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National and Sub-National Pediatric Cancer Mortality in Iran, 2000–2015

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Abstract

Background: Cancer, a common disease in adulthood, is a rare albeit slowly increasing condition among children. Currently, limited data are available on the incidence, prevalence, and mortality of these diseases in many regions, including developing countries. Herein, we are reporting national and sub-national estimates on deaths due to childhood cancers between 2000 and 2015 in Iran.

Methods: Cancer mortality rates were estimated using the national death registration system's data after addressing its incompleteness and misclassification, using demographic (complete birth history and summary birth history) and statistical analysis (spatiotemporal, Gaussian process regression, and generalized linear mixed models). We included data from cemeteries of two cities (Tehran and Isfahan) that were not included in the death registration system. We used census data and household expenditure and income surveys for data on population and other covariates used in the modeling.

Results: The overall age-standardized death rate (ASDR) of childhood cancers have decreased by 69.52% (80.67–49.71) in Iran (equal to an annual percent change of -3.63 [-4.53– -2.24]), declining from 12.24 (95% UI: 10.52–14.49) in 2000 to 3.73 (2.8–5.29) deaths per 100 000 in 2015. This decrement was equal to an annual percent change of 4.35% over these years. Leukemia, brain, and nervous system malignancies accounted for about 66% of all cancer-related mortalities among children and adolescents in 2015, which had a 10% increase compared to 2000. Moreover, trends at the sub-national level showed that the highest and lowest ASDR of childhood cancers ranged from 2.12 to 4.99 across provinces of Iran in 2015.

Conclusion: Although the overall mortalities have decreased, there is still inequality in the distribution of the recorded deaths. This inequality should be addressed with the improvement of the quality of care and better access to pediatric hospitals and oncologists in these areas.

Keywords: Cancer, Child, Epidemiology, Iran, Mortality

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Introduction

Cancer, a common disease in adulthood, is a rare albeit slowly increasing condition among children.[1] Although pediatric neoplasms affect a relatively small fraction of adolescents and children, cancers are among the leading causes of disease-related mortality in patients aged up to 14 years in several countries.[2] Pediatric cancers constitute only 1% of all cancer cases in developed countries, like the United States and European nations. However, studies show a 5-fold higher proportion for this measure in the developing world.[2,3] This difference not only highlights the contributing roles of risk factors or genetic, racial, and ethnical predisposition in areas like lower-income countries leading to the higher prevalence of these diseases but also calls for interventions to address the increasing need for diagnostic and therapeutic facilities in these regions.

Results of the Global Burden of Disease (GBD) 2015 study showed that, between 2005 and 2015, child cancer mortality decreased globally, however, still a substantial proportion of children with cancer were reported not to have survived.[1,3] In spite of the importance of updating health statistics on child mortalities due to neoplasms to monitor the efficacy of medical interventions, currently, limited data are available on the incidence, prevalence, and mortality of these diseases in many regions, including developing countries.[4,5] In recent years, Iran has established

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several registries like national cancer and mortality registry, to address this shortcoming, however, the data recorded in the country is associated with significant levels of incompleteness and misclassification.[6]

Using statistical models to overcome the errors and flaws in the available registries and datasets, the national and sub-national burden of diseases (NASBOD) study was designed to provide statistics on the incidence, prevalence, and mortality of different diseases in Iran.[7,8] Here, using the NASBOD study's findings, for the first time, we are reporting the national and sub-national estimates of deaths due to childhood cancers between 2000 and 2015 in this country.

Materials and Methods

Herein, cancer mortality rates are estimated using national death registration system data after addressing issues like the incompleteness and misclassification of diseases, using demographic modeling (complete birth history and summary birth history) and statistical analysis (spatiotemporal, Gaussian process regression, and generalized linear mixed models).[8]

Data Source

The data used in this study was a combination of several data sources, mainly the Death Registration System (DRS) and cemeteries records in Tehran and Isfahan, which had not been included in the DRS. The DRS data were obtained from the Ministry of Health and Medical Education for the years 1995 to 2010 while the datasets of Bagh-e-Rezvan cemetery in Isfahan and Behesht-e-Zahra cemetery in Tehran were available for years of 2007 to 2010 and 1995 to 2010, respectively. The details of the data source used in this project had been previously discussed.[8,9]

For the covariates of our study, we used census data of 1996, 2006, and 2011, including the population size of each area and the demographic information of inhabitants residing in the provinces of Iran.[7,8] We also used Household Expenditure and Income surveys to obtain data for years of schooling, wealth index, and urbanization as covariates in the models.[9,10] In the NASBOD study, International Classification of Diseases (ICD10) codes for defining the causes of death were used, and the codes were mapped to GBD cause list; as a result, estimates on cancer mortality were available for 29 major cancer groups for all ages in this project. Herein, we are reporting the recorded mortalities of cancers among individuals aged up to 15 years.[8]

Demographic Modeling

The incompleteness of the recorded cases is a drawback of the Iranian DRS data and to overcome this problem, we used the demographic modeling approach, details of which are presented elsewhere.[10,11] In our approach, due to different contributors to incomplete registration of child deaths compared to adults, different models for child and adult population were used. For a better estimation of child deaths, summary birth history and complete birth history data were also gathered and analyzed to bring an indirect estimate of child mortality trend, level, and incompleteness of the DRS records. The two datasets were analyzed using methods of maternal age cohort and maternal age period, outputs of which were ultimately combined using the LOESS regression.[7,10]

Statistical Modeling

There were two issues in estimating mortality rates, first, there were inadequate and missing data in each age, sex, province, and year group. To address these issues, we used the extrapolation of cancer types with spatiotemporal models. Gaussian process regression models were applied as an effective way to estimate the uncertainty of mortality rates in the causes of cancer deaths.[9,12,13] The complete statistical process is described in the study protocol paper of the project.[12]

Herein, we are reporting age-standardized death rates (ASDRs) using the national Iranian population structure of 2015 (only the population size younger than the age of 15 were used). All the statistical analyses of this study were performed using R software, version 3.1.1.[14] Results of this project are also presented online on the data visualization website; https://vizit.report/.

Results

The overall ASDR of childhood cancers have decreased by 69.52% (80.67–49.71) in Iran (equal to an annual percent change of -3.63 [-4.53– -2.24]), declining from 12.24 (95% uncertainty interval: 10.52–14.49) in 2000 to 3.73 (2.8–5.29) deaths per 100 000 in 2015. This decrement was equal to an annual percent change of -4.35% over these years. Similarly, the number of deaths attributable to all types of child cancers showed a decreasing pattern over this 15-year period. (Figure 1) Moreover, the decreases in ASDRs of childhood cancers were comparable among the two genders over these years (Figure 1).

In our study of mortalities among different age groups, children aged under 1 and aged between 1 and 4 had the highest recorded mortality rates in 2000, with the group aged under 1 showing slightly higher values. Moreover, with reductions of overall mortality rates of childhood cancers in our 4 age groups by 2015, the rates of childhood cancer mortality in children aged more than 4 years were still lower compared to the under 4 groups (Figure 2A).

Our results showed that leukemia, brain, and nervous system malignancies accounted for about 66% of all cancer-related mortalities among children and adolescents in 2015, which had a 10% increase compared to 2000, in which this number was calculated as 56% (Figure 2B, Figure 3, and Table 1). We also observed the changes in ASDRs of leukemia (2015: 1.71 [1.44–2.01] and 2000:

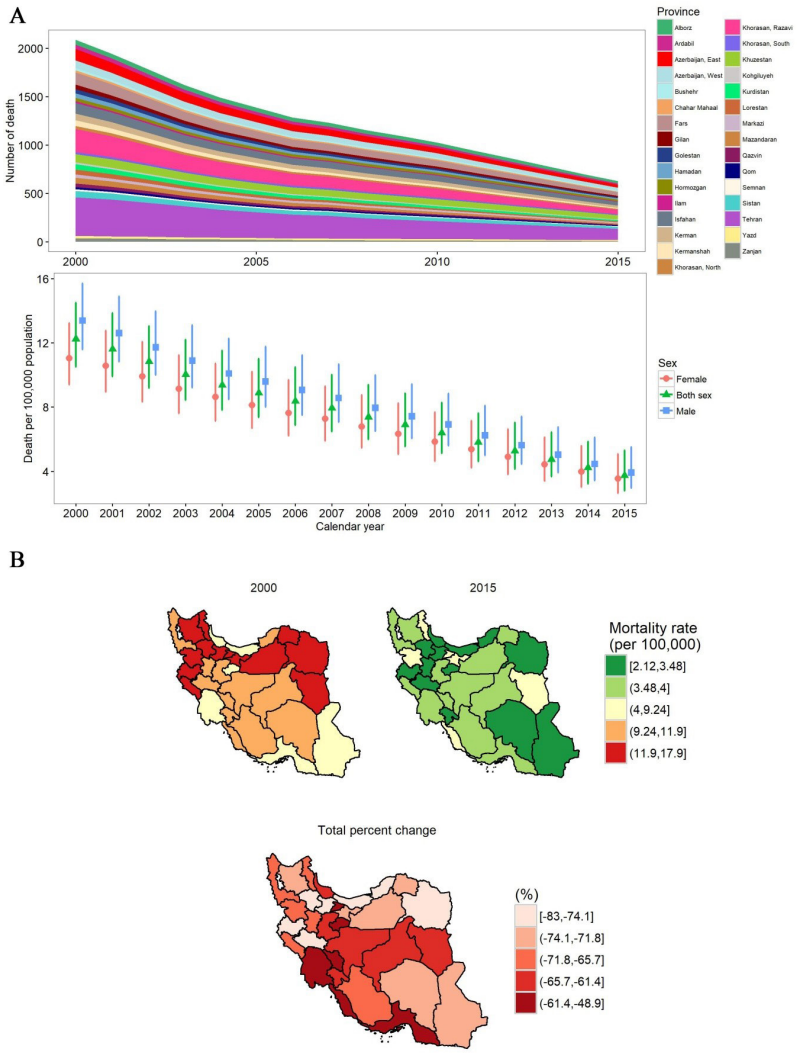

Figure 1. Mortality of Pediatric Cancers in Iran. (A) Age-standardized death rate and the number of deaths attributed to pediatric cancers in Iran between 2000 and 2015 (B) age-standardized death rate of childhood cancers in provinces of Iran in 2000 and 2015, in addition to the percent change over years of the study.

5.11 [4.63–5.62] deaths per 100 000), brain and nervous system cancers (2015: 0.75 [0.57–0.96] and 2000: 1.79 [1.50–2.10] deaths per 100 000), lymphoma (Hodgkin and Non-Hodgkin lymphoma) (2015: 0.42 [0.27–0.64] and 2000: 1.05 [0.79–1.38] deaths per 100 000), as well as kidney and other urinary system cancers (2015: 0.09 [0.03–0.17] and 2000: 0.46 [0.32–0.64] deaths per 100 000) (Figure 2B and Figure 3).

In the study of trends at the sub-national level, we observed that the highest and lowest ASDR of childhood cancers were 4.99 (3.51–8.03) in Tehran and 2.12 (1.62–2.92) in Mazandaran in 2015, respectively. Moreover, the ASDR resulting from pediatric neoplasms decreased in all provinces of Iran between 2000 and 2015, while the annual changes varied between -5.18% (-5.66– -4.06) in Zanjan to -3.06% (-4.54–0.57) in Khuzestan (Table 2 and Figure 4).

Discussion

In this study, we reported the national and sub-national mortalities of pediatric neoplasms in Iran between the years of 2000 and 2015. Our results showed that the number of deaths, as well as ASDR of childhood cancers, decreased over this 15-year period, while leukemia, brain/nervous system, and lymphoma were the three diseases with the highest mortalities in Iran.

Globally, death rates due to pediatric cancers are decreasing. This decreasing trend is more pronounced in higher-income countries, whereas areas with lower sociodemographic statues have been reported with lower increases in cancer-related death rates over the past decades.[15] Similar trends were also reported in the North African and Middle Eastern area. Comparison of the changes in cancer deaths in Iran and the Middle Eastern area suggested that rates were higher in the beginning years of the study in Iran, however, they were successfully reduced by 2015 in this country. At the national levels, the GBD 2015 study showed that the total number of deaths due to pediatric cancers between 1990 and 2015 decreased in Iran and this decrement was more prominent in the

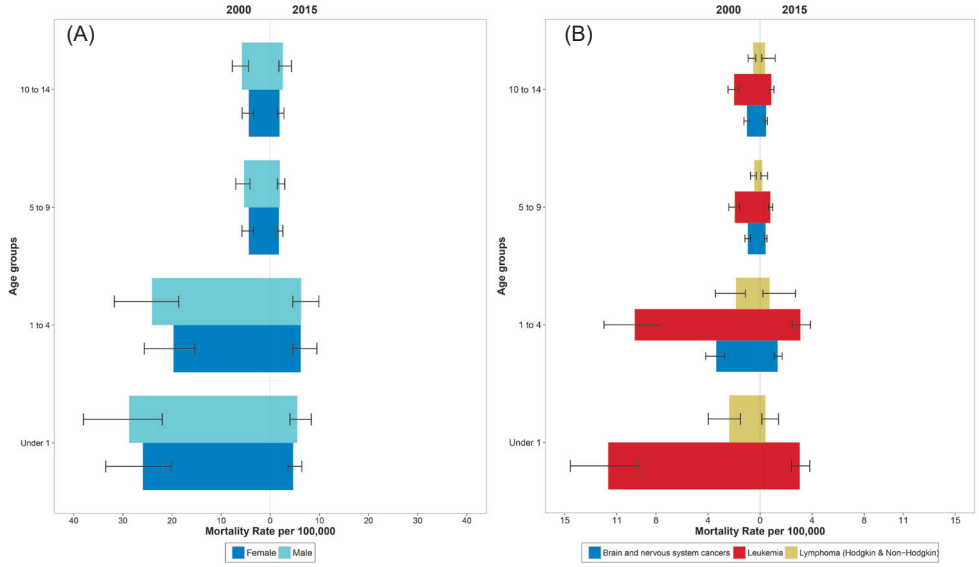

Figure 2. Mortality of Pediatric Cancers in Iran in 2000 and 2015. The overall age-standardized death rate of pediatric cancers in Iran in 2000 and 2015 in males and females (A) and cause-specific rates for the three major cancers (B) in age groups of under 1, 1 to 4, 5 to 9, and 10 to 14 years.

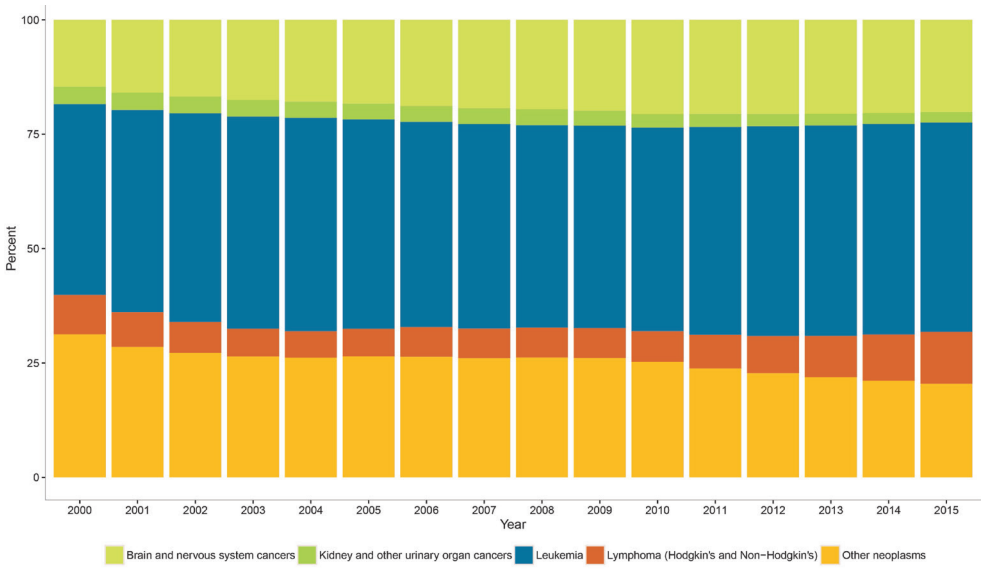

Figure 3. Decomposition of the Age-Standardized Death Rate of Pediatric Cancers by Type, in Iran between 2000 to 2015.

early years of this period and reached a plateau after 2010.[1] In this study, leukemia, brain cancer, and lymphoma were the three causes with the highest number of attributed deaths in children aged less than 5 years and aged 5 to 14 years (this study considered Hodgkin's lymphoma in a group different from non-Hodgkin types). Herein, we found comparable results for pediatric cancer mortality in Iran for the same period; a decreasing pattern was observed in both genders, while leukemia and brain malignancies topped the list. However, the GBD results lacked sub-national level data in Iran and were unable to compare sub-national measures of these causes.[1,2] Similarly, results of GLOBOCAN 2012 showed that leukemia caused 365 deaths in Iran in 2012, while the brain and nervous system, and lymphoma (Hodgkin and non-Hodgkin) followed this disease on the list with 131 and 96 recorded deaths. The reported deaths in this study are lower than expected, and given the results presented in this study and the GBD results, one can assume that GLOBOCAN results are far lower than actual values. In other words, the modeling approaches, the primary data sources used in the GLOBOCAN study, and its vulnerability to underreporting of the recorded cases (especially cases of leukemia, brain, and liver cancer) question the validity of these estimates. Moreover, this study provides only a cross-sectional view of the statistics, and due to changes

Table 1. Deaths Numbers and the Age-Standardized Death Rate (Per 100 000) of Pediatric Cancers Among Children Under 15 Years in Iran

Cancer		2000		2015		Change in ASDR
		Number of Deaths	ASDR	Number of Deaths	ASDR	
All cancer	Females	913.48 (711.28–1192.81)	11.05 (9.4–13.24)	290.93 (216.32–436.01)	3.54 (2.63–5.08)	-4.25 (-5.01–-2.87)
	Males	1173.53 (907.87–1553.9)	13.39 (11.59–15.69)	336.5 (241.47–529.49)	3.92 (2.95–5.5)	-4.42 (-5.07–-3.28)
	Both genders	2087.02 (1619.15–2746.7)	12.24 (10.52–14.49)	627.43 (457.78–965.5)	3.73 (2.8–5.29)	-4.35 (-5.04–-3.11)
Brain and nervous system cancers	Females	142.22 (114.58–176.3)	1.7 (1.42–2.02)	63.02 (50.32–78.74)	0.79 (0.61–1.02)	-3.35 (-4.36–-1.76)
	Males	164.97 (133.34–204.43)	1.87 (1.59–2.19)	58.79 (46.95–73.42)	0.71 (0.54–0.92)	-3.88 (-4.7–-2.63)
	Both genders	307.19 (247.93–380.72)	1.79 (1.51–2.11)	121.81 (97.27–152.16)	0.75 (0.58–0.97)	-3.63 (-4.53–-2.24)
Kidney and other urinary organ cancers	Females	31.78 (22.99–43.84)	0.41 (0.28–0.58)	6.65 (4.67–9.44)	0.08 (0.03–0.16)	-5.03 (-5.93–-2.68)
	Males	43.27 (31.55–59.29)	0.52 (0.38–0.71)	8.28 (5.88–11.62)	0.09 (0.04–0.18)	-5.17 (-5.9–-3.29)
	Both genders	75.06 (54.54–103.14)	0.47 (0.33–0.65)	14.93 (10.55–21.06)	0.09 (0.04–0.17)	-5.05 (-5.87–-3.03)
Leukemia	Females	387.98 (312.28–481.93)	4.66 (4.19–5.16)	140.97 (112.89–175.39)	1.65 (1.39–1.94)	-4.04 (-4.57–-3.36)
	Males	491.19 (395.42–611.09)	5.54 (5.05–6.07)	157.62 (126.62–195.96)	1.77 (1.5–2.06)	-4.25 (-4.71–-3.7)
	Both genders	879.17 (707.7–1093.02)	5.11 (4.63–5.62)	298.59 (239.51–371.35)	1.71 (1.44–2)	-4.16 (-4.65–-3.55)
Lymphoma (Hodgkin's and Non-Hodgkin's)	Females	69.65 (43.73–122.58)	0.81 (0.59–1.11)	25.25 (7.35–97.57)	0.29 (0.17–0.5)	-4.01 (-5.29–-0.95)
	Males	117.06 (73.6–208.75)	1.29 (1–1.65)	48.85 (15.39–162.36)	0.55 (0.38–0.79)	-3.59 (-4.81–-1.31)
	Both genders	186.71 (117.33–331.33)	1.05 (0.8–1.39)	74.1 (22.73–259.93)	0.42 (0.27–0.65)	-3.75 (-5.04–-1.17)
Other cancers	Females	281.86 (217.7–368.15)	3.48 (2.91–4.38)	55.04 (41.09–74.88)	0.72 (0.44–1.46)	-4.96 (-5.62–-3.11)
	Males	357.04 (273.95–470.34)	4.16 (3.57–5.07)	62.96 (46.63–86.12)	0.8 (0.49–1.55)	-5.05 (-5.65–-3.54)
	Both genders	638.89 (491.66–838.49)	3.83 (3.25–4.73)	118 (87.73–161)	0.76 (0.47–1.5)	-5.01 (-5.63–-3.37)

The changes in ASDR (age-standardized death rate) are presented as the estimated annually changes.

in quality of data registry and improvements of statistical modeling, temporal analyses of different GLOBOCAN data is subject to systemic biases.[16]

Several studies have reported the incidence and mortality of childhood cancers in different regions of Iran previously.[17-19] Mousavi et al conducted a review on published articles about childhood cancers in Iran and showed that in 2004, about 4.6 cases (per 100 000) died with cancer-related etiologies which resulted in 35 010 DALYs. This number seems to be an underestimation of the current status, probably due to inefficient death registry systems in Iran at the time.[19] In two other reports, the authors studied pediatric cancer epidemiology in the central and northern provinces of Iran. Given the relatively small sample size of these studies, their reported estimations were subject to biases. However, both of these

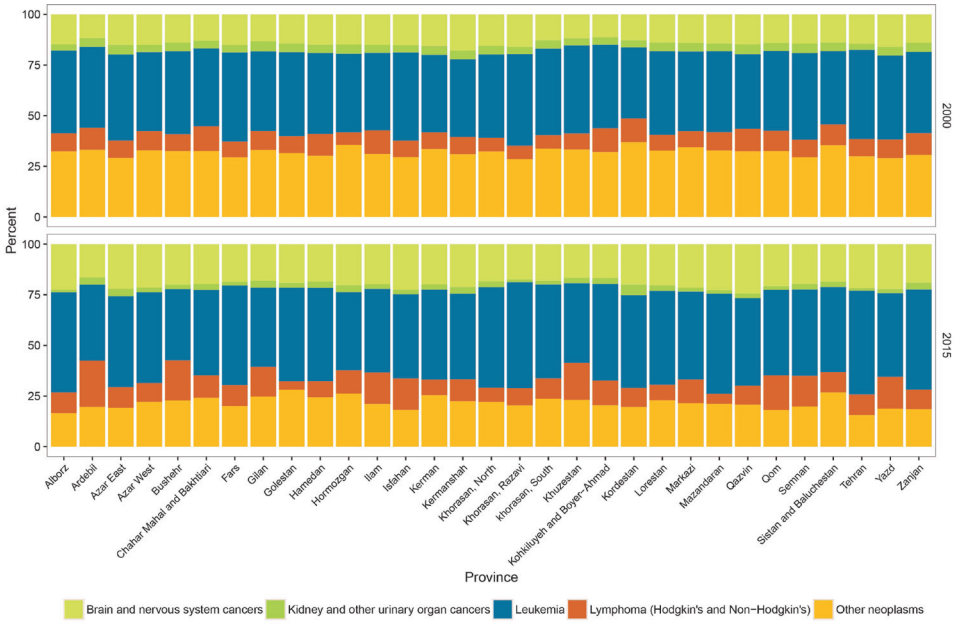

Figure 4. The Cause-Specific Age-Standardized Death Rate of Pediatric Cancers in Provinces of Iran in 2000 and 2015.

Table 2. Death Numbers and the Age-Standardized Death Rate (Per 100 000) of Pediatric Cancers Among Children Under 15 Years in Regions of Iran

Province	2000		2015		Change in ASDR
	Number of Deaths	ASDR	Number of Deaths	ASDR	
Alborz	48.3 (36.84–64.41)	12.19 (9.29–16.27)	25.49 (18.67–38.97)	4.8 (3.51–7.33)	-3.79 (-4.9–-1.32)
Ardebil	45.69 (36.21–59.82)	13.93 (11.04–18.19)	13.12 (8.96–22.88)	4.78 (3.26–8.34)	-4.11 (-5.13–-1.53)
Azerbaijan, East	117 (94.08–146.85)	13.76 (11.07–17.26)	31.15 (23.74–44.84)	3.78 (2.88–5.44)	-4.53 (-5.21–-3.18)
Azerbaijan, West	79.93 (63.82–101.59)	10.54 (8.42–13.36)	27.43 (20.94–39.32)	3.55 (2.71–5.09)	-4.14 (-4.98–-2.47)
Bushehr	23.51 (18.78–29.95)	9.93 (7.94–12.62)	11.1 (7.62–18.76)	4.05 (2.76–6.87)	-3.7 (-4.88–-0.85)
Chahar Mahal and Bakhtiari	23.28 (18.45–29.88)	9.68 (7.67–12.41)	8.48 (6.27–12.7)	3.81 (2.81–5.71)	-3.79 (-4.83–-1.6)
Fars	123.79 (98.49–157.31)	11.52 (9.17–14.62)	37.51 (28.39–54.46)	3.67 (2.78–5.33)	-4.26 (-5.06–-2.62)
Gilan	46.58 (37.27–59.83)	8.76 (7.02–11.18)	13.78 (10–21.41)	3.37 (2.46–5.21)	-3.84 (-4.87–-1.61)
Golestan	46.07 (36.54–58.95)	10.24 (8.13–13.08)	11.61 (8.99–15.83)	2.45 (1.89–3.34)	-4.76 (-5.35–-3.68)
Hamedan	47.01 (37.81–59.21)	10.41 (8.38–13.1)	11.33 (8.74–15.74)	3.1 (2.39–4.32)	-4.39 (-5.11–-3.03)
Hormozgan	32.92 (26.12–42.15)	8.28 (6.57–10.58)	19.05 (13.7–29.99)	3.96 (2.85–6.24)	-3.26 (-4.57–-0.31)
Ilam	18.59 (14.62–24.1)	12.71 (9.99–16.46)	4.46 (3.16–7.2)	3.79 (2.67–6.12)	-4.39 (-5.23–-2.42)
Isfahan	110.04 (85.2–144.36)	10.05 (7.78–13.16)	39.47 (27.99–62.79)	3.88 (2.75–6.16)	-3.84 (-4.94–-1.3)
Kerman	67.44 (54.06–85.73)	10.04 (8.06–12.72)	22.84 (17.38–32.44)	2.78 (2.11–3.94)	-4.52 (-5.21–-3.19)
Kermanshah	59.57 (47.86–75.6)	12.04 (9.68–15.25)	12.08 (9.11–17.87)	3.12 (2.35–4.62)	-4.63 (-5.28–-3.27)
Khorasan, North	32.38 (25.54–41.41)	13.99 (11.03–17.88)	9.51 (7.19–13.61)	3.93 (2.97–5.62)	-4.5 (-5.21–-3.06)
Khorasan, Razavi	236.5 (185.92–302.26)	16.09 (12.65–20.55)	46.52 (35–67.53)	2.99 (2.25–4.35)	-5.09 (-5.56–-4.1)
Khorasan, South	22.17 (17.3–28.8)	13.39 (10.46–17.36)	8.79 (6.47–13.44)	4.8 (3.53–7.34)	-4.01 (-4.98–-1.87)
Khuzestan	86.17 (67.14–113.08)	6.87 (5.36–8.98)	42.79 (29.98–71.39)	3.51 (2.46–5.85)	-3.06 (-4.54–0.57)
Kohkiluyeh and Boyer-Ahmad	17.83 (13.78–23.34)	9.54 (7.37–12.46)	5.91 (4.32–9.04)	3.34 (2.43–5.12)	-4.06 (-5.03–-1.91)
Kurdistan	55.39 (43.83–71.28)	13.83 (10.95–17.74)	14.23 (10.87–20.16)	4.25 (3.24–6.04)	-4.33 (-5.11–-2.81)
Lorestan	51.63 (41.55–65.01)	11.02 (8.88–13.86)	8.81 (6.78–12.26)	2.26 (1.74–3.15)	-4.97 (-5.47–-4.03)
Markazi	33.11 (26.59–41.93)	10.21 (8.19–12.92)	11.04 (8.12–16.93)	3.77 (2.77–5.78)	-3.94 (-4.91–-1.84)
Mazandaran	58.99 (46.52–75.95)	8.77 (6.92–11.25)	12.12 (9.3–16.77)	2.12 (1.62–2.92)	-4.74 (-5.35–-3.61)
National	2087.02 (1619.15–2746.7)	12.24 (10.52–14.49)	627.43 (457.78–965.5)	3.73 (2.8–5.29)	-4.35 (-5.04–-3.11)
Qazvin	38.83 (31.11–49.03)	14.17 (11.35–17.87)	8.28 (6.26–12.08)	3.19 (2.41–4.66)	-4.84 (-5.41–-3.68)
Qom	21.08 (15.55–29.76)	7.55 (5.56–10.66)	10.21 (6.85–17.92)	3.47 (2.32–6.08)	-3.38 (-4.89–0.58)
Semnan	17.74 (13.6–23.77)	13.92 (10.67–18.65)	5.25 (3.65–8.82)	3.93 (2.74–6.6)	-4.49 (-5.33–-2.38)
Sistan and Baluchestan	66.11 (48.75–96.31)	8.79 (6.48–12.8)	23.04 (16.36–37.51)	2.32 (1.65–3.79)	-4.6 (-5.45–-2.6)
Tehran	396.96 (286.62–564.57)	17.91 (12.93–25.46)	114.87 (80.86–184.75)	4.99 (3.51–8.03)	-4.51 (-5.39–-2.37)
Yazd	24.65 (19.12–32.16)	10.3 (7.98–13.42)	11.16 (7.86–18.3)	3.83 (2.69–6.28)	-3.93 (-5–-1.33)
Zanjan	37.78 (30.08–48.31)	15.08 (12.01–19.25)	5.99 (4.24–9.79)	2.57 (1.82–4.21)	-5.18 (-5.66–-4.06)

The changes in ASDR (age-standardized death rate) is presented as the estimated annually changes.

studies highlighted the importance of leukemia, nervous system tumors, and lymphoma in terms of incidence and mortality in this age group.[17,18] Changes in childhood cancer mortality over the years have been less studied in Iran or investigated in regional datasets. In this nationally representative project, our results showed that childhood cancer mortality, similar to many other areas in the world, decreased in the past 15 years. However, inequality in the distribution of this metric is still an important issue in this country.

The diagnosis of pediatric cancers in their early stages provides patients with a better prognosis, requires lower intensity therapies to be administered, and leads to lesser complications due to the disease itself and the treatment.[20] However, signs and symptoms associated with these causes are mostly non-specific and similar to simple pediatric diseases in clinical settings, thus access to pediatricians (compared to family physicians) and pediatric cancer centers, play important roles in this regard.[21-23] The current study's findings can help policymakers obtain an in-depth view of the health system's function and the inequality in the distribution of resources within the Iranian healthcare structure. In spite of experiencing decreases in death rates, many southern and central provinces reported higher measurements compared to other areas in 2015. The highlighted inequality calls for actions and policies to address the probably lower quality of care and access to necessary healthcare centers in these provinces; insufficient increases in the number of beds in pediatric hospitals, as well as the number of pediatric oncologists relative to population size in these areas in recent decades, are the contributors that should be investigated. Earlier studies have shown a major gap between the ratio of oncologists to the population in provinces across Iran, with the provinces of better socio-economic status or provinces adjacent to Tehran having a higher ratio.[24] Given the current structure

and challenges of the Iranian health system, increasing the number of oncologists and bed hospitals may be limited by a shortage of financial resources, however, redistribution of the human resources and bed hospitals seems to be a plausible option. Moreover, treating children with cancers requires more than just oncologists or bed hospitals; supportive care is also a huge issue.

Our study has several strengths; we used the largest available datasets in the country, applied robust statistical and demographic modeling approaches, and reported each number with its uncertainty interval, which represents both sample-derived and model-derived uncertainties. However, recording patients' information in data registries are usually associated with several errors, including duplicate registries, incomplete registration of data, and misclassification. Despite the urgent need for a more efficient death and cancer registry in Iran to address these problems and to provide a better image of the distribution of deaths in the country, we used the modeling approaches that account for effects of multiple covariates, to overcome these shortcomings. However, our results may have been tempered by several limitations. Firstly, our preliminary dataset covered a relatively short period of time, extrapolating of which may result in imprecise trends. We used statistical models, which would count the possible contribution of other covariates, besides the extrapolating mortality rates process, to produce reliable and robust results. Secondly, there were missing data points in the data available from different provinces of Iran; while the data coming from the central provinces were of higher quality, the areas with lower socioeconomic status had variable-quality data. To overcome this problem, we checked our datasets for possible inconsistencies and tried to interpolate any missing point data or significant deviations from the observed trends.

In conclusion, in this study, we have reported national and sub-national changes in mortalities of pediatric cancers in Iran for the first time. We observed that mortality rates of childhood cancers dropped in the past 16 years in almost all regions of Iran. Although mortality attributable to different neoplasms have declined over this period, leukemia, brain, and nervous system malignancies are still among the leading cancer-related causes of death in childhood. These results provide health policymakers with the necessary tool for better resource allocation; provinces with lower declines in childhood cancer mortality should be prioritized on the list, and more pediatric cancer centers and pediatric oncologists should be considered for these areas in the upcoming years. However, with improvements in data registries and computational approaches, these statistics could be updated in the future.

Authors' Contribution

The general design of paper: FK, FF, NR, FP. Designing of methods: FF, MY, AM, AS. Analysis: FF, AS, MY, SSM. Writing primary draft: NR, FP, MY, LT. Manuscript review: All authors.

Conflict of Interest Disclosures

The authors declare no conflict of interest.

Ethical Statement

The medical ethics committee of Tehran University of Medical Sciences exempted this study from regular reviews since it's a re-analysis of the existing data (code: IR.TUMS.EMRI.REC.1396.00175).

Availability of Data and Material

Results of this project are also presented online on the data visualization website; https://vizit.report/.

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