Incidence and mortality of primary bone cancers in China, 2014

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Abstract

Objective: In this study, we aimed to estimate the updated incidence and mortality of primary bone cancers based on population-based cancer registration data in 2014, collected by the National Central Cancer Registry of China (NCCRC).

Methods: In 2017, 339 registries' data were qualified based on data quality criteria set down by the NCCRC. Cases of primary bone cancers were retrieved from the national database. We estimated numbers of primary bone cancer cases and deaths in China using age-specific rates and corresponding national population stratified by area, sex, age-group (0, 1−4, 5−9, 10−14, …, 85+). Chinese standard population in 2000 and Segi's World population were applied for the calculation of age-standardized incidence and mortality rates.

Results: In 2014, 24,000 primary bone cancer cases and 17,200 deaths attributable to primary bone cancers were estimated to have occurred in China. The crude incidence rate of primary bone cancers was 1.76/100,000, with age-standardized incidence rate by Chinese standard population (ASIRC) and by World standard population (ASIRW) being 1.35/100,000 and 1.32/100,000, respectively. The crude mortality rate of primary bone cancers was 1.26/100,000, with age-standardized mortality rate by Chinese standard population (ASMRC) and by World standard population (ASMRW) being 0.88/100,000 and 0.86/100,000, respectively. Age-specific incidence curve was bimodally distributed with age, with the first peak occurring in the second decade of the life and the second peak in the elderly. Males had higher crude and age-standardized rates for both incidence and mortality compared with females. Both crude and age-standardized incidence rates were higher in rural areas than in urban areas, so were the crude and age-standardized mortality rates.

Conclusions: This population-based study presents the most recently available estimates on primary bone cancers in China, revealing that the males are 1.34 times as much as females suffering from primary bone cancers and the adolescents in puberty and the elderly are predominantly affected groups by these cancers. High-quality cancer registration data are a prerequisite for undertaking further study for gaining insight into the causes and risk factors for primary bone cancers in China.

Keywords: Incidence; mortality; population-based; primary bone cancers

Introduction

Primary bone cancers are relatively uncommon compared to tumors arising at other anatomical sites, making up less than 1% of all cancers (1-7). Given the relative rarity of primary bone cancers, there have been fewer studies

focusing on them compared to cancers at other sites (4), so little is known about their causes and risk factors (2,8), which consequently have prohibited effective prevention programs and counter measures towards them. Population-based cancer registration data are usually considered as a good source for gaining insight into the geographical and demographical patterns of the incidence, mortality and survival of primary bone cancers and informing us of their causes and risk factors. In 2012, the first ever report on the incidence and mortality of primary bone cancers in China over the period 2003−2007 was published (6,9), which concluded that primary bone cancers accounted for 0.67% of all cancers and 0.79% of deaths due to cancers. In our study, we made use of the newest available population-based cancer registration data and provided up-to-date epidemiological estimates about primary bone cancers in China in 2014.

Materials and methods

Data source

The National Central Cancer Registry of China (NCCRC), which is subordinate to National Cancer Center (NCC), is in charge of population-based cancer registration network in China. In 2017, NCCRC received population-based cancer registration data from 449 registries across China, which were distributed in 31 provinces, autonomous districts and municipalities directly under the central government and comprised 160 cities (urban areas) and 289 counties and county-level cities (rural areas). All submitted data were evaluated by going through quality control procedures to ascertain whether they meet quality criteria as stipulated in the Chinese Guideline for Cancer Registration (10) and Cancer Incidence in Five Continents Volume XI (11). Finally, registration data from 339 registries including 129 urban areas and 210 rural areas fulfilled quality criteria and were included for analysis. The 339 registries covered a population of 288,243,347 (144,061,915 in urban areas and 144,181,432 in rural areas; 146,203,891 males and 142,039,456 females), accounting for 21.07% of the national population. Data on primary bone cancers were extracted using the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) site codes C40.0−C41.9.

Population data sources

The population data for 2014 were provided by the

National Bureau of Statistics of China by area and sex. Population structures stratified further by age groups were inferred using the fifth and sixth National Population Census data for 2000 and 2010, by age groups (0, 1−4, 5−84 by 5 years, 85+ years), sex and area (urban/rural) (http://data.stats.gov.cn/). Briefly, each age-specific population by sex was calculated by multiplying sex-specific population by corresponding age-specific population composition by sex, which was derived by linear interpolation based on age-specific population compositions by sex at 2000 and 2010. More details were described in the study by Chen *et al.* (12,13).

Quality evaluation of registration data

The comparability, completeness and validity of data were evaluated using indicators including the percentage of cases morphologically verified (MV%), the percentage of death certificate-only cases (DCO%), the mortality to incidence (M/I) ratio and the percentage of the diagnosis of unknown basis (UB%) (14). Usually, the data included for analysis should meet the following criteria: MV (%) not lower than 66% for all cancers combined, DCO (%) lower than 15%, M/I between 0.6 and 0.8 and UB (%) lower than 5%. The corresponding values for MV%, DCO%, M/I and UB% were 41.63%, 4.28%, 0.72 and 1.03%, respectively. The quality indicators by sex at urban and rural registration areas each and combined were shown in *Table 1*. IARCcrgTools (version 2.05) issued by the International Agency for Research on Cancer/International Association of Cancer Registries (IARC/IACR) were used for data checking and evaluation.

Statistical analysis

Data from 339 registries were pooled for national estimates. Crude incidence and mortality rates were calculated by age groups, sex and area (urban/rural). The number of new cases and that of deaths were estimated using the age-specific incidence/mortality rates and the corresponding populations. Age-standardized rates were calculated using the direct standardization method by applying the Chinese standard population in 2000 and Segi's World standard population to the age-specific rates, to adjust for differences in the population structures when comparing rates between different population groups. The cumulative risk of developing or dying from primary bone cancers before 75 years of age (in the absence of competing causes of death) was calculated and presented as a

Table 1 Quality control indicators for primary bone cancers in China, 2014

Areas	Sex	M/I	%		
			MV	DCO	UB
All	Both	0.72	41.63	4.28	1.03
	Male	0.75	40.73	4.47	0.94
	Female	0.69	42.81	4.04	1.14
Urban areas	Both	0.70	44.73	6.31	1.67
	Male	0.73	43.10	6.71	1.66
	Female	0.65	46.76	5.82	1.69
Rural areas	Both	0.74	39.04	2.59	0.49
	Male	0.76	38.82	2.67	0.36
	Female	0.72	39.34	2.48	0.66

M/I, mortality to incidence ratio; MV, morphologically verified; DCO, death certificate-only; UB, unknown basis.

percentage. All rates were expressed per 100,000 person-years. SAS software (Version 9.4; SAS Institute Inc., Cary, NC, USA) was used for the statistical analysis.

Results

Incidence of primary bone cancers

In 2014, there was estimated to be 24,000 cases of primary bone cancers newly diagnosed, making up about 0.63% of all newly diagnosed cancers combined and ranked 21st as per incidence rate. The age-standardized incidence rates by Chinese standard population (ASIRC) and Segi's World standard population (ASIRW) were 1.35/100,000 and 1.32/100,000, respectively (*Table 2*). Among the population aged 0−74 years, the cumulative incidence rate was 0.14%.

Primary bone cancers occurred more frequently in rural areas than in urban areas. In urban areas, the ASIRC was 1.22/100,000 while in rural areas, it was 1.53/100,000 (*Table 2*).

Primary bone cancers affected more males than females, with their respective ASIRC of 1.55/100,000 and 1.16/100,000 and with the ASIRC ratio of 1.34. Male predominance was also found for both urban and rural areas (*Table 2*).

Age-specific incidence of primary bone cancers

As seen from *Figure 1*, the incidence curve of primary bone cancers with age was bimodally distributed for each sex and both combined as well. On the whole, the first peak occurred during the second decade of the life with incidence rate in the range of 1.18−1.28/100,000 in males and 0.76−1.03/100,000 in females, differing contingent on areas (urban/rural areas) while the second peak occurred amongst the elderly (*Figure 1*, *Table 3*).

Table 2 Primary bone cancers estimated incidence in China, 2014

Areas	Sex	Cases (×10⁴)	Crude rate (1/10⁵)	Ratio (%)	ASIRC (1/10⁵)	ASIRW (1/10⁵)	Cumulative rate 0−74 (%)	Rank
All	Both	2.40	1.76	0.63	1.35	1.32	0.14	21
	Male	1.37	1.95	0.65	1.55	1.51	0.16	18
	Female	1.04	1.55	0.61	1.16	1.13	0.12	20
Urban	Both	1.22	1.63	0.54	1.22	1.20	0.12	22
	Male	0.68	1.80	0.55	1.36	1.34	0.14	18
	Female	0.54	1.47	0.52	1.08	1.05	0.10	20
Rural	Both	1.18	1.91	0.77	1.53	1.49	0.16	21
	Male	0.69	2.13	0.77	1.78	1.73	0.18	18
	Female	0.49	1.66	0.75	1.28	1.24	0.13	20

ASIRC, age-standardized incidence rate adjusted by Chinese standard population in 2000; ASIRW, age-standardized incidence rate adjusted by Segi's World standard population.
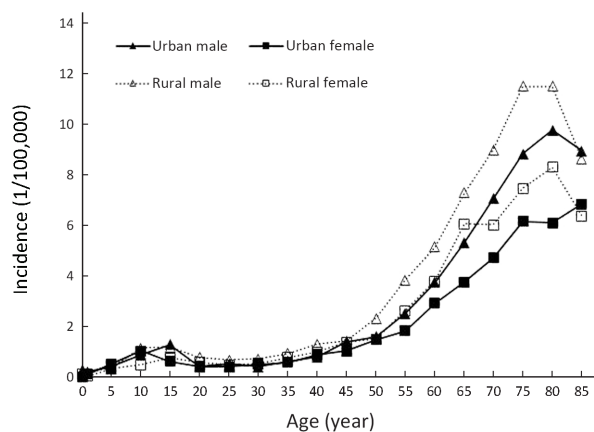
Figure 1 Age-specific incidence rates of primary bone cancers in China, 2014

Moreover, it was found that rural areas had higher incidence rates than urban areas for most age groups except for age groups 0−14 and 85+ (*Table 3*).

In children and adolescents aged less than 20 years of age, the first incidence peak occurred in females no later than in males, with first incidence peak being 0.75/100,000

in females aged 10−14 and 1.23/100,000 in males aged 15−19, respectively (*Table 3*).

Mortality of primary bone cancers

In 2014, primary bone cancers were estimated to have contribute to 17,200 deaths in China, comprising about 0.75% of all cancer deaths and ranked as 19st as per mortality rate. The age-standardized mortality rates by Chinese standard population (ASMRC) and Segi's World standard population (ASMRW) were 0.88/100,000 and 0.86/100,000, respectively (*Table 4*).

In urban areas, the mortality rate was 1.13/100,000, with ASMRC of 0.75/100,000 and ASMRW of 0.74/100,000, respectively. In rural areas, the corresponding rates were 1.41/100,000, 1.05/100,000 and 1.03/100,000. So obviously rural areas had higher mortality rate than urban areas (*Table 4*).

For males, ASMRC and ASMRW were 1.05/100,000 and 1.03/100,000, respectively and were larger than their counterparts in females, which were 0.71/100,000 and 0.69/100,000 (*Table 4*).

Table 3 Age-specific incidence rates of primary bone cancers in China, 2014 $(1/10^5)$

Age groups	All areas			Urban areas			Rural areas		
	Both	Male	Female	Both	Male	Female	Both	Male	Female
All	1.76	1.95	1.55	1.63	1.80	1.47	1.91	2.13	1.66
0−	0.15	0.22	0.06	0.16	0.30	0.00	0.13	0.12	0.14
1−	0.14	0.19	0.08	0.17	0.21	0.12	0.11	0.17	0.03
5−	0.40	0.39	0.42	0.46	0.40	0.52	0.35	0.37	0.32
10−	0.90	1.03	0.75	0.96	0.89	1.03	0.84	1.15	0.47
15−	0.97	1.23	0.69	0.96	1.28	0.61	0.99	1.18	0.76
20−	0.55	0.59	0.50	0.42	0.41	0.43	0.69	0.77	0.59
25−	0.51	0.59	0.43	0.46	0.51	0.40	0.58	0.67	0.48
30−	0.53	0.55	0.52	0.45	0.41	0.50	0.64	0.72	0.55
35−	0.72	0.76	0.67	0.60	0.62	0.59	0.86	0.93	0.79
40−	0.97	1.03	0.92	0.83	0.80	0.86	1.15	1.31	0.98
45−	1.30	1.41	1.18	1.21	1.39	1.02	1.40	1.43	1.38
50−	1.70	1.90	1.49	1.54	1.60	1.49	1.92	2.32	1.50
55−	2.61	3.05	2.15	2.18	2.52	1.83	3.25	3.84	2.64
60−	3.81	4.33	3.28	3.33	3.74	2.92	4.48	5.14	3.79
65−	5.45	6.17	4.73	4.54	5.32	3.76	6.68	7.29	6.05
70−	6.56	7.88	5.26	5.86	7.05	4.72	7.51	8.98	6.02
75−	8.23	9.93	6.68	7.42	8.82	6.15	9.40	11.48	7.45
80−	8.56	10.46	6.99	7.76	9.76	6.09	9.72	11.50	8.29
85+	7.49	8.80	6.63	7.67	8.94	6.83	7.22	8.60	6.36

Table 4 Primary bone cancer estimated mortality in China, 2014

Areas	Sex	Deaths (×10⁴)	Crude rate (1/10⁵)	Ratio (%)	ASMRC (1/10⁵)	ASMRW (1/10⁵)	Cumulative rate 0−74 (%)	Rank
All	Both	1.72	1.26	0.75	0.88	0.86	0.09	19
	Male	1.01	1.44	0.70	1.05	1.03	0.11	17
	Female	0.71	1.06	0.84	0.71	0.69	0.07	17
Urban	Both	0.85	1.13	0.65	0.75	0.74	0.08	20
	Male	0.50	1.31	0.61	0.91	0.90	0.09	17
	Female	0.35	0.95	0.72	0.60	0.59	0.06	19
Rural	Both	0.87	1.41	0.88	1.05	1.03	0.11	15
	Male	0.52	1.60	0.81	1.24	1.22	0.13	15
	Female	0.36	1.20	1.01	0.85	0.84	0.09	15

ASMRC, age-standardized mortality rate adjusted by Chinese standard population in 2000; ASMRW, age-standardized mortality rate adjusted by Segi's World standard population.

Age-specific mortality of primary bone cancers

As illustrated in *Figure 2*, the mortality rates of primary bone cancers were at low levels in the population aged younger than 40 years of age, but starting from 40 years of age and onwards, the mortality rates went up moderately with age and usually arrived at mortality peaks during the seventh and eighth decades. Similar age-specific mortality patterns were found for both males and females, though with the mortality rate in males larger than in females for almost age groups except for age group 5−9. As compared to urban areas, starting from age 40 years and onwards, rural areas had strikingly higher mortality rates (*Figure 2*, *Table 5*).

Discussion

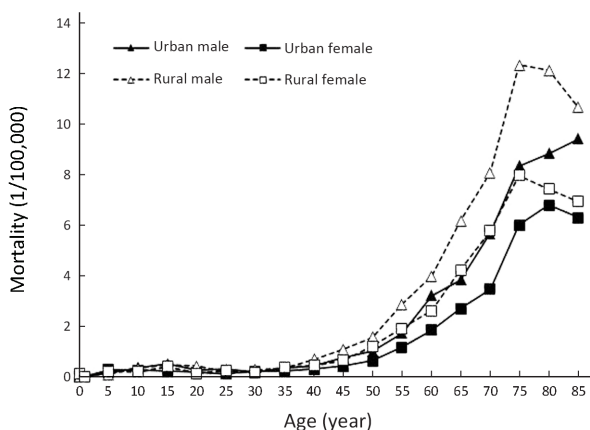To the best of our knowledge, there have been fewer

Figure 2 Age-specific mortality rates of primary bone cancers in China, 2014

reports concerning the epidemiology of primary bone cancers as compared to cancers at other body sites, and what's more, most of already existing studies came from developed countries or regions (1-3,15-17), so our study can bridge the gap by providing up-to-date estimates about the incidence and mortality of primary bone cancers in China. In our study, primary bone cancers had an ASIRW of 1.32/100,000 and comprised 0.63% of all newly diagnosed cancers in China, 1.51/100,000 and 0.65% in males and 1.13/100,000 and 0.61% in females, respectively. According to SEER cancer statistics based on SEER 18 in the period 2011−2015, primary bone cancers had an age-standardized incidence rate of 0.9/100,000 in the US, 1.1/100,000 in males and 0.8/100,000 in females, and represented 0.2% of all new cancer cases (18). In Europe, it was found that the age-standardized incidence rates for primary bone cancers across 40 national and subnational populations in 2013 varied in the range of 0.34−1.67/100,000, with 80% of those populations having incidence rates higher than 1.32/100,000 (19). In 2017, the Cancer Incidence in Five Continents (CI5) Volume XI compiled and published by IARC/IACR provided us up-to-date high-quality statistics on primary bone cancers across 343 registries located in 65 countries over the five-year period of 2008−2012, of which 36 registries came from China. We found that the incidence rates across the 36 registries in China exhibited five-fold differences in the range of 0.7−3.5/100,000 in males and 0.5−2.4/100,000 in females, and furthermore, among the top 100 list in the descending order of incidence rate worldwide, 24 registries for males and 21 for females were in China, respectively (11). So the incidence rates of primary bone cancers in China might be at relative high levels with wide geographical variations.

Table 5 Age-specific mortality rates of primary bone cancers in China, 2014 (1/10^5)

Age groups	All areas			Urban areas			Rural areas		
	Both	Male	Female	Both	Male	Female	Both	Male	Female
All	1.26	1.44	1.06	1.13	1.31	0.95	1.41	1.60	1.20
0–	0.07	0.09	0.06	0.08	0.15	0.00	0.06	0.00	0.14
1–	0.02	0.05	0.00	0.02	0.04	0.00	0.03	0.06	0.00
5–	0.18	0.12	0.24	0.21	0.16	0.28	0.15	0.09	0.21
10–	0.29	0.35	0.23	0.31	0.36	0.26	0.27	0.34	0.20
15–	0.41	0.49	0.31	0.37	0.50	0.22	0.45	0.49	0.41
20–	0.25	0.35	0.15	0.22	0.27	0.17	0.29	0.43	0.13
25–	0.21	0.25	0.17	0.21	0.30	0.12	0.22	0.20	0.23
30–	0.20	0.22	0.19	0.19	0.17	0.21	0.22	0.27	0.16
35–	0.31	0.34	0.28	0.28	0.34	0.21	0.36	0.34	0.37
40–	0.46	0.55	0.36	0.37	0.43	0.30	0.57	0.70	0.44
45–	0.72	0.90	0.53	0.59	0.74	0.43	0.87	1.08	0.66
50–	1.05	1.23	0.87	0.82	1.00	0.63	1.38	1.55	1.21
55–	1.83	2.19	1.46	1.45	1.73	1.17	2.40	2.86	1.91
60–	2.84	3.53	2.16	2.52	3.21	1.84	3.30	3.97	2.62
65–	4.08	4.83	3.33	3.25	3.82	2.69	5.21	6.17	4.22
70–	5.55	6.71	4.42	4.54	5.67	3.45	6.92	8.06	5.77
75–	8.32	9.99	6.79	7.11	8.34	6.00	10.06	12.31	7.95
80–	8.45	10.15	7.05	7.72	8.83	6.79	9.51	12.10	7.42
85+	7.87	9.89	6.55	7.53	9.40	6.28	8.35	10.64	6.93

As for mortality, not so much data as incidence are available internationally for comparison due to relative rarity of primary bone cancer (4). In our study, we found that primary bone cancers had an ASMRW of 0.86/100,000 and accounted for 0.75% of all cancer-attributable deaths in China; corresponding figures were 1.03/100,000 and 0.70% in males and 0.69/100,000 and 0.84% in females, respectively. In the US, the ASMRW was 0.4/100,000, 0.5/100,000 in males and 0.3/100,000 in females, respectively (18). In Europe, the mortality of primary bone cancers exhibited much wide variation in the range of 0.06−1.73/100,000 in 2013 (19).

With respect to the incidence patterns of primary bone cancers, consistent findings were found in our study as in previous studies (1-4,6,7) and were detailed as follows. Firstly, primary bone cancers have predilection for males, indicating more males suffer from primary bone cancers than females. In our study, ASIRW was found to be 1.51/100,000 in males and 1.13/100,000 in females, with male-to-female incidence rate ratio of 1.34. Huang *et al.* (7) reported a male-to-female incidence rate ratio of 1.22 over the period of 2003−2010 in Taiwan, China. In US, Anfinsen *et al.* analyzed incidence trends of primary bone

cancers overall and by histologic subtypes over 30 years and found that "the male to female ratio was largely between 1.2 and 1.6 for all types throughout the three 10-year periods" (3). In England, Whelan *et al.* reported a male-to-female incidence rate ratio of 1.3 between 2005 and 2007 (2). Kumar *et al.* pooled in data from Cancer Incidence in Five Continents (Vol X) for incidence analysis and concluded that "males had age-standardized rates that were almost 1.3 times the ASR (World) of women at a global level across all age groups" (4). Secondly, the incidence pattern with age is bimodally distributed with the first incidence peak occurring in the second decade of life and the second incidence peak in the elderly (1,2,4,6,7). In our study, as shown in *Table 3*, the first incidence peak occurred at age group 15−19 years (0.97/100,000), then declined between 20 and 40 years of age with incidence rate fluctuating within the range of 0.51−0.72/100,000 and started to increase gradually starting from 40 years and onwards, and finally arrived at the second peak at ages 80−84 years (8.56/100,000). Moreover, almost the same incidence patterns with age were found for each combination of sex and area. Thirdly, the first incidence peak of primary bone cancers during childhood and

adolescence occurred in females as early as or earlier than in males (2-4,7). In our study, the first incidence peak occurred at age group 10−14 in females with incidence rate of 0.75/100,000 but occurred at age group 15−19 in males with incidence rate of 1.23/100,000. Different from females in urban China where females experienced earlier incidence peak at their 10−14 years as compared to their male counterparts, females in rural China had their first incidence peak occurring at the same age group 15−19 as their male counterparts. This earlier incidence peak observed in females as compared with males lends further support to the hypothesis that hormonal changes and growth spurt at puberty may have a role in the pathogenesis of primary bone cancers (4).

There was a limitation in our study which might challenge the reliability of the study. As previously mentioned by Valery *et al.* in their study (8), the proportion of unspecified bone cancers is much higher in China as compared with those reported in developed countries, as corroborated by the low percentage of bone cancer cases with morphological verification at 41.63% in our study. Because bone metastases commonly occur subsequently when a prior solid tumor at other sites progresses to an advanced stage (20), so morphological features play a vital role for both discerning between primary bone cancers and metastatic bone cancers and grouping primary bone cancers into morphological subgroups. In view of high proportion of unspecified bone cancer cases in China, cautions need to be taken when interpreting those findings in our study. Firstly, high proportion of unspecified bone cancer point to the likelihood of including metastatic bone cancers for the calculation of both incidence and mortality, potentially biasing the incidence and mortality estimates upwards on the whole, especially for rural areas which had much lower MV% than urban areas (39.04% *vs.* 44.73%). As a result, accurate comparisons of incidence and mortality variations cannot be completely made between urban and rural areas. Secondly, because primary bone cancers consist of various morphological subtypes, including osteosarcoma, chondrosarcoma, Ewing's sarcoma, chordoma, etc. (2,3,7,8,20). In their previous studies, Howard *et al.* (1), Whelan *et al.* (2), Anfinsen *et al.* (3), Huang *et al.* (7), Valery *et al.* (8), Duong *et al.* (17) revealed markedly distinct age-specific incidence patterns with respect to morphological subtypes of primary bone cancers. Briefly, osteosarcoma has a bimodal distribution with the first incidence peak occurring during the second decade of life and the second incidence peak occurring in

the elderly (1-3,5,7,15,17), with 50%−60% occurring in the age group 0−24 and about 10%−15% in the age group 60 and above (2,5,7,15); chondrosarcoma shows a gradual increase of incidence with age but seldomly affects those aged less than 20, with less than 10% occurring in the first two decades of life (1-3,7); Ewing's sarcoma exhibits similar age-specific incidence pattern to that for osteosarcoma until the age of 40 after which very few cases of Ewing's sarcoma are diagnosed (3), with over 60% occurring in the age group 0−24 (1,2,21); chordomas mainly affected the elderly population (1,2,7). So the bimodally-distributed incidence patterns with age found in our study likely can be attributed to the mixture of different incidence patterns of various morphological subtypes of primary bone cancers, because in our study we analyzed the incidence trend with age for primary bone cancers combined (22).

It was found by Niu *et al.* that the epidemiological features of primary bone cancers differed between populations by making a comparison between patients diagnosed and treated at Beijing Jishuitan Hospital in China and the Mayo Chinic in the US (23), indicating that those findings from the previous studies, especially those from developed countries, may not apply to Chinese population. So more efforts should be made to improve the quality of cancer registration data while expanding the geographical coverage of cancer registration in China, by enhancing both completeness of and accuracy of items including antomatical location, histological subtypes, disease stage at diagnosis about primary bone cancers (24).

Conclusions

Based on population-based cancer registration data, our study provided up-to-date incidence and mortality estimates on primary bone cancers in China. We confirmed some findings as reported in previous studies that primary bone cancers have male predominance, with the number 1.34 times as much as that of females in China, and have a bimodally distributed incidence pattern with age, with the first peak in the second decade of life and the second peak in the elderly. The results of this study lay the ground for future study to delve into the causes and risk factors of primary bone cancers, which call for high-quality cancer registration as the prerequisite.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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