RESEARCH COMMUNICATION

Yogyakarta Pediatric Cancer Registry: An International Collaborative Project of University Gadjah Mada, University of Saskatchewan, and the Saskatchewan Cancer Agency

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Abstract

Introduction: In July 2001, a 'twinning" project was undertaken between University Gadjah Mada, Indonesia, and the Saskatchewan Cancer Agency, Canada to create a computerised Pediatric Cancer Registry at Sardjito Hospital, Yogyakarta city. Objectives: To analyse information from the Yogyakarta Pediatric Cancer Registry (YPCR) in order to i) determine the prevalence of pediatric cancers in Yogyakarta Special Region and, ii) compare the demographics of pediatric malignancies in the Special Region (population: 3.3 million), with those of the Saskatchewan Cancer Registry in the province of Saskatchewan (population: 1 million). Methodology: In May 2001, a computer dedicated to the YPCR was installed at Sardjito Hospital. Bilingual (English/Indonesian) data capture forms were developed for data extraction from hospital health records. Data items were then entered into a data base using the Statistical Package For Social Sciences (SPSS) program. Two projects were initiated: i) a prospective study from 2000-2009 of pediatric cancer cases from the YPCR, and ii) a comparison of demographics from both Cancer Registries during the time period 1996-2003. Comparative data were obtained for age, sex, diagnoses, and referral patterns. Results were analysed using the SPSS software program. Results: i) In the 10 year prospective study, 1,124 pediatric cancer cases were accrued in the Yogyakarta Registry, the majority being in the age group 0-5 years. Male:female::1.7:1. Leukemias were the most common diagnosis, followed by retinoblastoma and neuroblastoma. The majority of patients (68%) were referred from outside the catchment area of Yogyakarta Special Region. ii) In the 8 year archival comparative analysis, the most striking contrasts were a higher proportion of children with retinoblastoma and negligible numbers of pediatric brain tumors in the Yogyakarta Registry. Conclusion: This is the first published report of a computerised pediatric cancer registry in Indonesia. The differences in diagnostic frequencies noted above may, in part, be due to comparisons between the population-based Saskatchewan Cancer Registry versus the hospital-based Yogyakarta Pediatric Cancer Registry. The contrasts in demographics are multifactorial, and require further investigation.

Key Words: Hospital-based pediatric cancer registry - Indonesia

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Introduction

Developing countries contain over 75% of the world's population, but possess only 5% of the world's economic resources. Population-based cancer registries in these countries are few and far between for a number of reasons, not the least being lack of sustained funding and infrastructure, as well as absence of their recognition as a national health care priority (Magrath and Litvak, 1993). Of the approximately 250,000 world's children diagnosed with cancer each year, about 200,000 live in developing countries, where their disease is not recognised as a public health priority (Kellie and Howard, 2008). The cure rate for childhood cancer in developing countries has been estimated at 25% (Wilimas and Ribeiro, 2001). In some developing countries, the cure rate for acute lymphoblastic leukemia (ALL) approaches 35% (Nandakumar et al., 1995), well below cure rates of around 80% in developed countries (Pui et al., 2001). There is a dearth of information on pediatric cancer epidemiology in developing countries, which face such challenges as reliable census data, under-reporting of cases, accuracy of diagnoses, and certified documentation of deaths (Steliarova-Foucher et al 2004; Kellie and Howard, 2008). It has been estimated that in Asia, only 7% of the total population of the continent have been included in systems reporting cancer incidence (Mayor, 2008).

Indonesia, a developing nation and the world's fourth most populous, is an archipelago comprised of over 17,000 islands. It has an estimated population of 228,248,538

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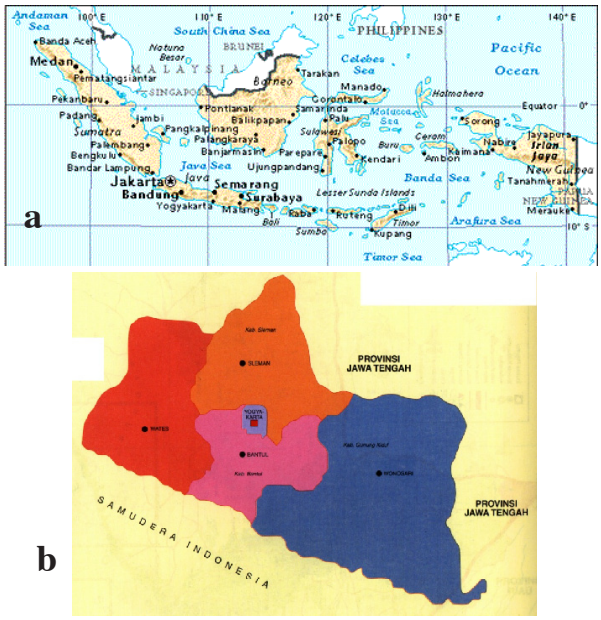

Figure 1. a) Map of Indonesia showing Location of Yogyakarta in South-central Java b) Closeup of Location of Yogyakarta City (red square) and the Five Regencies comprising Yogyakarta Special Region

(World Bank, 2008), about 30% of whom are children in the 0-14 year age range. Approximately 58 % of all Indonesians live on the main island of Java. Yogyakarta Special Region (YSR), located in south-central Java (Figures 1a, 1b), has an estimated population of 3,337,095 (www.datastatistik-indonesia.com). Dr. Sardjito Hospital located in Yogyakarta city, the Region's capital (Figure 1c), with an estimated population of 433,539 (www.datastatistik-indonesia.com), is the tertiary care referral hospital for pediatric cancer cases in the region, and also receives referrals from neighbouring provinces. In 1977, a pathology- based tumor registry reported on relative frequencies of adult cancers from Yogyakarta (Soeripto, 1977). Prior to 2001, no computerised pediatric cancer registry existed in Indonesia.

Cancer registries are either population-based or hospital-based. One of the oldest cancer registries in the world is the Saskatchewan Cancer Registry in Canada. It is a population-based Registry established in 1932, and covers the province of Saskatchewan (estimated population, 1 million) (Statistics Canada, 2006/2009). Computerised information is available on all cancers diagnosed since 1967. The Registry has an estimated case ascertainment of 99% (Ulmer, 2003). Challenges to establishing population-based cancer registries in developing countries include inadequate resources, lack of trained personnel, and requisite infrastructure to sustain this activity (Silva,1999). Hospital-based cancer registries in developing countries are likely to capture a large proportion of pediatric cases, which are usually managed at a tertiary care centre. Their data input derives from hospital records, outpatient files, and autopsy reports from within the same hospital. They generate information on, among other items, frequencies of cancer types, premature discontinuation of therapy, staging at diagnosis, treatment protocols, and patient survival. Their limitations include inability to determine cancer incidences, inexact demographic information, and incomplete long-term follow up data; patient characteristics and survival may not necessarily be representative of the patient population (Valsecchi and Steliarova-Foucher, 2008).

In July 2001, a Letter of Intent for collaborative education and research was signed by the Deans of the Faculties of Medicine, University Gadjah Mada, Yogyakarta, Indonesia, and University of Saskatchewan, Canada. A "twinning" project was launched for the creation of a computerised cancer registry at Sardjito Hospital, Yogyakarta city, Yogyakarta Special Region, in south- central Java. The objectives were:1. To develop a hospital-based, computerised Yogyakarta Pediatric Cancer Registry (YPCR) at Sardjito Hospital, as a first step towards consolidating a comprehensive Pediatric Cancer Program; 2. To compare demographics of childhood cancers between the hospital-based Yogyakarta Pediatric Cancer Registry and the population-based Saskatchewan Cancer Registry.

Materials and Methods

Computers, software and data collection

In 2001, a computer dedicated for the YPCR was installed in the Division of Pediatric Oncology/ Hematology (YPOHC) at Sardjito Hospital. In August that year, a cancer epidemiologist from University of Saskatchewan (JN) installed the SPSS program into the Registry computer. Bilingual (English and Indonesian) data capture forms were developed (Appendix 1), onto which information from hospital health records were written in, and then entered into the SPSS data base. Upon completion of data collection, the results were entered into the SPSS software program for analysis. Data collected included patient characteristics, demographic information, ICD-O (3rd Ed.) / ICD-10 classification of cancers, details of cancer treatments, follow-up status, and other information including the use of traditional healing methods.

Directory Personnel and Training

Following designation by the YPOHC Division Head of a Pediatric Oncologist (SM) as the Director of the proposed Registry, intensive training on Registry methodology was provided on-site at the Saskatchewan Cancer Registry office from July to August 2002. Quality control checks on retrieved data were performed according to established guidelines, with due diligence paid to completeness of records, standard consistency of data generated, and checks to avoid duplication of records. Next, a Data Manager was identified at YPOHC (IP), who was assigned the responsibility of coordinating data collation and entry. He received on-the-job training at Sardjito Hospital and worked closely with the hospital's Director of Health Records.

Subsequently, two initial studies were undertaken with the YPCR. Study 1: A review of all types of cancers in children under 18 years of age diagnosed at Sardjito Hospital over a ten year period from January 2000-December 2009. Study 2: A retrospective comparison of demographic data between the Saskatchewan and

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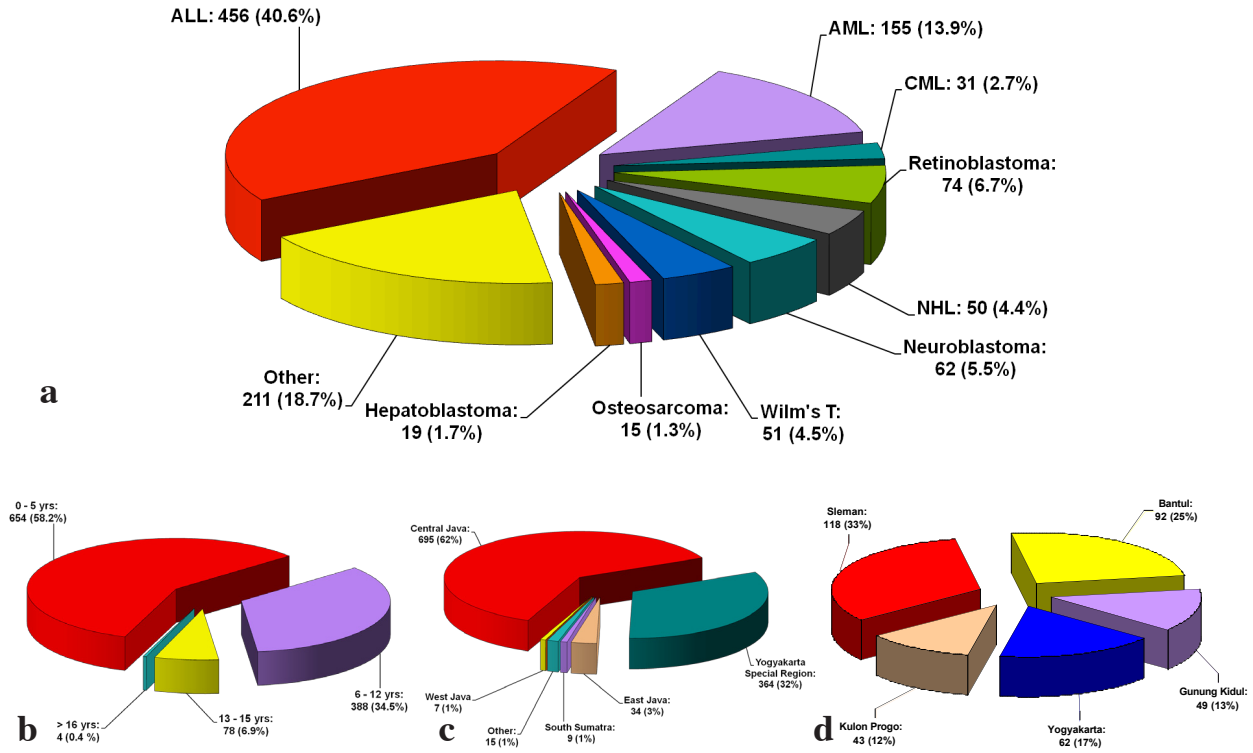

Figure 2. Pie Charts of Distribution of Pediatric Cancer Cases: a) Tumor Types; b) Age Groups; c) Regional Pattern of Referral According to Address at Diagnosis; and d) Address within Yogyakarta Special Region

Yogyakarta Cancer Registries over an eight year period, 1996-2003. Children under 18 years of age, identified from lists generated from the respective Registries, were included. Comparative data obtained for age, sex, common cancer diagnoses, and referral demographics were analysed.

Results

Study 1: During the 2000-2009 study period, a total of 1,124 children newly diagnosed with cancer were entered in the YPCR. In order of decreasing frequency, the 6 most common diagnoses were acute lymphoblastic leukemia (ALL-40.6%), acute myeloblastic leukemia (AML-13.9%), retinoblastoma (6.7%), neuroblastoma (5.5%), Wilm's tumor/nephroblastoma (4.5%) and non-Hodgkin lymphoma (4.4%) (Figure 2a). When categorised by age at diagnosis in 5 year blocks, the majority of children (58.2%) were in diagnosed during infancy and early childhood (ages 0-5 years), with a gradual and progressive decrease in late childhood and early adolescence A negligible number comprised teenagers 16 years of age or older (Figure 2b); this may be explained by the possibility that they were automatically referred to the adult wards at Sardjito Hospital or other tertiary care hospitals. When assessed by place of residence or referral by location within Yogyakarta Special Region, the defined catchment area, a finding of great interest was that almost two-thirds (62%) of all pediatric cancer patients at diagnosis were referred from beyond the boundaries of the catchment area (Figure 2c). Also of interest is that a minority of the referrals (1%) were from the neighbouring western island of Sumatra, these patients bypassing the largest cancer treatment facility in the country located in the capital city of Jakarta. In terms of referrals within the catchment area, the two Regencies that surround Yogyakarta, Sleman in the north and Bantul in the south, account for the two largest Regencies contributing new patient referrals at 33% and 25% respectively Figure 2d). When analysed by sex at diagnosis, 59.4% of children were boys (male:female::1.7:1), as shown in Figure 3.

Study 2: The duration of this comparative study between the hospital-based YPCR and the population-based SCR covered an 8 year period, 1996-2003. YPCR: A total of 592 patients were documented within the study period, 63% of whom were from outside the borders of Yogyakarta Special Region. Male::female was 1.4::1; 55% were in the 6-12 year age group at diagnosis. The 6 commonest pediatric cancers, in order of decreasing frequency, were leukemia (56.6%), retinoblastoma (6.9%), non-Hodgkin's lymphoma (6.7%), neuroblastoma (4.6%), hepatoblastoma (3%), and osteo-sarcoma (2.9%). SCR: a total of 391 patients were identified, all of whom

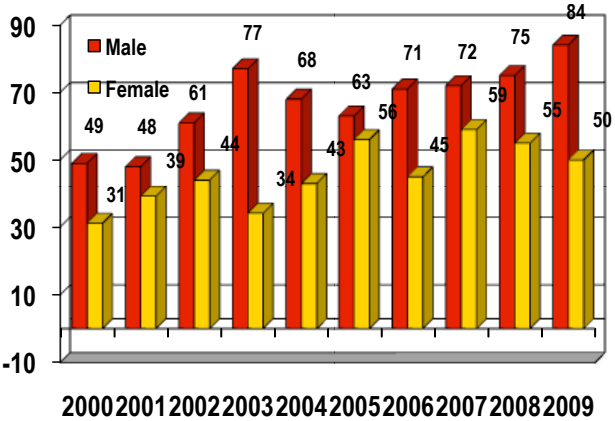

Figure 3. Comparison of Male to Female Patients

were from within the province. Male::female was 1:2; 33.2% were in the 0-5 year age group at diagnosis. The 6 commonest cancers were CNS tumors (21.3%), leukemia (19.4%), lymphomas (12.4%) Wilms tumor (3.9%), soft tissue sarcomas (3.4%), and osteosarcoma (3.1%). The most striking contrasts noted in the Yogyakarta Cancer Registry were the relatively higher proportion of boys, of children with retinoblastoma, and a paucity of patients with CNS tumors.

Discussion

A Cancer Registry, for the entire duration of its existence, remains a "work in progress" (Adamson, Law and Roman 2005), and requires frequent adjustment in response to the increasing complexity of data processing and data queries. Partnership or a "twinning" approach between developed and developing countries in undertaking to develop a Cancer Registry have proven their value in terms of longevity of a Registry, as well as clinical benefits by decreasing the rates of premature cessation of therapy, relapse, and mortality due to toxic effects of treatments (Ribeiro and Pui, 2005).

To our knowledge, this is the first published report of a computerised Pediatric Cancer Registry in Indonesia (Curado et al., 2007). The gold standard of any Registry is the accuracy of the data generated, in turn totally dependent on the quality of data being entered. The YPCR being a hospital-based registry (Atique et al., 2008).), the main data sources are the Sardjito Hospital inpatient wards and outpatient clinics health records, and pathology reports (Bhurgri et al., 2008).

Practical lessons gained from building a cancer registry in a developing country include: i) Registry data capture items should reflect the "lowest common denominator" for information gathering, i.e., the questions asked for data collection must be at a level that can be answered by the entire population, lay and professional. To ensure and maintain the viability of a Registry, it should be designed to meet predetermined needs at a basic level, with inbuilt capacity to expand and develop with maturity and experience. Starting at the "ground level" and keeping the goals of the Registry practical and attainable avoid frustrations that can hinder progress and prevent further development. ii) Shortages of health care personnel and infrastructure limit productivity, i.e. lack of funding to employ a full-time data entry clerk and/or a data coordinator. This leads to irregularity in data collation and entry, thereby hindering assessment of data quality control (Howard et al., 2007). iii) Preparatory education and workshops in advance of launching a Registry are essential, as is continuing support via the Internet re. consultations regarding diagnostic conundrums, interpretation of digital microphotographs of blood smears, bone marrows, and histopathological tissue sections, as well as management issues. iv) Simple and straightforward basic information, when analysed, can reveal trends that were not previously obvious or serve to confirm clinical suspicions/observations e.g., in the Yogyakarta Registry, the near absence of central nervous system tumors and an increased prevalence of retinoblastomas. These anomalies may, in part, be due to comparisons between a population-based registry (Saskatchewan) versus a hospital-based registry (Yogyakarta) (see Figure 4); further reasons would include, among others, variations in genetic expression, environmental factors, and population characterestics. Another factor relates to the possibility that some children with retinoblastomas or brain tumors may be directly admitted to, and exclusively cared for by, the ophthalmology and neurosurgery services respectively at Sardjito Hospital. In the case of central nervous system tumors, other explanations including missed diagnoses and those relating to socio-economic realities need to be considered. One such situation pertains to the "invisible" children who are die along the way from village to hospital. Since Indonesia is mainly an agricultural country with a predominantly rural population, parents' or families' perceptions and beliefs about sickness, disease, and cancer may preclude bringing a sick child to medical attention. Also, long travelling distances and limited transport facilities, and the economic burdens of traveling to, and taking up temporary residence in, Yogyakarta city can pose formidable challenges. Practical realities of dealing with family priorities preclude many newly diagnosed children from reaching a tertiary care referral centre (Parker, 1998). These factors may well account for most newly diagnosed children with cancer in presenting at tertiary care centres with advanced disease, resulting in poor outcomes (Bonilla et al., 2009). Even in an affluent country like the United States, it has been reported that minority populations may not travel to a cancer treatment centre when faced with lack of transportation (Guidry et al. 1997); a similar experience has been reported in South India (Kakuet al., 2008). Recognition of a child with a malignancy in the

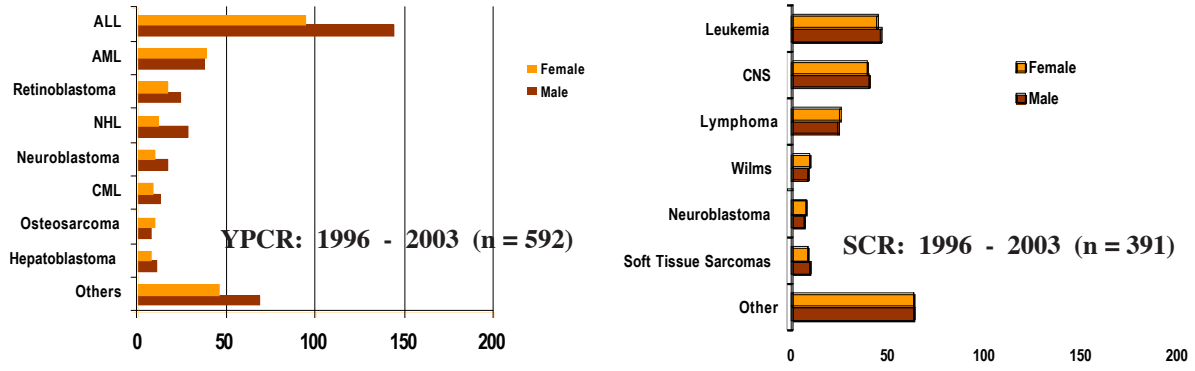

Figure 4. YPCR / SCR - Comparison by Type of Cancer at Diagnosis for Males and Females

rural home setting and subsequent referral to the nearest primary, secondary or tertiary health care centre does not occur with the same diligence or dispatch as in developed countries (Howard et al., 2008).

In order to raise awareness of childhood cancers in Indonesian villages and primary health care centres, an existing resource that can be utilised for early detection as well as to monitor and report outcomes at home is the Pemberdayaan Kesejahteraan Keluarga (Family Welfare Movement or PKK). The PKK is a women's organisation with members at every level of health care delivery throughout Indonesia. They serve multiple functions, including training of primary health care and family planning workers/community leaders; dissemination of information and educational materials on family planning and maternal and child health; and development of monitoring and evaluation strategy of Posyandus (primary rural health service units provided by, and for, the community, supported by health center staff) activities (Okamoto, 1993). At the very least, given the proper training and resources, their involvement would be invaluable in providing earlier recognition and referrals to secondary or tertiary health care centres for diagnosis and management of children with manifestations such as leukocoria, growths in or around the eye, unexplained strabismus, head tilt, or unsteady gait.

The key to developing a sustainable cancer program in a developing country lies in helping its health care professionals to become self-reliant and self-governing (Webb, 2009). This can be accomplished by providing them with the necessary training and guidance to enable them to operate independently, and as equal partners. The role of the "twinning" institution in the developed country should be one of nurturing and support, not of dominance (Braveman, 2001). Bilateral agreement on, and cooperative efforts towards, realistic goals and expectations of a cancer registry will help set the stage for building a successful cancer control program in a developing country.

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Appendix: Cancer Registry Data Capture Forms PEDIATRIC CANCER REGISTRY, YOGYA

A. DEMOGRAPHIC AND TREATMENT DATA

∑ Patient's Full Name / Nama Lengkap Pasein
∑ Patient's Birth Certificate Number / Nomor-Akte-Kelahiran Pasien
∑ Father's Name / Nama Ayah
∑ Father's Date Of Birth (dd/mm/yyyy)/ Tangal Lahir Ayah (hh/bb/

tttt)
∑ Father's ID Card Number / Nomor Kartu Tanda Penduduk Nama Ayah
∑ Father's Address and Village / Alamat Tetap Ayah dan Kampung Asal; - Area (Kelurahan) - Sector (Rukun Wilayah)
- Section (Rukun Tetangga) - Street (Jalan)
∑ Father's Village / Kampung Asal Ayah
∑ Mother's Name / Nama Ibu
∑ Mother's Date Of Birth (dd/mm/yyyy) / Tangal Lahir Ibu (hh/bb/tttt)
∑ Mother's ID Card Number / Nomor Kartu Tanda Penduduk Ibu
∑ Mother's Address / / Alamat Tetap Ibu
- Area (Kelurahan)- Sector (Rukun Wilayah)- Section (Rukun Tetangga) - Street (Jalan)
∑ Mother's Village / Kampong Asal Ibu

∑ Patient's Cancer Registry Unique Number / Kanker Register Nomor Unik Pasien
∑ Sex (M/F) / Jenis Kelamin (L/P)
∑ Hospital Number / Nomor Rumah Sakit
∑ Patient's Address at Diagnosis / Alamat Pada Saat Pemeriksaan Pasien
- Area (Kelurahan)- Sector (Rukun Wilayah)- Section (Rukun Tetangga)
∑ Patient's Current Address / Alamat Sekarang Pasien
- Area (Kelurahan)- Sector (Rukun Wilayah)
- Section (Rukun Tetangga)- Jalan (Street)
∑ Date of Birth (dd/mm/yyyy)/ Tangal Lahir (hh/bb/tttt)
∑ Ethnic Group / Suku-Keturunan
- Javanese (Orang Java)
- Maduranese (Orang Madura)
- Sundanese (Orang Sunda)
- Bantanese (Orang Bantan)
- Other (Orang Lain)
∑ Health District / Dinas Kesehatan Kabupaten
∑ Health Centre / Puskesmas
Appendix 1: Cancer Registry Data Capture Forms (p. 3/7)

∑ Name of Hospital where Diagnosed / Nama Rumah Sakit di Tempat Pemeriksaan
∑ Date of Admission to Hospital (dd/mm/yyyy)
/ Tanggal Peneriman di Rumah Sakit (hh/bb/tttt)
Hospital Number (Nomor Rumah Sakit)
∑ Tumor Type (Manchester Classification) / Jenis Tumor (Klasifikasi Manchester)
∑ Primary Site of Tumor (ICD-O-3 Classification) /
Bagian Tumor dimulai (Klasifikasi ICD-O-3)
∑ Tumor Morphology (ICD-M Classification) / Bentuk Tumor (Klasifikasi ICD-M)
∑ Method of Diagnosis / Cara Pemeriksaan
- clinical / Pengamatan Dokter Yes / No (Ya / Tidak)
- radiological / Penyinaran Yes / No (Ya / Tidak)

Xray / CT scan / MRI scan Roentgen / Penyinaran CT / Penyinaran MRI
- biopsy / Biopsi Yes / No (Ya / Tidak)
- other method (Cara lain) Yes / No (Ya / Tidak)

∑ Surgical Staging (Local Spread / Regional Spread / Systemic Spread) / Tinkatan Pembedehan (Penyebaran Setempat / (Penyebaran Meluas / Penyebaran Menyeluruh)
∑ Surgery – Date / Tanggal Pembedahan
- biopsy only / Hanya Biopsi Yes / No (Ya / Tidak) - partial resection / Diambil Sebagian Yes / No (Ya / Tidak) - complete resection / Diambil Seluruh Yes / No (Ya / Tidak) - other surgery (type//date dd/mm/yyyy) / Pembedahan Lainnya (macam// hh/bb/tttt)
∑ Chemotherapy / Kimoterapi
- Received / Terimah Yes / No (Ya / Tidak) - Protocol / Protokol Yes / No (Ya / Tidak) (If yes) Protocol name & number / (Kalau Ya) Protocol namah dan nomor
- Drugs / Jenis Obat [insert Saskatchewan Cancer Agency standard drug codes]
- Duration of chemotherapy / Lama Pengobatan Kimoterapi
- start date (dd/mm/yyyy) / Tanggal mulai (hh/bb/tttt)
- end date (dd/mm/yyyy) / Tanggal selasai (hh/bb/tttt)

∑ Radiation Therapy / Penyiran Yes / No (Ya / Tidak)
- Treatment Area / Bagian Yang Disinari
- Dose (cGY) / Dosis (centiGrey)
- Duration of radiation therapy (dd/mm/yyyy to dd/mm/yyyy) / Lama Pengobatan (hht/bb/tttt ke hht/bb/tttt)
- start date (dd/mm/yyyy) Tanggal mulai (hh/bb/tttt)
- end date (dd/mm/yyyy) Tanggal selasai (hh/bb/tttt)
∑ Tumor Behaviour / Perilaku Tumor
- Benign / Lamah- In Situ / Didalam- Invasive / Telah Menjalar- Uncertain / Tidak Pasti

∑ Patient's Cancer Registry Unique Number / Kanker Register Nomor Unik Pasien
∑ Follow Up Yes / No / Tindak Lanjut (Ya / Tidak)
∑ Status / Keadaan
- Dead / Meninggal- Alive / Masih Hidup - Lost to Follow Up / Tidak ada tindak lanjut
∑ If alive, status at last contact/Kalau masih hidup,keadaan kesehatan waktu terakhir dihubungi
- remission / relapse Sudah Sembuh / Kambuh Lagi
- date of last contact (dd/mm/yyyy) / Tanggal Kunjungan Terakhir ((hh/bb/tttt)
- place of contact (dd/mm/yyyy) / Tampat Kunjungan Terakhir ((hh/bb/tttt)
- Dr. Sardjito Hospital / Rumah Sakit Dr. Sardjito
- Kabupaten Hospital / Rumah Sakit Kabupaten
- Health Centre / Puskesmas
- Home / Rumah
- Other / Lain

∑ Record of remissions and relapses Rekordnya Sudah Sembuh / Kambuh Lagi
- Date of 1st Remission (dd/mm/yyyy) / Date of 1st Relapse (dd/mm/yyyy)
Tanggal Sudah Sembuh Pertama ((hh/bb/tttt) / Tanggal Kambuh Lagi Pertama ((hh/bb/tttt)
- Date of 2nd Remission (dd/mm/yyyy) / Date of 2nd Relapse (dd/mm/yyyy)
Tanggal Sudah Sembuh Kedua ((hh/bb/tttt) / Tanggal Kambuh Lagi Kedua ((hh/bb/tttt)
- Date of 3rd Remission (dd/mm/yyyy) / Date of 3rd Relapse (dd/mm/yyyy)
Tanggal Sudah Sembuh Ketiga ((hh/bb/tttt) / Tanggal Kambuh Lagi Ketiga ((hh/bb/tttt)
- Date of 4th Remission (dd/mm/yyyy) / Date of 4th Relapse (dd/mm/yyyy)
Tanggal Sudah Sembuh Keempat ((hh/bb/tttt) / Tanggal Kambuh Lagi Keempat ((hh/bb/tttt)

∑ Dead / Meninggal Yes / No (Ya / Tidak)
- Date of Death (dd/mm/yyyy) / Tanggal Kematian (hh/bb/tttt)
- Place of Death / Tempat Kematian
- Dr. Sardjito Hospital / Rumah Sakit Dr. Sardjito
- Kabupaten Hospital / Rumah Sakit Kabupaten
- Health Centre / Puskesmas
- Home / Rumah
- Other / Lain
- Cause of Death / Penyebab Kematian
- [ICD 10] code / [ICD 10]kode