated was completeness of data items. These measures are also associated with the accuracy of data since they show the percent of cases for which a specific data item was not accurately recorded [7]. Completeness of those data items which are essential for cancer registries are generally measured. These include age, sex, address, and diagnosis. The missing percentage for these items is recommended to be close to zero and each registry should set a level of tolerance for these missing percentages [7]. This is one of the areas where continuous quality control is very rewarding because missing data can be retrieved from medical records when they are still available [59]. It has been shown that when the completeness of data items falls below 80-90%, the risk of selection bias threatens the registry database and thus serious actions should be taken [130]. This risk is probable for two of the data items in the Tehran Cancer Registry, address and primary tumour, both of which are very important in the calculation of incidence rates by affecting the accuracy of the numerator.

Although the proportion of cases with missing age in the Tehran Cancer Registry is minimal (2%), it is important to note that when the percent of missing ages is sizable, the age-specific rates will be underestimated for the oldest age groups [7]. The reason is that the calculation of rates assumes that missing cases are distributed proportionately among age groups; however, in reality they are more likely to belong to older age groups. This might partly explain the observed decline in the incidence rate of breast cancer in Tehran in older age groups.

There was a notable difference between the proportion of cases missing primary site in Tehran (20%) and Manitoba (2.83%). There are three main reasons commonly cited for high percentage of missing primary site or primary site unknown [7]:

1. *Differences in healthcare practices:* e.g., clinicians tend to record "unknown" when they are in doubt about the diagnosis.

2. *Differences in healthcare policy:* i.e. there are less intensive investigations into the primary source of metastasis in patients known to be untreatable because of limited resources.

3. *Deficiencies in registry operation:* incomplete abstraction of medical records or inaccurate compliance with ICD-O coding system.

We are unable to differentiate these three influences; however, we suspect that all of them are involved to some degree in producing such a large difference in percentage of unknown primary site between the two registries.

The high proportion of cases with missing address in the Tehran Cancer Registry poses two potential problems [7]:

1. Since Tehran is a referral center for cancer patients in the whole country, inaccuracy in estimation of the numerator of incidence rates is probable.

2. For geographic comparisons within the registry area, the high percent of missing cases makes the analysis less accurate.

Moreover, as will be discussed subsequently, quality control studies performed in Tehran have revealed a high prevalence of inaccuracy even in the presence of address item [127].

The next category of data quality measures to be examined was measures of accuracy. Data accuracy can be measured using the percent of cases that pass "edits" for data

submission. This percent was the only available measure in this category. The software used for editing is different for each registry but both are designed for the same purpose. Although this percentage was significantly lower for the Tehran Cancer Registry, most of the crosschecks of the items in this registry showed a high degree of agreement (over 90%). The number of cases passing edits could even be higher by increasing staff training and adding continuous checks throughout a registration year. Another consideration is workload; if as indicated in the discussion of "structural aspects", the Tehran Cancer Registry has less staff than recommended for its caseload, there could be additional inaccuracy of data abstraction and coding. The solution is challenging in an environment of limited funding, as it involves recruiting more staff.

Percent of "histologically confirmed cases" was not reported for both registries; however, it was noted that there was a difference in its definition. Percent of "histologically confirmed cases" in the Tehran Cancer Registry includes only pathology reports but in Manitoba it also includes haematology and cytology reports, more accurately called "microscopically verified cases". Thus when Manitoba's percent of histologically confirmed cases is discussed, its estimates may well be increased, especially for haematologic and cervical cancers for which other microscopic examinations are routine [49]. Such differences in definitions have important implications for international comparisons.

The Tehran Cancer Registry provided one additional measure of accuracy derived from inter-abstractor audits. Audit information showed an agreement level of 73%, which is suggestive of an opportunity to improve data accuracy by training of the abstractors.

Timeliness, the last aspect of data quality investigated in this study, is important in terms of the usefulness of the data [17]. The fact that data from the Tehran Cancer Registry are being processed and reported with a large time lag impairs the utility of the data. However, this registry is very new and is currently collecting the cases retrospectively. Improved timeliness is expected to occur after the first few years of operation of the registry.

5.5 Effect of differences in rate components

The numerator, denominator, and age-specific rates all can influence the overall reported incidence rates. Additionally, differences in these components may raise the problem of incomparability of the statistics.

As regards the numerator of the incidence rate, it is very important that the standard definition of numerator of the rate (cancer incidence) is consistent across registries. While reviewing the structure and process characteristics of the two systems, we identified issues regarding comparability of numerators, in terms of definition, completeness, and accuracy.

The two centers follow different guidelines (IARC versus CCR), which results in discrepancies in the definition of numerator regarding multiple primary determination rules. Additionally, the data sources used to define cases are different in the two centers, i.e. screening and autopsy detected incidental cases are included in the numerator of incidence rate in Manitoba but not Tehran. As discussed we were able to adjust the rates to remove the effect of these differences as much as possible.

Another issue influencing the numerator is incompleteness and inaccuracy of the data. In this study, the rates have been adjusted as far as possible to remove the problems of incompleteness. The accuracy issues, however, are less quantifiable and more difficult to adjust for. For example, a high percentage of missing information for registered cases is an indication of inaccuracy. Some of these missing items can seriously endanger the accuracy of numerator. For example, an unpublished report of a quality control study in Tehran revealed that only 70% of the address items present in database were properly recorded, and a high proportion of cases had missing address (20%) [127]. Based on the information from registry staff, many of the cases report their place of residence inaccurately. The reason is that Tehran is a referral center for cancer diagnosis and treatment and a large number of patients come from other cities to visit Tehran hospitals. These patients tend to report the address where they will be staying in Tehran for that period as their place of residence and therefore will be incorrectly included as cases in the Tehran Cancer Registry. This suggests that a countable proportion of the numerator of the incidence rate in the Tehran Cancer Registry may be registered incorrectly, resulting in an over-estimate of rates. However, we are not able to adjust for such potential over-registration because of the probability of bias, i.e. we suspect that those from out of the city are more likely to have missing address.

Manitoba, on the other hand, takes the advantage of a central Canadian registry which double checks the information from all provinces and territories and notifies registries about cases that have been incorrectly registered. There is also a precise system of coding used by Manitoba Health which assigns each resident of Manitoba a unique and identifiable number and removes the problem of inaccuracy of address.

Population denominators are based on recent data capture for both centers; however, since the Tehran Cancer Registry covers only an urban area, population mobility is more problematic in this center. Given the fact that Tehran is a major business and occupation attraction site, the immigration rate is increasing and an updated census might show that the estimated population for 1998 is an underestimate. Thus these denominators could result in artificial increases in incidence rates.

Based on the above discussions both numerator and denominator data contributing to the incidence rate in Tehran might lead to over-estimates of cancer incidence in Tehran's population. Unfortunately we are not able to measure the magnitude of this over-estimation.

To complicate matters, the method of age-standardization must also be considered. In direct standardization method, age-specific incidence rates are calculated and adjusted to a standard and then their weighted average comprises the overall rate. Thus when we compare the overall rates between the two registries, we assume similar age-specific rates.

However, in the comparison of cancer incidence in Tehran and Manitoba, this assumption proved incorrect. After calculating the standardized incidence rates, we noticed that despite a younger population structure in Tehran, the incidence rate did not increase as much as we expected. Therefore, we examined and compared the age-specific rates in the two registries. These rates are demonstrated in Figure 5-2 for Manitoba and Tehran, with Ontario data included for comparative purposes.

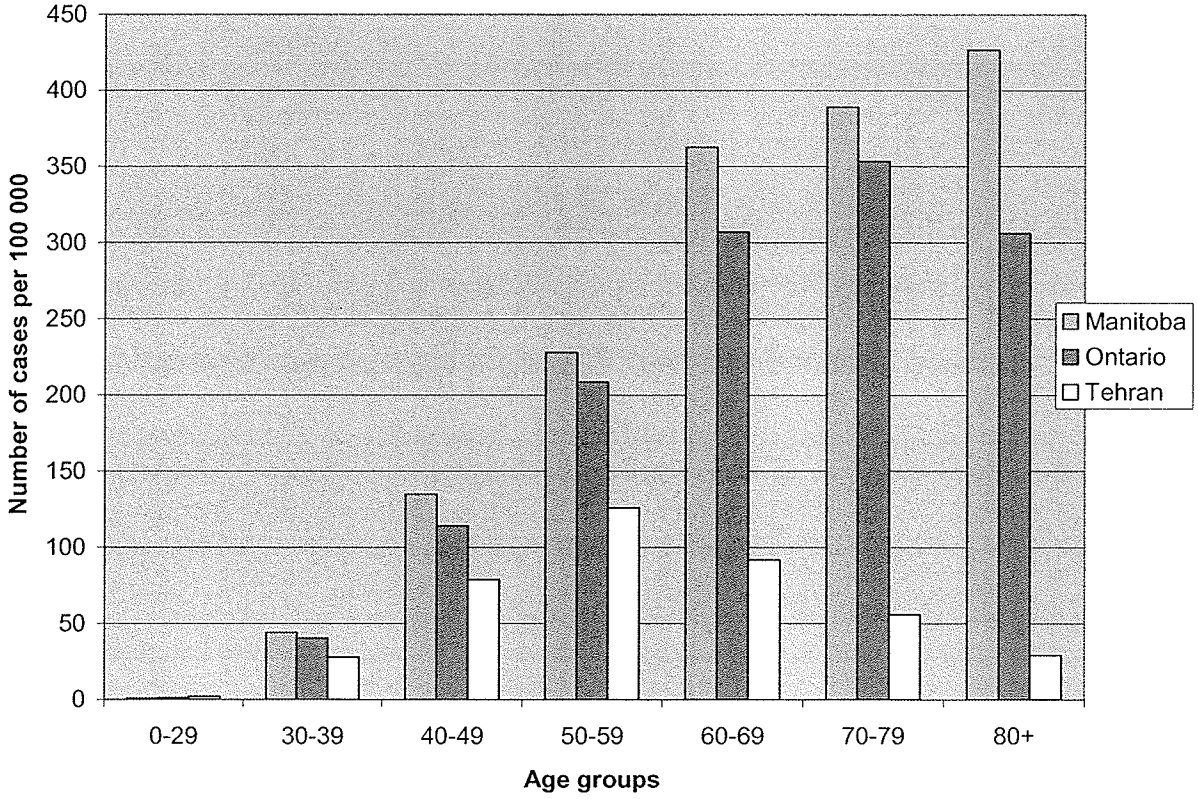


Figure 5-2: Breast cancer age-specific incidence rates in Manitoba, Tehran and Ontario

Interestingly, the age-specific rates showed different patterns in Tehran and Manitoba. Breast cancer cases are on average younger in Tehran than in Manitoba. Incidence of breast cancer increases steadily with age in Manitoba; however, it increases until 60 years of age in Tehran and then drops suddenly in older ages. This is in accordance with previous studies showing a lower average age of Iranian breast cancer cases and a higher prevalence of breast cancer in pre-menopausal Iranian women compared to western countries [99].

There are two possible explanations for the terminal drop in incidence statistics in Tehran as compared to the steady increases in Manitoba:

1. *Risk factor differences in younger and older age groups:* there are numerous studies in the literature providing evidence of differences in risk factors of breast cancer for pre-menopausal and post-menopausal women [e.g. 131-133]. Since pre-menopausal breast cancer is more common in Tehran [99], it is possible that differences in such risk factors between Tehran and Manitoba explain the different patterns in age-specific incidence rates. This possibility has also been suggested by IARC/IACR observations in low-risk populations where the incidence of breast cancer increases rapidly in pre-menopausal age groups but slows down or even drops in post-menopausal ages [134].

2. *Inability of Tehran Cancer Registry to capture cases in older age groups:* this can happen because of some structural and process characteristics of the Tehran Cancer Registry, e.g. the absence of access to information from physician offices and the missing information on age. It has also been shown that since old patients are more likely to be unable to recall their age, a large number of cases with missing age are found to cause underestimation of incidence in older age groups [7].

Some data were available to pursue the probability of the second explanation. We hypothesized that older female cancer patients are less likely to become hospitalized for two reasons: firstly, it is known that the elderly are more likely to be diagnosed in late and untreatable stages of disease [7], hence, their only point of contact with healthcare system may be physician offices; and secondly, old women in Tehran are generally less likely to visit hospitals compared to old men in Tehran and the elderly in Manitoba. Therefore, since the Tehran Cancer Registry does not receive information about cancer

cases who only visit physicians (i.e. not in hospitals), old women are more likely to escape being captured by the cancer registry.

To test this hypothesis, we examined the pattern of incidence rates in some other cancer sites for which it is known that incidence rates increase steadily with age [7]. Interestingly, for many other cancer sites in the Tehran Cancer Registry's 1998 report [135], the same age-specific pattern of incidence rate was visible. For example, colon and oesophageal cancers increased with age in Tehran's male population while they dropped in the oldest age groups in the female population (Figure 5-3 and Figure 5-4).

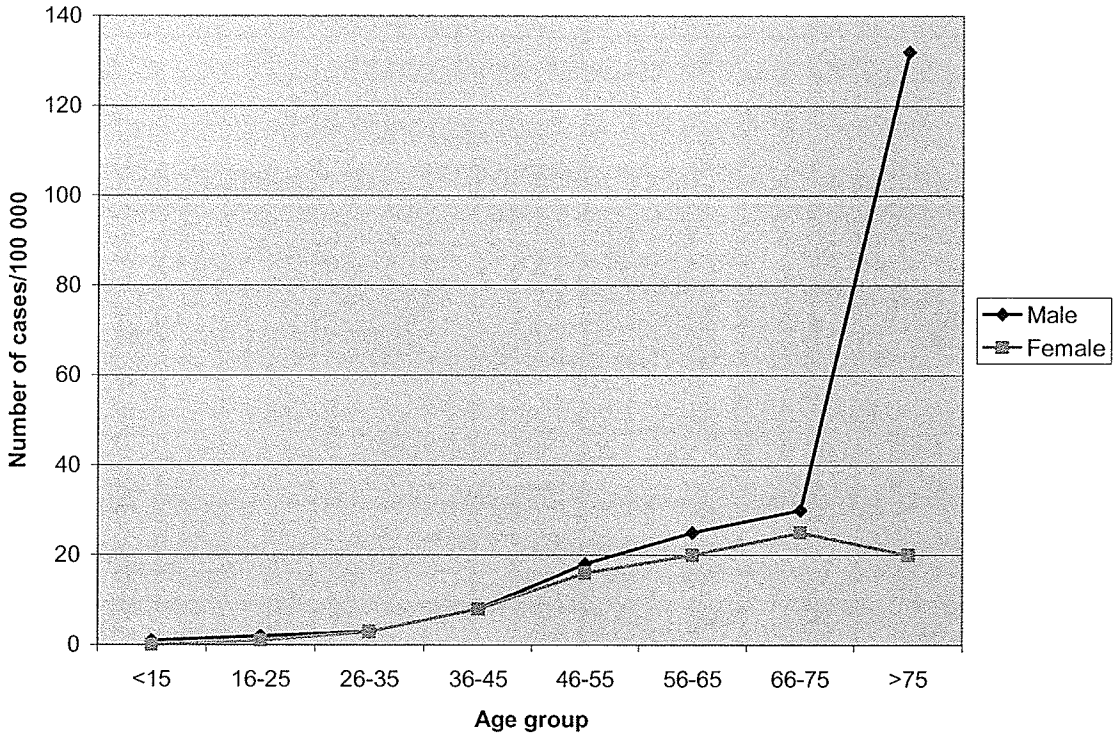


Figure 5-3: Number of cases of colon cancer per 100 000, in 1998, Tehran, males and females, by age group

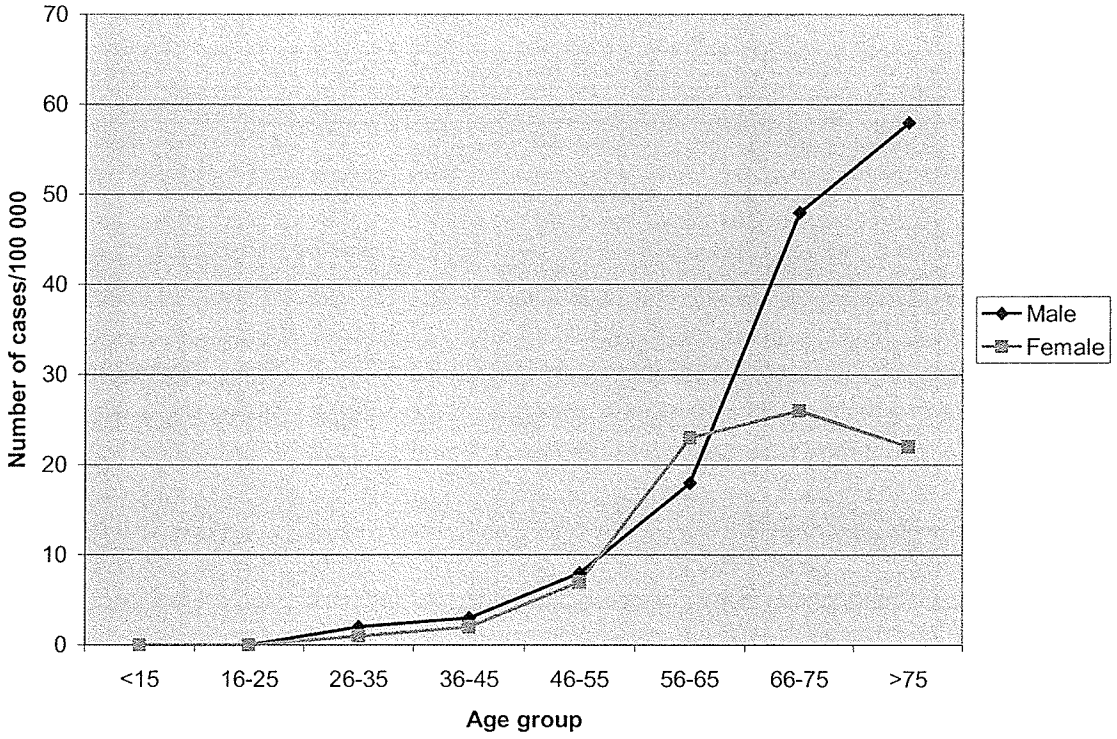


Figure 5-4: Number of cases of oesophageal cancer per 100 000, in 1998, Tehran, males and females, by age group

The observation of a pattern similar to that observed for breast cancer in different cancer sites supports our hypothesis. Subsequently, we compared the pattern of age-specific hospitalization rates for women and men in Tehran and Manitoba. Interestingly, the average annual hospitalization rates between 1995 and 1997 in Manitoba increased with age for women as well as men in the same pattern as cancer rates (Figure 5-5 [136]). In contrast, based on the data for four months of April to July of 2004 in one of the largest hospitals in Tehran (Imam Khomeini), the estimated annual hospitalization rates, increases in both older males and females in Tehran; however, this increase was dramatically greater for Tehran's male population (Figure 5-6 [137]). We acknowledge that these rates are estimates and from only one hospital in Tehran (as opposed to the population-based data available in Manitoba) but the pattern of the rates is the focus of this discussion. This analysis indicates that Tehran's female population may be less likely

to contact healthcare system and get hospitalized than the male population.

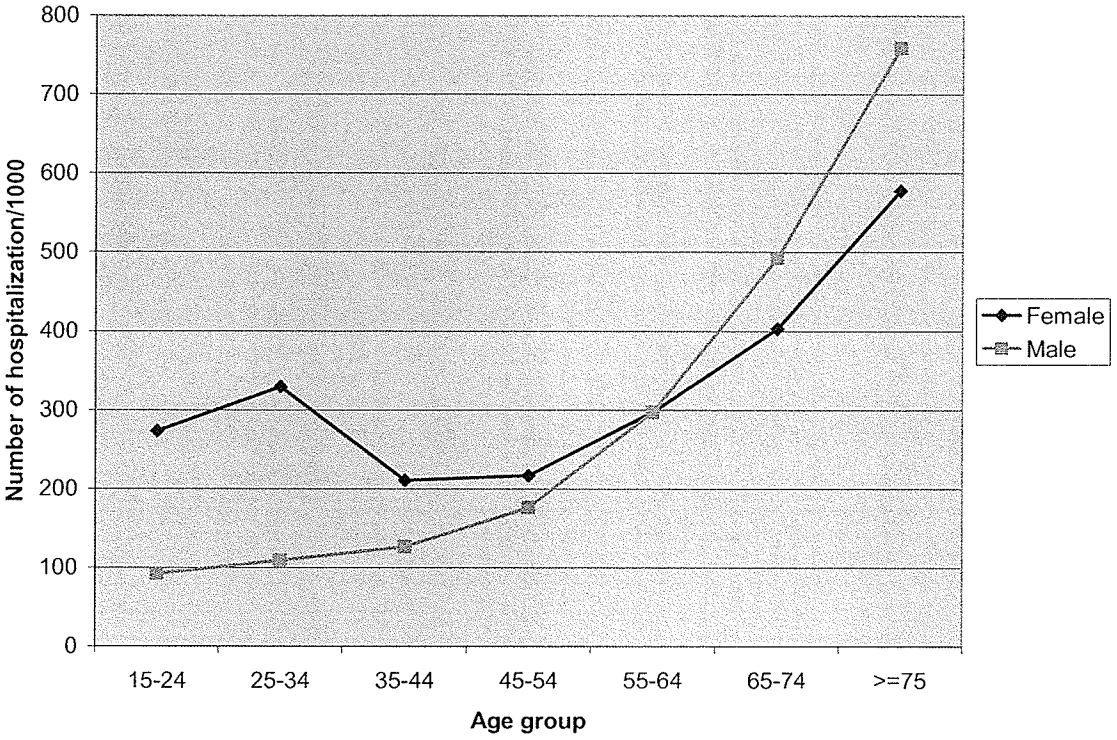


Figure 5-5: Average annual hospitalization rates per 1000, Manitoba, 1995-97, males and females, by age group

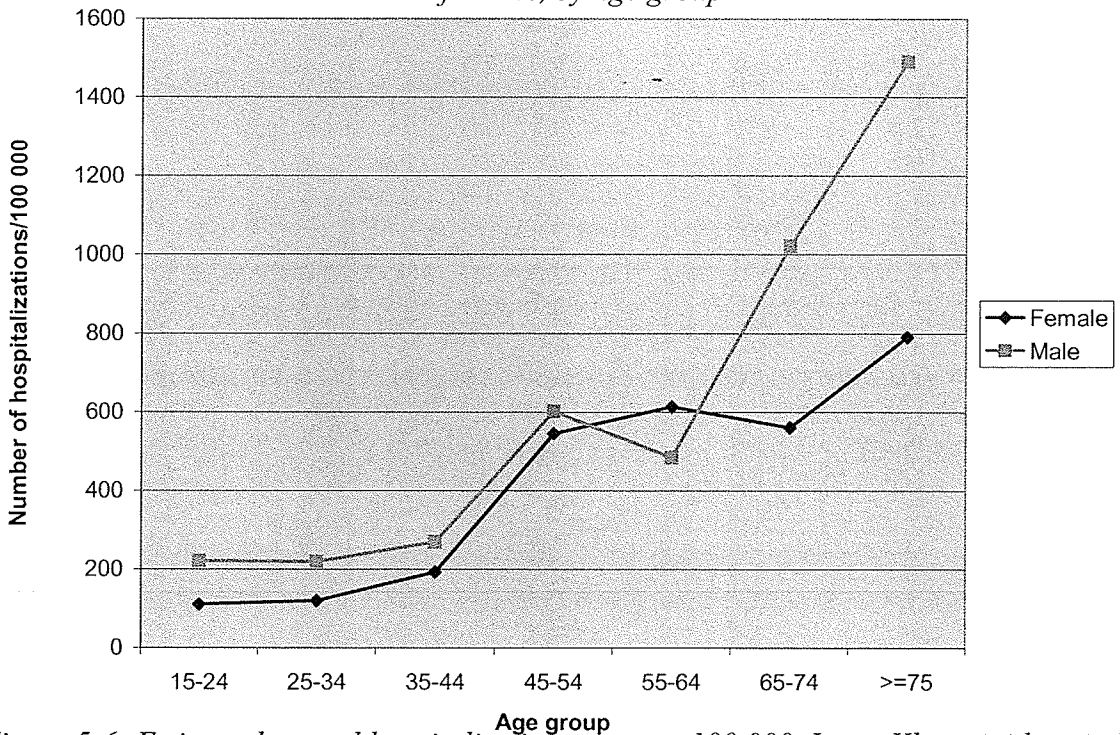


Figure 5-6: Estimated annual hospitalization rates per 100 000, Imam Khomeini hospital in Tehran, 2004, males and females, by age group

Although suggestive, this evidence is not conclusive, since it can be claimed that the reason for lower hospitalization rates in old women in Tehran is that they are healthier, although it is not very plausible.

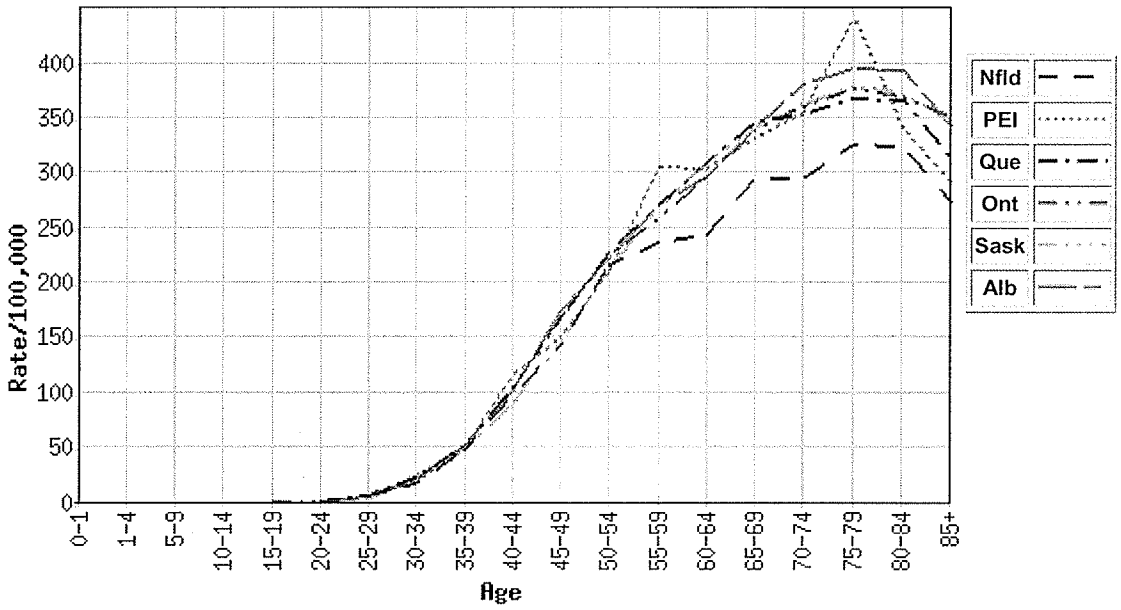
We also compared Manitoba's age-specific patterns to other Canadian populations with a comparable structure. In Figure 5-2, Ontario's age-specific rates are graphed as an example. It is evident in this graph that Ontario follows an interim pattern, i.e. the incidence rates increase with age and drop slightly in the oldest age category. This pattern is observed in most cancers that are epithelial in origin [138] for two reasons:

1. *Biologic resistance:* those who live to very old ages are generally genetically less vulnerable to cancer and because the proportion of biologically resistant population increases, the cancer incidence rate will decrease [7].

2. *Less efficient case ascertainment:* several other competing causes of death are present and cancer is not stated as a cause of mortality in death certificates [7].

To confirm this, we examined the pattern of age-specific incidence rates of breast cancer in the period of 1992-2001 in 10 provinces of Canada. We selected a period instead of a single year in order to remove random variations present in shorter periods. As depicted in Figure 5-7 [139], almost all provinces follow the same pattern as Ontario with the exception of two: New Brunswick and Nova Scotia. Interestingly, in this graph even Manitoba shows a slight decrease in incidence rates for the oldest age group. This can be explained by the possibility of an artefact caused by the random variation in a short one-year period, i.e. only 1998, which was chosen for the original analysis.

a. *provinces with sharp drop in oldest age groups*



b. *provinces with slight drop or increase in oldest age groups*

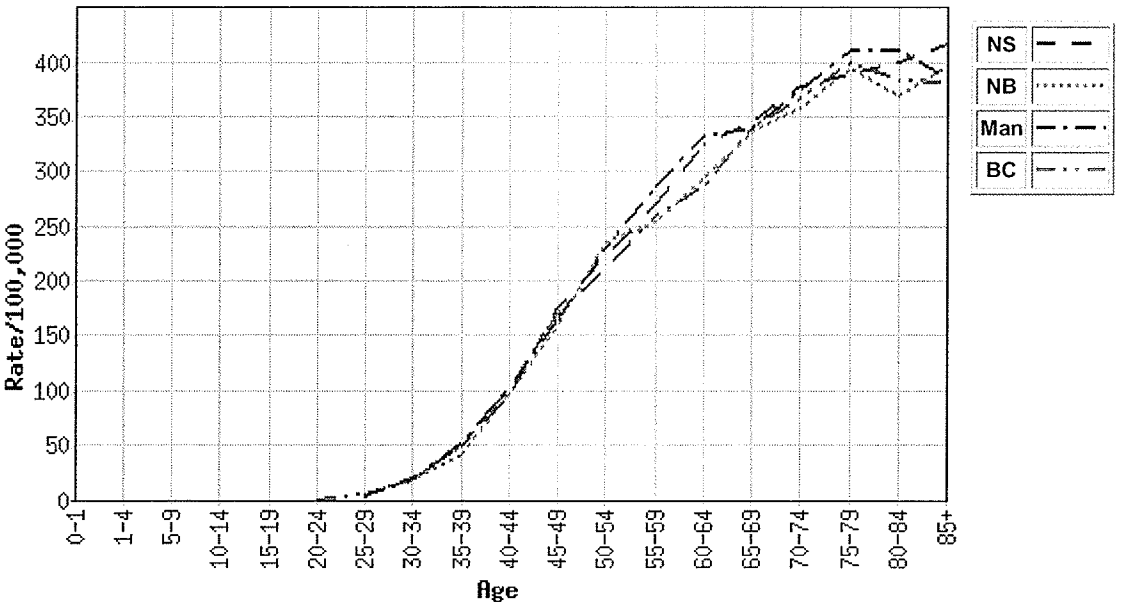


Figure 5-7: Cancer Incidence by Age Group and Province, Cancer of the Breast, Females, 1992-2001, Age-Standardized Incidence Rate per 100,000 (Canada 1991)

Some provinces have a more dramatic age-specific terminal drop, but others show only a slight drop or even an increase. This can be caused by relatively better case ascertainment techniques for old patients in some provinces. The two provinces with a terminal rise in this graph (Nova Scotia and New Brunswick) have confirmed their high data quality by consistently receiving NAACCR certification since 1997. The different patterns observed for Manitoba and Ontario incidence rates may also be explained by more successful case ascertainment techniques in the Manitoba Cancer Registry demonstrated by receiving the gold or silver level of NAACCR certification since 1996[24], while the Ontario Cancer Registry has not achieved certification this consistently [24].

One way to improve this aspect of registration is to collect information from physician offices who may be the only point of contact for some patients, especially for older women. One major obstacle to this is large population size, as in the case of Tehran's and Ontario's cancer registries. This problem makes contact with and access to all physician offices difficult and causes inherent inaccuracy in data from such large populations. A solution for this may be developing local as well as central registries to collect data from smaller subpopulations. This requires more funding which is not usually available in developing registries.

In summary, in this chapter we made an attempt to quantify and remove the effect of differences in process, structure, and data quality measures from reported incidence statistics in the two jurisdictions. The resultant adjusted incidence rates of breast cancer in the order of adjustment are summarized in Table 5-1.

Table 5-1: Summary of adjustments of breast cancer incidence rate in Tehran and Manitoba

Breast cancer incidence rate / Adjustment	Incidence rate in Manitoba /100 000 women	Incidence rate in Tehran /100 000 women
Crude rate	125.9	22.4
Age-standardized (using world standard population)	83.8	27.5
After removing the effect of differences in incidence definition (multiple primary determination rules)	71.5	27.5
After removing the effect of data sources (screening, autopsy)	69.4	27.5
Adjusting for the inaccessible population	69.4	27.9
Adjusting for the incompleteness of registration	70.3	33.5

It is important to notice that although all these adjustments were in the direction of correcting any probable "under-registrations" in Tehran, there is also a high probability of "over-registration" especially in the case of breast cancer. Breast cancer patients generally visit several hospitals and because of absence of a unique identifier, they might be double-registered through multiple sources, i.e. different hospitals or even both through hospitals and vital statistics. Also, as mentioned earlier, the inaccuracy of address item increases the probability of including cases from outside of the coverage population (22 areas of the Tehran Metropolitan Area), which will in turn result in overestimation of incidence rates for Tehran population. Such quite possible influences on the reported rates from Tehran were unfortunately unquantifiable for the current analysis but these effects should ultimately considered for their effect on the adjusted rates.

At last but not least, although the Manitoba Cancer Registry was used as an example of successful cancer registry and a "gold standard" in this study, some results revealed that even long-established and well-known registries, such as the one in Manitoba, are still developing and should still work to improve some aspects of their data. For example, there were structure and process shortfalls (e.g. Manitoba Registry regulations currently lack any penalties for failure to report cancer cases or they require more staff for quality control programs). In addition, this study showed that the position of a quality control technician, which is recommended for continuous quality control to achieve the best quality of data, was not existent in the Manitoba Cancer Registry until 1999. In turn, some of the quality measures of outcome indicated room for improvement. For example, even since the addition of this position, the Manitoba Cancer Registry has identified areas requiring quality improvement, such as the proportion of DCOs (a DCO rate of 1.6% indicates there are still cases which escape being captured by the registry through one of the many other different sources) and measure of completeness of case ascertainment that are not at 100%. Fortunately, quality is considered an ongoing concern, one that is a major focus of continuous analysis and vigilance by the staff of the Manitoba Cancer Registry.

5.6 Study limitations

- The first and most important study limitation was absence of an objective guideline for cancer registries around the world. The fact that Tehran and Manitoba used two different sources as their guidelines, made their comparison difficult. It would be desirable to have an objective set of standards to be used for international comparisons of cancer registries.

- Some of the data quality measures were not available from both cancer registries and, therefore, we were not able to compare those aspects of data quality.

- We were unable to quantify the effect of all the structural and process differences between the two registries, and therefore, we were not able to remove the influence of some important factors such as inaccuracy of incidence or census data.

- And lastly, since the incidence statistics were only available for one year from the Tehran Cancer Registry, an important goal of the study was not achievable. It was desirable to use the data from consequent years to find out the trend of data quality measures in the Tehran Cancer Registry and to predict when these measures will reach a plateau and therefore the incidence statistics can be used confidently for trend analyses and international comparisons.

Chapter 6: Conclusions and Recommendations

6.1 Conclusions

The results of this study demonstrated that the Tehran Cancer Registry, as a developing registry, is faced with many problems but is persevering to keep pace with international standards. There is some evidence of improvement as a result of their efforts, e.g. complete record linkage with vital statistics files for death information was absent for 1998 data but is now available. Some aspects of the cancer registry are expected to improve over time, although relative restrictions on resources and less comprehensive regulations compared to long-standing registries make it difficult for them to achieve high levels of data quality. Recognizing the hard work and dedication of the staff in a developing registry, continued enhancement to structural and process aspects, and ongoing support from international agencies such as IARC and IACR are needed for improvement and better performance of the developing registries. This will, in turn, help to increase international knowledge about cancer determinants and cancer epidemiology, ultimately contributing to international health.

This study showed that the reported incidence rates of breast cancer from international sources are not always accurate, especially when they are estimates. For example, the incidence rate of breast cancer for Iran, reported by GLOBOCAN 2002 [16], is estimated to be 17/100 000 women (standardized to the world standard population) which is approximately 30% lower than the rate reported by this center for 1998, even though the

international estimates refer to a more recent year and rates are expected to have even increased since 1998. The breast cancer rates for Canada are more realistic, at 84/100 000 women for 2002. It is notable that the reported rates for some countries are merely estimates based on averaging the available rates from countries of the same region (e.g. Iran incidence statistics in GLOBOCAN 2000 were only an average of available rates from some Middle Eastern countries [140]) or estimates based on inaccurate data from non-population-based cancer registries in that country (the case for Iran incidence statistics in GLOBOCAN 2002 [16]). Such inaccuracies in the published rates by international agencies could lead to false conclusions about the relative incidence of breast cancer in different countries, e.g. Canada in comparison to Iran.

In this study we used actual data rather than estimates from other countries. The results showed very different rates of breast cancer in the two regions of study. We then removed the effect of differences in registry practices as far as possible. Even after these adjustments, it appeared that there is still a large difference in breast cancer incidence.

Initially, we postulated that the large geographical variations in incidence of breast cancer could be due to two major factors: effectiveness of the cancer registry system and differences in the distribution of risk factors including genetic, life style, and environmental factors. Therefore, after removing the effect of differences in the cancer registration processes, we can conclude that the remaining difference in the statistics is due to variation in risk factor distribution. Evidence supporting this conclusion includes:

1. Analysis of age-specific rates showed a different age distribution of breast cancer cases in the two jurisdictions, with breast cancer occurring at a younger age in

Tehran. These differences may be due to under-registration of older breast cancer patients in Tehran and/or differences in risk factors in younger and older women. However, although the absence of data on older patients may explain the lower incidence rates in the oldest age groups, for the relatively low rates evident for middle aged women differences in risk factors are the most reasonable explanation. It is well established in the literature that the risk factors of breast cancer vary in pre-menopausal and post-menopausal women [131-133]. Since mean age of menopause is quite similar in the two jurisdictions (49.5 and 51 years for Iran and North America respectively [141, 142]), the difference in age specific rates implies that the risk factor differences may have caused the higher incidence of pre-menopausal breast cancer in Tehran population. In Manitoba, risk factors for both pre-menopausal and post-menopausal breast cancer appear to be prevalent.

2. All possible adjustments in this chapter were in the same direction of increasing Tehran rates or decreasing Manitoba rates or decreasing their difference. However, we found some evidence that rates could be over-estimated in the Tehran Cancer Registry: although we could not quantify the effect, the inaccuracy of address item and the fact that Tehran is a referral oncology center likely results in over-estimating the numerator of the incidence rate. There is also the possibility of inaccuracies in Tehran's census data with a tendency towards under-estimating the population because of high levels of migration which would in turn result in over-estimated incidence rates. Therefore, the difference in rates could be even larger than our estimation. However, our analysis provides a conservative

estimate of the difference, which is still substantial. Since differences in registry practices cannot explain the difference in rates, risk factor differences remain as the only other candidate.

6.2 Recommendations

- Firstly and most importantly, international efforts to improve cancer registry systems in developing countries must be continued. This study revealed that the registry staff in developing countries are working hard to establish and improve the cancer registration system in their jurisdictions; however, under-funding and technical problems are issues that are not easily solved without international agency supports. Many of these countries have limited resources for basic healthcare, and there are needs that are more immediate than cancer registries. But the fact that the cancer burden is increasing in these countries and the ability of cancer registries to contribute to national and international cancer control efforts, are important considerations for the not-so-distant cancer crisis.

- Manitoba has benefited considerably from having legislated mandatory reporting of cancer to the cancer registry. The Tehran Cancer Registry could also benefit from such legal support. This would be particularly important for complete case ascertainment, especially as regards accessing patient records from all hospitals.

- International standards for the minimum acceptable level of data quality measures should be developed and posted to serve as targets for registries. These could be

created based on the experience of countries in the same stage of registration to avoid unachievably high standards used by more developed registries.

- Long term stable funding will be important for the Tehran Cancer Registry to guarantee the future of this newly established registry.

- Confidentiality rules need to be documented by the Tehran Cancer Registry and as outlined in IARC/IACR guidelines, the registry staff should sign a confidentiality pledge when first employed.

- The number of staff in the Tehran Cancer Registry is not adequate for their caseload. Ideally the Tehran Cancer Registry should increase the number of staff to about 20 abstractors, although this recommendation is not currently possible without an increase in registry funding.

- It is also recommended that the Tehran Cancer Registry consider employing and training staff for continuous quality control. International agencies can contribute to the improvement of data quality by assisting them with funding and training quality control staff.

- It is essential for every registry to have a detailed manual to increase reliability and consistency of its data. For the Tehran Cancer Registry, this kind of manual could be developed or adapted from neighbouring countries or registries with similar conditions. (The Manitoba Cancer Registry adapted its manual partially from Alberta Cancer Registry but changed it to meet its purposes and considered CCR and NAACCR recommendations which it follows as well.)

- Developing registries could use additional direction on sources for training the staff, and should be sure to learn from other cancer registries worldwide. International organizations such as WHO can support attendance by representatives of developing countries in related international conferences to update and facilitate the adaptation of new knowledge in their countries.

- Follow back of cases, especially with the physician offices is challenging in Tehran. One solution for registries that cover a large population, e.g. Ontario and Tehran is to develop local cancer registries as well as a central cancer registry, which would collect data from the local registries. Budget permitting, collecting information from a smaller subpopulation by a local registry would likely improve access to data for all cases in the population and consequently will improve case ascertainment and completeness of the registry.

- Analysts performing international comparisons health data and specifically cancer data should be aware of differences in definitions among different countries. For example, in this study the definition of histologically confirmed cases differed for Tehran and Manitoba as did the definition of multiple primary tumours. Such differences may result in incomparability and must be considered before performing statistical comparisons.

- When additional years of data are available, a study of the trend of data quality measures in the Tehran Cancer Registry would be useful for predicting when data quality measures should reach a plateau; this will provide guidance as to when reported statistics from a developing registry should be ready to be used

confidently for international comparisons and trend analyses.

- Finally, the results of this study revealed that part of the difference in the geographical variation of breast cancer incidence can be explained by differences in structural and process characteristics, further indicated by data quality measures of the cancer registries. However, a large part of the difference remains unexplained. We recommend comparative studies of risk factors of breast cancer with a special focus on pre-menopausal versus post-menopausal risk factor differences in Canada and Iran. Studying the differences in the distribution of specific characteristics among low incidence and high incidence areas of breast cancer is a promising field for further research about aetiology of breast cancer.

References

1. Jensen OM, Whelan S. Planning a cancer registry. In: Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet R (eds.) Cancer Registration Principles and Methods (IARC Scientific Publication No. 95), IARC: Lyon, France, 1991: 22-28.
2. Shanmugaratnam K. Introduction. In: Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet R (eds.) Cancer Registration Principles and Methods (IARC Scientific Publication No. 95), IARC: Lyon, France, 1991: 1-2.
3. Gillian Matthews. Cancer Registries. In: Leadbeter D (ed.) Harnessing official statistics. Abingdon: Radcliffe Press. Available online at [retrieved April 1, 2005]: http://www.radcliffe-oxford.com/books/samplechapter/3542/ch1.pdf
4. Wagner G. History of cancer registration. In: Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet R (eds.) Cancer Registration Principles and Methods (IARC Scientific Publication No. 95), IARC: Lyon, France, 1991: 3-6.
5. SEER's training website, Cancer Registry Operations & Procedures, Cancer Registration, Unit 2: Types of Cancer registries, Hospital-based registries [retrieved April 1, 2005]: http://training.seer.cancer.gov/module_cancer_registration/unit2_hospital_based.html
6. Jensen AR, Overgaard J, Storm HH. Validity of breast cancer in the Danish Cancer Registry. A study based on clinical records from one county in Denmark. Eur J Cancer Prev 2002; 11:359-64.
7. Parkin DM, Chen VW, Ferlay J, et al. Comparability and Quality Control in Cancer

Registration. IARC Technical report No. 19, 1994; Lyon: France.

8. Storm HH, Dickman PW, Engeland A, et al. Do morphology and stage explain the inferior lung cancer survival in Denmark? Eur Resp J 1999; 13:430–5.
9. Tulinius H, Storm HH, Pukkala E, Andersen A, Ericsson J. Cancer in the Nordic countries, 1981–86. A joint publication of the five Nordic Cancer Registries. APMIS 1992; 31(Suppl): 1–194.
10. Engeland A, Haldorsen T, Dickman PW, et al. Relative survival of cancer patients – a comparison between Denmark and the other Nordic countries. Acta Oncol 1998; 37: 49–59.
11. World Health Organization. Cancer. In: The World Health Report. Life in the 21st century: A vision for all. Geneva: World Health Organization; 1998:88-90.
12. National Cancer Institute of Canada: Canadian Cancer Statistics 2003: www.cancer.ca
13. Friedenreich C, Aronson KJ, DeKoning k, et al. Review of Lifestyle and Environmental Risk Factors for Breast Cancer, Report of the Working Group on Primary Prevention of Breast Cancer. Canadian Breast Cancer Initiative [summary report], Minister of Public Works and Government Services Canada, 2001.
14. Miller AB, Bulbrook RD. UICC multidisciplinary project on breast cancer: the epidemiology, aetiology and prevention of breast cancer. Int J cancer 1986; 37: 173-177.
15. Mettlin C. Global breast cancer mortality statistics. CA Cancer J Clin 1999; 49:138–144.
16. IARC database, GLOBOCAN 2002 [retrieved June 16, 2005]: http://www-dep.iarc.fr/GLOBOCAN/database.htm

17. Hilsenbeck SG, Glaefke GS, Feigl P, et al. Quality Control for Cancer Registries. Washington, DC: US Department of Health and Human Services; 1985.

18. Prior P, Woodman CBJ, Collins S. International differences in survival from colon cancer: More effective care versus less complete cancer registration. Br J Surg 1998; 85: 101-104.

19. Parkin DM. Comparability and quality of data. In: Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB (eds.) Cancer Incidence in Five Continents, Vol. VIII (IARC Scientific Publications No. 155), IARC: Lyon, France, 2002.

20. Parkin DM, Sanghvi LD. Cancer registration in developing countries. In: Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet R (eds.) Cancer Registration Principles and Methods (IARC Scientific Publication No. 95), IARC: Lyon, France, 1991: 185-198.

21. Pisani P. Breast cancer: geographic variation and risk factors. J Environ Pathol Toxicol Oncol 1992; 11(5-6):313-6.

22. Al-Zahrani A, Baomer A, Al-Hamdan N, et al. Completeness and validity of cancer registration in a major public referral hospital in Saudi Arabia. Ann Saudi Med 2003; 23: 6-9.

23. Cancer Institute of Iran website, Cancer Registry, Cancer in Iran [retrieved June 16, 2005]: http://medicine.tums.ac.ir/cancer/canhist_files/frame.htm

24. North American Association of Central Cancer Registries, Registry Certification [retrieved March 7, 2005]: www.naaccr.org/index.asp?Col_SectionKey=12&Col_ContentID=54

25. Jensen OM, Storm HH. Purposes and uses of cancer registration. In: Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet R (eds.) Cancer Registration Principles and Methods (IARC Scientific Publication No. 95), IARC: Lyon, France, 1991: 7-21.

26. CancerCare Manitoba website, 2002 annual report [retrieved April 1, 2005]: http://www.cancercare.mb.ca/EPI/pdfs/2002Annual_report.pdf

27. Shamseddine A, Sibai AM, Gehchan N, et al. Cancer incidence in postwar Lebanon: findings from the first national population-based registry, 1998. Ann Epidemiol 2004; 14:663-8.

28. Traina A, Cusimano R, Liquori M, et al. Breast cancer incidence in the city and province of palermo in 1999-2002: a breast cancer registry report. Ann N Y Acad Sci 2004; 1028:473-80.

29. Quinn M, Babb P. Patterns and trends in prostate cancer incidence, survival, prevalence and mortality. Part I: international comparisons. BJU Int 2002; 90:162-73.

30. Rosen M, Lundin A, Nystrom L, et al. Incidence and mortality of breast cancer during a 25-year period. International and regional comparisons. Lakartidningen 2000; 97:294-9.

31. Silverstein MD, Nietert PJ, Ye X, et al. Racial disparities in the incidence of lung cancer: the Savannah River Region Health Information System cancer registry, 1991-95. J Health Care Poor Underserved 2003; 14:23-33.

32. Smith LH, Danielsen B, Allen ME, et al. Cancer associated with obstetric delivery: results of linkage with the California cancer registry. Am J Obstet Gynecol 2003; 189:1128-35.

33. Cooksley CD, Hwang LY, Waller DK, et al. HIV-related malignancies: community-based study using linkage of cancer registry and HIV registry data. Int J STD AIDS 1999; 10: 795-802.

34. Franceschi S, Dal Maso L, Arniani S, et al. Risk of cancer other than Kaposi's sarcoma and non-Hodgkin's lymphoma in persons with AIDS in Italy. Cancer and AIDS Registry Linkage Study. Br J Cancer 1998; 78: 966-70.

35. Young TK. Population Health: Concepts and Methods. New York: Oxford University Press, 1998.

36. Yale Cancer Center web site. Rapid Case Ascertainment [retrieved May 5, 2005]: http://info.med.yale.edu/ycc/rs02j.htm#

37. Westergaard T, Melbye M, Pedersen JB, et al. Birth order, sibship size and risk of Hodgkin's disease in children and young adults: a population-based study of 31 million person-years. Int J Cancer 1997; 72:977-81.

38. SEER's training website, Cancer Registry Operations & Procedures, Registry Operations, Unit 1, Section 3: population-based registries [retrieved April 1, 2005]: http://training.seer.cancer.gov/module_registry_operations/unit01_sec03_population.html

39. CDC website, Cancer Prevention and Control, 2004-2005 Fact Sheet, Cancer Registries: Foundation for Cancer Prevention and Control [retrieved April 1, 2005]: http://www.cdc.gov/cancer/npcr/about2004.htm

40. Parkin DM, Hakulinen T. Analysis of survival. In: Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet R (eds.) Cancer Registration Principles and Methods (IARC Scientific Publication No. 95), IARC: Lyon, France, 1991: 159-176.

41. Davis FG, McCarthy BJ, Berger MS. Centralized databases available for describing primary brain tumor incidence, survival, and treatment: Central Brain Tumor Registry of the United States; Surveillance, Epidemiology, and End Results; and National Cancer Data Base. Neuro-oncol 1999; 1:205-11.

42. SEER's training website, Cancer Registry Operations & Procedures, Registry Operations, Unit 1, Section 2: hospital-based registries [retrieved April 1, 2005]: http://training.seer.cancer.gov/module_registry_operations/unit01_sec02_hospital.html

43. SEER's training website, Cancer Registry Operations & Procedures, Cancer registration, Unit 2: Types of registries [retrieved April 1, 2005]: http://training.seer.cancer.gov/module_cancer_registration/unit2_registry_types.html

44. Young JL. The hospital-based cancer registry. In: Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet R (eds.) Cancer Registration Principles and Methods (IARC Scientific Publication No. 95), IARC: Lyon, France, 1991: 177-184.

45. Powell J. Data sources and reporting. In: Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet R (eds.) Cancer Registration Principles and Methods (IARC Scientific Publication No. 95), IARC: Lyon, France, 1991: 29-42.

46. South Carolina Department of Health and Environmental Control website, South Carolina Central Cancer Registry [retrieved April 1, 2005]: http://www.scdhec.net/co/phsis/biostatistics/SCCCR/AboutARegistry.htm

47. Trent Cancer Registry website, Cancer Registration in Trent [retrieved April 1, 2005]: http://www.trentcancer.nhs.uk/registration.html

48. Texas Department of State Health Services website, Electronic Pathology Laboratory

Pilot Project [retrieved April 1, 2005]: http://www.tdh.state.tx.us/tcr/EPLP_Update0604.html

49. Seddon DJ, Williams EM. Data quality in population-based cancer registration: an assessment of the Merseyside and Cheshire Cancer Registry. Br J Cancer 1997; 76: 667-674.

50. CancerCare Manitoba, Epidemiology and Cancer Registry Unit [retrieved April 1, 2005]: http://www.cancercare.mb.ca/EPI/index.shtml

51. Ministry of Health Malaysia website, Clinical Research Center, National Cancer Registry, About NCR [retrieved April 1, 2005]: http://www.crc.gov.my/ncr/about.htm

52. Karagas MR, Thomas DB, Roth GJ, Johnson LK, Weiss NS. The effects of changes in health care delivery on the reported incidence of cutaneous melanoma in western Washington State. Am J Epidemiol 1991; 133:58-62.

53. Stefoski Mikeljevic J, Johnston C, Adamson PJ, Wright A, Bishop JA, Batman P, Neal RD, Forman D. How complete has skin cancer registration been in the UK? A study from Yorkshire. Eur J Cancer Prev 2003; 12:125-33.

54. G. ENOW-OROCK. Cancer Registration: Principles and Methods. Yaounde Cancer Registry [retrieved April 1, 2005]:

http://64.233.183.104/search?q=cache:0AQoh6Mi-XIJ:www.gfmer.ch/Medical_education_En/Cameroon/Pdf/CANCER_REGISTRATION.pdf+autopsy+cancer+registry+data+source&hl=en

55. University of Manitoba website, Centers, Manitoba Center for Health policy, Use of

ICD-9 Codes in Vital Statistics Records [retrieved April 1, 2005]: http://www.umanitoba.ca/centres/mchp/concept/dict/vital_stats_icd9.html

56. Statistics Canada website, Canadian Cancer registry [retrieved April 1, 2005]: http://www.statcan.ca/cgi-bin/imdb/p2SV.pl?Function=getSurvey&SDDS=3207&lang=en&db=IMDB&dbg=f&adm=8&dis=2

57. Dolson DD, Gaudette LA. Estimating current year cancer incidence and mortality in Canada: an evaluation of data sources and methodology (Technical report). Ottawa: Statistics Canada, Canadian Center for Health Information, 1988; 11-16.

58. MacLennan R. Items of patient information which may be collected by registries. In: Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet R (eds.) Cancer Registration Principles and Methods (IARC Scientific Publication No. 95), IARC: Lyon, France, 1991: 43-63.

59. Skeet RG. Quality and quality control. In: Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet R (eds.) Cancer Registration Principles and Methods (IARC Scientific Publication No. 95), IARC: Lyon, France, 1991: 101-107.

60. Parkin DM, Wabinga H, Nambooze S. Completeness in an African cancer registry. Cancer Causes Control 2001; 12:147-152.

61. Kuntoro, LaPorte RE, Mazumdar S. Approaches to quality control with an application to a new cancer registry in a developing country. J Clin Epidemiol 1994; 47: 779-786.

62. Havener L (Ed). Standards for Cancer Registries Volume III: Standards for Completeness, Quality, Analysis, and Management of Data. Springfield (IL): North

American Association of Central Cancer Registries, 2004, 180 pp; available online at [retrieved April 1, 2005]: http://www.naaccr.org/filesystem/pdf/NAACCR%20Volume%20III%20Final%20PDF%20File%2011-29-04.pdf

63. Day NE, Davies TW. Cancer registration: integrate or disintegrate? BMJ 1996; 313:896.

64. Expert Advisory Group on Cancer. A policy framework for commissioning cancer services. A report by the to the chief medical officers of England and Wales. London: Department of Health, 1995.

65. Goldberg J, Gelfand HM, Levy PS. Registry evaluation methods: a review and case study. Epidemiol Rev 1980; 2: 210-220.

66. Pennsylvania Cancer registry. Quality Assurance in Data Base Systems. Pennsylvania Department of Health; 1984.

67. Giles GG, Thursfield V. Cancer statistics: everything you wanted to know about the cancer registry data but were too afraid to ask. ANZ J Surg 2004; 74: 931-4.

68. Lang K, Magi M, Aareleid T. Study of completeness of registration at the Estonian cancer registry. Eur J Cancer Prev 2003; 12: 153-156.

69. Warnakulasuriya KAAS, Acworth P, Bell J, et al. Incompleteness of oral cancer registration in south-east England, 1971-87. Br J Cancer 1994; 70: 736-738.

70. Rubin G, Umbach D, Shyu S, et al. Using Mark-Recapture methodology to estimate the size of population at risk for sexually transmitted diseases. Stat Med 1992; 11:1533-49.

71. Band PR, Gaudette LA, Hill GB, et al. The making of the Canadian cancer registry: cancer incidence in Canada and its regions, 1969 to 1988. Ottawa: Statistics Canada,

Canadian Council of Cancer Registries Health and Welfare Canada, 1993.

72. DeVor RE, Chang T, Sutherland JW. Statistical Quality Design and Control: Contemporary concepts and Methods. New York: Macmillan; 1992:4315-451.

73. Wolfgang PE. Cancer Incidence by County 1983-1987 (technical report). New York State Department of Health; 1987.

74. Dickinson HO, Salotti JA, Birch PJ, et al. How complete and accurate are cancer registrations notified by the National Health Service Central Register for England and Wales? J Epidemiol Community Health 2001; 55: 414-422.

75. Hawaii Tumor Registry. Proposal for Funding the Hawaii Tumor Registry 1 November 1989-31 October 1996 (Technical Report). Hawaii Tumor Registry; 1986.

76. Mukherjee AK, Leck I, Langley FA, et al. The completeness and accuracy of health authority and cancer registry records according to a study of ovarian neoplasms. Public Health 1991; 105: 69-78.

77. Brewster D, Muir C, Crichton J. Registration of colorectal cancer in Scotland: An assessment of data accuracy based on review of medical records. Public Health 1995; 109: 285-292.

78. Fulton JP, Buechner JS, Stanis D, et al. Assuring the quality of Cancer Registration in Rhode Island. R I Med J 1988; 71: 337-346.

79. SEER's training website, Cancer Registry Operations & Procedures, Cancer Registration, Unit 3: Cancer Data, Process of Data Collection [retrieved April 1, 2005]:

http://training.seer.cancer.gov/module_cancer_registration/unit3_how_collect.html

80. Clarke EA, Marrett LD, Kreiger N. Twenty Years of Cancer Incidence, 1964-1983: The Ontario Cancer Registry. Toronto: Ontario Cancer Treatment and Research Foundation, 1987.

81. Clarke EA, Marrett LD, Kreiger N. Appendix 3 (c) Cancer registration in Ontario: a computer approach, the Ontario Cancer Registry, OCTRF, Toronto, Ontario. In: Jensen OM, Parkin DM, MacLennan R, Muir CS, Skeet RG, eds. Cancer Registration: Principles and Methods. Lyon: International Agency for Research on Cancer, 1991:246-57.

82. Cancer Care Ontario website, methods used by Ontario Cancer Registry [retrieved April 10, 2005]: http://www.cancercare.on.ca/prevention_601.htm

83. Agency for Toxic Substances and Disease Registry website, Division of Health Assessment and Consultation, Health Outcome Data Evaluation [retrieved April 1, 2005]: http://www.atsdr.cdc.gov/HAC/pha/kafb2/kab_p1.html

84. Muir CS, Demaret E. Cancer registration: legal aspects and confidentiality. In: Jensen OM, Parkin DM, Maclennan R, Muir CS, Skeet R (eds.) Cancer Registration Principles and Methods (IARC Scientific Publication No. 95), IARC: Lyon, France, 1991: 199-207.

85. Watkins S. Legal and ethical aspects of cancer data. In: Fritz AG, Hutchison CL, Roffers SD (eds.) Cancer Registry Management: Principles and Practice, Kendall/Hunt: United States, 1997: 52-57.

86. Faris TH. Health information privacy and security. In: Fritz AG, Hutchison CL, Roffers SD (eds.) Cancer Registry Management: Principles and Practice, Kendall/Hunt: United States, 1997: 52-57.

87. IACR website, Guidelines of Confidentiality in Population-based Cancer Registration [retrieved April 2, 2005]: http://www.iacr.com.fr/confidentiality2004.pdf

88. Tingulstad S, Halvorsen T, Norstein J, et al. Completeness and accuracy of registration of ovarian cancer in the Cancer Registry of Norway. Int J Cancer 2002; 98: 907-911.

89. Crocetti E, Miccinesi G, Paci E, et al. An application of the two-source capture-recapture method to estimate the completeness of the Tuscany Cancer Registry, Italy. Eur J Cancer Prev 2001; 10: 417-423.

90. Brewster DH, Stockton D, Harvey J, et al. Reliability of cancer registration data in Scotland, 1997. Eur J Cancer 2002; 38: 414-417.

91. Kyllonen LE, Teppo L, Lehtonen M. Completeness and accuracy of registration of colorectal cancer in Finland. Ann Chir Gynaecol 1987; 76: 185-90.

92. Schouten LJ, Van-der-Does-Van-den-Berg A, Otter R, et al. Accuracy and completeness of the registration of childhood leukaemia in The Netherlands, 1989-1992. Eur J Cancer Part A 1997; 33: 891-894.

93. Vickers N, Pollock A. Incompleteness and retrieval of case notes in a case note audit of colorectal cancer. Qual Health Care 1993; 2: 170-4.

94. Phekoo K, Moller H, Richards M, et al. Comparison of a specialist haematological malignancy database against a regional cancer registry: Case ascertainment and diagnostic accuracy. Br J Haematol 2002; 119: 697-705.

95. Astrom M, Bodin L, Tidefelt U. Adjustment of incidence rates after an estimate of completeness and accuracy in registration of acute leukemias in a Swedish population. Leuk Lymphoma 2001; 41: 559-570.

96. Bah E, Hall AJ, Inskip HM. The first 2 years of the Gambian National Cancer Registry. Br J Cancer 1990; 62: 647-50.

97. Bah E, Parkin DM, Hall AJ, et al. Cancer in the Gambia: 1988-97. Br J Cancer 2001; 84: 1207-14.

98. Innos K, Rahu M. Epidemiological data sources in Estonia: a survey of registries and databases. J Epidemiol Biostat 2000; 5: 293-302.

99. Harirchi I, Ebrahimi M, Zamani N, et al. Breast cancer in Iran: a review of 903case records. Public Health 2000; 114: 143-145.

100. The Center for Disease Control and Prevention website, Cancer Registries: The Foundation for Cancer Prevention and Control [retrieved March 6, 2005]: http://www.cdc.gov/cancer/npcr/about2004.htm

101. Clive RE. Introduction to Cancer Registries. In: Fritz AG, Hutchison CL, Roffers SD (eds.) Cancer Registry Management: Principles and Practice, Kendall/Hunt: United States, 1997.

102. Donabedian A. Evaluating the Quality of Medical Care. Milbank Mem Fund Q 1966; 44: 166-206.

103. Parkin DM. President of IACR, Personal Communications with the author, June 2005.

104. Zinn JS, Mor V. Organizational structure and the delivery of primary care to older Americans. Health Serv Res 1998; 33: 354-80.

105. Donabedian A. The Quality of Care: How Can It Be Assessed? JAMA 1988; 260: 1743-48.

106. Microsoft Excel 2002 (10.6501.6626) SP3.

107. Natural Resources of Canada website, the Atlas of Canada, population pyramid of Manitoba by age and sex, 1996 [retrieved June 19, 2005]: http://atlas.gc.ca/site/english/maps/peopleandsociety/age/age1996/man_graph.gif/image_view

108. Schuz J, Schon D, Batzler W, et al. Cancer registration in Germany: current status, perspectives and trends in cancer incidence 1973-93. J Epidemiol Biostat 2000; 5:99-107.

109. Hong Kong cancer registry website, Frequently Asked Questions, What is the quality of the Hong Kong Cancer Registry data? [retrieved June 19, 2005]: http://www3.ha.org.hk/cancereg/faq.asp#Q3

110. Queensland Health website, Queensland cancer Registry [retrieved June 19, 2005]: http://www.health.qld.gov.au/hic/QHID/html/can_QCRdetails.asp

111. Bhurgri Y, Bhurgri A, Hasan SH. Comparability and Quality Control in Cancer Registration: Karachi (Data Monitoring 1995-2001). J Pak Med Assoc 2002; 52: 301-7.

112. California Healthline website, Health Privacy, past issues September 28, 2004. Bay Area Hospitals, Researchers Debate Privacy Policies for State Cancer Registry, available online at [retrieved July 29, 2005]: http://www.californiahealthline.org/index.cfm?Action=dspItem&itemID=105926&ClassCD=CL141

113. California Department of Health services, California Cancer Registry program. Policies and Procedures for Access to Reporting Entity Records and Collection of Confidential Data. Available online at [retrieved July 29, 2005]:

http://www.ccrcal.org/pdf/CCRfacilityAccessPolicy-v04.1-051705.pdf.

114. Government of British Columbia website, Ministry of Sustainable Resource Management, Resource Information Standards Committee, Guidelines for designing and implementing a water quality monitoring program in British Columbia, Recommended steps for the monitoring program design [retrieved July 7, 2005]: http://srmwww.gov.bc.ca/risc/pubs/aquatic/design/design-02.htm#4.

115. Meneck HR, Parkin DM, eds. Directory of computer systems used in cancer registries. IARC: Lyon, France, 1986.

116. Fritz A, Percy C. Implementing ICD-O-3: Impact of the New Edition. SEER Program, National Cancer Institute, available online at [retrieved July 8, 2005]: http://training.seer.cancer.gov/module_icdo3/downloadables/ICD-O-3%20abstract%20n%20article%20WORD.doc.

117. Miller BA, Feuer EJ, Hankey BF. The increasing incidence of breast cancer since 1982: relevance of early detection. Cancer Causes Control 1991; 2: 67-74.

118. White E, Lee CY, Kristal AR. Evaluation of the increase in breast cancer incidence in relation to mammography use. J Natl Cancer Inst 1990; 82: 1546-52.

119. Liff JM, Sung JF, Chow WH, et al. Does increased detection account for the rising incidence of breast cancer? Am J Public Health 1991; 81: 462-5.

120. Feuer EJ, Wun LM. How much of the recent rise in breast cancer incidence can be explained by increases in mammography utilization? A dynamic population model approach. Am J Epidemiol 1992; 136: 1423-36.

121. Sternby NH. The role of autopsy in cancer registration in Sweden, with particular reference to findings in Malmo. (IARC Scientific publication No. 112). IARC: Lyon, France 1991: 217-22.

122. Saxen EA. Trends: facts or fallacy? In: Magnus K (ed.) Trends in Cancer Incidence: Causes and Practical Implications. Hemisphere: Washington, DC, 1982: 5-16.

123. CancerCare Manitoba website, Prevention & Screening, Manitoba Breast Screening Program, Information for Health Professionals, 1995-2003 Statistical Report, available online at [retrieved July 8, 2005]:
http://www.cancercare.mb.ca/MBSP/pdfs/FS_Results95-03.pdf

124. CancerCare Manitoba website, Prevention & Screening, Manitoba Breast Screening Program, Who is eligible for this program? [retrieved July 8, 2005]:
http://www.cancercare.mb.ca/MBSP/mbsp_eligibility.shtml

125. Turano L, Laudico A, Esteban D, et al. Reduction of Death Certificate Only (DCO) Registrations by Active Follow Back. Asian Pac J Cancer Prev 2002; 3: 133-135.

126. Turner D, Kliewer E. Manitoba Cancer Registry Record Linkage Project (Case Ascertainment). Department of Epidemiology and Cancer Registry, CancerCare Manitoba; 2003.

127. [Final Report of the Quality Control Project of the Tehran Cancer Registry in 1998], unpublished report of the Tehran Cancer Registry, Source: Mosavi-Jarrahi A, Principal Investigator of the Tehran Cancer Registry Project, Personal Communications with the author, May 2005.

128. Parkin DM, Whelan SL, Ferlay J, Raymond L, and Young J (eds.) Cancer Incidence in Five Continents, Vol. VII (IARC Scientific Publications No. 143), IARC: Lyon, France, 1997.

129. Frost & Sullivan website, Frost & Sullivan healthcare practice, Tackling the Essentials to Successfully Fight Cancer - Frost & Sullivan's Oncology Decision Support Database, 2004; 2: available online at [retrieved July 9, 2005]: http://www.frost.com/prod/servlet/cpo/22745285

130. Hilsenbeck SG, Glaefke GS, Feigl P, et al. Quality Control for Cancer Registries. 1985, US Dept of Health and Human Services.

131. Friedenreich CM. Physical activity and breast cancer risk: the effect of menopausal status. Exerc Sport Sci Rev 2004; 32: 180-4.

132. Goodstine SL, Zheng T, Holford TR, et al. Dietary (n-3)/(n-6) fatty acid ratio: possible relationship to premenopausal but not postmenopausal breast cancer risk in U.S. women. J Nutr 2003; 133: 1409-14.

133. Hirose K, Tajima K, Hamajima N, et al. Association of family history and other risk factors with breast cancer risk among Japanese premenopausal and postmenopausal women. Cancer Causes Control 2001; 12: 349-58.

134. Moolgavkar SH, Stevens RG, Lee JA. Effect of age on incidence of breast cancer in females. J Natl Cancer Inst 1979; 62: 493-501.

135. [Final Report of the Research Project of the National Cancer Registry: Goals, Operation Report, and Project Progress]. Mohagheghi MA, Mosavi-Jarrahi A, Mortazavi H. Report of the year 1998; April 2002.

136. Kliewer E, Mayer T, Wajda A. The Health of Manitoba's Métis Population and Their Utilization of Medical Services: A pilot Study. Manitoba Health, CancerCare Manitoba joint report; May 2002.

137. Unpublished data from Imam Khomeini Hospital Admission Unit, Personal Communications, July 2005.

138. Cook PJ, Doll R, Fellingham SA. A mathematical model for the age distribution of cancer in man. Int J Cancer 1969; 4: 93-112.

139. Public Health Agency of Canada website, Cancer Surveillance Online, Cancer Incidence Charts, Cancer Incidence by Age Group [retrieved July 30, 2005]: http://dsol-smed.phac-aspc.gc.ca/dsol-smed/cancer/c_age_e.html

140. Ferlay J, Bray F, Pisani P, Parkin DM. Cancer Incidence, Mortality, and Prevalence Worldwide. GLOBOCAN 2000, IARC Press: Lyon, France, 2001.

141. Mohammad K, Sadat Hashemi SM, Farahani FK. Age at natural menopause in Iran. Maturitas 2004; 49: 321-6.

142. Bromberger JT, Matthews KA, Kuller LH, et al. Prospective study of the determinants of age at menopause. Am J Epidemiol 1997; 145: 124-33.

Appendix 1

Questionnaire I

(To be filled in by the head of the registry)

Study title: Are breast cancer incidence statistics internationally comparable? The effect of cancer registration practices on the data.

Name of registry center: **Date:**

Thanks for taking the time to participate in this study. This questionnaire consists of four parts. The first part is background information on breast cancer incidence statistics derived from published reports from Tehran and Manitoba cancer registries and transformed by investigators. The second part consists of questions that are aimed at describing the operation of the center you are working at. The third part asks about data quality measures that are available from your center. And finally, the fourth part asks about incidence definitions in your center. Please answer the questions based on your knowledge from the center you are working at.

Note 1: You have the choice of "no answer" for uncertain questions.

Note 2: "Cancer" includes "all invasive cancers excluding non-melanoma skin cancers" and "breast cancer" includes all cases of "invasive" breast cancer.

Section 1 (Background):

What is the most recent incidence rate of breast cancer that has been reported from both jurisdictions? ———————— for the year ———

How was the rate calculated (please specify how the numerator and denominator are measured)?

Numerator

———— = ————————————

Denominator

Is it crude or standardized? ————————

World Standard Population will be used for standardization if this process was required.

What method of standardization was used? Direct □ Indirect □
What is the standardized rate for each jurisdiction? Tehran: _____ Manitoba:_____

Section 2 (Registry Operation):

When did the center start working? Year ————
What kind of registry is it now? Population-based □ Hospital-based □
When did it become population-based? Year————
What area does it cover and who are defined as its residents? _____
What sources are used for data collection?
Medical records □ Outpatient clinics □ Private clinics and hospitals □
Pathology laboratories □ Autopsy services □ Haematology laboratories □
Death certificate □ General practitioners □ Hospices □ Health insurance □ Screening programs □ Central population register □
What is the method of data collection? Active □ Passive □
What data items are collected?
Name□ Sex□ Date of birth or Age□ Address□ Ethnic group□ Incidence date□
Most valid basis of diagnosis□ Topography (site)□ Morphology (histology)□
Behaviour□ Source of information□ Index number□ Personal identification number□
Place of birth□ Marital status□ Nationality□ Religion□ Occupation□ Certainty of diagnosis□ Country of birth of father and/or mother□ Method of first detection□
Multiple primaries□ Laterality□ Initial treatment□ Date of last contact□ Status at last contact□ Date of death□ Cause of death□ Place of death□ Data source (physician, laboratory, etc.) □ Actual source (name of the source) □ Date of registration□
Others ————
What system of coding is used for:
Topography: ICD-9□ ICD-10□ ICD-O□ If ICD-O is used edition_____ Others____
Morphology: ICD-9□ ICD-10□ ICD-O□ If ICD-O is used edition _____ Others___
Behaviour: ICD-9□ ICD-10□ ICD-O□ If ICD-O is used edition_____ Others____
How is the data abstracted? Computerized □ Manually □
How is the data stored? Computerized □ Manually □

Section 3 (Data Quality Measures):

Please provide any measures that are available for the year under study and if these measures are also available for previous years please provide answers for 5 most recent years.

Measures of case-finding completeness:

Is DCO rate calculated for breast cancer? Yes □ No □

If yes, what is this rate? ————

If yes, how was it calculated?

Numerator

————— = ————————

Denominator

Are there any independent case ascertainment studies performed in your registry center?

Yes □ No □

If yes, what is the estimate of completeness in percent? %————

Is observed/expected ratio calculated for breast cancer? Yes □ No □

If yes, what is the ratio? ————

How was it calculated?

Numerator

————— = ————————

Denominator

Is incidence/mortality rate ratio calculated for breast cancer?

Yes □ No □

If yes, what is the ratio? ————

How was it calculated?

Numerator

————— = ————————

Denominator

Measures of item completeness:

Is there any study which has drawn Shewhart control chart or have measured unknown percent for important data items (age, sex, address)? Yes □ No □

If yes, what is the percent of missing data for each of the above items or which do not meet completeness requirements?_____

Is the percent of cases with unknown origin calculated? Yes □ No □
If yes, what is this percent? % ————

Measures of accuracy and reliability:
Is the percent of histologically confirmed cases calculated for breast cancer cases or all cancer sites? Yes □ No □
If yes, what does histologically confirmed include?
Pathology report □ haematology report □ cytology report □
What is the percent? For breast cancer: %———— For all cancers: %————
Has any re-abstracting audits been performed? Yes □ No □
If yes, what is the estimated accuracy? %————
Are edits routinely performed? Yes □ No □
If yes, what percent have passed final edits? %————
Is there any study available on inter-abstractor agreement for reliability? Yes □ No □
If yes, what is the kappa statistics? ————

Measures of timeliness:
Is there any measure of timeliness available for this center? Yes □ No □
If yes, what measure is used?
Accrual method (% of cases diagnosed within X months of closing a diagnosis year) □
Median diagnosis to registration interval □
What is the available measure?
%———— of cases are diagnosed within —— months of closing a diagnosis year
Median diagnosis to registration interval is——months

Section 4 (Comparability):

What definition is used for distinction between recurrence or extension of an existing cancer and development of a new primary?

Is screening used as a means for case-finding? Yes □ No □

Is autopsy used as a means for case-finding? Yes □ No □

Thanks for your participation.
☺

Appendix 2

Questionnaire II

Study title: Are breast cancer incidence statistics internationally comparable? The effect of cancer registration practices on the data.

Name of registry center: **Date:**

Thanks for taking the time to participate in this study. This questionnaire consists of 35 questions which ask about standard quality control procedures that are employed in your center. Please answer these questions based on your knowledge from the center you are working at. For the questions that you answered yes, please explain the procedure briefly with reference to important details and for the questions that you answered no, please highlight the important obstacles for performing that procedure.
Note: You have the choice of "no answer" for uncertain questions.

Quality Assurance Procedures

1. Is cancer registry authorized by any legislation and/or regulations? Yes □ No □

If the answer is yes, please answer questions 1.1-1.7 about any indication of the following in the legislation and/or regulations:

1.1 Are standards for reporting requirements (e.g. terminology definitions) stated?

Yes □ No □

_____

_____

1.2 Is there any statement about providing access to patient records by relevant facilities?

Yes □ No □

_____

_____

1.3 Are there any penalties for failure to report cases or grant access?

Yes □ No □

1.4 Are any standards for data quality stated (e.g. DCOs should be less than 5%)?

Yes □ No □

1.5 Are there any standards for confidentiality and disclosure of data?

Yes □ No □

1.6 Are the registry staff protected from liability for the release of the record information?

Yes □ No □

1.7 Do the legislation and/or regulations specify source of funding of the central registry?

Yes □ No □

2. Are reportable tumours precisely defined (e.g. ambiguous terminology, reference date)?

Yes □ No □

3. Is the number of staff based on estimated number of case reports to the registry?

Yes □ No □

4. Are the staff specifically trained for the activities they do?

Yes □ No □

5. Is continuing education provided to cancer registry staff?

Yes □ No □

6. Does the registry have access to 100% of the hospitals in its reporting area?

Yes □ No □

7. Does the registry obtain information about cases completely diagnosed and treated outside hospital settings?

Yes □ No □

8. Does the registry follow-back to physicians' offices?

Yes □ No □

9. Does the registry notify all reporting facilities about reporting requirements (e.g. data items to be collected, all relevant considerations such as data confidentiality)?

Yes □ No □

10. Does the registry capture tumours of all at risk population in the coverage area?

Yes □ No □

11. Is registry data collected and kept with careful confidential considerations to prevent any unauthorized access?

Yes □ No □

12. Do the staff sign confidential pledge?

Yes □ No □

13. Are "death certificate only" cases followed back before being registered as DCOs?

Yes □ No □

14. Is there any data linkage between the complete file of registry for a specific year with completed file of vital statistics?

Yes □ No □

15. Is there any training for registry staff on case reportability?

Yes □ No □

16. Is there any training for the staff for rules of multiple primary determination?

Yes □ No □

17. Are there regular audits (independent reviews) for completeness of case finding?

Yes □ No □

18. Are there regular recoding audits?

Yes □ No □

19. Are there regular re-abstracting audits?

Yes □ No □

20. Does the registry compare expected and observed cases at regular intervals in a year?

Yes □ No □

21. Does the center monitor if incidence is greater than mortality rate for all cancer sites?

Yes □ No □

22. Are quality control programs part of the registry activities?

Yes □ No □

23. Is there adequate funding available for quality control programs?

Yes □ No □

24. Are there staff determined for quality control activities?

Yes □ No □

25. Is there any manual which documents completely the current and historic practices?

Yes □ No □

If yes, answer next question:

25.1 Does this document include definitions and methods used by the registry?

Yes □ No □

26. Are the edits used for data entered to the registry system?

Yes □ No □

27. Does the registry provide process controls (monitor statistically the results that are aggregated to find if they are within normal limits by examining errors and stability of data over time and across regions)?

Yes □ No □

28. Are detected errors fed back to the staff?

Yes □ No □

Thanks for your participation.

☺

Appendix 3

RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

Title of Study: "Are breast cancer incidence statistics internationally comparable? The effect of cancer registration practices on the data."

Principal Investigator: "Parisa Airia,
Manitoba, phone
Supervisor: "Dr. Donna Turner,

Sponsor: University of Manitoba

You are being asked to participate in this study since you are among the most knowledgeable people regarding cancer registration in this center.
A total of 10-15 participants will participate in this study. Please take your time to review this consent form and discuss any questions you may have with the study staff. By filling in the questionnaire, you will demonstrate your consent for participation in this study.

Purpose of Study

This research study is being conducted to find out the influence of differences in cancer registration practices on geographical variations in breast cancer incidence rates, since differences in cancer registration efficacy might result in differences in quality of data reported by these registries. We also want to demonstrate the types of problems encountered by developing registries to build an efficient system, recognizing and appreciating their efforts to do so despite the difficulties.

Study procedures

This study will compare two cancer registries from the Cancer Institute of Iran in Tehran, Iran and CancerCare Manitoba in Winnipeg, Canada. Review of publications and two questionnaires, one of which will be filled in by head of the cancer registries and the other filled in by the key informants from the two registries, are the main two sources for finding the answers to the study questions.

If you take part in this study, you will be asked to fill in a questionnaire consisting of 35 questions which will take you 30 to 45 minutes to answer. You can keep the questionnaire with you as long as you require to fill it in and return it to the study investigator preferably within two weeks. In this questionnaire you will be asked some questions about standard quality control procedures that are performed in your center.

These questions are about legal aspects of registry, documentation, confidentiality, reporting, quality control, staff, and training.

These questions are designed to describe the operations of your cancer registry center and to identify strengths as well as opportunities for improvement in the system from your point of view which might affect the quality of data reported by the center you are working at.

The results of the study will form the thesis project of the main investigator and she will provide your cancer registry center with a copy of her dissemination after she has defended her thesis.

Risks and Benefits

You will be spending 30-45 minutes of your time to fill in this questionnaire; however, this can be done at anytime convenient for you.
Although the questions may identify both strengths and weaknesses of your cancer registration system, the information will be used in a positive way to demonstrate how a registry works despite any challenges. Our intent is to provide data that will support local cancer registry efforts and indicate how various international organizations might help to improve the quality of data from different registries and thus make data more comparable.

Confidentiality

Information gathered in this research study may be published or presented in public forums; however, your name and other identifying information will not be used or revealed. Despite efforts to keep your personal information confidential, absolute confidentiality cannot be guaranteed. Your personal information may be disclosed if required by law.

Organizations that may inspect and/or copy this information for quality assurance and data analysis include the University of Manitoba, CancerCare Manitoba, and the Cancer Institute of Iran.

The University of Manitoba Health Research Ethics Board may review records related to the study for quality assurance purposes.

Voluntary Participation/Withdrawal from the Study

Your decision to take part in this study is voluntary. You may refuse to participate or you may withdraw from the study at any time. Your decision not to participate or to withdraw from the study will not affect the performance evaluation of your centre.

Questions

You are free to ask any questions that you may have about the study and your rights as a research participant. If any questions come up during or after the study or if you have a research-related problems or concerns, contact the principal investigators: Dr. Parisa Airia at , or Dr. Donna Turner at

For questions about your rights as a research participant, you may contact The University of Manitoba, Bannatyne Campus Research Ethics Board Office at (204) 789-3389.

Do not fill in the questionnaire unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.