RESEARCH ARTICLE

Trends and Analysis of Cancer Incidence for Common Male and Female Cancers in the Population of Punjab Province of Pakistan during 1984 to 2014

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Abstract

Background: The Pakistan Atomic Energy Commission Cancer Registry (PAECCR) program has made availability of a common cancer incidence database possible in Pakistan. The cancer incidence data from nuclear medicine and oncology institutes were gathered and presented. Materials and Methods: The cancer incidence data for the last 30 years (1984-2014) are included to describe a data set of male and female patients. The data analysis concerning occurrence, trends of common cancers in male and female patients, stage-wise distribution, and mortality/follow-up cases is also incorporated for the last 10 years (2004-2014). Results: The total population of provincial capital Lahore is 9,800,000. The total number of cancer cases was 80,390 (males 32,156, females 48,134). The crude incidence rates in PAECCR areas were 580.8/10^5 during 2010 to 885.4/10^5 in 2014 (males 354.1/10^5, females 530.1/10^5). The cancer incidence rates for head and neck (15.70%), brain tumors (10.5%), and non-Hodgkin lymphoma (NHL, 9.53%) were found to be the highest in male patients, whereas breast cancer (46.7%), ovary tumors (6.80%), and cervix (6.31%) cancer incidence rates were observed to be the most common in female patients. The age range distribution of diagnosed and treated patients in conjunction with the percentage contribution of cancer patients from 15 different cities of Punjab province treated at the Institute of Nuclear Medicine and Oncology, Lahore are also included. Leukemia was found to be the most common cancer for the age group of 1-12 years. It has been identified that the maximum number of diagnosed cases were found in the age range of 51-60 years for males and 41-50 years for female cancer patients. Conclusions: Overall cancer incidence of the thirty years demonstrated that head and neck and breast cancers in males and in females respectively are the most common cancers in Punjab province in Pakistan, at rates almost the highest in Asia, requiring especial attention. The incidence of brain, NHL, and prostate cancers among males and ovarian and cervix cancers among females have increased rapidly. These data from a major population of Punjab province should be helpful for implementation of appropriate planning, prevention and cancer control measures and for determination of risk factors within the country.

Keywords: Cancer incidence - breast cancer - cancer diagnosis - cancer survival - Pakistan

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Introduction

Cancer is a major cause of elevating death tolls across the globe (Jemal et al., 2010) and even the most developed countries are continuously experiencing a surge in cancer incidence trends (Simard et al., 2012). Cancer registration provides a firm basis for cancer control efforts and research into changing patterns of incidence, mortality, survival and prevalence is of obvious importance and the cancer registration research in the Asian Pacific region requires strengthening effective intervention efforts to reduce the burden of disease. (Moore, 2013). Population based cancer registry collects the data on cancer incidence and mortality from covered population to survey and describes the epidemics in certain areas. Cancer registry plays an important role in illustrating the epidemic, gives

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fundamental information in expressing cancer trends (Park et al., 2013; Brecht et al., 2014), interpret cancer causes (Schlesinger et al., 2013), follow-up patients (Sengoku et al., 2014), evaluate survival (Hanna et al., 2010), enhance planning and promote cancer control policies and individual patients care (Parkin, 2006). Continuous efforts have been made to alleviate the risk of various cancerous diseases in the Asian pacific region (Shin et al., 2012). Recently, particular interest has been seen in the detailed study of cancer incidence trends by race/ethnicity, gender, and age group (Liu et al., 2012; van Laar et al., 2013). According to the data published by WHO International Agency for Research on Cancer (IARC) (GLOBOCAN 2012), there were 14, 100, 000 new incidence cases, and 8, 200, 000 new death cases in 2012 in the world. There were 8, 000, 000 new incidence cases and 5, 300,000 new death cases in the less developing regions (Ferlay et al., 2012; Chen et al., 2013). The cancer incidence and mortality rates are continuously increasing in the Asian Pacific region (Parkin et al., 2002; Curado et al., 2008; NCRP 2013; Liu et al., 2014).

Pakistan is the seventh most populous country in the world and is a republic in south Asia. It shares international geographical boundaries with China and Soviet Central Asian Republics in the north, with Iran and Afghanistan on the west and northwest and cultural similarities with India in the east and southeast. As a developing country of the region, Pakistan faces a huge burden of cancer diseases with a significant rising incidence trends (Ferlay et al., 2004). In Pakistan, an improvement has been experienced in the oncology infrastructure over a period of time (Begum et al., 2012; Are et al., 2013) but low cancer survival rates are still prevalent due to lack of awareness about cancer among the population, poor health facilities and infrastructure, social stigmas, difficult economic conditions, and cancer detection at advanced stages (Hanif et al., 2009). At present, a national level cancer registry database is nonexistent in Pakistan, and the only data available is from hospitals or institutional databases (Bhurgri et al., 2007). The significance of cancer incidence is critical in ensuring effective implementation of cancer control programs. To obtain a deeper insight into this cancer epidemic, implementation of breast cancer screening with stress on public health education is a major responsibility of any government (Siegel et al., 2012). However, at the same time, the projected number of new cancer cases and cancer deaths should be interpreted cautiously, because these estimates are model-based and may vary considerably from year to year for reasons other than changes in cancer occurrence (Parkin et al., 2005; Aziz et al., 2010). Cancer risk continues to increase in the developing countries of South Asia, including Pakistan, Iran, Sri Lanka, India, Bangladesh, Nepal, and Bhutan, where cancer is presently responsible for about 25% of all deaths (Moore et al., 2010). Therefore, the coordination of activities within South Asia must be a high priority for cancer control in this region (Salim et al., 2010). There are a number of active registries in the region and population-based data are now available for a considerable number of countries. However, the presentation and availability of data from Pakistan is virtually nonexistent at a global scale. This hinders substantially the epidemiological research into the causes of cancer and the enactment of effective control programs (Jemal et al., 2005; Agha et al., 2006) as the complete cancer incidence data helps in providing valuable information for upgrading the initiation of cancer early diagnostic, prevention, and treatment programs (Parkin et al., 2005; Mazhar et al., 2009). We have checked, sorted, analyzed and presented the incidence data under the auspices of the Pakistan Atomic Energy Commission Cancer Registry (PAECCR) from 1984 to 2014 for the major population of Punjab province and provincial capital Lahore, Pakistan in order to utilize the data in making decision of cancer prevention and control strategies, clinical trials and scientific researches. Some work has been reported for southern part of the country (Bhurgri et al., 2004; Bhurgri et al., 2005). Cancer registration (PAECCR) can be traced back to more than 30 years. However, the progress of the registry system in Pakistan had been relatively slow in other three provinces.

According to the recent population statistics, total population of Pakistan and Punjab province is 190,580,000 and 82,000,000 respectively. The total population of provincial capital Lahore is 9,800,000. In Pakistan, approximately 320,000 new cancer cases are diagnosed each year (Ferlay et al., 2012). Among these, nearly 256,000 patients are being treated at Pakistan Atomic Energy Commission (PAEC) cancer institutes. The Institute of Nuclear Medicine and Oncology (INMOL) is one of the PAEC cancer institutes that handle thousands of new cancer cases per year. The institutional data on cancer incidence at INMOL have been registered and properly maintained since 1984, and are frequently used to report on cancer cause statistics, cancer management, and identification of risk factors. The aim of this study was to disseminate cancer incidence data, common cancer trends, and cancer occurrence by age group for male and female cancer patients in a developing country. This could be helpful in understanding the problems and assessing the challenges that need to be addressed. The patient registration record maintained at INMOL institute has all the key information covering a wide range of demographic and medical information. The demographic information includes age, gender, race/ethnicity, birthplace, and residence, and the medical information includes physical findings, screening information, and diagnostic and follow-up procedures, including annual information about treatment, recurrence, and patient status.

The institutional cancer incidence data includes 80,390 males and females patients. These also include patients treated from Lahore and from 15 other major cities of Punjab province i.e., (Gujranwala, Sialkot, Shikhopura, Kasur, Sargoda, Okara, Bhakkar, Gujrat, Narowal, Bhowialnagar, Vehari, M. Bahaud Din, Naankana, Bahwalpur and Pakpattan). In 1990, only 1,463 cancer patients were registered at INMOL from the local population. This data set had 665 male and 798 female patients. The number of new patients continued to increase every year and reached up to 2,220 patients in 2000 with 975 male and 1,245 female patients. In 2014, a total of 4,722 new cancer patients were registered (1,893 male and 2,829 female patients). The total number of cancer cases
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was 80,390 (males 32,156, females 48,134).

The 10 most common cancers for male and female patients have been identified for the last 10 years (2004-2014) and the trends followed by the most common cancers both in male and female patients have been presented against a time variable. The most common male cancers are head and neck cancers, affecting 15.70% of the diagnosed patients. In female patients, breast cancer is the most common, affecting 46.66% of the diagnosed female patients with incidence increasing every year at rates almost highest in Asia.

The patterns and trends suggest that cancers in male and female patients increased up to 67% and up to 98.6%, respectively. The results exhibiting the typical cancer occurrence profile for different age groups have also been elaborated. The trend profile illustrates that cancer incidence among young patients aged 31-40 years are also increasing rapidly. Leukemia has been identified as the most common cancer in patients aged 1-12 years, constituting 21% of total childhood malignancies. In patients aged 15-44 years, head & neck and breast cancer are the most common cancers while brain, NHL, prostate, lung, ovary, cervix, cancers are predominant in people over 45 years of age. The data analysis reveals that in the year 2014, the overall cancer occurrence was 39.8% among the patients aged 30-50 years. In the next section, the institutional setup and data collection and analysis mechanism at INMOL is briefly described.

Materials and Methods

Currently there are 18 nuclear medical centers working under PAEC, extending excellent diagnostic and therapeutic facilities all over Pakistan. INMOL has been declared a Center of Excellence in Southeast Asia by the International Atomic Energy Agency (IAEA), where oncolgic diagnosis and treatment facilities of various cancers and noncancerous diseases are being provided using unsealed and sealed radioactive sources, respectively, in nuclear medicine and clinical oncology. INMOL has 80 beds for inpatients and 40 for a chemotherapy day ward. On average, approximately 450 specific chemotherapy drugs are dispensed per week in these wards. In addition, it has leukemia bays that can accommodate 11 acute leukemia patients and 2 isolation rooms concurrently. For diagnostic purposes, there are 3 gamma cameras, computed tomography scanner, mammography units, an ultrasound unit, and an X-ray machine at INMOL. A new pediatric hematological malignancy unit with 15 beds and a dedicated clinical laboratory and blood transfusion facilities has also become functional. The commissioning of a 16.5MeV Cyclotron, PET-CT and a complete surgery department have further facilitated the local and surrounding population with the latest diagnostic facilities. Institutes are also conducting research in collaboration with national and international scientific bodies such as IAEA and the World Health Organization. The treatment of cancer is carried out using radiotherapy and chemotherapy modalities. By observing high standards of professional and clinical practice at INMOL, the College of Physicians and Surgeons Pakistan (CPSP) has recognized INMOL as the accredited training centre for fellows of (CPSP) students in the fields of nuclear medicine, oncology, medical physics and radiology. INMOL is providing services in nuclear medicine, oncology (medical oncology and radiotherapy), radioimmunoassay, medical physics, radiology (radiography, mammography, and ultrasonography), clinical pathology laboratory, radio pharmacy and social welfare.

The institute is quality management system ISO 9001:2008 certified and it especially emphasizes maintaining and updating all cancer patients’ records for review and data analysis. The cancer incidence record has been developed by employing the characteristic parameters necessary for accurate treatment. Records of malignant cancers granted registration numbers have been maintained and identified annually. The patient files and computerized records are simultaneously maintained for future reference. The individual patient records contain all necessary information (name, address, age, gender, contact, origin, disease history, treatment details, etc). The procedural efforts used to maintain data records of cancer-diagnosed patients includes demographics and screening Information, diagnostic findings and cancer information, cancer therapy and follow-up procedures, post treatment cancer surveillance and calculation of survival rates and assessment concerning the efficacy of treatment modalities. The disease classification and details of organ-wise male and female cancer patient data are maintained through locally developed computer software (CANSOFT I and CANSOFT II) that contain all necessary information. The privacy for the individual cancer patient’s record is maintained in the use of information on cancer data for statistical analysis and research (Aziz et al., 2010). The institutional cancer statistics are compiled from the yearly data set summary records of cancer patients, hospital inpatient records, and other statistical collections such as diagnostic statistics. The clinical oncology protocol books contain the organ-specific cancer details and records stored at INMOL are protected by PAEC rules. Pakistan Atomic Energy Commission Cancer Registry (PAECCCR) Program has greatly improved the database management at the institutes for collection and availability of the accurate common male and female cancers incidence data for analysis in Pakistan and these results from nuclear medicine and oncology institutes has been discussed in the next section.

Results

Many cancers are initially recognized either by their symptoms or through screening (Parkin et al., 2005). Although a number of cancers share risk factors, most cancers have a unique set of risk factors. The risk of death due to particular cancers may be reduced through engaging intensive monitoring of individuals at high risk, reducing external risk factors, detecting and treating cancers early in their development, and treating them in accordance with the best available evidence.

The averages of 10 common cancers in male patients for the 2004-2014 are described in Figure 1. The most common cancers are head and neck with 15.70%.
followed by brain (10.50%), non-Hodgkin lymphoma (NHL) cancer (9.53%), prostate (8.30%), lung (7.50%), urine bladder (6.70%) and leukemia (6.00%). The other common cancers include metastasis of unknown origin (MUO, 5.10%), Hodgkin’s disease (4.40%), larynx cancer (4.30%), rectum (3.90%) and colon and bone cancers with a contribution of 3.50% and 3.0% respectively. The other common cancers are distributed among esophagus, acute lymphocytic leukemia (ALL) and other miscellaneous types of cancer diseases; together these account for 7% of the remaining percentage.

Figure 2 also illustrates the last 10-year averages of 10 common cancers in female patients in the population of Lahore and the surrounding area treated at INMOL. The most common cancer in female patients is breast cancer, with an incidence of 46.66% and increasing every year. The other common registered cancers after breast are ovary (6.80%), cervix (6.30%), MUO (5.10%) and uterine (4.50%). The rest of the cancers percentages are distributed among non-Hodgkin lymphoma (NHL) cancer (4.0%), thyroid (3.80%), brain (3.50%), leukemia (3.15%), head and neck (2.50%), and other miscellaneous types of cancer (13.9%). In contrast to western data of female patients with lung cancer (Jemal et al., 2005), it is not present in the 10 most common diseases among our female population; it is, however, the fifth most common cancer disease among males.

The cancer trends for male and female patients over the last 30 years and the proportion of cancer incidence data attributed to male and female cancer patients from (1984-2014) is illustrated in Figure 3. An overall cancer incidence rate of 7.6% has been noted during the last 10 years. New Admission/Readmission data for male and female cancer patients are presented in Figures 4 and 5. The last 10-year trend of the 3 most common male cancers is illustrated in Figure 6. The most common among male patients, head and neck cancer, shows a slowly increasing trend, whereas brain has become the second most common disease with an elevating pattern. Similarly, NHL cancer has shown an elevating trend among the male population during the last 10 years.

The profile of the 3 most common female cancers from (2004-2014) is also shown in Figure 7, indicating that breast cancer is continuing to increase among the female population. The second and third most common cancers found were ovarian cancer and cervix cancer. For the sake of clarity, the cancer incidence and mortality/follow-up cases are reported for the years 2004-2014 in Figures 8 and 9. The total number of cancer cases treated was 80,390 cancer patients with 32,156 males and 48,134 female patients. The age-group cancer occurrence data is shown in Figure 10. Leukemia is the most common cancer in patients aged 1-12 years, contributing to 21% of total childhood malignancies. The incidence of leukemia has been reported in patients who are exposed to radiation, exposed to benzene, pesticides, or herbicides. Breast cancer is dominant in female patients, contributing to about 46.66% of total cancer diagnoses in female patients. The exact causes of breast cancer are not known, but research has shown that women with certain risk factors are more likely to develop breast cancer.
Figure 10 illustrates that cancer incidence among the young population of Lahore between the ages of 41-50 years is also increasing rapidly. Breast cancer is mostly seen among women between the ages of 41-60 years and can be controlled by an early diagnosis (all women over the age of 40 years should have mammography every year). In 2014, the average age for the maximum number of diagnosed cases in males was 51-60 years, followed by 61-70 years. The average age for the maximum number of diagnosed cases in females was 41-50 years, followed by 51-60 years. A typical cancer occurrence profile of the local population is presented in Figure 10. Age-specific incidence depicts the trends of commonly occurring cancers in the specific age groups.

The age-specific incidence of female breast cancer had two peaks: age of 41-50 years and 51-60 and similar two peaks data has also been reported by others (Zhang et al., 2012; Wu et al., 2013). Further studies focused on breast cancer could clarify whether this “two-peaks” was a common phenomenon. In the age group of 41-50 years, the incidence of cancer was the highest both in males or females and this incidence data is helpful for various types of tumors in age groups for planning to carry out cancer prevention.

Almost 62.40% of patients from other remote cities of Punjab province have been treated at INMOL. As illustrated in Figure 11, INMOL is serving a massive population and the percentage of treated patients here is
far greater than other cities of Punjab. These also include patients treated at INMOL from 16 major cities of Punjab province i.e., (Lahore, Gujranwala, Sialkot, Shikhopura, Kasur, Sargoda, Okara, Bhakkar, Gujrat, Narowal, Bhawalnagar, Vehari, M. Bahaud Din, Naankana, Bahwalpur and Pakpattan). The figure reveals that over 37% of cancer cases from Lahore are being treated at INMOL, and this can be attributed to lack of diagnosis and treatment facilities in most of the other cities of the province. This is also relevant in terms of increase in death toll due to nonexistent cancer detection practices at early stages, and lack of awareness in rural areas and other cities of Punjab province of Pakistan. The institutional cancer incidence data includes 80,390 males and females patients. The crude incidence rates in PAECCR areas were 580.77/10^5 during 2010 to 885.35/10^5 in 2014 (males 354.14/10^5, females 530.11/10^5).

**Discussion**

In PAECCR program, adequate amount of resources input is given annually and the collection of vast data it produces every year, interpreting and using these data to leverage more cost-effective policies and interventions against cancer epidemic cannot be overestimated. This is a challenging task since a whole range of factors are involved in cancer case identification, progression and reporting (Cheunget et al., 2013; Barayan et al., 2014; Kharazmi et al., 2014; Perdue et al., 2014). Pin-pointing this complexity requires systematic thinking of the major indicators inferred from PAECCR. The typical curve-shaped line graphs of incidence and mortality (as shown in Figure 8) reflect the fact that cancers are caused by the accumulative effects of multiple factors (Cheung et al., 2013). Each of these factors exerts its effect at a certain possibility and it takes time for multiple factors to pool enough effect to develop cancers. Thus the younger the age of a population group, the lower the chances for them to get cancers; and as the age of the population grows older, their chances for developing cancers become greater. The drops, in age group 01-20 and age group 71-90, in the incidence rates among all the age groups may be explained by reduction, due to low and high age, in risk behaviors (e.g., smoking, unprotected sex, alcohol consumption, unhealthy life style), in exposure to environmental carcinogenesis factors and in uptake of cancer screening, diagnosis and treatment services.

The incidence and mortality in the gender differences may be attributed due to number of reasons. Since the males and females differ in lifestyles and in exposure to environmental factors with significance of cancer genesis and prognosis, they had varied susceptibility for different types of cancers due to gender related discrepancies in physiology and genetics. There is lack of awareness among males and females living in urban and rural areas and they respond differently to cancer related symptoms, prevention and treatment services that lead to uneven registration of cancer incidence cases and deaths (Hanna et al., 2010; Takiar et al., 2011; Hao et al., 2012; Gao et al., 2013). In Pakistan, most cancer diagnosis and treatment services are only available from large hospitals that are often far away from rural population and outside the jurisdiction of their local cancer registries. This poses accessibility barriers not only for rural population, especially the aged ones, to get cancer services but also for local rural cancer registries to obtain relevant cancer case records for check and complete required data (Tripathi et al., 2014). A substantial part of rural children did not register formal residence until their school age and some children are diagnosed with and died of cancers without entry in cancer registry.

Breast cancer is the first biggest cause of cancer related deaths in women and one out of nine women has lifetime risk of developing breast cancer. Pakistan has the highest incidence in Southeast Asia, where 35% to 40% women in the age of 40 years has a risk of developing breast cancer. According to UICC and WHO report, 47% of newly diagnosed breast cancers in Pakistan are already in advanced stage. Annual medical examination must be performed by well trained health worker after 40 years of age and at least every three years starting from the age of 20 and any signs of the disease should be further evaluated. It is evident from percentage distribution of various cancers by age groups that breast cancer among the women in age group 31-40 is continuously increasing in Pakistan and the data is consistent with other part of the world (Gabriel et al., 2010; Leclere et al., 2013; Mousavi et al., 2013). According to the (PAECCR) data for the population of Lahore, breast cancer ranks the most common cancer among Pakistani women, and it was also the most frequently diagnosed cancer in Punjab province followed by ovarian cancer and cervix cancer which is consistent with the overall cancer incidence rate from 2000-2014. The breast cancer incidence shows similar trends in the other parts of the country and is consistent with the south east Asian region trends (Afsharfard et al., 2013; Zhao et al., 2012; Hao et al., 2012; Takiar et al., 2010). The incidence of thyroid cancer failed to rank in the top 10 male cancers, whereas, it is the seventh most common female cancer in (PAECCR) cancer registries. MUO, Uterus, NHL and brain cancers were the other most common female cancers in Punjab province in Pakistan. At the same time, the incidence rates of head and neck, brain, NHL, prostate and lung cancers among the males has increased, therefore, prevention and control should be implemented on these cancers. The data of Punjab province major cities cancer registration
areas in Pakistan shows that the incidence of cancer is rising, and it is consistent with the cancer registries outcome, but some cancer incidence showed more than 15% higher incidence rates in head and neck and 10% in brain cancers in males and breast cancer in 46.66% females. According to the cancer features of the Punjab province, there is a need to strengthen early diagnosis and treatment of cancer screening work, to further improve the geographical distribution of the province cancer registry, making basic and clinical research in depth and combining cancer prevention with control for effective handling the cancer disease. In Pakistan, (PAECCR) has becomes a valuable tool of assessing need for screening and planning and evaluating screening services for breast and cervix cancers.

Overall cancer incidence data consists of total 80,390 male and female patients treated during the period 1984-2014. The cancers in male and female patients increased up to 67% and up to 98.6%, respectively. In present communication, the described trends in the cancer incidence and mortality have important illustrative aspects. There is a clear need to handle cancer control differently and to take full consideration of the discrepancies between the males and females, rural and urban residents, young, middle aged and the elder persons. As the disease is not caused by single or limited major factors, the cancer control depends on comprehensive planning and targeting at multiple factors which requires enduring efforts covering the whole lifespan of target population. The cancer incidence remains the highest until the old age groups and there is no time point when it becomes too late for an individual to take action for prevention to become cancer free which progresses from a minimum accumulative effects of influencing factors (Moore et al., 2013). In this regard, further improvement and efforts to pay special attention to under reporting of cancer incidence and mortality cases for children and the elders in rural areas (Belasco et al., 2014; Tripathi et al., 2014). The disease detection through comprehensive risk assessment, adequate biomarkers and skilled professionals may prove cost-effective. The utilization and interpretation of PAECCR to take full account of all factors related to cancers genesis, prognosis and cancer registry program. It is pertinent to mention that PAECCR program has made substantial progress during 2004-2014 and provided valuable data during (1984-2014) for devising better cancer prevention and control strategies for future. It is extremely importance that emphasis needs to be given for determination of the variation in incidence and mortality data on the basis of ethnicity, socioeconomic and geographical background factors to precisely predict the trends over time for cancer in general or specifically based on organ sites and to devise adequate methodology for cancer prevention and control issues and for development of futuristic cancer registry based research.

In conclusions, PAECCR cancer registry incidence data during (1984-2014) has been presented to share the information and challenges to be addressed in third world countries like Pakistan. This may help in devising effective cancer control strategies for trends shown by common prevalent cancers by focusing energies in the right direction to detect cancer at early stages. For cancer alleviation, there is also a dire need to organize public awareness workshops and training sessions to assist the oncologists in cancer treatment practices in Pakistan, by encompassing elements of surgical, medical, and radiation oncology. In assessing these trends, it is important to recognize that small changes seen in the most common cancers mean a substantial shift in the numbers of new cases, whereas the same shift in less common cancers can have a relatively small impact. The data reveal that risk of cancer incidence increases with age.

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